



Ontario Health

Cancer Care Ontario

Guideline 26-2 Version 3

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

Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer

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Report Date: March 31, 2021

An assessment conducted in February 2024 deferred the review of Guideline 26-2 Version 3. 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](#))

Guideline 26-2 Version 3 is comprised of 5 sections. You can access the summary and full report here:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/256>

Section 1:	Recommendations
Section 2:	Guideline - Recommendations and Key Evidence
Section 3:	Guideline Methods Overview
Section 4:	Systematic Review
Section 5:	Internal and External Review

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For information about the PEBC and the most current version of all reports, please visit the OH (CCO) website at <https://www.cancercareontario.ca/en/guidelines-advice> or contact the PEBC office at: Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775
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PEBC Report Citation (Vancouver Style): Members of the Colorectal Cancer Survivorship Guideline Development Group. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer. Toronto (ON): Ontario Health (Cancer Care Ontario); 2021 March 31. Program in Evidence-based Care Evidence-Based Series No.: 26-2 Version 3.

Journal Citation (Vancouver Style): Kennedy E, Zwaal C, Asmis T, Cho C, Galica J, Ginty A, and Govindarajan A. An Evidence-Based Guideline for Surveillance of Patients after Curative Treatment for Colon and Rectal Cancer. *Current Oncology*. 2022; 29(2):724-740.
<https://doi.org/10.3390/curroncol29020062>

Journal Citation (Vancouver Style): Galica J, Zwaal C, Kennedy E, Asmis T, Cho C, Ginty A, and Govindarajan A. Models of Follow-Up Care and Secondary Prevention Measures for Survivors of Colorectal Cancer: Evidence-Based Guidelines and Systematic Review. *Current Oncology*. 2022; 29(2):439-454. <https://doi.org/10.3390/curroncol29020040>

PUBLICATIONS RELATED TO THIS REPORT

- Members of the Gastrointestinal Cancer Disease Site Group. Follow-up of patients with curatively resected colorectal cancer. 2012 Mar 20 [Education and Information 2012 Mar 20]. Program in Evidence-based Care Practice Guideline No.: 2-9 Education and Information 2012.
- Sussman J, Souter LH, Grunfeld E, Howell D, Gage C, Keller-Olaman S, et al. Models of care for cancer survivorship. Sussman J, Fletcher G, reviewers. Toronto (ON): Cancer Care Ontario; 2012 Oct 26 [ENDORSED 2017 March 28]. Program in Evidence-based Care Evidence- Based Series No.: 26-1 Version 2 ENDORSED.
- Cancer Care Ontario Person-Centred Care Guideline: Endorsement and Adaptation of CG 138: Patient experience in adult NHS services: improving the experience of care for people using adult NHS services. 2015 May 2015. Person-Centred Care Program.
- Follow-Up Model of Care for Cancer Survivors: Recommendations for the Delivery of Follow-up Care for Cancer Survivors in Ontario. 2019 March. Cancer Care Ontario Survivorship Program.

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Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer

Section 1: Recommendations

This section is a quick reference guide and provides the guideline recommendations only. For key evidence associated with each recommendation, see [Section 2](#).

GUIDELINE OBJECTIVES

This guideline is an update to a previous version (i.e., GL 26-2 Version 2). The main objectives are:

1. To determine the surveillance regimen that leads to the largest benefit for stage I-IV colorectal cancer survivors treated with curative intent.
2. To determine preferred models of follow-up care in Ontario.
3. To identify signs and symptoms of potential recurrence and determine when to investigate.
4. To evaluate patient information and support needs during the survivorship phase.

TARGET POPULATION

Adult colorectal cancer survivors defined as patients who have completed primary, curative treatment for colorectal cancer stages I to IV and are without evidence of disease.

INTENDED USERS

This guideline is targeted to:

1. Clinicians (e.g., medical oncologist, radiation oncologist, surgeon, advanced practice nurse, physician assistant, primary care provider [family physician, nurse practitioner, family practice nurse]) involved in the delivery of care for colorectal cancer survivors.
2. Healthcare organizations and system leaders responsible for offering, monitoring, or providing resources for colorectal cancer survivorship protocols.

PREAMBLE

The Supplemental Information section that follows the recommendations provides links to webpages with tools to help with communication, patient education, and decision aids; a list of signs and symptoms; and a list of psychosocial supports and informational needs of patients that may impact follow-up requirements and decisions.

RECOMMENDATIONS

Recommendation 1
<p>For patients with stage I-III colon cancer:</p> <ul style="list-style-type: none">• A medical history and physical examination should be performed every six months for three years.• Computed tomography (CT) of the chest, abdomen and pelvis (CT CAP) should be performed at one and three years OR one CT CAP could be performed at 18 months.

<ul style="list-style-type: none"> • The use of carcinoembryonic antigen (CEA) is optional if CT imaging is being performed. • Surveillance colonoscopy should be performed one year after the initial surgery. The frequency of subsequent surveillance colonoscopy should be dictated by the findings of the previous one, but it generally should be performed every five years if the findings of the previous one is normal.
Qualifying Statements for Recommendation 1
<ul style="list-style-type: none"> • The use of CEA in combination with CT CAP does not lead to a survival advantage compared to CT CAP alone. • CEA is optional in patients with elevated CEA prior to treatment provided that CT CAP imaging is being performed. • If complete colonoscopy was not performed in the course of diagnosis and staging (e.g., due to obstruction), a complete colonoscopy should be performed within six months of completing primary therapy. • There was insufficient evidence to support these recommendations for patients with rectal cancer, patients with stage IV colon cancer, and patients over the age of 75 years. Therefore, the follow-up in those patients is at the discretion of the treating physician. • There was no evidence to support follow-up in patients with stage I-III colon cancer beyond three years. Therefore, follow-up after this time period is at the discretion of the treating physician. • These recommendations do not apply to patients with rectal cancer undergoing non-operative management or to patients with increased risk of cancer including but not limited to inflammatory bowel disease, familial adenomatous polyposis, and Lynch syndrome. • Patients should be informed of these current recommendations and the treating physician should discuss the specific risks and benefits of these recommendations with their patient.

Table 1.1 Recommended evaluation and intervals for routine surveillance of stage I-III colon cancer survivors

Intervention	Interval	
	Years 1 to 3	Years 4 and 5
Physical examination	Every 6 months	At discretion of treating physician
CEA	At discretion of treating physician	At discretion of treating physician
CT of the Chest, Abdominal and Pelvic Imaging (CT CAP)	CT CAP at Years 1 and 3 OR CT CAP at 18 months	At discretion of treating physician
Colonoscopy	At 1 year following surgery, the frequency of subsequent surveillance colonoscopies should be dictated by the findings of the previous one but generally should be performed every 5 years if the findings of the previous one are normal.	

CEA=carcinoembryonic antigen; CT=computed tomography

Recommendation 2

While there is limited evidence to support a shared care model for the follow-up of patients with colorectal cancer, this approach was supported by the Working Group and Expert Panel.

Follow-up care is complex and requires multidisciplinary, coordinated care of the patient delivered by the cancer specialist, family physician or nurse practitioner, and allied health professionals.

The roles and responsibilities of the multidisciplinary team members need to be clearly defined and the patient needs to know when and how to contact each member of the team.

Qualifying Statement for Recommendation 2

- It is expected that implementation of a shared care model will need to be region specific based on the available resources and provider models in each individual region.

Recommendation 3

The signs and symptoms of recurrence may be subtle and must be considered in the context of the patient's overall health and pre-existing conditions. There is insufficient evidence to recommend any individual sign or symptom or combination of signs and symptoms as a strong predictor of recurrence.

Patients should be educated about the potential signs and symptoms of recurrence and know which member of the multidisciplinary care team they should contact if they develop any new or concerning signs or symptoms.

A list of signs and symptoms of colorectal cancer recurrence can be found in the Supplemental Information section following the recommendations.

Recommendation 4

Psychosocial support about the risk of recurrence and provision of empathetic, effective, and coordinated communication are most highly valued by patients for post-treatment physical effects and symptom control.

Continuing professional education should emphasize the importance of communication skills and coordination of communication between the patient and family, and healthcare providers.

A list of late and long-term physical and psychosocial effects of colorectal cancer and links to communication resources and tools can be found in the Supplemental Information section following the recommendations.

Supplemental Information: Colorectal Cancer Follow-up Resources

1. Colorectal Cancer Follow-up Resources

Communication Skill Resources and Training

Physiciansapply.ca

- Communication and Cultural Competence Program, Communication Skills Module: Medical Communication skills
- Modules that focus on communication between health professionals and patients
- <https://physiciansapply.ca/commskills/introduction-to-medical-communication-skills/>

Ontario Health (CCO) Follow-up Model of Care for Cancer Survivors: Recommendations for the Delivery of Follow-up Care for Cancer Survivors in Ontario. March 2019.

- These Recommendations aim to provide guidance to healthcare providers and administrators on implementing optimal delivery of follow-up care for all cancer survivors by clarifying: the roles of primary care providers and specialist teams; settings in which this care should be provided; and processes involved in organization of follow-up care.
- <https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/58736>

Ontario Health (CCO) Person-Centred Care Guideline

- The objective of this guideline is to establish a standardized set of recommendations for providing person-centred care in the delivery of adult oncology services in Ontario.
- This guideline provides guidance for use by all clinicians and staff within adult oncology service settings, and for use by patients (and/or family members and caregivers) and their care providers to inform the provision of person-centred care.
- <https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/38631>

R.E.D.E. to Communicate®: Foundations of Healthcare Communication

- This course introduces clinicians to the R.E.D.E. Model of relationship-centered communication and how it applies to any clinical practice. This peer-led course is grounded in evidence-based practices, adult learning theory and experiential learning.
- <https://my.clevelandclinic.org/departments/patient-experience/depts/experience-partners/training/foundations-of-healthcare>

Decision Aids

Ottawa Hospital Research Institute

- <https://decisionaid.ohri.ca/AZlist.html>

Patient Education (How to) Materials

Canadian Association of Psychosocial Oncology (CAPO) <https://www.capo.ca/>

- Evidence-informed guidelines can be found
- <https://www.capo.ca/guidelines>

Canadian Association of Nurses in Oncology (CANO/ACIO)

- Survivorship resource based upon literature reviews of the topics in table of contents
- www.cano-acio.ca/survivorship_manual

American Society of Clinical Oncology (ASCO)

- Models of long-term follow-up care
- <https://www.asco.org/practice-policy/cancer-care-initiatives/prevention-survivorship/survivorship/survivorship-3>

Canadian Cancer Society (CCS)

- Follow-up after treatment for colorectal cancer
- <https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/treatment/follow-up/?region=on>

University of Ottawa Psychosocial Oncology Laboratory: Fear of Cancer Recurrence

- <https://socialsciences.uottawa.ca/psychosocial-oncology-laboratory/resources>

CancerCare Manitoba

- Moving Forward after Colorectal Cancer
- <https://www.cancercare.mb.ca/For-Health-Professionals/follow-up-care-resources/index.html>

Discussion (related) tools

Canadian Oncology Symptom Triage and Remote Support (COSTaRS)

- <https://ktcanada.ohri.ca/costars/> (intended for nurses)

Canadian Association of Psychosocial Oncology

- [The Emotional Facts of Life with Cancer: A Guide to Counselling and Support for Patients, Families and Friends](#)

Ontario Health (CCO)

- Follow-up Model of Care for Cancer Survivors
- <https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/58736>

CancerCare Manitoba

- Follow-up Care Plan
- <https://www.cancercare.mb.ca/For-Health-Professionals/follow-up-care-resources/index.html>

2. Signs and Symptoms of Colorectal Cancer Recurrence

Signs and symptoms of colorectal cancer are subtle and complex. Patients with local or distant recurrence may be symptomatic or asymptomatic. Symptoms of recurrence depend on the site of recurrence and may vary between patients.

Local recurrence refers to the cancer coming back in the same area of the colon or rectum where the original cancer was found and where the surgery took place. Distant recurrence refers to the cancer spreading to other areas and is most often in the liver and/or lungs. Both local and distant recurrence are most likely to occur in the first two years following treatment.

The list below represents some of the signs and symptoms of recurrence that were put together by a group of cancer specialists. If you are experiencing any of these symptoms, especially if they are new, it is important to discuss this with your healthcare provider.

Sign or Symptom	Type of Recurrence	
	Local	Distant
Abdominal pain	X	X
Dry cough		X
Rectal bleeding	X	
Changes in bowel habit	X	
Fatigue	X	X
Nausea	X	X
Unexplained weight loss	X	X
Anemia	X	X
Pain	X	
Stoma bleeding	X	
Palpable mass	X	X
Abdominal pain from hepatomegaly		X
Jaundice		X
Pleuritic chest pain or shortness of breath		X
Anorexia, cachexia, and weight loss		X
Dyspnea		X
Loss of appetite		X
Signs and/or symptoms specific to rectal cancer*		
Pelvic pain	X	
Sciatica	X	
Difficulty with urination or defecation	X	

*There are no signs or symptoms specific to colon cancer that would not also apply to rectal cancer.

3. Common and/or Substantial Long-term and Late Effects

There are many health needs and concerns and physical and psychosocial long-term and late effects of colorectal cancer that both the physician and patient need to be aware of to mitigate discomfort, effectively manage symptoms, and improve quality of life. The highest priority supportive care needs for colorectal cancer survivors are for information and education and physician communication, particularly around the risk of recurrence. Psychosocial support about the risk of recurrence and provision of empathetic, effective, and coordinated communication should be emphasized more than post-treatment physical effects and symptom control.

Physical Long-term and Late Effects	
<ul style="list-style-type: none"> • Issues with bowel function <ul style="list-style-type: none"> ○ Frequent and/or urgent bowel movements ○ Loose bowels ○ Incontinence ○ Gas and/or bloating • Postoperative issues <ul style="list-style-type: none"> ○ Possible but low risk of incisional hernia ○ Possible but low risk of bowel obstruction • Peripheral neuropathy (associated with treatment using oxaliplatin) • Chemotherapy-related cognitive side effects • Issues with fertility • Sexuality function (e.g., vaginal dryness and pain with intercourse, erectile dysfunction, retrograde ejaculation) • Stoma care and life-style adjustments for patient who have received ostomy • Possible changes in urinary function • Chronic pain • Fatigue • Nutritional and diet considerations 	
Psychosocial Long-term and Late Effects	
<ul style="list-style-type: none"> • Psychological distress • Depression • Anxiety • Worry • Fear of recurrence • Changes in sexual function/fertility 	<ul style="list-style-type: none"> • Body and/or self-image • Relationships • Other social role difficulties • Return to work concerns • Financial challenges • Support for family

Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer

Section 2: Guideline - Recommendations and Key Evidence

GUIDELINE OBJECTIVES

This guideline is an update to a previous version (i.e., GL 26-2 V2). The main objectives are:

1. To determine the surveillance regimen that leads to the largest benefit for stage I-IV colorectal cancer survivors treated with curative intent.
2. To determine preferred models of follow-up care in Ontario.
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TARGET POPULATION

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2. Healthcare organizations and system leaders responsible for offering, monitoring, or providing resources for colorectal cancer survivorship protocols.

PREAMBLE

The Supplemental Information section that follows the recommendations provides links to webpages with tools to help with communication, patient education, and decision aids; a list of signs and symptoms; and a list of psychosocial supports and informational needs of patients that may impact follow-up requirements and decisions.

RECOMMENDATIONS, KEY EVIDENCE, AND JUSTIFICATION

Recommendation 1
<p>For patients with stage I-III colon cancer:</p> <ul style="list-style-type: none">• A medical history and physical examination should be performed every six months for three years.• Computed tomography (CT) of the chest, abdomen and pelvis (CT CAP) should be performed at one and three years OR one CT CAP could be performed at 18 months.• The use of carcinoembryonic antigen (CEA) is optional if CT imaging is being performed.• Surveillance colonoscopy should be performed one year after the initial surgery. The frequency of subsequent surveillance colonoscopy should be dictated by the

<p>findings of the previous one, but it generally should be performed every five years if the findings of the previous one is normal.</p>
<p>Qualifying Statements for Recommendation 1</p> <ul style="list-style-type: none"> • The use of CEA in combination with CT CAP does not lead to a survival advantage compared to CT CAP alone. • CEA is optional in patients with elevated CEA prior to treatment provided that CT CAP imaging is being performed. • If complete colonoscopy was not performed in the course of diagnosis and staging (e.g., due to obstruction), a complete colonoscopy should be performed within six months of completing primary therapy. • There was insufficient evidence to support these recommendations for patients with rectal cancer, patients with stage IV colon cancer, and patients over the age of 75 years. Therefore, the follow-up in those patients is at the discretion of the treating physician. • There was no evidence to support follow-up in patients with stage I-III colon cancer beyond three years. Therefore, follow-up after this time period is at the discretion of the treating physician. • These recommendations do not apply to patients with rectal cancer undergoing non-operative management or to patients with increased risk of cancer including but not limited to inflammatory bowel disease, familial adenomatous polyposis, and Lynch syndrome. • Patients should be informed of these current recommendations and the treating physician should discuss the specific risks and benefits of these recommendations with their patient.
<p>Key Evidence and Justification for Recommendation 1</p> <p>A Cochrane review by Jeffery et al. [1] including 15 randomized controlled trials (RCTs) and 12,528 patients showed that there was no survival benefit for intensifying the follow-up regimen (overall survival hazard ratio [HR], 0.91; 95% confidence interval [CI], 0.80 to 1.04; colorectal-specific survival, 0.93; 95% CI, 0.81 to 1.07).</p> <p>Furthermore, there was no difference in detection recurrence with intensifying the follow-up regimens (relapse-free survival HR, 1.05; 95% CI, 0.92 to 1.21); however, significantly more surgical procedures for recurrence were performed in the higher intensity follow-up regimens (relative risk [RR], 1.98; 95% CI, 1.53 to 2.56) [1].</p> <p>Subgroup analysis showed that there was no difference in overall survival in studies using CEA versus no CEA, CT versus no CT, or more than two CT scans versus two or fewer CT scans. These data also showed that 90% of the recurrences were found within 36 months of follow-up [1].</p> <p>COLOFOL was a multicentre trial that randomized 2509 patients treated for stage II and III colorectal cancer to high-intensity follow-up consisting of a CEA at one month postoperatively followed by CEA, CT CAP at six, 12, 18, 24 and 36 months, or low-intensity follow-up consisting of CEA at one month postoperatively followed by CEA and CT CAP at 12 and 36 months after surgery. The results of this study showed no difference in overall survival or cancer-specific recurrence rate between the high- and low-intensity groups (risk difference, 1.1%; 95% CI, -1.6 to 3.8; and risk difference, 2.2%; 95% CI, -1.0-5.4%, respectively). There were no significant differences in overall survival between cancer stages [2].</p>

FACS was a multicentre trial that randomized 1202 patients treated for Dukes' stage A-C cancer to minimum follow-up (CT CAP at 12 to 18 months if requested at study entry by the treating clinician) or one of three other higher-intensity groups that included CEA and CT CAP combined (CEA every 3 months for 2 years then every 6 months for 3 years; CT CAP every 6 months for 2 years and then annually for 3 years), CEA alone, or CT CAP alone. The results of this study showed that overall and disease-specific survival were similar between the minimum follow-up and higher-intensity regimens. This study also showed that detection of recurrence at scheduled visits was higher in the higher-intensity follow-up groups and this led to more surgical procedures for recurrence in the higher-intensity follow-up groups. There were no differences in overall survival between groups for patients with Dukes' A, B, or C [3].

In summary, the evidence consistently shows that there is no survival benefit for intensifying the follow-up regimen. While higher-intensity regimens may allow for earlier detection of recurrence than lower-intensity regimens, early detection does not lead to better overall survival or colorectal-specific survival at an aggregate level.

Table 1.1 Recommended evaluation and intervals for routine surveillance of stage I-III colon cancer survivors

Intervention	Interval	
	Years 1 to 3	Years 4 and 5
Physical examination	Every 6 months	At discretion of treating physician
CEA	At discretion of treating physician	At discretion of treating physician
CT of the Chest, Abdominal and Pelvic Imaging (CT CAP)	CT CAP at Years 1 and 3 OR CT CAP at 18 months	At discretion of treating physician
Colonoscopy	At 1 year following surgery, the frequency of subsequent surveillance colonoscopies should be dictated by the findings of the previous one but generally should be performed every 5 years if the findings of the previous one are normal.	

CEA=carcinoembryonic antigen; CT=computed tomography

Recommendation 2

While there is limited evidence to support a shared care model for the follow-up of patients with colorectal cancer, this approach was supported by the Working Group and Expert Panel.

Follow-up care is complex and requires multidisciplinary, coordinated care of the patient delivered by the cancer specialist, family physician or nurse practitioner, and allied health professionals.

The roles and responsibilities of the multidisciplinary team members need to be clearly defined and the patient needs to know when and how to contact each member of the team.

Qualifying Statement for Recommendation 2
<ul style="list-style-type: none"> It is expected that implementation of a shared care model will need to be region specific based on the available resources and provider models in each individual region.
Key Evidence and Justification for Recommendation 2
<p>Three guidelines, an environmental scan of Canadian provincial agencies, two systematic reviews, two RCTs, and two cohort studies provided evidence for this recommendation [1,4-11]. The certainty of the evidence is low to moderate in favour of a shared care model; most of the evidence is from small cohort studies and consensus opinion. The recommendations and information from the guidelines and provincial agencies come from a combination of selected evidence and consensus. The evidence and consensus support a combination or coordination of care among healthcare providers.</p> <p>Evidence from the systematic reviews showed that there was no difference in patient outcomes, including overall survival and recurrence, whether care was provided by surgeons, primary care physicians, or nurse practitioners.</p>

Recommendation 3
<p>The signs and symptoms of recurrence may be subtle and must be considered in the context of the patient’s overall health and pre-existing conditions. There is insufficient evidence to recommend any individual sign or symptom or combination of signs and symptoms as a strong predictor of recurrence.</p> <p>Patients should be educated about the potential signs and symptoms of recurrence and know which member of the multidisciplinary care team they should contact if they develop any new or concerning signs or symptoms.</p> <p>A list of signs and symptoms of colorectal cancer recurrence can be found in the Supplemental Information section following the recommendations.</p>
Key Evidence and Justification
<p>Evidence for this recommendation comes from two guidelines and two studies [4,8,12,13]. The certainty of the evidence is low as the recommendations for signs and symptoms is based primarily on consensus opinion.</p>

Recommendation 4
<p>Psychosocial support about the risk of recurrence and provision of empathetic, effective, and coordinated communication are most highly valued by patients for post-treatment physical effects and symptom control.</p> <p>Continuing professional education should emphasize the importance of communication skills and coordination of communication between the patient and family, and healthcare providers.</p> <p>A list of late and long-term physical and psychosocial effects of colorectal cancer and links to communication resources and tools can be found in the Supplemental Information section following the recommendations.</p>

Key Evidence and Justification

Two guidelines and one systematic review provided information about the types of information and education that are important to patients and how they are provided [4,8,14]. The certainty of the evidence is moderate as the guidelines were based on consensus opinion and the systematic review was based primarily on cohort studies and surveys. However, the systematic review was quite thorough, and an RCT may not be the most appropriate or feasible study design to investigate psychosocial issues.

IMPLEMENTATION CONSIDERATIONS

The previous Program in Evidence-Based Care (PEBC) guideline from 2016 recommended that follow-up for all stage II and III colorectal cancer survivors should include: (i) history and physical exam and CEA every 6 months for 5 years, (ii) CT abdomen and chest annually for 3 years, (iii) CT pelvis annually for 3 years for rectal cancer only, and (iv) colonoscopy at one year following surgery [3, 14]. These recommendations were based on guidelines from groups including the American Society of Clinical Oncology, the Cancer Council Australia and the Australian Cancer Network the American Cancer Society, the New Zealand Guideline Group, the National Comprehensive Cancer Network, and the European Society of Medical Oncology. Therefore, while the previous guideline was based on high-quality guidelines from other jurisdictions, this updated version is based on newer primary evidence.

The main changes in the current guideline are that the recommendations apply to stage I-III colon cancer survivors and do not apply to rectal cancer (all stages) and stage IV colon cancer. This guideline also recommends two CT scans at 12 and 36 months rather than three CT scans and that the use of CEA in combination with CT is optional.

During the internal and external review, it became apparent to the Working Group that there seemed to be significant variations in the follow-up of colorectal cancer patients across the province. Therefore, an assessment of current practice patterns across the province will be necessary to understand the extent and possible reasons for the variation as well as to develop tailored solutions to address it. Furthermore, sustained knowledge translation activities to foster ongoing discussion of the primary evidence will also be critical to reducing variation. One of the central components of this knowledge translation will be that while early detection of colorectal recurrence does not lead to improved survival, it does not mean that surgery for colorectal recurrence is not effective and patients should continue to be referred for surgical consultation. In addition, this knowledge translation will need to communicate that “more” investigations may possibly expose patients to greater harm and lead to overutilization of health resources.

At minimum, patients should be informed of these current guideline recommendations and the treating physician should discuss the specific risks and benefits of these recommendations with their patient based on the specific details of their case.

UPDATE 2021

The previous version of this document was assessed in accordance with the PEBC Document Assessment and Review Protocol. Clinical experts expressed concerns that new evidence had been published regarding the use of lower- versus higher-intensity follow-up for colorectal cancer survivors. While the previous versions were based on high-quality guidelines from other jurisdictions and organized in individual modalities, the updated version is based on newer primary evidence and organized as regimens with options allowing for individual patient requirements and needs.

RELATED GUIDELINES

- Members of the Gastrointestinal Cancer Disease Site Group. Follow-up of patients with curatively resected colorectal cancer. 2012 Mar 20 [Education and Information 2012 Mar 20]. Program in Evidence-based Care Practice Guideline No.: 2-9 Education and Information 2012.
- Sussman J, Souter LH, Grunfeld E, Howell D, Gage C, Keller-Olaman S, et al. Models of care for cancer survivorship. Sussman J, Fletcher G, reviewers. Toronto (ON): Cancer Care Ontario; 2012 Oct 26 [ENDORSED 2017 March 28]. Program in Evidence-based Care Evidence- Based Series No.: 26-1 Version 2 ENDORSED.
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FURTHER RESEARCH

Future work developing a province-wide, interactive, computer-based decision support tool that individually tailors the follow-up regimen for patients should be considered and evaluation of outcomes (regimen selected, compliance, survival) could be used to further support implementation of these guideline recommendations.

Supplemental Information: Colorectal Cancer Follow-up Resources

1. Colorectal Cancer Follow-up Resources

Communication Skill Resources and Training

Physiciansapply.ca

- Communication and Cultural Competence Program, Communication Skills Module: Medical Communication skills
- Modules that focus on communication between health professionals and patients
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Ontario Health (CCO) Follow-up Model of Care for Cancer Survivors: Recommendations for the Delivery of Follow-up Care for Cancer Survivors in Ontario. March 2019.

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Ontario Health (CCO) Person-Centred Care Guideline

- The objective of this guideline is to establish a standardized set of recommendations for providing person-centred care in the delivery of adult oncology services in Ontario.
- This guideline provides guidance for use by all clinicians and staff within adult oncology service settings, and for use by patients (and/or family members and caregivers) and their care providers to inform the provision of person-centred care.
- <https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/38631>

R.E.D.E. to Communicate®: Foundations of Healthcare Communication

- This course introduces clinicians to the R.E.D.E. Model of relationship-centered communication and how it applies to any clinical practice. This peer-led course is grounded in evidence-based practices, adult learning theory and experiential learning.
- <https://my.clevelandclinic.org/departments/patient-experience/depts/experience-partners/training/foundations-of-healthcare>

Decision Aids

Ottawa Hospital Research Institute

- <https://decisionaid.ohri.ca/AZlist.html>

Patient Education (How to) Materials

Canadian Association of Psychosocial Oncology (CAPO) <https://www.capo.ca/>

- Evidence-informed guidelines can be found.
- <https://www.capo.ca/guidelines>

Canadian Association of Nurses in Oncology (CANO/ACIO)

- Survivorship resource based upon literature reviews of the topics in table of contents
- www.cano-acio.ca/survivorship_manual

American Society of Clinical Oncology (ASCO)

- Models of long-term follow-up care
- <https://www.asco.org/practice-policy/cancer-care-initiatives/prevention-survivorship/survivorship/survivorship-3>

Canadian Cancer Society (CCS)

- Follow-up after treatment for colorectal cancer
- <https://www.cancer.ca/en/cancer-information/cancer-type/colorectal/treatment/follow-up/?region=on>

University of Ottawa Psychosocial Oncology Laboratory: Fear of Cancer Recurrence

- <https://socialsciences.uottawa.ca/psychosocial-oncology-laboratory/resources>

CancerCare Manitoba

- Moving Forward after Colorectal Cancer
- <https://www.cancercare.mb.ca/For-Health-Professionals/follow-up-care-resources/index.html>

Discussion (related) tools

Canadian Oncology Symptom Triage and Remote Support (COSTaRS)

- <https://ktcanada.ohri.ca/costars/> (intended for nurses)

Canadian Association of Psychosocial Oncology

- [The Emotional Facts of Life with Cancer: A Guide to Counselling and Support for Patients, Families and Friends](#)

Ontario Health (CCO)

- Follow-up Model of Care for Cancer Survivors
- <https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/58736>

CancerCare Manitoba

- Follow-up Care Plan
- <https://www.cancercare.mb.ca/For-Health-Professionals/follow-up-care-resources/index.html>

2. Signs and Symptoms of Colorectal Cancer Recurrence

Signs and symptoms of colorectal cancer are subtle and complex. Patients with local or distant recurrence may be symptomatic or asymptomatic. Symptoms of recurrence depend on the site of recurrence and may vary between patients.

Local recurrence refers to the cancer coming back in the same area of the colon or rectum where the original cancer was found and where the surgery took place. Distant recurrence refers to the cancer spreading to other areas and is most often in the liver and/or lungs. Both local and distant recurrence are most likely to occur in the first two years following treatment.

The list below represents some of the signs and symptoms of recurrence that were put together by a group of cancer specialists. If you are experiencing any of these symptoms, especially if they are new, it is important to discuss this with your healthcare provider.

Sign or Symptom	Type of Recurrence	
	Local	Distant
Abdominal pain	X	X
Dry cough		X
Rectal bleeding	X	
Changes in bowel habit	X	
Fatigue	X	X
Nausea	X	X
Unexplained weight loss	X	X
Anemia	X	X
Pain	X	
Stoma bleeding	X	
Palpable mass	X	X
Abdominal pain from hepatomegaly		X
Jaundice		X
Pleuritic chest pain or shortness of breath		X
Anorexia, cachexia, and weight loss		X
Dyspnea		X
Loss of appetite		X
Signs and/or symptoms specific to rectal cancer*		
Pelvic pain	X	
Sciatica	X	
Difficulty with urination or defecation	X	

*There are no signs or symptoms specific to colon cancer that would not also apply to rectal cancer.

3. Common and/or Substantial Long-term and Late Effects

There are many health needs and concerns and physical and psychosocial long-term and late effects of colorectal cancer that both the physician and patient need to be aware of to mitigate discomfort, effectively manage symptoms, and improve quality of life. The highest priority supportive care needs for colorectal cancer survivors are for information and education and physician communication, particularly around the risk of recurrence. Psychosocial support about the risk of recurrence and provision of empathetic, effective, and coordinated communication should be emphasized more than post-treatment physical effects and symptom control.

Physical Long-term and Late Effects	
<ul style="list-style-type: none"> • Issues with bowel function <ul style="list-style-type: none"> ○ Frequent and/or urgent bowel movements ○ Loose bowels ○ Incontinence ○ Gas and/or bloating • Postoperative issues <ul style="list-style-type: none"> ○ Possible but low risk of incisional hernia ○ Possible but low risk of bowel obstruction • Peripheral neuropathy (associated with treatment using oxaliplatin) • Chemotherapy-related cognitive side effects • Issues with fertility • Sexuality function (e.g., vaginal dryness and pain with intercourse, erectile dysfunction, retrograde ejaculation) • Stoma care and life-style adjustments for patient who have received ostomy • Possible changes in urinary function • Chronic pain • Fatigue • Nutritional and diet considerations 	
Psychosocial Long-term and Late Effects	
<ul style="list-style-type: none"> • Psychological distress • Depression • Anxiety • Worry • Fear of recurrence • Changes in sexual function/fertility 	<ul style="list-style-type: none"> • Body and/or self-image • Relationships • Other social role difficulties • Return to work concerns • Financial challenges • Support for family

Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer

Section 3: Guideline Methods Overview

This section summarizes the methods used to create the guideline. For the systematic review, see [Section 4](#).

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Ontario Health (Cancer Care Ontario) (OH [CCO]). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer control.

The PEBC supports the work of Guideline Development Groups (GDGs) in the development of various PEBC products. The GDGs are composed of clinicians, other healthcare providers and decision makers, methodologists, and community representatives from across the province.

The PEBC is a provincial initiative of OH (CCO) supported by the Ontario Ministry of Health (OMH). All work produced by the PEBC is editorially independent from the OMH.

JUSTIFICATION FOR GUIDELINE

The OH (CCO) Transitions in Care Program is updating the Ontario Follow-up Care Guidance Summaries and the Gastrointestinal Disease Site Group (GI DSG) reported that new studies have been published examining the timing of follow-up tests for colorectal cancer recurrence monitoring. Therefore, it was determined that an update to the guideline was needed.

GUIDELINE DEVELOPERS

This guideline was developed by the Colorectal Cancer Survivorship GDG (Appendix 1), which was convened at the request of the Oncology Nursing and Transitions in Care team, PEBC GI DSG and the GI Cancer Advisory Committee

The project was led by a small Working Group of the Colorectal Cancer Survivorship GDG, which was responsible for reviewing the evidence base, drafting the guideline recommendations, and responding to comments received during the document review process. The Working Group had expertise in radiation oncology, surgical oncology, medical oncology, nursing, family health, cancer survivorship and health research methodology. Other members of the Colorectal Cancer Survivorship GDG and members of the GI DSG served as the Expert Panel and were responsible for the review and approval of the draft document produced by the Working Group. Conflict of interest declarations for all GDG members are summarized in Appendix 1, and were managed in accordance with the [PEBC Conflict of Interest Policy](#).

GUIDELINE DEVELOPMENT METHODS

The PEBC produces evidence-based and evidence-informed guidance documents using the methods of the Practice Guidelines Development Cycle [15,16] This process includes a systematic review, interpretation of the evidence by the Working Group and draft recommendations, internal review by content and methodology experts, and external review by Ontario clinicians and other stakeholders.

The PEBC uses the AGREE II framework [17] as a methodological strategy for guideline development. AGREE II is a 23-item validated tool that is designed to assess the methodological rigour and transparency of guideline development and to improve the completeness and transparency of reporting in practice guidelines.

The currency of each document is ensured through periodic review and evaluation of the scientific literature and, where appropriate, the addition of newer literature to the original evidence base. This is described in the [PEBC Document Assessment and Review Protocol](#). PEBC guideline recommendations are based on evidence of the magnitude of the desirable and undesirable effects of an intervention or accuracy of a test, and take into account the certainty of the evidence, the values of key stakeholders (e.g., patients, clinicians, policy makers, etc.), and the potential impact on equity, acceptability and feasibility of implementation. A list of any implementation considerations (e.g., costs, human resources, and unique requirements for special or disadvantaged populations, dissemination issues, etc.) is provided along with the recommendations for information purposes. PEBC guideline development methods are described in more detail in the [PEBC Handbook](#) and the [PEBC Methods Handbook](#).

Search for Guidelines

As a first step in developing this guideline, a search for existing guidelines was undertaken to determine whether any guideline could be endorsed. Evidence-based guidelines with systematic reviews that addressed at least one research question were included and if the guideline had a score of 5/7 or above on the rigor of development section of the AGREE II. For question 1: guidelines published before 2018; and for questions 2-4: guidelines published before 2016, were considered. Guidelines without systematic reviews were excluded.

The following sources were searched for guidelines on March 8, 2019 with the search term(s) colorectal cancer, follow-up, surveillance, and survivors. National Institute for Health and Care Excellence Evidence Search, Canadian Medical Association Journal Infobase, Scottish Intercollegiate Guidelines Network, American Society of Clinical Oncology, National Health and Medical Research Council - Australia Clinical Practice Guidelines Portal, and Cancer Council Australia - Cancer Guidelines Wiki. OVID MEDLINE and EMBASE were searched for guidelines using the same search as primary literature described in Section 4.

Assessment of Guidelines

The search resulted in 22 guidelines being found. Of those, 17 were published before 2018 and were excluded and/or had no information regarding questions 2-4. Therefore, no guideline met the endorsement criteria from the Working Group. As well, new studies were released in 2019 and were not a part of the guidelines found. However, five guidelines did meet the inclusion criteria and were used to inform the recommendations [4,6,8,18,19]. A summary of guideline recommendations can be found in Appendix 4.

GUIDELINE REVIEW AND APPROVAL

Internal Review

For the guideline document to be approved, 75% of the content experts who comprise the GDG Expert Panel must cast a vote indicating whether or not they approve the document, or abstain from voting for a specified reason, and of those that vote, 75% must approve the document. In addition, the PEBC Report Approval Panel (RAP), a three-person panel with methodology expertise, must unanimously approve the document. The Expert Panel and RAP members may specify that approval is conditional, and that changes to the document are required. If substantial changes are subsequently made to the recommendations during external review, then the revised draft must be resubmitted for approval by RAP and the GDG Expert Panel.

Patient and Caregiver-Specific Consultation Group

Three patients/survivors/caregivers participated as Consultation Group members for the Colorectal Cancer Survivorship GDG Working Group. They reviewed copies of the project plan and draft recommendations and provided feedback on their comprehensibility, appropriateness, and feasibility to the Working Group's Health Research Methodologist. The Health Research Methodologist relayed the feedback to the Working Group for consideration.

External Review

Feedback on the approved draft guideline was obtained from content experts and the target users through two processes. Through the Targeted Peer Review, several individuals with content expertise are identified by the GDG and asked to review and provide feedback on the guideline document. Through Professional Consultation, relevant care providers and other potential users of the guideline are contacted and asked to provide feedback on the guideline recommendations through a brief online survey.

DISSEMINATION AND IMPLEMENTATION

All guidelines are published on the OH (CCO) website and may be submitted for publication to a peer-reviewed journal. The Professional Consultation of the External Review is intended to facilitate the dissemination of the guideline to Ontario practitioners. Section 1 of this guideline is a summary document to support the implementation of the guideline in practice. OH (CCO)-PEBC guidelines are routinely included in several international guideline databases including the CPAC Cancer Guidelines Database, the CMA/Joule CPG Infobase database, NICE Evidence Search (UK), and the Guidelines International Network (GIN) Library.

Implementation of guidelines developed by the PEBC may be undertaken by Transitions in Care Program.

ACKNOWLEDGEMENTS

The Colorectal Cancer Survivorship GDG would like to thank the following individuals for their assistance in developing this report:

- Sheila McNair, Emily Vella, Donna Maziak, Jonathon Sussman Eric Winqvist, Lisa Del Giudice, Stan Feinberg, Sharlene Gill, Mary Smith and Alice Wei for providing feedback on draft versions.
- Faith Maelzer for conducting a data audit.
- Sara Miller for copy editing.

Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer

Section 4: Systematic Review

INTRODUCTION

In 2020, it is expected that approximately 26,900 Canadians will be diagnosed with colorectal cancer (Canadian Cancer Society) [20]. Recent studies have found five-year recurrence rates for patients who have curative surgery for colorectal cancer is approximately 20-30% [1,2,13,21-24]. Recurrence may occur either locally or metastasize to other organs, most commonly the liver and/or lungs.

The principal aim of follow-up programs after curative resection of colorectal cancer is to improve survival. To achieve this goal, patients are screened for early recurrent disease with the intent of intervening early with a second curative intent surgery. Decades of experience has shown that approximately 20% [1] of patients who can undergo a surgery for recurrence can be cured. This has led to interest in surveillance with a rationale of finding these patients with recurrence at a time when they can be cured. While it is often considered better for patients to undergo a greater amount of testing, surveillance that is too high intensity may lead to second curative intent surgery only to find more metastases developing shortly after surgery resulting in patients being subjected to risk without cure. Moreover, finding recurrence early to facilitate earlier introduction of palliative chemotherapy has not been clearly shown to provide a survival benefit. Therefore, evidence to show that detecting early recurrence leads to improved survival is key to establishing the effectiveness of a surveillance program. Furthermore, the effectiveness of the surveillance program must also be considered in terms of the health resources, costs, and possible harms of surveillance.

As no single test is best for all sites of recurrent disease, a combination of tests is often used and mostly commonly includes CT CAP, CEA, and colonoscopy. These tests are directed to areas of potential disease and conducted at pre-established intervals. Since the incidence of recurrent disease occurs at an exponential rate over the first two years, surveillance tests are performed more frequently during this time period and then less frequently thereafter.

While the current Ontario guidelines recommend higher-intensity follow-up for patients with colorectal cancer, more recently, there has been increasing evidence comparing higher-intensity and lower-intensity regimens. Therefore, the purpose of this paper was to update this guideline by performing a systematic overview to critically evaluate the literature to determine (i) the surveillance regimen for colon and rectal cancer survivors providing the largest overall benefit; (ii) the preferred model of care for this surveillance regimen; (iii) signs and symptoms predictive of recurrence; and (iv) post-treatment informational and support needs of colorectal cancer survivors.

OH (CCO) aims to build upon the previous guideline and create a document that i) synthesizes the evidence, taking into account patient information and support needs; ii) allows healthcare professionals to provide quality follow-up care; and iii) provides advice for identifying signs and symptoms of potential colorectal cancer recurrence and the long-term and late effects of colorectal cancer.

This systematic review has been registered on the PROSPERO (International prospective register of systematic reviews) website (<https://www.crd.york.ac.uk/prospero/>) with the registration number CRD42020132109.

RESEARCH QUESTIONS

This guideline is an update to a previous version (i.e., GL 26-2 V2) and the research questions were adapted from it.

1. What is the surveillance regimen for stage I-IV colorectal cancer survivors resected with curative intent providing the largest benefit?
 - a. What is the evidence comparing higher-intensity versus lower-intensity surveillance programs for colorectal cancer survivors treated with curative intent?
 - b. What specific surveillance regimens provided the largest overall benefit for colorectal cancer survivors treated with curative intent?
2. Are there preferred models of follow-up care in Ontario, i.e., should patient follow-up be done by a medical oncologist, radiation oncologist, surgeon, nurse practitioner, physician assistant, or family physician.
3. Which symptoms and/or signs signify a potential recurrence of colorectal cancer and warrant investigation?
4. What are the individual needs and long-term and late effects for colorectal cancer survivors?
 - a. What are the post-treatment informational and support needs for patients regarding local recurrence and common long-term and late effects of colorectal cancer?
 - b. What are the common and/or substantial long-term and late treatment effects of colorectal cancer?

METHODS

This evidence review was conducted in two planned stages, including a search for systematic reviews followed by a search for primary literature. These stages are described in subsequent sections.

Search for Systematic Reviews

A search was conducted for existing systematic reviews on May 1, 2019. The databases searched were OVID MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews for years 2011 to May 1, 2019. For search terms, please see Appendix 2. This guideline is an update therefore search date was based on the previous guideline's dates and the search terms were similar to the original guideline.

Systematic reviews were included if they met the following criteria: English-language systematic review that covered any of the guideline questions. If more than one systematic review met the inclusion criteria, then one systematic review for each outcome was selected by CZ based on its quality, and the best match with our study selection criteria stated below. Systematic reviews were assessed using the ROBIS tool [25].

Search for Primary Literature

For each outcome or research question, a search for primary literature was conducted on June 5, 2019. Below are methods for locating and evaluating primary literature. For any included systematic reviews, an updated search for primary literature was performed. If any included systematic review was limited in scope (e.g., not fully addressing the research questions or project outcomes), then a search for primary literature to address the limitation in scope was conducted. An updated search was conducted on November 16, 2020.

Literature Search Strategy

Based on the results of the search for systematic reviews, OVID MEDLINE and EMBASE databases were searched for years 2011 to present for each research questions or parts thereof. Please see Appendix 2 for the full search strategy.

Study Selection Criteria and Process

Articles were selected for inclusion if they met the following criteria:

- Study designs: RCTs, retrospective and prospective cohort with at least 30 participants, comparative cohort with at least 30 participants per group
- Population: patients with colorectal cancer whose primary treatment was with curative intent and were without evidence of disease
- Other: length of study follow-up minimum two years, use of multivariate analysis

Articles were excluded if they were: letters, comments, editorials, non-English publications, or abstracts.

A review of the titles and abstracts was conducted by CZ and MS independently. For studies that warranted full-text review, CZ reviewed each study independently with another reviewer (EK) if uncertainty existed.

Data Extraction and Assessment of Risk of Bias

All primary studies that met the inclusion criteria underwent data extraction by CZ and MS in collaboration, with all extracted data and information audited subsequently by an independent auditor. Ratios, including HRs, were expressed with a ratio of <1.0 indicating benefit for the experimental group for a given outcome.

RCTs were assessed for quality and potential bias using the Cochrane Risk of Bias tool [26] and all non-RCTs were assessed using the Cochrane Risk of Bias in Non-Randomized Studies - of Interventions (ROBINS-I) tool [27].

Synthesizing the Evidence

Meta-analyses were not planned for questions 2, 3 and 4 owing to the outcomes being measured differently across studies. The base of the evidence for question 1 was a systematic review where meta-analyses were already conducted and deemed not necessary.

Assessment of the Certainty of the Evidence

The certainty of the evidence per outcome for each comparison and/or research question, taking into account risk of bias, inconsistency, indirectness, imprecision, and publication bias was assessed.

RESULTS

Search for Guidelines

In total, 22 guidelines were found. Of those, 17 were too old while the remaining had no information regarding questions 2-4. Five guidelines had recommendations that were used to inform the recommendations provided herein [4,6,8,18,19]. None of the recommendations were deemed fully endorsable. A summary of the guidelines' recommendations can be found in Appendix 4.

Search for Systematic Reviews and Primary Literature

There was a total of 3830 articles found through the literature search and the updated search. Three hundred eighty-eight articles were selected for full-text review.

Literature Search Results

There were 25 systematic reviews considered for full-text review. Four met the inclusion criteria; others were excluded for being narrative reviews or not relevant to the scope of the guideline. The four remaining systematic reviews were chosen for relevancy to the topics and

were assessed for quality using the ROBIS tool to assess the risk of bias [25]. The risk of bias was considered low overall for each review. See Appendix 5 for systematic review quality assessment results.

A search for primary literature was conducted for all questions. Three hundred fifty-three studies underwent a full-text review and 14 were retained (Table 4-1). See Appendix 3 for PRISMA diagram and Appendix 5 for quality assessment results.

Table 4-1 Studies selected for inclusion.

Question/Topic	Number of sources that were included
High- vs. low-intensity follow-up	1 SR [1]
Surveillance and modalities	3 SRs [28-30] 2 RCTs [3]
Models of follow-up care	3 guidelines [4,6,8] 2 SRs [1,7] 2 RCTs [5,10] 2 cohort studies [9,11]
Signs and symptoms	2 guidelines [4,8] 1 RCT [12] 1 cohort study [13]
Informational and support needs	2 guidelines [8,18] 1 SR [14]
Long-term and late effects	4 guidelines [4,6,8,18] 1 SR [14]

Abbreviations: RCT=randomized controlled trial; SR=systematic review

Outcomes

Question 1: What is the surveillance regimen for stage I-IV colorectal cancer survivors resected with curative intent providing the largest benefit?

- a. What is the evidence comparing higher-intensity versus lower-intensity surveillance programs for colorectal cancer survivors treated with curative intent?
- b. What specific surveillance regimens provided the largest overall benefit for colorectal cancer survivors treated with curative intent?

a. What is the evidence comparing higher-intensity versus lower-intensity surveillance programs for colorectal cancer survivors treated with curative intent?

The evidence for Question 1a is provided from a Cochrane review by Jeffery et al. [1] conducted in 2019 evaluating the outcomes associated with high- and low-intensity follow-up programs in patients with colorectal cancer treated with curative intent. This review included 19 RCTs comparing different follow-up strategies that included comparisons of follow-up vs. no follow-up, follow-up strategies of varying intensity (e.g., differing frequency or quantity of testing or both), and follow-up in different healthcare settings (primary care vs. hospital). A total of 13,216 patients undergoing follow-up after treatment for colorectal cancer from 1995 to 2019 were included. Of the 19 RCTs, seven were conducted before 2005, all included male and female patients treated for adenocarcinoma of the colon or rectum, and approximately one-third of the patients were treated for rectal cancer. Various follow-up modalities were used singly or in combination including clinical history, physical examination, CEA, CT scan, and colonoscopy. Intensity of the follow-up was defined by the individual studies. The primary

outcome of the review was overall survival and secondary outcomes included colorectal cancer-specific survival, relapse-free survival, salvage surgery, symptomatic recurrence, quality of life, and adverse effects (see Table 4-2 for results). For the outcomes included in this meta-analysis, more than 90% of the participants studied had a median follow-up duration greater than 48 months.

Certainty of Evidence

The systematic review [1] was assessed using the ROBIS tool to assess the risk of bias [25]. The GRADE assessment completed by the systematic review found the quality of evidence of the included studies to be high for overall survival, salvage surgery, relapse-free survival; moderate for colorectal cancer-specific survival, symptomatic recurrence, quality of life; and low for adverse events. The risk of bias was considered low for each domain and overall. See Appendix 5 for Quality Assessment Scores.

Outcomes of Interest

The outcomes of interest identified by the Working Group based on clinical expertise for the purpose of the guideline were: overall survival, colorectal cancer-specific survival, relapse-free survival, salvage surgery, symptomatic recurrence, and patient experience and/or quality of life.

Overall Survival

Among 15 trials reporting overall survival, there were 1453 deaths in 12,528 patients. The analysis showed no significant difference between high-intensity and low-intensity follow-up (HR, 0.91; 95% CI, 0.80 to 1.04, $p=0.16$). In absolute terms, the average effect of high-intensity follow-up was 24 fewer deaths per 1000 patients with a range of 60 fewer to nine more deaths per 1000 patients. There was no evidence of heterogeneity. Subgroup analyses did not show any significant differences between studies comparing programs with: (i) frequent CT scans versus two or less CT scans, (ii) use of CEA versus no CEA, (iii) more visits and tests versus fewer visits and tests, or (iv) general practitioner (GP) or nurse-led (community) versus surgeon-led hospital follow-up (see Table 4-3). Sensitivity analyses were robust to trials at high risk of bias and study age (excluding those trials that completed accrual by 1996).

Colorectal Cancer-specific Survival

Among 11 trials reporting colorectal cancer-specific survival, there were 925 colorectal cancer deaths in 11,771 patients, of whom 99.6% were followed for greater than 48 months. There was no significant difference in colorectal cancer-specific death between high- and low-intensity follow-up (HR, 0.93; 95% CI, 0.81 to 1.07, $p=0.31$). In absolute terms, the average effect with high-intensity follow-up was five fewer colorectal cancer deaths per 1000 patients with a range of 14 fewer to five more deaths. There was no evidence of heterogeneity. Sensitivity analyses were robust to studies at high risk of bias and study age.

Relapse-free Survival

Among 16 trials reporting relapse-free survival, there were 2254 relapses in 8047 patients, of which 97.9% were followed for greater than 48 months. There was no significant difference between high- and low-intensity follow-up (HR, 1.05; 95% CI, 0.92 to 1.21, $p=0.46$). In absolute terms, the average effect with high-intensity follow-up was 12 more relapses per 1000 participants with a range of 48 more to 19 fewer relapses per 1000 patients. There was no heterogeneity ($I^2=41%$, $p=0.05$) and sensitivity analysis was robust to studies at high risk of bias and study age.

Salvage Surgery

Salvage surgery was defined as surgery for relapse with curative intent. Thirteen studies reported that salvage surgery was performed in 457 of 5157 patients with 90.6% followed for greater than 48 months. Salvage surgery was more frequent with high-intensity follow-up (RR, 1.98; 95% CI, 1.53 to 2.56, $p < 0.00001$). In absolute terms, the average effects were 60 more salvage surgeries per 1000 patients in the more intensive follow-up group with a range of 33 to 96 more episodes per 1000 patients. There was no significant heterogeneity ($I^2 = 31\%$, $p = 0.14$) and the sensitivity analysis was robust to studies at high risk of bias and study age.

Symptomatic Recurrence

Symptomatic (interval) recurrence was defined as relapse of colorectal cancer detected between scheduled follow-up visits. Seven studies reported 376 symptomatic recurrences in 3933 patients, of which 100% were followed for greater than 48 months. There was a significant decrease in the number of symptomatic recurrences with high-intensity follow-up (RR, 0.59; 95% CI, 0.41 to 0.86, $p = 0.0063$). In absolute terms, the average effect with high-intensity follow-up was 52 fewer symptomatic recurrences per 1000 patients with a range of 18 to 75 fewer episodes per 1000 patients. There was heterogeneity detected ($I^2 = 66\%$, $p = 0.007$) and sensitivity analysis was robust to studies at high risk of bias and study age.

Quality of Life

Six studies reported quality of life outcomes including depression, anxiety, fear of recurrence, psychological distress, satisfaction, and overall quality of life for both high- and low-intensity follow-up regimens. However, these data could not be combined due to the different outcomes reported and various uses of both validated and non-validated scales to report these outcomes. None of these studies showed any significant differences between high and low intense follow-up for any of the outcomes.

Adverse Effects

Adverse effects or harms were defined as any colonoscopy complications and were reported by two studies. Three perforations and four gastrointestinal hemorrhages requiring transfusion were reported from a total of 2292 (0.3%) colonoscopies. Results were only available from one study and suggested that high-intensity follow-up may increase the colonoscopy complication rate (RR, 7.30; 95% CI, 0.75 to 70.69, $p = 0.09$), 326 participants). The quality of this study was low.

Cost of Surveillance

Three studies reported cost by intensity of follow-up. Two studies reported higher costs for high-intensity follow-up whereas one study found no difference in cost between high- and low-intensity follow-up schedules.

Conclusions

In summary, high-intensity follow-up led to more salvage surgery and fewer symptomatic recurrences, but these benefits did not translate into a significant improvement in overall survival or colorectal cancer-specific survival. Subgroup analysis showed that type of provider and the type of setting did not have any effect on overall survival. Furthermore, quality of life outcomes did not differ between high- and low-intensity follow-up, but these data could not be combined in an overall analysis.

Table 4-2. Results of Jeffery et al. meta-analysis, high- versus low-intensity follow-up

Systematic Review	Outcomes	Number of studies	Hazard Ratio	Heterogeneity	GRADE assessment of quality for outcome
Jeffery, 2019 [1]	Overall survival	15 studies	HR 0.91, 95% CI 0.80 to 1.04	I ² =18%, p=0.25	High
	Colorectal cancer-specific survival	11 studies	HR 0.93, 95% CI 0.81 to 1.07	I ² =0%, p=0.57	Moderate
	Relapse-free survival	16 studies	HR 1.05, 95% CI 0.92 to 1.21	I ² =41%, p=0.05	High
	Salvage surgery	13 studies	RR 1.98, 95% CI 1.53 to 2.56	I ² =31%; p=0.14	High
	Symptomatic (interval) recurrences	7 studies	RR 0.59, 95% CI 0.41 to 0.86	I ² =66%; p=0.007	Moderate

Abbreviations: CI=confidence interval; HR=hazard ratio; RR=relative risk

Table 4-3. Subgroup analysis for overall survival for Jeffery et al. meta-analysis

Subgroup analysis	Number of Studies	X ² Statistic
(More vs. fewer tests) vs. (2 tests vs. minimal or no FU)	11 studies (7 vs. 4)	X ² =0.34; p=0.56; I ² =0%
CT versus no CT	10 studies (7 vs. 3)	X ² =0.31; p=0.58; I ² =0%
CEA versus no CEA	7 studies (6 vs. 1)	X ² =0.15; p=0.7, I ² =0%
2 or more CT versus less than 2 CT	9 studies (6 vs. 3)	X ² =0.99; p=0.32; I ² =0%

Abbreviations: CEA=carcinoembryonic antigen; CT=computed tomography; FU=follow-up

b. What specific surveillance regimens providing the largest overall benefit for colorectal cancer survivors treated with curative intent?

Summary of Studies

While the Cochrane meta-analysis by Jeffery et al. was comprehensive, one of its main limitations was that various combinations and frequencies of investigations were “lumped” together into high-intensity versus low-intensity versus minimal follow-up [1]. As a result, it was not possible to compare different combinations of investigations or tests between regimens or to evaluate these investigations and tests individually.

Three other systematic reviews and two RCTs included in the Cochrane meta-analysis were identified that compared specific regimens and/or effectiveness of individual modalities [3,28-30]. The COLOFOL trial compared higher-intensity follow-up consisting of CEA at one month postoperatively followed by CEA and CT CAP at six, 12, 18, 24, 30 and 36 months versus low-intensity follow-up consisting of CEA at one month postoperatively followed by CEA and CT CAP at 12 and 36 months. The primary outcome for this study was overall survival [2]. The FACS trial directly compared three specific regimens to minimal follow-up: CT alone, CEA alone, and CT and CEA combined. In addition, a factorial analysis was performed comparing individual modalities including CT versus no CT and CEA versus no CEA. The primary outcome was surgery for recurrence with curative intent [3].

Three systematic reviews evaluated the effectiveness of individual modalities. One review evaluated CEA, CT, and colonoscopy [29], one review evaluated CEA only [28], and one review evaluated colonoscopy only [30] (see Appendix 4 Tables 4-2 and 4-3 for Study Characteristics and Results).

Certainty of Evidence

The systematic reviews were assessed using the ROBIS tool to assess the risk of bias [25]. The risk of bias was considered low for each domain and overall. The RCTs were evaluated using the Cochrane Risk of Bias Tool 2.0 [26] and found to be of a low risk of bias (see Appendix 5 for Quality Assessment Scores).

Results for Individual Modalities

CT Scan

Pita-Fernández et al. performed a meta-analysis comparing high-intensity with low-intensity follow-up regimens with overall survival as the primary outcome [29]. This review included 11 RCTs (4055 patients). This systematic review was published before the Cochrane review and therefore does not include some of the newer studies. Overall survival was reported for individual diagnostic tests including CEA, CT, and colonoscopy (see Table 4-4). These results showed that having a CT scan (vs. no CT scan) led to improved overall survival (HR, 0.80; 95% CI, 0.66 to 0.98).

The FACS RCT factorial analysis showed that having a CT scan led to an increase in recurrence detected by scheduled follow-up (15.3% vs. 7.3%, $p < 0.001$), but this did not lead to a significance difference in overall detection of recurrence (18.1% vs. 15.6%, $p = 0.25$) [3]. There was significantly more surgical treatment of recurrence in the CT vs. no CT group (8.2% vs. 4.5%, $p = 0.009$). This also did not translate into a significant difference in overall survival (25.8% vs. 25.1%, $p = 0.79$) or disease-free survival (13.8% vs. 14.3%, $p = 0.92$).

CEA test

The meta-analysis by Pita-Fernández et al. showed a trend toward improved survival with CEA (vs. no CEA) (HR, 0.73; 95% CI, 0.51 to 1.05), but this did not reach statistical significance [29].

Similarly, no significant differences between CEA and no CEA for recurrences detected by scheduled follow-up (12.5 vs. 10.2%, $p = 0.21$) or detection of overall recurrence was found by the FACS study factorial comparison (17.3% vs. 16.5%, $p = 0.72$). There was no difference in the rate of surgical salvage between the CEA vs. no CEA testing groups (6.6% vs. 6.0%, $p = 0.65$) [5].

A health technology assessment by Shinkins et al. included a meta-analysis of 52 studies assessing the sensitivity and specificity of single and serial CEA testing for detection of cancer recurrence [28]. The results of the pooled analysis with a threshold of 5 ug/L used in 23 studies (4585 patients) showed a sensitivity of 71% (95% CI, 64 to 76) and a specificity of 88% (95% CI, 84 to 92). Therefore, for 1000 people tested, 14 cases of recurrence were detected, six cases were missed, and 118 people were referred unnecessarily for further testing.

Colonoscopy

The meta-analysis by Pita-Fernández et al. showed that colonoscopy (vs. no colonoscopy) (HR, 0.65; 95% CI, 0.53 to 0.81) led to improved overall survival [29].

Fuccio et al. conducted a meta-analysis of 27 studies to examine the colorectal cancer detection rates and timing of colorectal cancer recurrence at anastomotic and non-anastomotic locations [30]. They found that the risk of colorectal cancers at anastomoses was significantly lower 24 months after resection than earlier; 70.5% of all colorectal cancers at anastomoses were detected within 24 months of surgery and 90.8% within 36 months of surgery. The risk for colorectal cancer at non-anastomotic locations was significantly reduced more than 36 months after resection compared with earlier and 53.7% of all non-anastomotic colorectal cancers were detected within 36 months of surgery.

In the FACS trial, three luminal recurrences were detected in 601 (0.5%) patients at the two-year colonoscopy in the groups being monitored by CT imaging. Three new cancers were detected in 1202 patients (0.2%) (all groups) at the five-year colonoscopy [3].

The original PEBC guideline states that a postoperative colonoscopy should be performed one year following surgery. The frequency of subsequent surveillance colonoscopies should be dictated by the findings of this initial postoperative colonoscopy and in general should be performed a minimum of every five years [4]. However, if a complete colonoscopy was unable to be performed preoperatively, then a postoperative colonoscopy is recommended within six months of surgery. This original recommendation was based on the results of the National Polypectomy Study [31].

Clinic Visits

The meta-analysis by Pita-Fernandez et al. showed that clinic visits (vs. no clinic visits) (HR, 0.57; 95% CI, 0.035 to 0.92) led to improved overall survival [29].

Results for Specific Regimens: Intense vs. Minimum Follow-up

COLOFOL RCT

To compare follow-up intensities, 2509 patients treated for stage II and III colorectal cancer were randomized to high-intensity follow-up consisting of a CEA test at one month postoperatively followed by CEA and CT CAP at six, 12, 18, 24 and 36 months; or low-intensity follow-up consisting of a CEA test at one month postoperatively followed by CEA and CT CAP at 12 and 36 months after surgery [2].

The five-year overall mortality rate was 13.0% (95% CI, 11.3% to 15.1%) in the high-intensity group versus 14.1% (95% CI, 12.3% to 16.2%) in the low-intensity group with a risk difference of 1.1% (95% CI, -1.6% to 3.8%; $p=0.43$).

The colorectal cancer-specific mortality rate was 10.6% (95% CI, 9.0% to 12.5%) in the high-intensity group versus 11.4% (95% CI, 9.7% to 13.3%) in the low-intensity group with a risk difference of 0.8% (95% CI, -1.7% to 3.3%; $p=0.52$).

The risk of detected colorectal cancer-specific recurrence was not significantly increased at 21.6% (95% CI, 19.4% to 24.0%) in the high-intensity group versus 19.4% (95% CI, 17.3% to 21.8%) in the low-intensity group with a risk difference of 2.2% (95% CI, -1.0% to 5.4%; $p=0.15$).

Adherence to protocol

In COLOFOR, the proportion of patients with no protocol violations was 94.2% and 94.3% in the high- and low-intensity groups, respectively, with rates and reason being similar [2].

Summary of COLOFOR Results

Among patients who had undergone curative surgery for stage II or III colorectal cancer, surveillance with CEA and CT more frequently compared with less frequently did not result in a significant rate reduction in five-year overall mortality or colorectal cancer-specific mortality [2].

FACS RCT

While there was a significant difference between high-intensity (CEA only vs. CT only vs. CT and CEA combined) compared to minimum follow-up for detection of recurrence by scheduled follow-up (18.7% vs. 20.4% vs. 15.9% vs. 12.6%, $p=0.06$), there was not a difference in mortality (27.0% vs. 27.8% vs. 23.8% vs. 23.3%, $p=0.49$) or deaths attributed to colorectal cancer (16.0% vs. 15.1% vs. 12.6% vs. 12.6%, $p=0.73$) between the three more intensive groups and the minimum follow-up group, respectively [3]. Overall, two-thirds of recurrences were detected at scheduled follow-up investigation (see Table 4-4 for Summary of Results for FACS).

The primary outcome for FACS was surgical treatment of recurrence with curative intent. Overall, 6.3% (76/1202) of patients underwent salvage surgery for recurrence, with no difference among participants according to Dukes' stage (A, 5.1%; B, 7.4%; C, 5.6%, $p=0.56$) [5].

Salvage surgery for recurrence was higher in the three more intensive follow-up groups compared with the minimum follow-up group (CEA only 6.3%; CT only 9.4%; CEA and CT 7.0% vs. minimum follow-up 2.7%, $p=0.008$). This translated into adjusted odds ratios for surgically treated recurrence of 2.4 (95% CI, 1.02 to 5.65, $p=0.04$) for CEA only, 3.69 (95% CI, 1.63 to 8.38, $p=0.002$) for CT only, and 2.78 (95% CI, 1.19 to 6.49, $p=0.02$) for CEA and CT combined relative to minimum follow-up.

A key finding of the trial was that patients at all stages of primary tumour benefit equally from follow-up (Dukes' A: 13/249, 5%; Dukes' B: 32/537, 6%; Dukes' C: 20/346, 6%; $p=0.80$) [5].

Overall, the absolute differences in the proportion of patients treated with curative intent surgery between the high-intensity regimens and minimal follow-up was 3.6%-6.7%, indicating that between 12 and 20 patients need to be followed to identify one potentially curable recurrence. No further evidence regarding the time to re-recurrence or death or quality of life was provided for this subset of patients undergoing salvage surgery [3].

Adherence to protocol

In FACS, significantly more unscheduled tests were performed in patients not receiving regular CT scans, with 16.3% versus 4.7% ($p<0.001$) receiving one or more unscheduled CEA tests, 20.3% versus 3.7% ($p<0.001$) receiving one or more unscheduled CT tests, and 16.0% versus 4.3% ($p<0.001$) receiving one or more unscheduled colonoscopies [3].

Summary of FACS results

Among patients who had undergone curative surgery for primary colorectal cancer, surveillance with CEA only and CT only improved detection of recurrence treated with curative intent compared with minimal follow-up. There was no advantage to combining both strategies. If there is a survival advantage to any strategy, it is likely to be small (<5%) [3].

Conclusions

There was no significant difference in overall or colorectal cancer-free survival in patients in higher-intensity versus lower-intensity regimens. Recurrences in the more intensely followed groups may have been detected earlier allowing for effective salvage treatment but this did not lead to better overall survival. Specific reasonable low-intensity follow-up regimens are from COLOFOL and FACS and are: CEA and CT CAP at 12 and 36 months and CT CAP at 12 to 18 months, respectively [2,3]. Use of CT scan in follow-up led to an improvement in overall survival in the meta-analysis and an improvement in recurrence detection in scheduled follow-up but not in overall detection of recurrence. The use of a CEA test did not show an improvement in the overall survival in the meta-analysis or detection recurrence in the FACS. Varying thresholds provide varying sensitivity and specificity levels. Colonoscopy was used to find polyps as they are potential precursors of colorectal cancer.

Question 2: Are there preferred models of follow-up care in Ontario, i.e., should patient follow-up be done by a medical oncologist, radiation oncologist, surgeon, advanced practice nurse, physician assistant, or primary care provider (e.g., family physician, nurse practitioner, family practice nurse)?

Three guidelines retrieved in the literature search had recommendations regarding models of follow-up care based on a combination of selected evidence and consensus [4,6,8]. All guidelines recommend a combination of follow-up from care providers. The OH (CCO)

guideline recommendation is that although the most common practice for follow-up care in Ontario involved specialist-coordinated care within an institution, discharge from specialist-led care to a community-based family physician-coordinated or institution-based registered nurse (RN)-coordinated care is a reasonable option [4]. The Cancer Council Australia (CCA) colorectal cancer guideline concludes that follow-up care can be delivered as a combination of visits to the surgeon or associated gastroenterologist, with ongoing care by the GP and clinical RN consultant [8]. National Comprehensive Cancer Network (NCCN) guidelines state that the oncologist and the primary care provider should have defined roles in the surveillance period [6] (see Appendix 4 Table 4-1 for Guideline Recommendations Summary).

The primary evidence for this question was found in two systematic reviews [1,7], two RCTs [5,10], and two cohort studies [9,11]. The first systematic review is the recent Cochrane review by Jeffery et al. [1]. The second systematic review is a qualitative review by Berian et al. of 16 studies that examined patients' perceptions and expectations of routine surveillance and 14 studies (8 quantitative and 6 qualitative) that identified the types of providers that patients prefer to guide that surveillance [7].

The two RCTs compared providers: GP versus surgeon [5] and RN versus surgeon [10]. One cohort study examined the patient preferences during an outpatient follow-up program [11], and the other cohort study followed two groups of patients with or without an added nonphysician clinician [9] (see Appendix 4 Table 4-4 for Study Characteristics).

Environmental Scan

As this question focuses on preferred models of follow-up care in Ontario, an environmental scan of other Canadian Cancer Agencies' models of care for colorectal cancer follow-up was also conducted. From the environmental scan, five provinces had information freely available on their website (British Columbia, Alberta, Saskatchewan, Manitoba, Nova Scotia). In these provinces, there is a combination or coordination of care between the oncologist/surgeon and the family physician and/or primary care nurse practitioner. All provincial cancer agencies also discuss a treatment plan or provide an information package for the patient and the primary care physician. Only the guidance from Alberta Health Services provided an evidence base for the recommendations (see Appendix 4 and Table 4-5 for Environmental Scan Summary).

Certainty of Evidence

The guidelines were assessed using the AGREE II [17] and all scored between 65% and 86% on the rigor of development domain indicating a high-quality guideline. The systematic reviews were assessed for risk of bias using the ROBIS tool [25], and all were deemed to have low risk of bias. The RCTs were assessed using the RoB 2.0 [26], and the risk of bias for each outcome used in this review was rated as low in each study. The cohort studies were assessed using the ROBBINS tool [27], and were deemed to have a moderate risk of bias (see Appendix 5 for Quality Assessment scores).

Importance of Outcomes

To compare models of follow-up care delivery, the Working Group members determined based on clinical experience, that overall survival, recurrence of colorectal cancer, patient satisfaction, quality of life, and unannounced follow-ups (adherence) are critically important outcomes.

For the purpose of this section, comparisons were made between providers as described in the studies for the outcomes evaluated. This included terms such as GP, RN, specialist, and nurse specialist. However, for the purpose of this document we use the terms family physician and nurse practitioner to reflect current practice across the province of Ontario.

Hospital versus GP or RN follow-up***Overall survival***

The evidence examining overall survival is determined from one systematic review. Jeffery et al. evaluated RCTs that compared different healthcare professionals and found no differences in a subgroup analysis ($X^2=0.40$; $p=0.53$; $I^2=0\%$) between GP or RN-led follow-up (2 studies) and hospital follow-up (13 studies) [1]. The overall effect on overall survival was similar (HR, 0.91; 95% CI, 0.80 to 1.03, $p=0.14$).

Adherence

Coebergh van den Braak et al. found that patients at hospitals with a trained nonphysician clinician specialized in oncology had greater adherence to postoperative follow-up compared with patients visiting an outpatient clinic without (84.3 vs. 73.9%, $p=0.001$) [9].

GP versus Surgeon Follow-up***Recurrence***

Augestad et al. performed an RCT with 110 patients comparing GP and surgeon provider groups [5]. A total of four hospitals and 148 GPs participated in the trial. The GP intervention included the GPs being provided with follow-up information for the patients referred to them and both the GPs and patients were given a decision-support pamphlet containing information about their recurrence risk, the national follow-up guideline schedule, signs and symptoms of recurrence, and contact information in case of questions. A total of 48 (10.7%) patients had serious clinical events (an episode in which cancer recurrence was suspected such as a reported symptom or clinical finding) that occurred at both scheduled and unscheduled follow-up visits. There was no difference between the GP and surgeon provider groups with respect to mean time to diagnosis of recurrence (35 vs. 45 days, $p=0.46$), the number of patients with cancer recurrence (6 [10.9%] vs. 8 [14.5%] patients), surgical treatment of recurrence with curative intent (3 [5.5%] vs. 4 [7.3%] patients), or overall mortality (1 [1.8%] vs. 4 [7.3%] deaths).

Quality of Life

In Augestad et al., the European Organisation for Research and Treatment of Cancer QoL Questionnaire (EORTC QLQ) was completed at baseline and at three, six, nine, 12, 15, 18, 21, and 24 months after surgery [5]. There was no significant difference in the overall quality of life score; however, on the EORTC QLQ C-30 subscales, significant effects were observed in favour of GP follow-up for role functioning ($p=0.02$), emotional functioning ($p=0.01$), and pain ($p=0.01$). A total of 34 patients (31%), 14 (12.7%) in the surgeon group and 20 (18.3%) in the GP group ($p=NS$) experienced a false positive test (17). Fewer patients in the GP group than the surgeon group required visits to hospital for consultations and tests (250 vs. 528 visits). Overall, associated travel costs per patient over 24 months of follow-up were lower for the GP group ($p<0.001$).

The systematic review by Berian et al. included two studies comparing GP-led versus surgeon-led follow-up showed no difference in health-related quality of life, anxiety, or depression [7]. Both studies used the Hospital Anxiety and Depression Scale, the Short Form-12 Physical and Mental Health Component Scores, and the Patient Visit-Specific Questionnaire.

Adherence

In Augestad et al., the decision support tool used in the intervention to aid the GPs and patients was designed to increase adherence to guidelines [5]. The study found that the GPs had more healthcare contacts (regular, emergency, and telephone consultations [678 vs. 508])

and ordered more diagnostic tests (592 vs. 513) than the surgeons but there was no difference in mean costs per cycle (healthcare contacts; $p=0.76$, diagnostic tests; $p=0.39$).

RN versus Surgeon Follow-up

Recurrence of colorectal cancer

In Strand et al., 110 patients with rectal cancer were randomized to three years of follow-up care by an RN or a surgeon [10]. The RN and surgeon used the same follow-up regimen. There were no instances of local recurrences for either group. Distant metastases were detected in eight patients in the RN follow-up group and in seven patients in the surgeon group (8/54 [14.8%] vs. 7/56 [12.5%], $p=0.953$).

Patient Satisfaction

In Strand et al., patient satisfaction was high for patients randomized to both the RN and surgeon group on a visual analogue scale (9.5/10 vs. 9.4/10, $p=0.106$) [10]. During follow-up, there was no difference in the number of patients who felt anxious after the consultation between the RN and surgeon group (4/54 [7.4%] vs. 6/56 [10.7%], $p=0.546$). All but one patient felt safe and secure after the consultation and all patients except one in each group felt that the time provided for their consultation was sufficient and that they could ask all the questions they had planned.

Unannounced follow-ups

Strand et al. reported that the RN had longer consultation visits with patients than the surgeon (23 [17-33] vs. 15 [10-20] minutes, $p=0.001$) and were more likely to order extra blood samples (16 [29%] vs. 4 [7%] samples $p=0.003$), but the two groups ordered a similar number of additional radiological investigations (6 [11%] vs. 2 [3.6 %] tests, $p=NS$) [10].

GP versus RN versus Specialist

Patient Preference

The perceived role of surveillance delivery by three provider types (RN specialist, GP/family physician, and specialist [oncologist or surgeon]) was examined in 14 studies included in Berian et al. [7]. Five studies showed a preference for specialist-led care; four studies found equivalent preference for RN- and specialist-led follow-up; four studies showed equivalent preference for specialist- and GP-led care, and one study showed strong preference for RN-led follow-up over specialist-led follow-up (see Appendix 4 Table 4-6 for Perceptions of Follow-up Care Themes). Overall, patients reported high satisfaction with follow-up and believed that continued follow-up was important for the detection of recurrence. Although preferences varied for a given type of provider to conduct follow-up surveillance, satisfaction was generally high regardless of provider.

In Weildraaijer et al., patients from outpatient clinics from six hospitals completed a 10-point Likert-scale questionnaire (54% response rate) to assess their caregiver preference for reporting symptoms [11]. The patients gave similar scores with respect to appreciation of caregivers: 8/10 for GPs (interquartile range [IQR] 7-9), 8/10 for hospital RNs (IQR 7-9), and 8/10 medical specialists (IQR 8-8). However, an analysis of patient factors found that male sex, patients older than 65 years, and patients with chronic comorbid conditions were more likely to prefer to consult their GP or primary care nurse. Women, patients with stage III disease, and patients treated with adjuvant chemotherapy were more likely prefer to consult a secondary care provider, such as a hospital nurse or medical specialist. For many non-acute symptoms, patients responded significantly more often that they would contact their GP; however, they would contact both primary and secondary care providers simultaneously for fear of recurrent

disease (odds ratio [OR], 1.21; 95% CI, 0.90 to 1.62), rectal bleeding (OR, 0.97; 95% CI, 0.73 to 1.28), and weight loss (OR, 1.29; 95% CI, 0.98 to 1.71)].

Conclusions

Systematic review evidence showed no difference in overall survival between GP- or RN-led follow-up in the community and follow-up done in hospitals. In two RCTS that compared GP or RN-led care to a surgeon, there was no difference in the recurrence of colorectal cancer. However, these studies were small and had a small number of surgeons, GPs and nurses in each of the trials [5,10]. In those studies that examined quality of life and colorectal cancer follow-up, patients indicated that follow-up was important but did not express a clear preference for the type of provider (see Table 4-4 for comparisons). Patient satisfaction was high for all providers and preference was dependent on the patient’s symptoms and individual needs. The adherence to guidelines was found to be higher with a nonphysician clinician and with GPs without a significant increase in the number of tests ordered. Patients’ preferences for provider depend on the patient and their circumstances.

Table 4-4. Summary of Primary Literature Results between Follow-up Providers

Study	Outcome	GP or RN	Hospital	GP	Surgeon	RN	Surgeon
Overall survival							
Jeffrey [1]		No difference					
Recurrence							
Augestad [5]	Mean time until diagnosis			No difference			
	Cancer recurrence			No difference			
	Died by metastatic			No difference			
Strand [10]	Metastatic cancer					No difference	
QoL							
Augestad [5]	Overall QoL			No difference			
	Role functioning			GP better p=0.02			
	Emotional function			GP better p=0.01			
	Pain			GP better p=0.01			
	False positives			No difference			
	Hospital travels (+cost)			GP better p<0.001			
Patient satisfaction							
Strand [10]	Pt satisfaction					No difference	
	Anxiety					No difference	
	Sufficient time spent					No difference	
Unannounced follow-ups							
Strand [10]	Longer consultation time					RN longer p=0.001	
	Blood samples					RN more p=0.003	
	Radiological tests					No difference	
Adherence							
Augestad [5]	Healthcare contacts			GP had more			
	Diagnostic tests			GP had more			
Coeburgh vander Braak [9]	Scheduled surveillance	Hospital with dedicated NPC better p=0.001					
Pt. preference							
Weildraaijer [11]	Pt preference			No difference			

Berian Sys review, n= number of articles [7]	Pt preference	Preference for specialist led: n=5				
		Preference for RN led over specialist: n=1				
		Equivalent RN vs. specialist led: n=4				
				Equivalent specialist vs. GP led: n=4		

Abbreviations: GP=general practitioner; NPC=nonphysician clinician; Pt=patient; QoL=quality of life; RN=specialist nurse; Sys=systematic

Question 3. What signs and symptoms signal a potential recurrence of colorectal cancer and warrant further investigation?

The evidence for this question comes primarily from the original colorectal cancer follow-up PEBC guideline, the CCA colorectal cancer guideline, one RCT, and one retrospective study [4,8,12,13]. The PEBC guideline recommendations were based on consensus opinion of the Working Group members [4]. The Australian guideline practice points were based on selected evidence and consensus [8] (see Appendix 4 Table 4-1 for Guideline Recommendations Summary). The RCT that compared surgeon and GP follow-up also examined the symptoms found with recurrent disease [12]. The cohort study by Duineveld et al. calculated the percentage of symptoms reported during interval visits that led to the detection of a recurrence during a surveillance program [13] (see Appendix 4 Table 4-7 for Study Characteristics and Results) (see Table 4-5 for Summary of Results).

Certainty of Evidence

The guidelines were assessed using the AGREE II [17] and scored between 75% and 86% on the rigor of development domain indicating a high-quality guideline. The RCT was assessed using the RoB 2.0 [26] and had overall low risk of bias. The cohort study was assessed using the ROBBINS tool and found to have a low risk of bias [27] (see Appendix 5 for Quality Assessment scores).

Summary of Results

In the previous version of this guideline, common signs and symptoms associated with colorectal cancer recurrence were based on expert opinion and included: abdominal pain, particularly in the right upper quadrant or flank (liver area), dry cough, and vague constitutional symptoms (i.e., fatigue, nausea, and unexplained weight loss) [4]. Specific to rectal cancer are pelvic pain, sciatica, and difficulty with urination or defecation.

The CCA guideline reported that if the patient is symptomatic, the symptoms will depend on whether this is a local recurrence or a distant recurrence [8]. Local recurrences may include both anastomotic or luminal recurrences and symptoms may include rectal bleeding, anemia, altered bowel habits, or varying degrees of bowel obstruction. Patients with nodal or surgical bed recurrences may have palpable mass or pain from a mass affecting neighbouring structures. In patients with rectal cancer with pelvic recurrences, pain is a common symptom. In distant or systemic recurrence, the most common sites are hepatic followed by pulmonary metastases. Symptoms vary depending on the site of recurrence and may include symptoms such as abdominal pain from hepatomegaly, jaundice, pleuritic chest pain, and shortness of breath. Patients with extensive disease may also have anorexia, cachexia, and weight loss.

In the surgeon or general practitioner follow-up RCT of 110 patients, Augested et al. found 14 patients had cancer recurrence of which seven had symptoms [12]. Four patients had abdominal pain (two had disseminated recurrence, one had a liver recurrence, and one had a

local recurrence); the patient with blood in stool had a recurrence in the liver; the patient with weight loss had recurrence in the lung, and the patient with stoma bleeding had local and lymph node recurrence.

In the retrospective cohort study by Duinveld et al., 74/446 patients (16.6%) had a recurrence, which was detected in 31 patients during a non-scheduled visit and 26 (84%) of those patients were symptomatic: 15 (58%) had abdominal pain; 11 (42%) had altered defecation; six (23.1%) had weight loss; four (15%) had pain in back of pelvis; two (8%) had fatigue; two (8%) had dyspnea; two (8%) had loss of appetite; and three (12%) were listed as having other symptoms including urine retention, hematuria, or cough [13]. Fourteen patients (54%) had more than one symptom and 26 (35%) recurrences were in more than one location. There were 38 local recurrences; 14/38 (37%) were symptomatic and 24/38 (63%) were asymptomatic. There were 82 distant recurrences; 36/82 (44%) were symptomatic and 46/82 (56%) were asymptomatic.

Table 4-5. Summary of Signs and Symptoms

Sign or symptom	Guideline		Study		Type of Recurrence	
	PEBC [4]	CCA [8]	Augestad [12]	Duineveld [13]	Local	Distant
Abdominal pain	X		X	X	X	X
Dry cough	X			X		X
Rectal bleeding	X	X	X	X	X	
Changes in bowel habit	X	X		X	X	
Fatigue	X			X	X	X
Nausea	X				X	X
Unexplained weight loss	X		X	X	X	X
Anemia		X			X	X
Pain					X	
Stoma bleeding			X		X	
Palpable mass		X			X	X
Abdominal pain from hepatomegaly		X				X
Jaundice		X				X
Pleuritic chest pain or shortness of breath		X				X
Anorexia, cachexia, and weight loss		X				X
Dyspnea				X		X
Loss of appetite				X		X
Signs and/or symptoms specific to rectal cancer*						
Pelvic pain	X	X		X	X	
Sciatica	X				X	
Difficulty with urination or defecation	X			X	X	

*There are no signs or symptoms specific to colon cancer that would not also apply to rectal cancer.

Abbreviations: CCA=Cancer Council Australia; PEBC=Program in Evidence-based Care

Conclusions

The evidence for this question is based on consensus recommendations from guidelines and small studies. Limited studies show that approximately 35% to 50% of patients with

recurrence will present with symptoms. Since the signs and symptoms of both local and distant recurrence can be subtle, it is important to investigate new signs and symptoms for possible recurrence.

Question 4. What are the individual needs and long-term and late effects for colorectal cancer survivors?

- a) **What are the post-treatment informational and support needs for patients regarding local recurrence and common long-term and late effects of colorectal cancer?**
- b) **What are the common and/or substantial long-term and late treatment effects of colorectal cancer?**

a. What are the post-treatment informational and support needs for patients regarding local recurrence and common long-term and late effects of colorectal cancer?

The evidence for this question comes from two guidelines and one systematic review [8,14,18]. The European Society of Coloproctology (ESC) developed recommendations based on 24 high-quality European guidelines [18]. The CCA colorectal cancer guideline developed practice points based on selected evidence and consensus [8]. The systematic review included 54 descriptive and observational studies integrated in a narrative synthesis to summarize the health needs and concerns of people with colorectal cancer [14] (see Appendix 4 Table 4-1 for Guideline Recommendations Summary and Table 4-8 for Summary of Supportive Care Needs from Kotronoulas et al. [14]).

Certainty of Evidence

The guidelines were assessed using the AGREE II [17] and all scored between 78% and 86% on the rigor of development domain indicating a high-quality guideline. The systematic review was assessed using the ROBIS tool [25] and was deemed to have low risk of bias (see Appendix 5 for Quality Assessment scores).

Patient information needs

Five guidelines in the ESC summary stated that structured preventive care with health-promoting initiatives should be part of supportive care provided to colorectal cancer survivors [18]. The CCA colorectal cancer guideline indicated that the provision of adequate information to patients with colorectal cancer is related to increased psychological well-being and that good communication skills are vital [8]. The group identified six main principles of information provision relevant to the care of colorectal cancer patients:

- Treatment options should be explained clearly, with realistic information about potential effectiveness and adverse effects.
- Patients should be invited to guide the clinician to provide the level of detail they wish to receive and to enable their desired level of active involvement in decision making.
- Clinicians should review both the patient's understanding of the information, and their reactions to it, as a means of increasing integration and providing emotional support.
- Written materials should be provided, and clinicians should consider offering audio recordings of key consultations. The involvement of a specialist nurse or counsellor, provision of a follow-up letter, and participation in educational programs may also assist in recall of information.
- Information should be made available over time and, if desired, review appointments that allow time for further integration of information should be scheduled.
- Patients' carers and families should also be kept well informed.

A systematic review of the supportive care needs of people living with and beyond cancer of the colon and/or rectum identified 54 good- to moderate-quality studies that used qualitative and or quantitative methods to explore health needs and concerns [14]. One hundred thirty-six individual needs were identified and classified into eight conceptual domains that included: (i) physical and cognitive, (ii) psychosocial and emotional, (iii) family related, (iv) social, (v) interpersonal and intimacy, (vi) daily living, (vii) Information/education, and (viii) patient-physician communication (see summary and definitions in Appendix 4 Table 4-8).

A total of 136 individual needs were reported across the reviewed studies. Approximately one-half of these needs (n=70) concerned the information and education domain (n=36) and physician communication domain (n=34).

Table 4-6 lists the individual needs and their specific domains in order of priority based on the frequency of reporting within and across the reviewed studies. It is important to note that nine of the top 10 priority needs pertained to information and education and physician communication while only one concerned the physical and cognitive domain. Furthermore, these results indicated that it is not just the information that is being given but the way in which the healthcare professional provides this information (i.e., coordinated, honest, unhurried, and empathetic). It is also important to note that of all the physical symptoms, fatigue and pain seem to be of highest priority to the patients.

Table 4-6. Top 20 most prominent individual needs for people with colorectal cancer

Ranking	Domain	Need for....
1	Psychosocial/emotional	Emotional support and when trying to deal with fear of the cancer returning or spreading
2	Information/education	More information about diet/nutrition in the form of a pamphlet or by a hospital dietician
3	Information/education	More information about the long-term self-management of symptoms and complications at home, e.g., persistent fatigue and bowel symptoms
4	Health system/patient-clinician communication	Information that is clear/straight-forward, up-to-date, honest, unhurried, and given in a sensitive way especially if no curative treatment is available
5	Health system/patient-clinician communication	Written information/publications, especially about treatment options/processes
6	Information/education	More information about cancer staging and prognosis
7	Physical/cognitive	Help with fatigue/lack of energy postoperatively
8	Information/education	More information about the risk of and/or symptoms of disease recurrence
9	Information/ education	More information about the short-term and long-term effects of treatment on quality of life
10	Health system/patient-clinician communication	On-going communication/contact with and support from a trustworthy clinician
11	Physical/cognitive	Help with pain (abdominal) postoperatively associated with adhesions/infected wounds/non-healing wounds
12	Information/education	More information about the exact diagnosis and what it means
13	Information/education	More information about test results and procedures
14	Health system/patient-clinician communication	Healthcare professional who treats the patient like a person, not just another case, listens to what the patient has to say, is open and sincere, and

		acknowledges and shows sensitivity to patients' feelings/emotions and/or to family/friends' feelings
15	Family-related	Help with the worries/concerns of one's family, especially children
16	Health system/patient-clinician communication	Better coordination/communication among healthcare professional's primary and secondary care
17	Interpersonal/intimacy	Help to adjust to changes in/problems with sexuality, especially if partnered
18	Information/education	More information about what to expect following discharge or following chemotherapy, especially people with no stoma
19	Psychosocial/emotional	Support when dealing with uncertainty about the future
20	Information/education	More information about specific treatment modalities (mainly chemotherapy) and side effects while on treatment

Conclusions

The highest priority supportive care needs for colorectal cancer survivors are for information and education and physician communication particularly around the risk of recurrence. While the information was important so was the way in which this information was provided to patients that included a coordinated, honest, unhurried, and empathetic approach. While physical symptoms were also important, they were not rated as highly as information, education, and physician communication.

b. What are the common and/or substantial long-term and late treatment effects of colorectal cancer?

Four guidelines and one systematic review addressed long-term and late effects of colorectal cancer [4,6,8,14,18]. The previous PEBC colorectal cancer follow-up guideline drafted a list of common and/or substantial long-term and late effects based on a combination of the evidence identified and expert opinion and refined the draft through an informal consensus process [4]. This list was updated and refined via the OH (CCO) Survivorship Care program in 2019. The CCA colorectal cancer guideline developed practice points based on selected evidence and consensus [8]. The ESC included 12 guidelines that addressed issues of supportive care and handling of late effects [18]. The NCCN used a combination of selected evidence and consensus to develop principles of survivorship for colorectal cancer long-term follow-up care [6] (see Appendix 4 Table 4-1 for Guideline Recommendations Summary).

Certainty of Evidence

The guidelines were assessed using the AGREE II [17] and all scored between 65% and 86% on the rigor of development domain indicating a high-quality guideline. The systematic review was assessed using the ROBIS tool [25] and was deemed to have low risk of bias (see Appendix 5 for Quality Assessment scores).

Summary of Evidence

The PEBC, ESC, NCCN, and CCA colorectal cancer guidelines and the systematic review by Kotronoulas et al. identified 39 physical and psychosocial long-term and late effects of colorectal cancer [4,6,8,14,18] (see Table 4-7 for Summary of long-term and late effects).

Table 4-7. Common and/or substantial long-term and late effects summary listed from guidelines and systematic review

Guidelines and Systematic Review		PEBC 2019 [4]	ESC 2019 [18]	NCCN 2019 [6]	CCA 2018 [8]	Kotronoulas 2017 [14]
Effects						
Physical						
Surgery-related	Frequent and/or urgent bowel movements	X	X	X	X	X
	Loose bowels	X	X		X	X
	Gas and/or bloating	X				X
	Incisional hernia	X				
	Increased risk of bowel obstruction	X				
Medication-related	Peripheral neuropathy (associated with treatment using oxaliplatin)	X	X	X		
	Chemotherapy-related cognitive side effects	X	X	X		
Radiation-related	Localized skin changes (i.e., colour, texture, and loss of hair)	X				
	Rectal ulceration and/or bleeding (radiation colitis)	X				
	Anal dysfunction (incontinence)	X				
	Bowel obstruction (from unintended small bowel scarring)	X				
	Infertility	X				
	Sexuality dysfunction (e.g., vaginal dryness, erectile dysfunction, retrograde ejaculation)	X	X		X	X
	Second primary cancers in the radiation field (typically about seven years after radiotherapy)	X				
	Bone fracture (e.g., sacral region)	X				
Other	For patients who received ostomy, stoma care and life-style adjustments will be required	X	X	X		X
	Urinary dysfunction		X	X		
	Pain		X			X
	Fatigue		X	X		X
	Lymphedema		X			
	Anastomotic stenosis		X			
	Adhesions		X			X
	Insomnia		X	X		X
	Odour				X	
Dietary Issues					X	
Psychosocial						
	Psychological distress	X	X	X		
	Depression	X				
	Anxiety	X				X
	Worry	X				X
	Fear of recurrence	X	X			X
	Cognitive side-effects	X				

	Changes in sexual function/fertility	X				X
	Body and/or self-image	X	X		X	X
	Relationships	X			X	X
	Other social role difficulties	X			X	X
	Return to work concerns	X				X
	Financial challenges	X				X
	Support for family					X
	Stoma issues					X

Abbreviations: CCA=Cancer Council Australia; ESC=European Society of Coloproctology; NCCN=National Comprehensive Cancer Network; PEBC=Program in Evidence-based Care

Conclusions

Follow-up care is complex and there are many physical and psychosocial long-term and late effects of colorectal cancer that both the physician and patient need to be aware of to mitigate discomfort, effectively manage symptoms, and improve quality of life.

Ongoing, Unpublished, or Incomplete Studies

Protocol ID	Title and details of trial
NCT00995202	<p>PRODIGE 13 Follow-Up Care with or Without CEA Assessments in Patients Who Have Undergone Surgery for Stage II or Stage III Colorectal Cancer.</p> <p>This is a multinational/multicentre study. Patients are randomized to 1 of 2 follow-up arms.</p> <p>Standard follow-up: Patients undergo clinical assessments every 3 months until year 3 and every 6 months until year 5. They are then assessed at least yearly thereafter. Patients undergo abdominal ultrasound every 3 months until year 3 and then every 6 months until year 5; chest x-ray every 6 months until year 3 and then annually until year 5; and colonoscopy at 3 years after surgery then every 3 to 6 years thereafter.</p> <p>Reinforced follow-up: Patients undergo clinical assessments every 3 months until year 3 and every 6 months until year 5. They are then assessed at least yearly thereafter. Patients undergo alternate assessments every 3 months comprising thoraco-abdomino-pelvic CT scan or abdominal ultrasound until year 3 and then every 6 months until year 5. They also undergo colonoscopy at 3 years after surgery then every 3 to 6 years thereafter. Actual Enrolment: 1997 participants. Status: Active, not recruiting. Last modified April 2020. Estimated completion date: December 2020</p>
NCT03853278	<p>Developing and Testing a Self-management Support Intervention in Colorectal Cancer Survivors: A Mixed-methods Study</p> <p>The intervention includes a colorectal cancer self-management information booklet, a DVD, two individual skill training and 12 follow-up telephone calls. These are to establish participants' self-management skills and healthy lifestyle, including physical activity and healthy eating fruits and vegetables. The control group will receive health education leaflets Last modified: September 2020. Estimated completion date: October 31, 2020</p>
NCT03622437	<p>Individual Follow-up After Rectal Cancer - Focus on the Needs of the Patient</p> <p>In a patient-led follow-up program, the surveillance for recurrent disease is combined with detection and treatment of late adverse effects and supportive survivorship care. The follow-up involves a high degree of patient-involvement, aiming at meeting the individual patient's needs. The intervention is tested in</p>

	a multicenter randomized trial, comparing the patient-led follow-up to standard routine follow-up, involving prescheduled outpatient visits. Last modified: August 2018. Estimated completion date: August 31, 2021
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DISCUSSION

There are several changes in recommendations in this current guideline compared to the previously 2016 guideline. This is because the previous guideline was based on other high quality guidelines from other jurisdictions from 2004 to 2010 (i.e., ASCO, NCCN, CCA) and this updated guideline is based on an updated review of the primary evidence.

The main changes in this current guideline are that the recommendations apply to stage I-III colon cancer survivors and do not apply to rectal cancer (all stages) or stage IV colon cancer. This guideline also recommends two CT CAP scans at 12 and 36 months or one CT CAP scan at 18 months rather than three CT scans and the use of CEA is optional.

The results of the Cochrane review that included 19 RCTs and over 13,000 patients in which 90% were followed for a minimum of 48 months showed that there was no difference in overall survival between patients who received more than two CT scans versus two or fewer CT scans or patients who had CEA testing versus those who did not receive CEA testing. These results are supported by the COLOFOL study that showed patients having CEA and CT CAP at 12 and 36 had the same five year overall survival as patients who had CEA and CT CAP at 12 and 36 months. The FACS study showed that minimum follow-up with one CT CAP at 18 months led to the same detection of recurrence, eligible for surgery with curative intent at three years compared to CEA and CT CAP every six months for two years, then annually for three years. The FACS study also showed that CEA and CT CAP combined had no survival advantage compared to CT CAP alone. Furthermore, both the COLOFOL and FACS study also showed that most recurrences occurred within three years of curative intent treatment.

While these results suggest that early detection does not lead to improved survival, it is important to note that surgery for recurrence may be effective in some patients with five-year survival ranging from 25-37% [32]. A possible explanation for these findings is tumour biology. For example, finding an early or rapidly progressing recurrence with a high-intensity surveillance protocol in a patient with poor tumour biology may lead to earlier surgery, but this is unlikely to have any effect on overall survival since there is a high risk of developing further metastatic disease following surgery. Furthermore, complications from unnecessary surgery may delay subsequent treatment that may further impact survival. On the other hand, a patient with a recurrence that remains stable for several months (i.e., not detected early) is likely to have a lower risk of developing further metastasis and is more likely to be cured or have improved overall survival with surgery. Conversely, while the evidence for early detection and overall survival was quite robust, the number of patients undergoing surgery in the RCTs for curative intent was relatively small and therefore underpowered to detect small but significant differences in overall survival and disease-specific survival.

During the internal and external review, it became apparent to the Working Group that there seemed to be significant variation in the follow-up of colorectal cancer patients across the province. Therefore, an assessment of current practice patterns across the province will be necessary to understand the extent and possible reasons for this variation. Furthermore, sustained knowledge translation will be critical to reduce variation. Key components of this knowledge translation will need to include that early detection of colorectal recurrence does not lead to improved survival and that “more” investigations may possibly expose patients to more harm and lead to overutilization of health resources.

The Working Group members believe that it is critical that shared models care incorporate strategies to integrate and coordinate care between the patient and their family

and all their providers for the model to be effective. In particular, patients need to know which provider to contact for any particular issues and how to contact this provider. Prior to implementing shared care models on a large scale, it will be important to consider innovative strategies such as virtual care that may help to integrate and coordinate care. More recently, Qaderi et al. [33] conducted a qualitative review of healthcare provider and patient preparedness for alternative colorectal cancer follow-up and found that remote follow-up leads to enhanced involvement of patients in their own care and recommended that more flexible and dynamic methods of follow-up using technology should be used and focus on enhanced communication and role definitions among clinicians.

It is also important to acknowledge that there is likely not a “one size fits all” shared care model that can be used uniformly across the province and therefore this model of care will need to be specifically tailored for the organization, region, and Ontario Health Team.

Perhaps one of the most interesting findings of this review was that the highest priority informational and supportive needs of patients during follow-up was predominantly about fear of recurrence. Therefore, it is important for treating specialists to specifically discuss the risk of recurrence with their patients as much as symptom management at their follow-up visits. Even more importantly is that patients highly value the way in which information is presented to them by their healthcare provider. Patients consistently emphasize the importance of coordinated, honest, unhurried, and empathetic delivery of information by their healthcare providers. Based on these findings the Working Group members have recommended providers consider, and institution and organizations encourage, participation in Continuing Professional Development that focuses on advanced communication skills training.

Limitations

While the results of this Cochrane review were quite robust, one of the limitations of this study was that regimens were categorized as higher- versus lower-intensity regimens and therefore a higher-intensity regimen in one study may have been similar to the lower-intensity regimen in another study. Therefore, it was not possible to determine the optimal follow-up regimen based on these Cochrane results.

However, both the COLOFOL and FACS study did directly compare specific follow-up regimens. The COLOFOL study showed that CT CAP at 12 and 36 months postoperatively has similar overall survival to higher-intensity follow-up with CT CAP at six, 12, 18, 24, 30 and 36 weeks postoperatively [2]. And similarly, the FACS trial showed that minimum follow-up with CT CAP at 12-18 months had similar overall survival to higher-intensity follow-up regimens including CEA only, CT only, and CEA and CT over a five-year follow-up period [3].

Furthermore, while there did not seem to be any differences in quality of life or harm between the regimens, these data were extremely limited. Similarly, the number of rectal cancer and stage IV patients included in these studies was extremely small and therefore these results cannot be generalized to these groups at this time.

While a shared care model is preferred, there was little information on which shared care model is most ideal or how this should be implemented. There were very few studies that incorporated virtual care or remote follow-up as part of this model.

While patient informational and supportive needs were highly consistent across studies, the quality of evidence came primarily from cross sectional surveys and therefore is subject to recall and response rate bias. There was also limited information on racial disparities in the quality of follow care.

Conclusions

There is an increasing body of evidence that early detection provided by intensifying follow-up regimens for colorectal cancer does not lead to improved overall or disease-specific

survival. Therefore, use of lesser-intensity follow-up regimens is reasonable. Future studies to assess the effect of intensifying follow-up for rectal cancer and stage IV patients as well as quality of life, harm, cost, resource utilization, patient preference for follow-up care, and racial disparities are warranted.

Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer

Section 5: Internal and External Review

INTERNAL REVIEW

The guideline was evaluated by the GDG Expert Panel and the PEBC Report Approval Panel (RAP) (Appendix 1). The results of these evaluations and the Working Group's responses are described below.

Expert Panel Review and Approval

Of the 15 members of the GDG Expert Panel, 13 members voted and two abstained, for a total of 87% response in December 2020. Of those who voted, 12 approved the document (92%). The main comments from the Expert Panel and the Working Group's responses are summarized in Table 5-1.

Table 5-1. Summary of the Working Group's responses to comments from the Expert Panel.

Comments	Responses
1. Would like a clearer minimum regimen and finding it difficult to have such a minimal follow-up.	We have made a clear minimum regimen and added a CT CAP at 36 months to the minimal follow-up regimen.
2. Would like clarification of other regimens and clarification of their use.	We have added a Table in the recommendations and clearer guidance on reasonings and possible use of other regimens in the implementation section.
3. Would like stage IV patients removed or to be clarified regarding their follow-up.	We have changed the recommendation to: There was insufficient evidence for or against higher-intensity follow-up patients with rectal cancer and stage IV colon cancer.
4. Would like the first qualifying statement removed since it is not relevant.	It has been removed.
5. In Recommendation 2, I would like qualifying statement to reflect the weak evidence for shared care model but the consensus of the Working Group and panel.	We have added a qualifying statement stating that.
6. Need to update the list for radiation-related long-term and late effects.	We have made the list of late and long-term effects into one section for all physical effects since many effects may occur for any of the treatment modalities and had a radiation oncologist review the list for accuracy.

RAP Review and Approval

Three RAP members reviewed this document in August 2020. The RAP approved the document in September 2020. The main comments from the RAP and the Working Group's responses are summarized in Table 5-2.

Table 5-2. Summary of the Working Group’s responses to comments from RAP.

Comments	Responses
1. Recommendation 1 - I suggest you rearrange the statement concerning salvage surgery.	We moved the statement regarding salvage surgery to the qualifying statements section.
2. In Recommendation 4, you mention the long-term affects but maybe they should be listed.	We added a list of long-term and late treatment affects in the Supplemental Information in Section 1 and 2.
3. What regimens in Table 1 are considered high or low intensity?	We added labels to better describe the specifics of the regimens.

Patient and Caregiver-Specific Consultation Group

Four patients/survivors/caregivers participated as Consultation Group members for the Working Group. They reviewed the draft recommendations and provided feedback on its comprehensibility, appropriateness, and feasibility to the Working Group’s Health Research Methodologist. The main comments from the Consultation Group are summarized in Table 5-3.

Table 5-3. Summary of the Working Group’s responses to comments from the Consultation Group.

Comments	Responses
1. Preferred the term ‘advantages and disadvantages’ in the Appendix 1, to the term ‘risk and benefits’ in Recommendation 1.	We changed the wording in Recommendation 1 from ‘discussing risk and benefits’ to discussing advantages and disadvantages’
2. Like the order of the recommendations with the preferred provider being the second recommendation.	We moved question 4 back to question 2.
3. Would like to see a list of signs and symptoms in the Appendix	We have added a list in the Appendix.
4. Like the focus on the patient and especially communication. Would like to see families added as well.	Where appropriate, family was added with the patient.
5. Shouldn’t all regions be the same?	The Working Group recognizes that this would be best and changed the wording to accept the fact that currently, the implementation of a shared care model will need to be region specific based on the available resources and provider models in each individual region.

EXTERNAL REVIEW

External Review by Ontario Clinicians and Other Experts

Targeted Peer Review

Seven targeted peer reviewers from Ontario, British Columbia and New York who are considered to be clinical and/or methodological experts on the topic were identified by the

Working Group. Five agreed to be the reviewers (Appendix 1). Five responses were received. Results of the feedback survey are summarized in Table 5-4. The main comments from targeted peer reviewers and the Working Group’s responses are summarized in Table 5-5.

Table 5-4. Responses to nine items on the targeted peer reviewer questionnaire.

Question	Reviewer Ratings (N=5)				
	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the guideline development methods.			1	1	3
2. Rate the guideline presentation.		1		3	1
3. Rate the guideline recommendations.		1	1	2	1
4. Rate the completeness of reporting.				2	3
5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?		1	2	2	
6. Rate the overall quality of the guideline report.		1		3	1
	Strongly Disagree (1)	(2)	Neutral (3)	(4)	Strongly Agree (5)
7. I would make use of this guideline in my professional decisions.		1	1	3	
8. I would recommend this guideline for use in practice.		1		3	1
9. What are the barriers or enablers to the implementation of this guideline report?	<p>Enablers:</p> <ul style="list-style-type: none"> • good, updated evidence to support recommendations <p>Barriers:</p> <ul style="list-style-type: none"> • changing provider behaviour • patient fears that doing less will adversely affect them • too complex a document • the wide variability among the provided options for Recommendation 1 will be a barrier to implementation. • the move to less intense approaches may be met with scrutiny and concerns if there are medico-legal implications • implementing and measuring the impact of Recommendations 2, 3, and 4 may be difficult. • available healthcare resources to successfully implement these recommendations may be currently lacking 				

Table 5-5. Summary of the Working Group’s responses to comments from targeted peer reviewers.

Comments	Responses
<p>1. The guideline recommendations allow many different options for surveillance. Therefore, it does not provide clear guidance for the surveillance of an individual patient, apart from minimal standards. A preferred strategy among the available surveillance strategies would be helpful. It does not provide clear guidance for the surveillance of an individual patient, apart from minimal standards.</p>	<p>We have added a preamble that explains the reasons behind the regimens and the use of the supplement that provides pros and cons of each regimen.</p>
<p>2. A clear distinct recommendation for each of the follow-up modalities (CEA, colonoscopy, CT CAP imaging testing) as separate recommendations may make it clearer and easier to find both in the text and in the table</p>	<p>The Working Group believes that the regimens are best grouped together since the amount of individual modalities changes with each one.</p>
<p>3. As this document is an update from a prior version, a section that demonstrate key similarities or substantial differences from the prior version would be helpful. This is not essential but would be helpful particular to help implementation of any changes needed.</p>	<p>A section was added at the end of the recommendation section to provide information regarding the differences between the older and newer version.</p>
<p>4. I think they could have stratified the patient population into different streams for different risk groups. E.g., for an elderly population vs. younger.</p>	<p>There was not evidence to provide stratifications and the Working Group members believe that the practitioner and the patient can decide together what regimen to use based on the patient’s needs.</p>
<p>5. I think it should be made clearer what is recommended for the stage IV and rectal cancers even if it is the same (as a separate recommendation item), what to do beyond 5 years (as a separate recommendation item)</p>	<p>The Working Group had added a line in the recommendations section for each issue.</p>
<p>6. One thing that would have been helpful is some a grading or discussion of considering different intensities of surveillance based on stage of disease, and probability of disease progression.</p>	<p>The Working Group had added a line in the recommendations section for each issue.</p>
<p>7. Are there data to support this assertion that more intense surveillance is less patient centred? This assumes that patient-centred care means patients value less interaction with the healthcare system. I am not sure this is always the way that patients view it? But I do not have a very sophisticated understanding of what patient centred care means in this context. Perhaps a definition of ‘patient centred’ or ‘values’ should be added somewhere in the document</p>	<p>The Working Group has removed this issue in the supplement.</p>
<p>8. Consider discussing how questions or concerns regarding possible medico-legal implications are to be addressed within shared care interprofessional collaborations that implement the guidelines to lesser-intensity follow-up regimens.</p>	<p>This issue is important but out of scope for the guideline.</p>

9. Utility of CEA in patients who have high CEA preoperatively vs. normal.	The Working Group added a qualifying statement to Recommendation 1 to address this issue.
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Professional Consultation

Feedback was obtained through a brief online survey of healthcare professionals and other stakeholders who are the intended users of the guideline. All colorectal cancer surgeons, primary care physicians, radiologists and other imaging professionals, medical oncologists, nurses/nurse practitioners in the PEBC database were contacted by email to inform them of the survey (n=182). Thirteen responses (7.1%) responses were received. Ten stated that they did not have interest in this area or were unavailable to review this guideline at the time. The results of the feedback survey from 13 people are summarized in Table 5-6. The main comments from the consultation and the Working Group’s responses are summarized in Table 5-7.

Table 5-6. Responses to four items on the professional consultation survey.

	N=13 (7.1%)				
General Questions: Overall Guideline Assessment	Lowest Quality (1)	(2)	(3)	(4)	Highest Quality (5)
1. Rate the overall quality of the guideline report.	0	1	0	6	6
	Strongly Disagree (1)	(2)	(3)	(4)	Strongly Agree (5)
2. I would make use of this guideline in my professional decisions.	0	1	4	3	5
3. I would recommend this guideline for use in practice.	0	1	2	4	6
4. What are the barriers or enablers to the implementation of this guideline report?	Enablers: <ul style="list-style-type: none"> • Ability to have flexibility to be patient centred • Access to communication tools • Table of simplified recommendations Barriers: <ul style="list-style-type: none"> • Ensuring wide-spread communication/use not just for leaders but for point-of-care staff • Education of physicians and teams • Acceptance of a minimal schedule • Shared care practices vary by region and access to providers 				

Table 5-7. Summary of the Working Group’s responses to comments from professional consultants.

Comments	Responses
1. Need more explanation for Recommendation 1.	We have added a preamble to better clarify the use of Recommendation 1 and Table 1.1
2. Is there an age or comorbidity cut-off after which we should no longer offer surveillance? I did not see this in the document but maybe a qualifying statement that in the opinion of the treating physician, the patient would be interested in and	The Working Group found that insufficient evidence for or against higher versus lower intensity follow-up regimens for patients over the age of 75 years and added that information into the Qualifying Statements.

healthy enough to receive treatment, in particular surgery, for an asymptomatic recurrence.	
3. This report does not give information about symptoms of colorectal cancer recurrence. I found the summary on page 39 very helpful and wonder if something like that could be in the summary recommendations	The table with signs and symptoms has been referred to in the recommendations.
4. Recommendation 4 is not clearly worded; it is much clearer in the full report, talking about the importance of psychosocial support.	The Working Group modified Recommendation 4 to make it clearer.
5. Interesting to know that there is no difference in overall survival and patient satisfaction regarding follow-up method. This, hopefully, may help to ease up congestion in cancer centres if these patients can be followed up by their GP/nurse practitioner in community (additional training may be beneficial for community-based team).	No action required.
6. You might also consider making a statement about the emergence of circulating tumour DNA since this will be available to patients and practitioners will want some idea of what if any recommendations are made by CCO.	Out of scope.
7. This guideline report is the document BEHIND a one-page document required for primary care. Therefore, a tool developed by the Centre for Effective Practice would be ideal so that knowledge translation will take place. Otherwise, this large document will be at risk of being filed and not implemented.	The Working Group will add these ideas to the Implementation Considerations section.
8. I would also strongly advise that the one-page document is linked to the Electronic Medical Record with reminders and actionable items to facilitate the primary care provider to be prompted to follow the guideline.	
9. Education pieces done in concert with the Ontario College of Family Physicians and Centre for Effective Practice will be instrumental for knowledge translation.	
10. Lastly, the use of Facebook, Twitter, TikTok, and Instagram are key pieces both to educate the public on the standards to expect and to educate primary care.	

CONCLUSION

The final guideline recommendations contained in Section 2 and summarized in Section 1 reflect the integration of feedback obtained through the external review processes with the document as drafted by the GDG Working Group and approved by the GDG Expert Panel and the PEBC RAP.

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Appendix 1: Affiliations and Conflict of Interest Declarations

In accordance with the [PEBC Conflict of Interest \(COI\) Policy](#), the guideline authors, the colorectal cancer Survivorship Guideline Group/Expert Panel members, and internal and external reviewers were asked to disclose potential conflicts of interest.

Table 1. Members of the colorectal cancer Survivorship Guideline Working Group

Name	Affiliation	Declarations of Interest
Erin Kennedy Surgeon	Mount Sinai Hospital Toronto, ON	None
Tim Asmis Medical Oncologist	Ottawa Hospital Cancer Centre Ottawa, ON	None
Anand Govindarajan Surgeon	Mount Sinai Hospital Toronto, ON	None
Jacqueline Galica Registered Nurse	Queen's University Kingston, ON	None
Charles Cho Radiation Oncologist	Southlake Regional Cancer Centre Newmarket, ON	None
Alexandra Ginty Family Physician	Dorval Medical FHT Oakville, ON	None
Caroline Zwaal Health Research Methodologist	Program in Evidence-based Care, McMaster University Hamilton, ON	None

Table 2. Members of the colorectal cancer Survivorship Guideline Expert Panel

Name	Affiliation	Declarations of interest
Hugh Langley Family Physician	Cancer Centre of South-eastern Ontario Kingston, ON	None
Craig Earle Medical Oncologist	Canadian Partnership Against Cancer Toronto, ON	None
Kate Edgar Nurse Practitioner	Cobourg Health Centre Cobourg, ON	None
Gail Larocque Nurse Practitioner	Ottawa Hospital Cancer Centre Ottawa, ON	None
Rachel Halligan Family Physician	Grand River Regional Cancer Centre Kitchener, ON	None
Mala Bahl Medical Oncologist	Trillium Health Partners Mississauga, ON	None
Scott Berry Medical Oncologist	Kingston Health Sciences Centre Kingston, ON	None
Jim Biagi Medical Oncologist	Kingston Health Sciences Centre Kingston, ON	None

Sami Chadi Surgeon	Toronto Western Hospital University Health Network Toronto, ON	>\$500 Stryker Endoscopy for consulting
Rachel Goodwin Medical Oncologist	The Ottawa Hospital Ottawa, ON	Was a consultant at and on Advisory board for Ipsen, Eiasi, Novartis, Celgene, Novartis, Pfizer Grants: Multiple, including investigator trials, plus Pharma driven trials.
Robert Gryfe Surgeon	Mount Sinai Hospital Toronto, ON	None
Khalid Hirmiz Radiation Oncologist	Windsor Regional Hospital Windsor, ON	None
Maria Kalyvas Medical Oncologist	Kingston Health Sciences Centre Kingston, ON	None
Paul Karanicolas Surgeon	Odette Cancer Centre Sunnybrook Hospital Toronto, ON	None
Aamer Mahmud Radiation Oncologist	Kingston Health Sciences Centre Kingston, ON	Received a grant from CCSEO on knowledge transfer and published abstracts relevant to the topic of the guideline

Table 3. Members of the Report Approval Panel and Declarations of Interest

Name	Affiliation	Declarations of interest
Donna Maziak	Ottawa General Hospital Ottawa, ON	None
Eric Winqvist	London Health Sciences Centre London, ON	None
Jonathon Sussman	Juravinski Cancer Centre Hamilton, ON	None

Table 4. Members of the Targeted Peer Review and Conflicts of Interest

Name	Affiliation	Declarations of interest
Lisa Del Giudice	Sunnybrook Health Sciences Centre Toronto, ON	Salary as a Regional Primary Care Cancer Screening Lead, Cancer Care Ontario, Ontario Health
Stan Feinberg	North York General Hospital North York, ON	I routinely do colonoscopy on post operative colorectal cancer. This could potentially impact my income.
Sharlene Gill	BC Cancer Agency Vancouver, BC	None

Mary Smith	Queens University Kingston, ON	None
Alice Wei	Memorial Sloan Kettering Monmouth New Jersey, USA	Histosonics- consultant \$1200 USD AstraZeneca - consultant \$3500 USD Intuitive Surgical - travel Bayer - travel

Table 5: Members of the Patient Consultation Group and Conflicts of Interest

Name	Declaration of Interest
Bob Tuck	None
Lise Craig	None
Lauri Petz	None
Marissa Myers	None

Appendix 2: Literature Search Strategy

MEDLINE

1. exp colorectal neoplasms/
2. colorectal cancer:.mp.
3. rectal cancer:.mp.
4. CRC:.mp.
5. or/1-4
6. surveillance:.mp.
7. follow-up:.mp.
8. survivor:.mp.
9. prevent:.mp.
10. (late adj2 effect:).mp.
11. or/6-10
12. 5 and 11
13. recurrence/
14. neoplasm recurrence, local/
15. recurren:.mp.
16. or/13-15
17. 12 and 16
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19. limit 18 to yr="2011-current"
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21. meta-analy\$.tw.
22. metaanal\$.tw.
23. (systematic adj (review\$1 or overview\$1)).tw.
24. meta-analysis as topic/
25. or/20-24
26. cochrane.ab.
27. (cinahl or cinhal).ab.
28. embase.ab.
29. scientific citation index.ab.
30. bids.ab.
31. cancerlit.ab.
32. or/26-31
33. reference list\$.ab.
34. bibliograph\$.ab.
35. hand-search\$.ab.
36. relevant journals.ab.
37. manual search\$.ab.
38. or/33-37
39. selection criteria.ab.
40. data extraction.ab.
41. 39 or 40
42. review.pt.
43. review literature as topic/
44. 42 or 43
45. 41 and 44
46. comment.pt.

47. letter.pt.
48. editorial.pt.
49. or/46-48
50. 25 or 32 or 38 or 45
51. 50 not 49
52. practice guideline/
53. practice guideline\$.mp.
54. 52 or 53
55. 51 or 54
56. 19 and 55
57. 19 not 49
58. (comment or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case reports or historical article).pt.
59. 19 not 58
60. 59 and 55
61. 59 not 55
62. case series.mp.
63. 61 not 62
64. 59 not 62

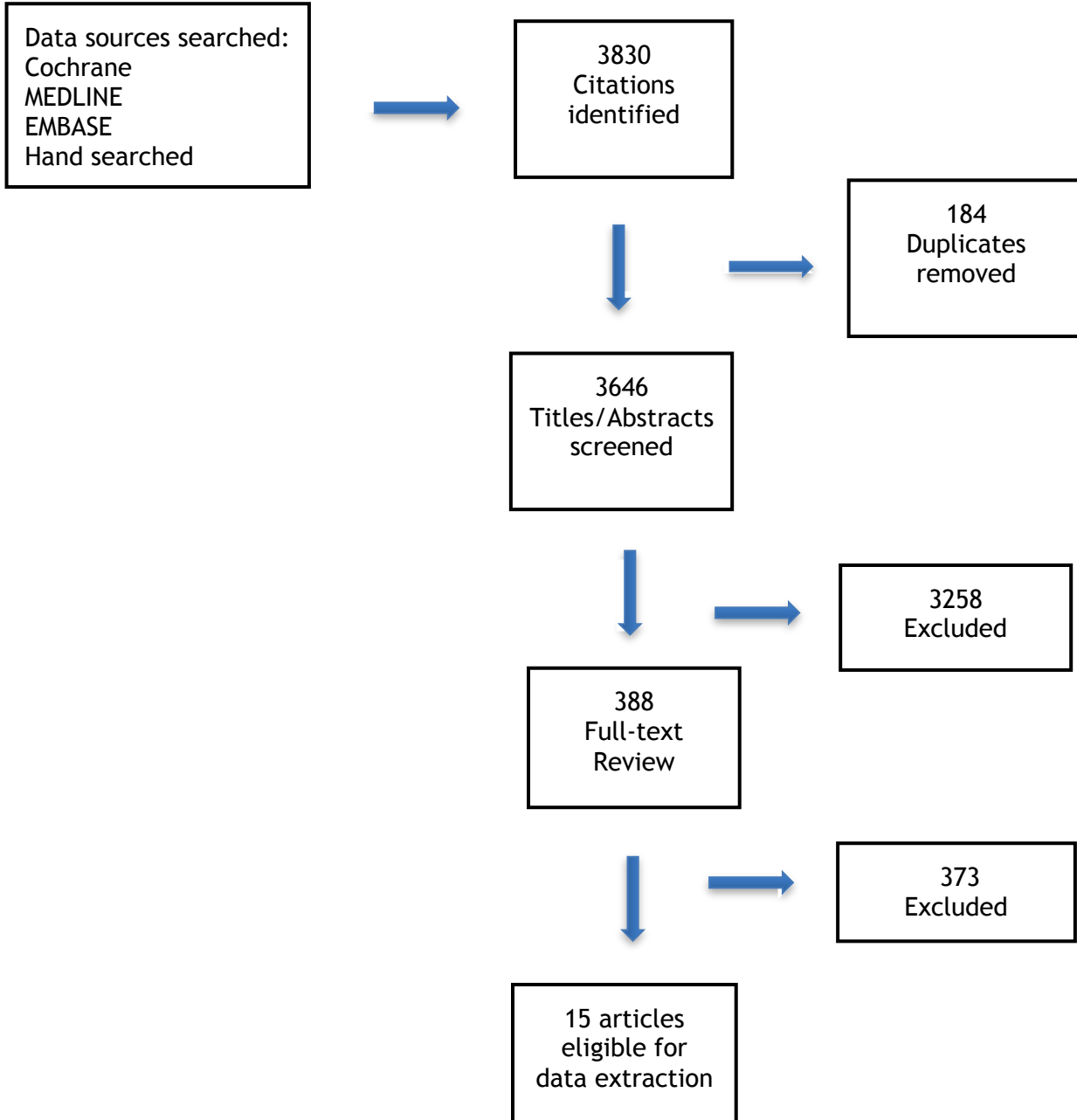
EMBASE

1. exp colorectal cancer/ or exp colorectal carcinoma/ or exp colorectal tumor/ or exp colorectal tumour/
2. colorectal cancer:.mp.
3. rectal cancer:.mp.
4. CRC:.mp.
5. or/1-4
6. surveillance:.mp.
7. exp follow-up/
8. after care/
9. long term care/
10. follow-up:.mp.
11. survivor:.mp.
12. prevent:.mp.
13. (late adj2 effect:).mp.
14. or/6-13
15. 5 and 14
16. exp recurrent cancer/ or exp recurrent disease/
17. recurren:.mp.
18. 16 or 17
19. 15 and 18
20. limit 19 to (human and english language)
21. limit 20 to yr="2011-current"
22. exp meta-analysis/
23. ((meta adj analy\$) or metaanaly\$).tw.
24. (systematic adj (review\$1 or overview\$1)).tw.
25. or/22-24
26. cancerlit.ab.
27. cochrane.ab.

28. embase.ab.
29. (cinahl or cinhal).ab.
30. scientific citation index.ab.
31. bids.ab.
32. or/26-31
33. reference list\$.ab.
34. bibliograph\$.ab.
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36. manual search\$.ab.
37. relevant journals.ab.
38. or/33-37
39. data extraction.ab.
40. selection criteria.ab.
41. 39 or 40
42. review.pt.
43. 41 and 42
44. letter.pt.
45. editorial.pt.
46. 44 or 45
47. 25 or 32 or 38 or 43
48. 47 not 46
49. exp practice guideline/
50. practice guideline\$.tw.
51. 49 or 50
52. 48 or 51
53. 21 and 52

Appendix 3: PRISMA Flow Diagram

Figure 3.1 Primary Literature Search Results Plus Updated Search Results



Appendix 4: Evidence Tables

Table 4-1 Guideline Recommendation Summary for colorectal cancer follow-up

Guideline	Question 1. Regimen
Ontario Health (CCO; Cancer Care Ontario) Colorectal Follow-up Guideline [4]	<p>Medical history, physical examination, and CEA every 6 months for 5 years. Abdominal / Pelvic / Chest Computed Tomography (CT) every 12 months for 3 years. Colonoscopy at 1 year following initial surgery OR within 6 months of completing surgery if a complete colonoscopy was not performed pre-operatively, then every 5 years.</p> <p>Only colonoscopy after 5 years.</p>
European Society of Coloproctology (ESC) 2019 Summary of European Union Countries' Guidelines [18]	<p>Clinical visits should be part of routine follow-up after colorectal cancer These visits should be performed until 5 years after surgery with a more frequent regimen in the first 2 to 3 years. CEA (might be restricted to stage II and III). This should be done every 3-6 months during the first 2-3 years, and then every 6-12 months until 5 years after surgery. Chest imaging should be routinely performed during follow-up of colorectal cancer (every 3-12 months for at least 5 years after surgery) but might be omitted in stage I colon cancer. Non-endoscopic pelvic imaging should have a role in follow-up after colorectal cancer, but could be restricted to pT2N0 and stage II-III rectal cancer: CT, whether in combination with other methods, is the preferred modality for the detection of pelvic recurrence. However, timing is unclear. A complete colonoscopy should be performed within 3-6 months of surgery if this was not done preoperatively. Surveillance colonoscopy should be routinely performed during the follow-up after colorectal cancer.</p>
National Comprehensive Cancer Network 2019 Colon [6]	<p>Stage I: Colonoscopy 1 year after surgery: if advanced adenomas, repeat in 1 year, otherwise in 3 years and then every 5 years Stage II, III: For 2 years, history and physical every 3-6 months and then every 6 months for 5 years. If patient is a potential candidate for further intervention: CEA every 3-6 months for 2 years, then every 6 months for a total of 5 years. Chest/abdominal/pelvic CT every 6-12 months (category 2B for frequency <12 months) for a total of 5 years. Colonoscopy in 2 years after except if no pre-op colonoscopy due to obstruction lesion, colonoscopy in 3-6 months. If advanced adenoma, repeat in 1 year. Otherwise repeat in 3 years and every 5 years. Stage IV: Same as above with the following differences: Chest/abdominal/pelvic CT every 3-6 months (category 2B for frequency <6 months) for a total of 5 years.</p> <p>Nothing after 5 years - principles of survivorship.</p>

<p>National Comprehensive Cancer Network Rectal 2019 [19]</p>	<p>Transanal local excision only. Proctoscopy (with EUS or MRI with contrast) every 3-6 months for the first 2 years, then every 6 months for a total of 5 years. Colonoscopy at 1 year after surgery. If advanced adenoma, repeat in 1 year. Otherwise repeat in 3 years, then every 5 years. Stage I with full surgical staging: Colonoscopy at 1 year after surgery. If advanced adenoma, repeat in 1 year. Otherwise repeat in 3 years, then every 5 years. Stage II-IV: History and physical every 3-6 months for 2 years, then every 6 months for a total of 5 years. CEA every 3-6 months for 2 years, then every 6 months for a total of 5 years. Chest/abdominal/pelvic CT; for stage II I every 6-12 months (category 2B for frequency <12 months) for a total of 5 years. For stage IV every 3-6 months (category 2B for frequency <6 months) for a total of 5 years.</p> <p>Colonoscopy in 1 year after surgery except if no pre-operative colonoscopy due to obstructing lesion, colonoscopy in 3-6 months. If advanced adenoma, repeat in 1 year. If not, repeat in 3 years and then every 5 years.</p> <p>Nothing after 5 years - principles of survivorship.</p>
<p>Cancer Council Australia 2017 and 2018 [8]</p>	<p>Evidence-based recommendations GRADE D Intensive follow-up after curative surgery for colorectal cancer should include CEA and CT scan, with the aim of early detection of recurrence or residual disease where there is the possibility for curative resection.</p> <p>PET/CT scan can be used as an effective adjunct for detection of recurrence, especially when the CEA and/or CT scans are suggestive of recurrence.</p> <p>Practice points:</p> <ul style="list-style-type: none"> • These recommendations apply only to asymptomatic patients. All patients who develop symptoms should be investigated rigorously. • Colonoscopy should be performed at 12 months after surgery to exclude missed lesions. If the initial colonoscopy was incomplete, then a colonoscopy should be performed at the latest 6 months after surgery. If the colonoscopy is normal, refer to the Clinical Practice Guidelines for Surveillance Colonoscopy for subsequent colonoscopies. • Intensive follow-up for colorectal cancer should be considered for patients who have had potentially curable disease, although optimal modality and frequency are yet to be firmly established. • Intensive follow-up can detect recurrences earlier, thus surgical resection for curative intent is possible. However, this is not associated with improved survival. • CEA and CT scans are readily accessible and relatively sensitive investigations. <p>After the routine review post discharge, patients should be reviewed at 3- to 6-monthly intervals for the first year (3 monthly in those patients who had poor prognostic factors such a positive margin, T4 disease and/or lymph node involvement, patients with stage III disease who decline chemotherapy), 6-monthly for the next 2 years and then yearly for a total of 5 years.</p> <p>Clinical assessment includes history and physical examination. Regular CEA measurement (at each consultation) and annual CT should be considered in follow-up protocols as they may provide useful in early detection of recurrence and the potential for</p>

	<p>surgery with curative intent. Positron emission tomography (PET/CT) can be an effective alternative to standard CT after detection of a significant rise in CEA.</p> <p>Nothing after 5 years.</p>
Guideline	Question 2. Signs and Symptoms
CCO colorectal cancer FU survivorship guidance [4]	<p>Any new and persistent or worsening signs/symptoms to watch for, especially: abdominal pain, rectal bleeding, changes in bowel habit.</p> <p>Vague constitutional symptoms such as: fatigue, nausea, unexplained weight loss</p> <p>Additional new and persistent or worsening signs/symptoms to watch for, specific to rectal cancer: pelvic pain, sciatica, difficulty with urination or defecation.</p>
Cancer Council Australia 2017 [8]	<p>Patients with local recurrence may be symptomatic or asymptomatic.</p> <p>Symptoms of local recurrence depend on the site of recurrence and therefore can vary between patients.</p> <p>In patients with anastomotic or luminal recurrences, symptoms are usually similar to those of patients with primary colorectal cancer in that patients usually present with rectal bleeding, anemia or altered bowel habits. Depending on the extent of the local recurrence, patients may also present with varying degrees of bowel obstruction. Where there has been a previous low rectal anastomosis, the luminal recurrence may be readily palpable on digital rectal examination during routine follow-up. In patients who have previously undergone an abdominoperineal excision, clinical findings may be limited.</p> <p>Patients with nodal or surgical bed recurrences may present with pain from mass effect on neighbouring structures (such as obstruction of ureters or neuropathic pain from the sciatic nerve compression) or may present as a palpable mass.</p> <p>Patients with pelvic recurrences are typically symptomatic, with pain as the most common presentation.</p> <p>Asymptomatic patients may present with a rising serum CEA level or have a new abnormality detected on surveillance imaging or surveillance colonoscopy.</p>
Guideline	Question 3 a. Patient information needs
ESC 2019 Summary of EU [18]	<p>Proposed initiatives were structured stoma care, treatment of low anterior resection syndrome (loperamide, fibre supplementation, irrigation, pelvic physiotherapy, neurostimulation), nutritional education, and referral to urologist/sexologist/pelvic physiotherapist, occupational reintegration, and psychosocial interventions such as treatment of fear of cancer recurrence.</p> <p>Five guidelines suggested that structured preventive care with health-promoting initiatives should be part of supportive care to colorectal cancer survivors.</p>
Cancer Council Australia 2018 [8]	<p>Persisting unmet need for psychosocial care has been reported.</p> <p>International guidelines recommend routine screening of patients for psychological distress using validated, reliable, objective measures. Screening should occur not only at diagnosis but also at key points of the illness trajectory and into survivorship to ensure late-onset distress is not missed.</p> <p>Psychological interventions are effective in the short and long term. For colorectal cancer patients this includes educational interventions, cognitive-behavioural therapy, relaxation training, and supportive group therapy, reduced length of hospital stays, days to stoma proficiency, and anxiety and depression, and improved quality of life.</p>

	Information needs: research has shown that the provision of adequate information is related to increased psychological wellbeing. Effective communication skills are key, patient should be well-informed.
Guideline	Question 3b. Common and/or substantial long-term and late effects
CCO colorectal cancer FU survivorship guideline [4]	<p>Physical:</p> <ul style="list-style-type: none"> • Surgery-related: frequent and/or urgent bowel movements or loose bowels (often improves over first few years), gas and/or bloating, incisional hernia, increased risk of bowel obstruction • Medication-related: peripheral neuropathy (associated with treatment using oxaliplatin), chemotherapy-related cognitive side effects (including difficulty with short-term memory and the ability to concentrate) • Radiation-related: localized skin changes (i.e., colour, texture, and loss of hair), rectal ulceration and/or bleeding (radiation colitis), anal dysfunction (incontinence), bowel obstruction (from unintended small bowel scarring), infertility, sexuality dysfunction (e.g., vaginal dryness, erectile dysfunction, retrograde ejaculation), second primary cancers in the radiation field (typically about seven years after radiotherapy), bone fracture (e.g., sacral region) • Other: for patients who received ostomy, stoma care and life-style adjustments will be required <p>Psychosocial:</p> <ul style="list-style-type: none"> • Psychological distress (e.g., depression, anxiety, worry, fear of recurrence) • Cognitive side effects • Changes in sexual function/fertility • Challenges with body and/or self-image, relationships, and other social role difficulties <p>Return to work concerns and financial challenges</p>
ESC 2019 Summary of EU [18]	Late effects mentioned in the guidelines were bowel dysfunction (low anterior resection syndrome chronic diarrhea), stoma problems, anastomotic stenosis, adhesions, urinary and sexual problems, pain, neuropathy, fatigue, lymphedema, cognitive dysfunction, insomnia, psychosocial problems, body image issues and fear of recurrence.
NCCN Colon 2019 [6]	Long-term: oxaliplatin-induced peripheral neuropathy, fatigue, insomnia, cognitive dysfunction, body image issues (related to ostomy), and emotional/social distress. Late-term effects: chronic diarrhea or incontinence (e.g., patients with stoma).
NCCN Rectal 2019 [19]	Long-term: oxaliplatin-induced peripheral neuropathy, fatigue, insomnia, cognitive dysfunction, and emotional/social distress. Late effects: bowel function changes (e.g., patients with stoma), Urogenital dysfunction following resection and/or pelvic irradiation is common.
Cancer Council Australia 2018 [8]	Physical: Bowel issues (frequent bowel movements, constipation, and diarrhea), leakage in patients with stomas, skin and stoma problems, odour, sexual dysfunction (erectile dysfunction in men; dyspareunia, vaginal dryness, pain in women), and disturbed body image. Social: Patients may avoid and fear social interactions, and experience disrupted intimate relationships.
Guideline	Question 4. Provider for Follow-up Care Recommendations
CCO colorectal cancer FU survivorship guideline [4]	The most common practice for follow-up care in Ontario involves specialist-coordinated care within an institution. Emerging evidence suggests that, for colorectal cancer survivors who have completed all their treatment, discharge from specialist-led care to community-based family physician-coordinated or institution-based nurse-coordinated care is a reasonable option.

NCCN 2019 (Both) [6,19]	Oncologist and primary care provider should have defined roles in the surveillance period.
Cancer Council Australia 2018 [8]	It had not been established whether outcomes differ by provider of follow-up care. For example, it has not been established whether intensive (hospital-based) follow-up is associated with survival advantage over care provided by a general practitioner or clinical nurse consultant in colorectal cancer. Follow-up can be delivered as a combination of visits to the surgeon or associated gastroenterologist, with ongoing care by the GP and clinical nurse consultant.

Abbreviations: CEA=carcinoembryonic antigen; CCO=Cancer Care Ontario; CT=computed tomography; EUS=endoscopic ultrasound; FU=follow-up; GP=general practitioner; MRI=magnetic resonance imaging; NCCN=National Comprehensive Cancer Network; PET=positron emission tomography

Table 4-2 Summary of Study Characteristics and Results for Question 1b

Evaluation	Study	Patients	Study Design	Outcomes	Results
Meta-analysis/HTAs					
CEA CT	Shinkins, 2017 [28]	52 studies - from Nicolson, 2015, FACS and re-analysis of FACS	Meta-analysis	Diagnostic accuracy of one test, trends and levels of CEA to trigger further investigation	<p>Pooled analysis for 5 µg/l of 23 studies (4585 participants):</p> <ul style="list-style-type: none"> • Sensitivity: 71% (95% CI: 64% to 76%) • Specificity: 88% (95% CI: 84% to 92%) <p>Pooled analysis for 2.5 µg/l of 7 studies (1515 participants):</p> <ul style="list-style-type: none"> • Sensitivity: 82% (95% CI: 78% to 86%) • Specificity: 80% (95% CI: 59% to 92%) <p>Pooled analysis for 10 µg/l of 7 studies (2341 participants):</p> <ul style="list-style-type: none"> • Sensitivity: 68% (95% CI: 53% to 79%) • Specificity: 97% (95% CI: 90% to 99%) <p>In the secondary analysis of FACS data at 5 µg/l,</p> <ul style="list-style-type: none"> • Sensitivity: 50% (95% CI: 40% to 60%) • Specificity (%) 93.3 (91% to 95%) • Positive predictive value: 62% (51% to 72%) • Negative predictive value: 90% (87% to 92%)
Colonoscopy CEA CT Clinic Visits	Pita-Fernandez 2015 [29]	11 studies with 4055 patients Curative surgery	Meta-analysis	Intensive strategies: overall survival, recurrence, evaluate diagnostic tests	<p>Overall Survival</p> <p>Colonoscopy: 8 studies: HR=0.75 (0.64-0.87)</p> <p>4 studies comparing with less vs. more: HR=0.86 (0.69-1.06)</p> <p>4 studies with vs. without colonoscopy: HR=0.65 (0.53-0.81)</p> <p>CEA testing: Total studies: 4 HR=0.69 (0.52-0.93)</p>

		1995- June 2014			<p>Studies with less vs. more CEA: 1 HR=0.57 (0.35-0.92) Studies with vs. without CEA: 3 HR=0.73 (0.51-1.05)* includes FACS</p> <p>CT: Total studies: 6 HR=0.80 (0.66-0.98) Studies with less vs. more CT: 0 Studies with vs. without CT: 6 HR=0.80 (0.66-0.98)* includes FACS</p> <p>Clinic visits: Total studies: 3 HR=0.59 (0.46-0.75) Studies with less vs. more CV: 2 HR=0.59 (0.44-0.79) Studies with vs. without CV: 1 HR=0.57 (0.35-0.92)</p>
Colonoscopy	Fuccio, 2019 [30]	<p>15,589 stage I-IV patients from 27 studies that used colonoscopy for surveillance after curative CRC surgery</p> <p>1986-2017</p> <p>The mean length of follow-up: 18-108 months</p>	Meta-analysis	<p>Primary outcomes were rates and timing of CRCs at anastomotic and non-anastomotic location.</p>	<p>296 non-anastomotic CRCs were detected over more than 16 years: cumulative incidence, 2.2% of CRCs; (95% CI: 2-3%)</p> <ul style="list-style-type: none"> risk of CRC at a non-anastomotic location was significantly reduced more than 36 months after resection compared with before this time point (non-anastomotic CRCs at 37-48 months vs. 6-12 months after surgery, OR= 0.61; 95% CI, 0.37-0.98; p=0 .031) 53.7% of all non-anastomotic CRCs were detected within 36 months of surgery. <p>158 CRCs were detected at anastomoses over more than 16 years: cumulative incidence; 2.7% of CRCs; (95% CI: 2-4%)</p> <ul style="list-style-type: none"> risk of CRCs at anastomoses was significantly lower 24 months after resection than before: CRCs at anastomoses at 25-36 months after surgery vs. 6-12 months, OR=0.56; 95% CI, 0.32-0.98; p=0 .036) 90.8% of all CRCs at anastomoses were detected within 36 months of surgery.
Randomized Controlled Trials					
Colonoscopy CEA CT	Wille-Jørgensen, 2018 [2]	2509 patients with stage II	RCT	To assess the effect of scheduled measurement of CEA and CT as	<p>Study Design: High-frequency group: CEA and CT CAP at 6, 12, 18, 24, and 36 months after surgery, n=1253 patients.</p>

		or III CRC resection		follow-up to detect recurrent CRC	<p>Low-frequency group: CEA and CT CAP at 12 and 36 months after surgery, n=1256 patients</p> <p>Results:</p> <ul style="list-style-type: none"> The 5-year overall patient mortality rate: high vs. low 13.0% (161/1253) vs. 14.1% (174/1256) (risk difference, 1.1% p=0.43) The 5-year colorectal cancer-specific mortality rate: high vs. low frequency: 10.6% (128/1248) vs. 11.4% (137/1250) (risk difference, 0.8%; p=0.52) The colorectal cancer-specific recurrence rate: high vs. low frequency: 21.6% (265/1248) vs. 19.4% (238/1250) (risk difference, 2.2%; p=0.15)
Colonoscopy CEA CT	Mant, 2017 Primrose, 2015 FACS [3]	1202 patients with CRC resection	RCT	To assess the effect of scheduled measurement of CEA and CT as follow-up to detect recurrent CRC	<p>Study Design:</p> <ol style="list-style-type: none"> CEA only follow-up: CEA q 3 months for 2 years, then q 6 months for 3 years with single CT CAP at 12 to 18 months CT only follow-up: CT CAP q 6 months for 2 years and then annually for 3 years CEA and CT follow-up: CEA and CT CAP as per Group 1 and 2 Minimum follow-up: No scheduled follow-up except a single CT CAP at 12 to 18 months <p>Results:</p> <ul style="list-style-type: none"> Two-thirds of recurrences (134, 66.0%) were detected by a scheduled follow-up investigation: 87 (64.9%) by CT; 43 (32.1%) by CEA measurement More recurrences were detected in the CT arm than in the CEA testing arm (9.4% vs. 6.3%; p=0.16). The factorial comparison showed a significant absolute benefit only for CT (absolute difference 3.7%; p=0.01). COL detected: 3 local recurrences of rectal tumours; 3 synchronous tumours; 2 metachronous tumours; low-risk adenomas in 76 patients (20.7%, n=367); high-risk adenomas in 22 patients (5.9%, n=367).

Abbreviations: CAP=chest, abdomen, pelvis; CEA=carcinoembryonic antigen; CI=confidence interval; COL=colonoscopy; CRC=colorectal cancer; CT=computed tomography; FACS=follow-up after colorectal surgery; HR=hazard ratio; HTA=health technology assessment; OR=odds ratio; q=measured; RCT=randomized controlled trial

Table 4-3 Summary of Results for FACS RCT [3] for Question 1b

Description	Individual randomization arms					Factorial comparison groups					
	CEA testing only	CT only	CEA + CT	Min	P value	CEA testing	No CEA testing	P value	CT	No CT	P value
Surgical treatment with curative intent, n (%)	19 (6.3)	28 (9.4)	21 (7.0)	8 (2.7)	0.008	40 (6.6)	36 (6.0)	0.65	49 (8.2)	27 (4.5)	0.009
Mortality											
Total deaths, n (%)	81 (27.0)	83 (27.8)	72 (23.8)	70 (23.3)	0.49	152 (25.4)	153 (25.5)	0.97	155 (25.8)	151 (25.1)	0.79
Deaths attributed to colorectal cancer, n (%)	48 (16.0)	45 (15.1)	38 (12.6)	38 (12.6)	0.73	86 (14.3)	83 (13.8)	0.84	83 (13.8)	86 (14.3)	0.92
Patients with recurrence still surviving n (%)	14 (4.7)	14 (4.7)	15 (5.0)	7 (2.3)	0.33	29 (4.8)	21 (3.5)	0.25	29 (4.8)	21 (3.5)	0.25
Patients with recurrence treated with curative intent still surviving, n (%)	11 (3.7)	11 (3.7)	13 (4.3)	5 (1.7)	0.29	24 (4.0)	16 (2.7)	0.20	24 (4.0)	16 (2.7)	0.20
Median survival post recurrence (months)											
All patients with recurrence	23.7 (n=56)	25.5 (n=61)	38.0 (n=48)	14.6 (n=38)	0.16	27.7 (n=104)	23.1 (n=99)	0.44	29.2 (n=109)	20.7 (n=94)	0.08
Treated surgically with curative intent	51.2 (n=19)	43.6 (n=28)	58.7 (n=21)	76.9 (n=8)	0.18	56 (n=40)	51.3 (n=36)	0.82	52.0 (n=49)	59.1 (n=27)	1.00
Not treated surgically with curative intent	19.0 (n=37)	13.0 (n=33)	22.2 (n=27)	10.6 (n=30)	0.11	19.1 (n=64)	12.6 (n=63)	0.04	15.6 (n=60)	12.6 (n=67)	0.54
Diagnosed with recurrence											
All sites, n (%)	56 (18.7)	61 (20.4)	48 (15.9)	38 (12.6)	0.06	104 (17.3)	99 (16.5)	0.72	109 (18.1)	94 (15.6)	0.25
Liver, n	23	30	19	15		42	45		49	38	
Lung, n	23	18	17	11		40	29		35	34	
Locoregional, n	18	19	15	14		33	33		34	32	
Other, n	12	8	9	14		21	22		17	26	
Recurrences detected by scheduled follow-up, n (%)	35 (11.7)	52 (16.1)	40 (13.2)	9 (3.0)	<0.001	75 (12.5)	61 (10.2)	0.21	92 (15.3)	44 (7.3)	<0.001
CEA level, n	30	0	13	0		43	0		13	30	
CT imaging, n	3	49	26	9		29	58		75	12	

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Colonoscopy, n	0	3	1	0		1	3		4	0	
Surgical treatment with curative intent, n (%)	19 (6.3)	28 (9.4)	21 (7.0)	8 (2.7)	0.008	40 (6.6)	36 (6.0)	0.65	49 (8.2)	27 (4.5)	0.009
Patients receiving more than specified follow-up											
Received ≥ 1 unscheduled CEA, n (%)	40 (13.3)	17 (5.7)	11 (3.6)	58 (19.3)	<0.001	51 (8.5)	75 (12.5)	0.023	28 (4.7)	98 (16.3)	<0.001
Received ≥ 1 unscheduled CT scan, n (%)	56 (18.7)	14 (4.7)	8 (2.6)	56 (18.6)	<0.001	64 (10.6)	70 (11.7)	0.57	22 (3.7)	122 (20.3)	<0.001
Received ≥ 1 unscheduled Colonoscopy, n (%)	43 (14.3)	13 (4.3)	13 (4.3)	53 (17.6)	<0.001	56 (9.3)	66 (11.0)	0.33	26 (4.3)	96 (16.0)	<0.001
Total missed > 1 scheduled test or had received any unscheduled test, n (%)	111 (37.0)	47 (15.7)	69 (22.8)	113 (37.5)	<0.001	180 (29.9)	160 (26.7)	0.21	116 (19.3)	224 (37.3)	<0.001

Abbreviations: CEA=carcinoembryonic antigen; CT=computed tomography; NS=non-significant

Table 4-4 Results of studies of follow-up providers

Study	Provider used / surveillance person/ schedule	Number of Patients	Median Observation (months)	Overall Recurrence Rate (%)	Timeliness /compliance	Rate of late effects/ metastases	Time to recurrence	Quality of Life / Patient Satisfaction	Unannounced follow-ups
Augestad, 2013 [12] RCT	GPs Surgeons	55 55	75% for 12 mos, and 52% for 24 mos	10.9 14.5	Response rate of 96% for QoL questionnaire	NA	35 days 45 days (Reported as serious clinical event)	No significant effect on QoL main outcome measures; EORTC QLQ C-30 subscales reported significant effects in favour of GP follow-up	3 4 (Number of metastases surgeries)
Strand, 2011 [10] RCT Rectal cancer patients	Surgeon RN	56 54	36	0	All patients completed the questionnaire	7 8 Distant metastases	NA	Overall high patient satisfaction; VAS 9.4 for surgeon and 9.5 for RN	4 surgeries for distant metastases, 9 received palliative chemotherapy
Coeburgh van den Braak, 2018 [9] Prospective	NPC No NPC	394 287	34.3 for DFS; 67.9 for OS	12.5	Involvement of an NPC resulted in a higher adherence to follow-up (84.3 vs. 73.9%, p=0.001)	NA	NA	NA	NA

Abbreviations: CEA=carcinoembryonic antigen; CRC=colorectal cancer; DFS=disease-free survival; EORTC QLQ=European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire; GP=general practitioner; mo=month; NA=not applicable; NPC=nonphysician clinician; OS=overall survival; RCT=randomized controlled trial; RN=specialist nurse

Table 4-5 Environmental Scan of Canadian Cancer Agencies online sources.

Agency/ district	Oncologist	Surgeon	FP	RN	Combination	Treatment plan or information to patient
BC Agency 2018	X		X		Oncologist provides reports to FP during treatment. FU is done by FP and will contact the oncologist if there are any concerns with test results	Report http://www.bccancer.bc.ca/coping-and-support-site/Documents/FollowupProgram-After-Colorectal-Treatment-English.pdf
Alberta Health Services 2019	X	X	X	X	Patient post-treatment surveillance can be led by their general practitioner (GP), a RN practitioner, surgeon, or their medical/radiation oncologist.	Information about the late effects of colorectal cancer treatment, risk reduction strategies, and health promotion recommendations, should be provided to patients completing treatment, as well as their primary healthcare providers. https://www.albertahealthservices.ca/assets/info/hp/cancer/if-hp-cancer-guide-gi002-colon-surveillance.pdf
Saskatchewan Cancer Agency 2019			X			Follow-up recommendations should be provided to the patients and their primary care physicians. http://www.saskcancer.ca/images/pdfs/health_professionals/clinical_resources/clinical_practice_guidelines/colorectal_cancer/Colorectal%20guideline%20%20Feb%202019.pdf
CancerCare Manitoba 2017			X	X	FPs and nurse practitioners play a key role in caring for patients during and after their cancer treatment. The treatment plan is created by the oncologist and given to the patient	Moving Forward after Colorectal Cancer Program Part 1 - the Personalized Follow-Up Care Plan and Treatment Summary Part 2 -Colorectal Cancer Information Part 3 - General Moving Forward After Cancer Treatment booklet https://www.cancercare.mb.ca/For-Health-Professionals/follow-up-care-resources/index.html
Nova Scotia 2016		X	X		For patients without primary care providers, surveillance will be provided by the rectal cancer surgeon. A standardized letter will be sent to the primary care provider by the treating oncologist including the recommended surveillance schedule to be followed.	Coordination and Communication of Surveillance Plan to FP and patients http://www.nshealth.ca/sites/nshealth.ca/files/patientinformation/nsccp0061.pdf

FP=Family Physician; FU=follow-up; RN-registered nurse

Table 4-6 Perceptions of Follow-up Care themes from Berian et al. [7]

Perceptions of Follow-Up Care Themes	Number of studies with Positive perceptions	Number of studies with Negative perceptions
Emotional reactions to follow-up (E.g., positive=reassurance, negative=anxiety)	N=7	N=2
Overall satisfaction or perceived quality of care	N=4	N=1
Access to care or frequency of visits	N=4	N=0
Follow-up is important to detect recurrence	N=3	N=0
Follow-up is important to improve survival	N=2	N=0
Information exchanged during follow-up (e.g., ability to ask questions, questions answered)	N=3	N=2
Communication between providers	N=0	N=2
Follow-up includes sufficient sensitivity to patients' quality of life	N=0	N=3

Table 4-7 Study Characteristics for Question 3

Study	Follow-up Program Intensity	Number of Patients and disease type	Median Observation (months)	Overall Recurrence and Time to Recurrence	Rate of late effects/ metastases	Signs and symptoms associated with risk of recurrence (Number and %)
Duineveld, 2016 [13] Retrospective cohort	CEA testing every 3 to 6 months during the first 3 years and 6 months during the following 2 years; abdominal imaging every 6 months for first 2 years and annually for following 3 years	446; 93 (21%) stage I carcinoma, 176 (39%) stage II, 176 (39%) stage III; majority carcinoma of left colon (55%)	34	74 pts (16.6%) 43 (58%), detected during a scheduled follow-up visit; 41 (95%) asymptomatic 31 (42%), found during non-scheduled interval visits; 26 (84%) of these patients were symptomatic Time to recurrence: 13.7 months	9 lung metastases	Symptoms reported during interval visits leading to detection of recurrent disease Abdominal pain: 15 (57.7) Altered defecation: 11 (42.3) Weight loss: 6 (23.1) Pain in back of pelvis: 4 (15.4) Fatigue: 2 (7.7) Dyspnea: 2 (7.7) Loss of appetite: 2 (7.7) Other (including urine retention, hematuria or cough): 3 (11.6) >1 symptom: 14 (53.8)
Augested, 2014 [12]	CEA testing and clinical exam every 3 months during the first 2 years	110;	24	14 pts (12.7%) 7 had symptoms	48 serious clinical events (SCE; episode leading to	Of 48 SCEs; 31 (65%) were initiated by emerging symptoms 17 (35%) were initiated by test findings.

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RCT	and 6 months during the following 3 years; chest x-ray and liver ultrasound every 6 months for first 2 years and annually for following 3 years; colonoscopy at 1 and 4 years	Dukes' stage A, B or C colon cancer		7 found during visit Time to Recurrence: 45 days in surgeon group and 35 days in the GP group (p=0.46)	suspicion of cancer recurrence)	14 pts had true colon cancer recurrence. 7 pts had symptoms: Abdominal pain -4 Blood in stool -1 Weight loss -1 Stoma bleeding -1 7 pts had radiologically detected lesions (n=4) and elevated CEA levels (n=3)
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Abbreviations: CEA=carcinoembryonic antigen; GP=general practitioner; pts=patients; RCT=randomized controlled trial; SCE=serious clinical events

Table 4-8 Summary of Supportive Care Needs from Kotronoulas et al. [14]

Domain	Operational Definition	Individual supportive care need (number of studies mentioning the need: percentage of patients identifying the need in studies)
Information/ education (showing top 10 needs of 34 listed in SR)	Need for help with lack of information, uncertainty about diagnosis/treatment, uncertainty/lack of knowledge about self-care	2. More information (32-49%) about: Diet/nutrition (15: 46-98%) in the form of a pamphlet (1:90%) or by a hospital dietician (1:53%)
		3. Long-term self-management of symptoms and complications at home, e.g. persistent fatigue and bowel symptoms (15: 7-89%)
		6. Cancer staging and prognosis (9: 59-60%)
		8. Risk of recurrence (6: 46-63%) and/or symptoms of disease recurrence (3: 89%)
		9. Short-term and long-term effects of treatment on quality of life (9: 40-78%)
		12. Exact diagnosis and what it means (7: 52-80%)
		13. Test results and procedures (7: 21-77%)
		18. What to expect following discharge (4) or following chemotherapy (1) especially people with no stoma (2)
Health system/patient-clinician communication (showing top 10 needs of 34 listed in SR)	Need for help with insufficient communication between patients and clinicians, satisfaction with care, participation in decision-making, preferences in communication	4. Information that is clear/straight-forward, up-to-date, honest, unhurried, and given in a sensitive way (13:14-99%), especially if no curative treatment is available (13: 29-38%)
		5. Written information/publications (8: 21-75%) especially about treatment options/processes (3: 72-78%)
		10. On-going communication/contact with and support from a trustworthy clinician (8: 16-56%)
		14. Healthcare professional who treats the patient like a person, not just another case (2: 14-32%) listens to what the patient has to say (1: 94%), is open and sincere, and acknowledges and shows sensitivity to patients' feelings/emotions (3: 16%) and/or to family/friends' feelings (1).
		16. Better coordination/communication among healthcare professionals (primary and secondary care) (7: 15-68%)
		Follow-up visit by a specialist nurse to provide support with post-treatment concerns. (5)

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		Information customised to individual needs and abilities to handle information. (5) Quick access to information, coordinated health services, investigations and treatment (5: 22-98%) Participation in decision-making in a shared manner (4: 22-72%) Post-operative follow-up/information provided by a hospital doctor (3:46-93%)
Psychosocial/ emotional (showing top 5 needs of 10 listed in SR)	Need for help with psychological/emotional symptoms such as depressive mood, anxiety, fear/worry, despair	1. Emotional support and reassurance (7: 16-33%) when trying to deal with fear of the cancer returning or spreading (12: 20-56%) 19. Support when dealing with uncertainty about the future (6: 33-35%) Support to come to terms with the diagnosis and deal with feelings of shock and mental isolation (3) Psychological support (1) especially in relation to feelings of abandonment after treatment is over (2) Support with concerns about being a burden or dependent on others (2: 29%)
Family-related (showing top 4 needs of 4 listed in SR)	Need for help with dysfunctional family relationships, fears/concerns for family future	15. Help with the worries/concerns of one's family (4: 24-38%) especially children (3: 55%) Support with concerns about the family's future (3) Help with the information needs of family (2: 16%) Help with compromised emotional closeness with family (1)
Social/societal (showing top 5 needs of 8 listed in SR)	Need for help with experience of social isolation, inefficient social support, diminished socialisation	Access to peer support groups for colorectal cancer survivors (4: 63%) Help with embarrassment/loss of dignity/pride due to stoma issues/uncontrolled bowel movements in social situations (2: 31-36%) Know the proximity/location of a toilet at all times (1: 72%) Plan social events ahead (1: 35%) Access support groups to help others (1)
Interpersonal/ intimacy (showing top 5 needs of 5 listed in SR)	Need for help with altered body image or sexuality, sexual health problems, compromised intimacy with partner, loss of fertility	17. Help to adjust to changes in/problems with sexuality especially if partnered (7: 12-48%) Help to adjust to altered body image/appearance (6) Help with concerns about sexual impotence/dysfunction (3) Help with concerns about sexual relationships (1: 18%) especially initiating future relationships if unpartnered (1) Help with changed partner roles and compromised intimacy (1)
Practical/daily living (showing top 5 needs of 12 listed in SR)	Need for help with transportation, living will, out-of-hours accessibility, funeral care, financial strain, experience of restriction in daily living tasks such as housekeeping, exercise	Help in adjusting to the daily restrictions posed by treatment toxicity/altered bowel function/stoma (5: 26%) Support with transportation/access barriers/issues/difficulties especially for rural patients (3: 19- 34%) e.g., accessible hospital parking (2: 17%) Support with financial issues (3: 23-27%) and/or work-related issues (2: 15-25%) Help in recovering/achieving full potential and dealing with the debilitating effects of the illness (3) Support with establishing dietary changes/timing of meals (specially to avoid gas from the stoma or having to change the stoma bag) (3)
Physical/ cognitive	Need for help with symptom management of cancer-related	Help with symptom control (7: 6-62%) especially: 7. Fatigue/lack of energy (5: 23-32%) post-op (4:12-27%)

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(showing top 10 needs of 10 listed in SR)	problems and treatment-related toxicity, and cognitive dysfunction	11. Pain (abdominal) (6: 23-28% post-op associated with adhesions/infected wounds/non-healing wounds (3)
		Defecation problems (gas/wind, diarrhoea, constipation) (5: 21-26%)
		Digestive problems/dysfunction (5: 18-31%) (nausea, indigestion; appetite; taste)
		Sleep loss (2) post-op (2: 29%)
		Cognitive alteration (2)
		Weight changes (loss/gain) (1)
		Infection (1)
		Peripheral neuropathy (1)
Management of comorbid illnesses (1)		

Abbreviation: SR=systematic review

Appendix 5: Quality Assessment Scores

AGREE II - Guidelines

Guideline	Domain 1: Scope and Purpose	Domain 2: Stakeholder Involvement	Domain 3: Rigor of Development	Domain 4: Clarity of Presentation	Domain 5: Applicability	Domain 6: Editorial Independence
OH (CCO) [4]	100%	58.3%	75%	83.3%	18.7%	83.3%
ESC [18]	95.2%	42.8%	78.5%	85.7%	28.5%	78.5%
NCCN - colon [6]	75%	61.1%	67.7%	69.4%	66.7%	83.3%
NCCN-rectal [19]	72.2%	75%	65.6%	69.4%	66.7%	83.3%
CCA [8]	95.2%	90.4%	85.7%	71.4%	60.7%	85.7%

Abbreviations: CCA=Cancer Council Australia; ESC=European Society of Coloproctology; NCCN=National Comprehensive Cancer Network; OH (CCO)=Ontario Health (Cancer Care Ontario)

ROBIS - Systematic Review/Meta-analysis

Study	Domain 1: Study Eligibility Criteria	Domain 2: Identification and Selection of studies	Domain 3: Data Collection and Study Appraisal	Domain 4: Synthesis and Findings	Overall Risk of Bias
Jeffery, 2019 [1]	Low	Low	Low	Low	Low
Fuccio, 2019 [30]	Low	Low	Low	Low	Low
Shinkins, 2017 [28]	Low	Low	Low	Low	Low
Berian, 2017 [7]	Low	Low	Low	Low/unclear	Low
Kotronoulas, 2017 [14]	Low	Low	Low	High	Low
Pita-Fernández, 2015 [29]	Low	Low	Low	Low	Low

Risk of Bias - RCTs

Study	Domain 1: Randomization Process	Domain 2: Deviation from Intervention	Domain 3: Missing Outcome Data	Domain 4: Measurement of Outcome	Domain 5: Reported Result	Overall Risk of Bias
Wille-Jorgensen, 2018 [2]	Low/Some concerns	Low/Some concerns	Low	Low	Low	Low
Mant, 2017 FACS [3]	Low	Some concerns	Low	Low	Low	Low
Augestad, 2013 [5]	Low	Low	Low	Low	Low	Low
Strand, 2011 [10]	Low	Low	Low	Low	Low	Low
Augestad, 2014 [12]	Low	Low	Low	Low	Low	Low

Abbreviations: RCTs=randomized controlled trials

Risk of Bias - Cohort Studies

Study	Domain 1: Bias due to confounding	Domain 2: Bias due to selection of participants	Domain 3: Bias in measurement of interventions	Domain 4: Bias due to departure of interventions	Domain 5: Bias due to missing data	Domain 6: Bias in measurement of outcomes	Domain 7: Bias in selection of the reported results	Overall Risk of Bias
Coebergh van den Braak, 2018 [9] Prospective	Moderate	Moderate	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Wieldraaijer, 2018 [11] Retrospective	Moderate	Low	Low	Moderate	Low	Low	Low	Moderate
Duinveld, 2016 [13] Retrospective	Low	Low	Low	Low	Low	Low	Low	Low

Appendix 6: Guideline Document History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES and KEY CHANGES
	Search Dates	Data		
Original 2012	2000-June 2011	Full Report	Earle C, Annis R, Sussman J, Haynes AE, Vafaei A. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer. Toronto (ON): Cancer Care Ontario; 2012 Feb 3. Program in Evidence-based Care Evidence-Based Series No.: 26-2.	N/A
Version 2 2016	2000 to June 2011: question 6 additional data from 26-1, 2012	New data added to original Full Report	Members of the Colorectal Cancer Survivorship Group. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer. Toronto (ON): Cancer Care Ontario; 2012 Feb 3 [Being Updated 2018 Jun]. Program in Evidence-based Care Evidence-Based Series No.: 26-2 Version 2	Table 1 in Section 1 footnote: “Patients with rectal cancer who have not received pelvic radiation should receive a rectosigmoidoscopy every 6 months for 2-5 years. Change the footnote to “for rectal cancer patients who are considered at high risk of local recurrence by the treating physician, sigmoidoscopy may consider at intervals less than 5 years”
Version 3 2020	June 2011 to November 2020	New data	TBD	Key changes include the new evidence that had been published regarding the use of lower- versus higher-intensity follow-up for CRC survivors. While the previous versions were based on high-quality guidelines from other jurisdictions and organized in individual modalities, the updated version is based on newer primary evidence and organized as regimens with options allowing for individual patient requirements and needs.

Abbreviations: CRC=colorectal cancer; N/A=not applicable; TBD=to be determined