



Complete Summary

GUIDELINE TITLE

Follow-up of patients with curatively resected colorectal cancer.

BIBLIOGRAPHIC SOURCE(S)

Figueredo A, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, Zuraw L, Zwaal C. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. *BMC Cancer* 2003 Oct 6;3(1):26. [62 references] [PubMed](#)

Gastrointestinal Cancer Disease Site Group. Figueredo A, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, Zuraw L, Zwaal C. Follow-up of patients with curatively resected colorectal cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2004 Jan [online update]. 30 p. (Practice guideline report; no. 2-9). [67 references]

GUIDELINE STATUS

This is the current release of the guideline.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Curatively resected colorectal cancer

GUIDELINE CATEGORY

Evaluation
Management
Prevention
Screening

CLINICAL SPECIALTY

Colon and Rectal Surgery
Internal Medicine
Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To provide recommendations as to whether follow-up of patients after curative resection of colorectal cancer improves survival

TARGET POPULATION

Adult patients with curatively resected colorectal cancer, defined as patients who have had all apparent disease removed by surgery

INTERVENTIONS AND PRACTICES CONSIDERED

Follow-up of patients after curative resection of colorectal cancer including consideration of:

1. Screening tests
2. Frequency of follow-up visits
3. Patient compliance with follow-up programs

MAJOR OUTCOMES CONSIDERED

- Recurrence rate
- Number of second bowel cancers
- Radical reoperation rate
- Overall survival rate
- Complication rate
- Patient compliance

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original guideline: June 2002

MEDLINE (1966 to September 2001), CANCERLIT (1983 to August 2001), and the Cochrane Library (2001, Issue 3) were searched with no language restrictions. "Colonic neoplasms" (Medical subject heading [MeSH]), "rectal neoplasms" (MeSH), and "colorectal neoplasms" (MeSH) were combined with "recurrence" (MeSH), "prognosis" (MeSH), "compliance" (MeSH), "survival analysis" (MeSH), and the following phrases used as text words: "follow-up" and "surveillance". These terms were then combined with the search terms for the following study designs or publication types: practice guidelines, systematic reviews or meta-analyses, randomized controlled trials, cohort studies, and retrospective studies. In addition, the Physician Data Query (PDQ) clinical trials database on the Internet (http://nci.nih.gov/search/clinical_trials/) and the conference proceedings of the 1997 to 2001 annual meetings of the American Society of Clinical Oncology (ASCO) were searched for reports of new or ongoing trials. The reference lists from retrieved papers were searched for additional trials.

January 2004 Update

The literature search was updated in January 2004 using the MEDLINE (1966 to January [week 1] 2004), EMBASE (1996 to week 52, 2003), and Cochrane Library (2003, issue 3) databases and the 2003 American Society of Clinical Oncology proceedings. The Physician Data Query clinical trials database was also searched for relevant trials.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence if they were fully published reports or published abstracts of:

1. Randomized or non-randomized studies and systematic reviews comparing groups of patients receiving different follow-up programs after curative resection of colorectal cancer, and overall patient survival was reported
2. Cohort studies that investigated compliance with follow-up programs after curative resection of colorectal cancer, and overall patient survival was reported

January 2004 Update

The inclusion criteria for updates to this practice guideline have been revised to:

1. Randomized trials comparing groups of patients receiving different follow-up programs after curative resection of colorectal cancer, and reporting overall patient survival
2. Meta-analyses of these randomized trials

Although survival was the main outcome of interest, results of trials were also searched for recurrence rates, time to recurrence, asymptomatic recurrences, reoperation rates for recurrences, complications, and compliance with follow-up programs.

While not considered for inclusion in any analysis where randomized trials were available, some cohort studies were retained for discussion.

NUMBER OF SOURCE DOCUMENTS

Original guideline: June 2002

Two published meta-analyses, one position paper, one guideline that included a systematic literature review, six randomized trials, eight nonrandomized comparative cohort studies, and three cohort studies of compliance with follow-up were reviewed.

January 2004 Update

Twelve additional papers were obtained during updating.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Original Guideline: June 2002

Due to the multiple factors that can affect survival results (e.g., variety and frequency of screening tests, compliance with tests and interventions, comorbidity), both clinical and statistical heterogeneity among study results was expected. Prior to the estimation of risk reduction, each study was appraised individually, the mortality rates for both groups were assessed for heterogeneity using scatter plots, and visual impressions were confirmed by calculating heterogeneity coefficients with significance levels set at 0.10 as recommended in the statistical literature. Mortality rates were pooled using Review Manager 4.1 (Metaview© Update Software), which is available through the Cochrane Collaboration. The numbers used for data pooling were those reported or those calculated from tables or survival curves in published reports of study results.

Results were reported as mortality odds ratios (OR) with 95% confidence intervals (CI) obtained by the random effects model of DerSimonian and Laird. An OR less than one favours the more intense follow-up and an OR greater than one favours less intense follow-up.

It was planned, a priori, to conduct a subgroup analysis to examine the pooled results of all studies by intensity of follow-up programs compared and by inclusion of blood carcinoembryonic antigen (CEA) testing. This decision was based on the proposed hypothesis that increasing the frequency of assessments and the number of tests would result in earlier diagnosis of recurrences and lead potentially to improved patient survival. Blood carcinoembryonic antigen testing was considered important in previous studies. To conduct the analyses by intensity of follow-up, the studies were divided into two subgroups: those that compared regular follow-up (i.e., assessments at least once a year) versus minimal follow-up, and those that compared intensive follow-up (i.e., regular follow-up added with more frequent assessments and/or other tests) versus regular follow-up. As the direction of expected effect in these subgroup analyses were stated a priori, the p-values provided are one-sided only.

Mortality rates from the randomized trials were pooled, and the results were used to develop recommendations for follow-up after curatively resected colorectal cancer. Mortality rates from the non-randomized studies were combined in a separate analysis because it was considered inappropriate to combine results of randomized and non-randomized studies. In addition, results of cohort studies of compliance were pooled separately to examine the impact of patient compliance with follow-up on their survival.

January 2004 Update

Only published data from randomized trials or from meta-analyses of randomized trials have been used in any analyses for this update. A quality analysis of the eligible trials, not performed in the original practice guideline (PG), was undertaken individually by two authors, using the methodology described in Detsky et al, and is reported in the Update section. Summary statistics, expressed as OR in the approved practice guideline, are reported as Relative Risk Ratios (RR) with 95% confidence interval for all meta-analyses in both the published and updated version. An RR less than one favours the more intense follow-up and an RR more than one favours less intense follow-up. Survival rates from the randomized trials were pooled, and the results were used to develop recommendations for follow-up programs.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Original Guideline: June 2002

Intense debate during several sessions centred on the interpretation of the presented evidence as well as the common practices and the guideline developers' role in clarifying for other physicians what is an acceptable follow-up program. The evidence presented clearly demonstrated a survival benefit for patients receiving programs of more intense follow-up. The evidence for the schedule of visits and screening tests to detect disease recurrence is soft or non-existent. The evidence for the use of colonoscopy to detect second colorectal cancer and its precursors derive from investigations of the Polyp Surveillance Study in the United States. Further, there are other goals for follow-up than to increase survival, including psychosocial support, documentation of disease course, and close contact to test new therapies. Common practice has been to follow patients at high risk of recurrence (stages II and III) with clinical assessment and blood tests including carcinoembryonic antigen (CEA) every three to four months for the first two or three years and every six to 12 months to complete five years following resection. Blood CEA monitoring seems to uncover resectable liver metastases, is relatively inexpensive, and causes minimal inconvenience. Patients also have a colonoscopy in the perioperative period, and if adenomatous polyps are present, colonoscopy is repeated yearly or, if no polyps are detected, every three to five years. This practice was recommended in a document prepared by the Gastrointestinal Cancer Disease Site Group (DSG) in January 1997 (see Appendix 2 of the original guideline document) and a group of American Society of Clinical Oncology (ASCO) experts recently supported similar views. These recommendations encompass the available evidence from clinical trials and what is known about the clinical biology of colorectal cancer recurrences and second tumours, and should serve as a guide to other physicians. The Gastrointestinal Cancer DSG is fully aware that further trials are needed to determine which tests lead to the detection of resectable recurrent disease and whether patients' quality of life is also improved.

January 2004 Update

Since the original practice guideline was approved, the Polyp Surveillance Study performed in the United States has been updated. This Polyp Surveillance Study guideline continues to provide evidence for the use of colonoscopy to detect second colorectal cancer and its precursors.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

- The guideline authors reviewed published cost analyses. Two papers were obtained that detailed the high economic cost of intensive follow-up programs.
- A program of colorectal cancer follow-up similar to those described by Vernava et al, and using U.S. costs per test given by Nelson, would have an approximate five-year cost per patient of \$10,000, half of this amount due to colonoscopy. This cost does not include surgical procedures (\$8,000 per operation) for asymptomatic disease, most of which cannot be curatively resected. Several other investigators have also emphasized these high economic costs. Similar costs will occur in the Canadian context.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 153 practitioners in Ontario (29 medical oncologists, 20 radiation oncologists, and 104 surgeons). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The Gastrointestinal Cancer Disease Site Group (DSG) reviewed the results of the survey.

Final approval of the original guideline report was obtained from the Practice Guidelines Coordinating Committee (PGCC).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Original Guideline: June 2002

- Patients with curatively resected colorectal cancer should be alerted to the future risk of disease recurrence, which is related to tumour stage, and to the development of a second colorectal cancer.
- There is evidence from one randomized trial and a meta-analysis of six randomized trials of a small survival benefit with more intensive follow-up compared to less intensive follow-up. This benefit is due to the early diagnosis and resection of limited recurrent disease in the liver, lungs, or local sites. It is not known at this time whether this diagnosis of resectable recurrences is due to the early assessment of symptoms or to the use of screening tests (blood carcinoembryonic antigen, chest-x-ray, liver ultrasound, or colonoscopy). There is insufficient evidence on which to base a recommendation for specific screening tests.
- In light of the uncertainty of the schedule of visits and screening tests to be recommended, and based on the rate of recurrent disease and second neoplasms, and on current practices, the guideline developers advise:
 1. In patients who are at high risk of relapse (stages IIb and III disease) and who are fit and willing to undergo investigations and treatment:
 - Prompt assessment for symptoms of potential disease relapse (see Appendix 1 of the original guideline document)

January 2004 Update

- For patients at high risk of recurrence (stages IIb and III), clinical assessment is recommended when symptoms occur or at least every six months for three years and then yearly for at

least five years, instead of for at least three years as recommended in the original guideline.

- During those visits patients may have blood carcinoembryonic antigen, chest x-rays, and liver ultrasound;
- When recurrences of disease are detected, patients should be assessed by a multidisciplinary oncology team including surgical, radiation, and medical oncologists to determine the best treatment options.

2. In patients at high risk of relapse but who have comorbidities that may interfere with prescribed tests or potential treatment for recurrence, or who are unwilling to undergo prescribed tests or potential treatment for recurrence:

- Clinical assessments yearly or for suggestive symptoms of relapse.

3. In all patients with resected colorectal cancer (stages I, II, and III) and based on the U.S. Polyp Study:

- Colonoscopy postoperatively if not yet done:
 - If polyps are present, excise as they are potential precursors of colorectal cancer; repeat colonoscopy yearly as long as polyps are found.
 - If there are no polyps, repeat colonoscopy in three to five years.

(see Appendix 2 in the original guideline document).

- Patients should be encouraged to participate in clinical trials investigating screening tests added on to their clinical assessment. These trials of follow-up need to target patients with resectable recurrent disease who are fit for required surgery.

January 2004 Update

- For patients at lower risk of recurrence (stages I and Ia) or those with comorbidities impairing future surgery, only visits yearly or when symptoms occur are recommended. All patients should have a colonoscopy before or within 6 months of initial surgery, repeated yearly if villous or tubular adenomas >1 cm are found; otherwise, repeat every 3 to 5 years.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by randomized trials and meta-analyses.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Of six randomized trials comparing one follow-up program to a more intense program, only two individual trials detected a statistically significant survival benefit favouring the more intense follow-up program. Pooling of all six randomized trials demonstrated a significant improvement in survival favouring more intense follow-up (relative risk ratio 0.80; 95% confidence interval, 0.70 to 0.91; $p=0.0008$). Although the rate of recurrence was similar in both of the follow-up groups compared, asymptomatic recurrences and reoperations for cure of recurrences were more common in patients with more intensive follow-up. Trials including blood carcinoembryonic antigen monitoring and liver imaging also had significant results, whereas trials not including these tests did not.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Figueredo A, Rumble RB, Maroun J, Earle CC, Cummings B, McLeod R, Zuraw L, Zwaal C. Follow-up of patients with curatively resected colorectal cancer: a practice guideline. BMC Cancer 2003 Oct 6;3(1):26. [62 references] [PubMed](#)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Jun (revised online 2004 Jan)

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Gastrointestinal Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please visit the [Cancer Care Ontario Web site](#).

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Gastrointestinal Cancer Disease Site Group (DSG) disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Follow-up of patients with curatively resected colorectal cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 2004 Jan. Electronic copies: Available from the [Cancer Care Ontario Web site](#).
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995 Feb;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 14, 2004. The information was verified by the guideline developer on June 2, 2004.

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