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MANATŪ HAUORA

Management of Early Colorectal Cancer

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New Zealand GUIDELINES GROUP
Te Rōpū Rarangi Tohutohu
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Evidence-based
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Guideline

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Funding and independence

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Statement of intent

NZGG produces evidence-based best practice guidelines to help health care practitioners, policy-makers and consumers make decisions about health care in specific clinical circumstances. The evidence is developed from systematic reviews of international literature and placed within the New Zealand context.

While NZGG guidelines represent a statement of best practice based on the latest available evidence (at the time of publishing), they are not intended to replace the health practitioner's judgment in each individual case.

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Cover concept: The cover image draws on Rongoa Māori and shows Koromiko (hebe stricta) leaves. These are used for their balancing and toning effect on the bowel.

The guideline and its summary are available at www.nzgg.org.nz – search on publication title.

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Kei to kamakama te tikanga

Promptness will carry the day

Contents

List of tables

List of figures

About the guideline

Purpose of the guideline

The purpose of this guideline is to provide an evidence-based summary of current New Zealand and overseas evidence to inform best practice in the management of people with early colorectal cancer. The guideline will be relevant and useful to all secondary and tertiary care practitioners involved in the care of people with early colorectal cancer (ie, not metastatic or recurrent).

Need for a guideline

Improving early detection and diagnosis of cancer and improving access to timely and appropriate treatment are identified as goals of the *New Zealand Cancer Control Strategy Action Plan 2005–2010*.[1] The development and implementation of guidelines support the achievement of these goals by contributing to improvements in national consistency and quality in cancer services. This guideline was commissioned by the Ministry of Health to meet this identified need.

Scope of the guideline

This guideline covers the period from preoperative assessments through to treatment and includes recommendations for follow-up. The guideline specifically addresses the management of people with invasive adenocarcinoma of the colon or rectum. The guideline provides recommendations for secondary and tertiary care providers and assumes the patient has already been referred because of suspicious bowel symptoms or has undergone initial testing in primary care. Guidelines on the referral of patients are on the New Zealand Guidelines Group (NZGG) website (see *Suspected cancer in primary care)*.

It should be noted that the management of people with more advanced colorectal cancer (including metastatic disease) at diagnosis or later and people with high-risk familial colorectal cancer syndromes are beyond the scope of this guideline, so these cancers have been excluded. Squamous cell carcinomas have also been excluded. Colorectal cancer screening in asymptomatic people or the prevention of colorectal cancer in the general population is also beyond the scope of this guideline.

Colorectal cancer includes cancer of both the colon and the rectum. It is important to distinguish colon from rectal cancer as management may differ. During meetings, the Guideline Development Team (GDT) debated the definition of the upper proximal limit of the rectum and agreed on the following definition:

> The rectum has an anatomical definition of being the confluence of the taenia and the origin of the sigmoid mesentery. This has been shown in a recent study of fifty patients to have a median of 19 cm (range: 11–35 cm) from the anal verge. The anterior peritoneal reflection was found at a median of 11 cm (range: 8–17 cm).[2] Trials of radiotherapy in rectal cancer have been restricted to tumours up to 16 cm from the anal verge. These definitions should be taken into account when interpreting trial data.

Target audience for the guideline

The guideline is intended primarily for the providers of care for New Zealanders with early colorectal cancer. It is also expected that the guideline will have implications for health service provider organisations and funders and may be read by patients with early colorectal cancer and their carers.

NZGG is committed to involving consumers in the development of all NZGG guidelines. Consumers are a part of the GDT, helping to determine the clinical questions to be included in the guideline, reviewing the evidence and forming the guideline recommendations.

Treaty of Waitangi

NZGG acknowledges the importance of the Treaty of Waitangi to New Zealand. It considers the Treaty principles of partnership, participation and protection as central to improving Māori health.

NZGG's commitment to improving Māori health outcomes means it works to identify and address Māori health issues relevant to each guideline. In addition, NZGG works to ensure Māori participation is a key part of the guideline development process. It is important to differentiate between involving Māori in the guideline development process (the aim of which is participation and partnership) and specifically considering Māori health issues pertinent to that guideline topic at all stages of the guideline development process. While Māori participation in guideline development aims to ensure the GDT considers Māori health issues, this is no guarantee of such an output; the entrenched barriers Māori may encounter when involved in the health care system (in this case, guideline development) need to be addressed. NZGG attempts to challenge such barriers by specifically identifying points in the guideline development process where Māori health must be considered and addressed. The guideline also weaves issues of relevance for Māori health throughout the document. Specific issues for Māori as a population group are described in Chapter 1, *Introduction and guideline context*.

Guideline development process

NZGG follows specific structured processes for guideline development. These processes in relation to this guideline are described is in this section, with further details outlined in Appendix 1, *Guideline development*.

Scoping phase

In 2009, the Ministry of Health's Bowel Cancer Taskforce identified the existing Australian National Health and Medical Research Council (NHMRC) endorsed *Clinical practice guideline for the prevention, diagnosis and management of colorectal cancer*[3] (chapters 8 to 23) as the guideline it would like adapted for use in New Zealand. NZGG responded to a request from the Ministry of Health to adapt this existing guideline to New Zealand circumstances.

The Ministry of Health required NZGG to assess the extent to which the NHMRC-endorsed guideline (chapters 8 to 23) could be adapted for the New Zealand context. NZGG convened the scoping Expert Advisory Group (EAG), comprising members nominated by the Ministry of Health. A one-day, face-to-face meeting was held where the NHMRC recommendations were reviewed and EAG members agreed on which recommendations were acceptable in their current format, and which needed updating either because new evidence had emerged or because the New Zealand context differed. In addition, the EAG identified a small number of new questions it believed were necessary for a New Zealand guideline to address. Fifteen clinical questions were proposed and agreed by the EAG (including questions for updating and new questions); these questions were systematically reviewed. For more details, see Appendix 1, *Guideline development*.

Where NHMRC recommendations have been accepted by the EAG, these are included in this guideline. Where NHMRC recommendations have been updated or where new questions have been added by the EAG, the reasons for the updates and new questions have been made clear.

For further information on how the NHMRC recommendations were developed, see the full text guideline at www.nhmrc.gov.au/publications/synopses/cp106/cp106syn.htm

Guideline development

Following agreement of the acceptance or otherwise of the NHMRC recommendations with the Ministry of Health, the multidisciplinary Guideline Development Team (GDT) was convened. The GDT comprised members nominated by a diverse range of stakeholder groups; the original EAG members remained part of the group and others joined to represent the interests of most stakeholder groups. The agreed new questions developed during the scoping phase were used to inform the search of the published evidence, from which the GDT derived systematic evidenced-based statements for best practice. A two-day, face-to-face meeting of the full GDT was held, plus additional teleconferences, where evidence was reviewed and recommendations were developed.

This guideline thus comprises a series of recommendations directly derived from the NHMRC guideline and accepted by the EAG where no additional research was required, and new recommendations based on the latest research evidence.

Full methodological details are in Appendix 1, *Guideline development*. This appendix also includes details of the GDT members and lists the organisations that provided feedback during public consultation on the guideline. See also Appendix 4, *Abbreviations and glossary*.

Summary

Key messages

- A patient navigator, care coordinator or support person should be involved to support patients and their families/whānau following a diagnosis of colorectal cancer and to assist in guiding them along the patient care pathway.
- Service providers should ensure that information about colorectal cancer care and support services meets the needs of different ethnic groups and their families/whānau.
- All people with colon or rectal cancer should be discussed at a Tumour Board meeting.
- Elective surgery for both colon and rectal cancers should be carried out by surgeons who have undergone specific training and exposure to these surgeries and who sustain a sufficient caseload and experience to maintain surgical skills.
- For people with resected node positive colon cancer (Stage III) who are to receive postoperative chemotherapy, combination chemotherapy with oxaliplatin and a fluoropyrimidine is recommended. People with resected node negative colon cancer (Stage II) with poor prognostic features may also be offered postoperative chemotherapy, and health practitioners should discuss the risks and benefits of treatments, including the uncertain benefits of treatment and the potential side effects.
- Preoperative or postoperative adjuvant therapy should be considered by a multidisciplinary team for all people with rectal cancer.
- People with colorectal cancer should be given written information outlining planned follow-up (eg, a discharge report) at discharge from treatment, including what they should expect regarding the components and the timing of follow-up assessments.

Summary of clinical practice recommendations

This is a summary of recommendations developed by the Guideline Development Team. The recommendations are grouped under headings and subheadings that correspond to the individual chapters and sections within chapters. Further details of the clinical questions, the New Zealand Guidelines Group (NZGG) and National Health and Medical Research Council (NHMRC) grading systems (for individual studies and recommendations based on the body of evidence) and other methodology are in Appendix 1, *Guideline development*.

1 Introduction and guideline context

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Ethnic disparities and cultural issues			
A patient navigator, care coordinator or support person should be involved to support patients and their families/whānau following a diagnosis of colorectal cancer, and to assist in guiding them along the patient care pathway			✓
Service providers should ensure that information about colorectal cancer care and support services meets the needs of different ethnic groups and their families/whānau			✓
Māori-specific and Pacific-specific cancer services or service components should be provided where a need is identified			✓
Health systems planners and service providers should improve access to services for ethnic groups, for example, by developing and supporting outreach and community-based clinics			✓
Health systems planners should support and develop Māori and Pacific participation in the colorectal cancer care workforce at all levels			✓
Service providers should collect and report accurate, high-quality ethnicity data at all stages of the patient pathway to ensure that the effectiveness of health services in reducing disparities can be monitored			✓
Service providers should monitor practice, including review of patient experiences, to foster culturally competent, patient-centred care			✓

2 General principles of care

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Multidisciplinary teams			
All people with colon cancer should be discussed at a Tumour Board meeting			B
All people with rectal cancer should be discussed at a Tumour Board Meeting			B
Every health practitioner involved in colorectal cancer care should actively participate in a multidisciplinary team			✓
The Tumour Board and multidisciplinary team involved in colorectal cancer care should provide culturally appropriate and coordinated care, advice and support			✓
The outcomes of Tumour Board and multidisciplinary team meetings should be communicated to the person with colorectal cancer and their general practitioner, and should be clearly documented in the medical records			✓
Supportive and rehabilitative care			
Psychosocial care is important. Psychological interventions should be a component of care as they can improve the quality of life for patients with cancer	I	Strongly recommended	
Supportive and rehabilitative care should be available to all people with colorectal cancer			✓
Communication and information provision			
During consultation, practitioners should make available to people with colorectal cancer the level and amount of information that will be most effective in enabling them to understand their condition and treatment options			✓
People with colorectal cancer should be acknowledged as key partners in the decision-making about their cancer management			✓

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2 General principles of care continued...			
Recommendations by chapter	**Grading systems used**		
	NHMRC level of evidence	**NHMRC practice recommendation**	**NZGG grade**
Practitioners should provide people with colorectal cancer information about their diagnosis, treatment options (including risks and benefits) and support services			✓
Practitioners should give people with colorectal cancer information about managing bowel function, particularly diet, following surgery			✓
Practitioners should encourage people with colorectal cancer to take notes or record a consultation and have a support person present			✓
Practitioners should maintain a patient hand-held record, where available			✓
Service providers and practitioners should ensure that high-quality evidence-based information resources in a variety of formats and languages are available for people with colorectal cancer			✓

3 Preoperative assessments

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Preoperative assessment for colon cancer should include clinical examination, complete blood count, liver and renal function tests, carcinoembryonic antigen (CEA), chest x-ray and contrast-enhanced computed tomography (CT) of the abdomen/pelvis/liver			C
Preoperative assessment should include colonoscopy of the entire large bowel. Where complete examination is not possible, imaging of the proximal colon with CT colonography (or with barium enema if CT colonography is not available) is recommended			C
If proximal parts of the colon are not directly visualised preoperatively, postoperative repeat colonoscopy should be undertaken within 12 months			C
In selected cases, preoperative microsatellite instability (MSI)/immunohistochemistry may be helpful in guiding surgical management			✓
PET-CT scanning is not recommended as part of routine preoperative assessment of non-metastatic colon cancer			C
Preoperative assessment for rectal cancer should include clinical examination, complete blood count, liver and renal function tests, carcinoembryonic antigen (CEA), chest x-ray and contrast-enhanced CT of the abdomen/pelvis/liver			C
Preoperative assessments for rectal cancer should include MRI for identifying circumferential resection margin (CRM) involvement and local staging			B
Preoperative assessment of possible T1 rectal cancers may include endorectal ultrasound (EUS) for local staging, as an alternative to MRI of the pelvis			B
Endorectal ultrasound should not be used as the sole assessment to predict CRM involvement in people with rectal cancer			B

4 Management of epithelial polyps

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Adenomas with focal malignancy may be managed safely by endoscopic polypectomy provided strict criteria for patient selection and histopathological assessment are adhered to. In particular, adenomas with focal malignancy should be well or moderately differentiated and excision should be complete	III-2	Recommended	

5 Preparation for surgery

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
All patients who have a reasonable chance of a postoperative stoma should be prepared for this possibility. This includes a visit, where possible, by the stomal therapy nurse	III-2	Recommended	
Bowel preparation is current standard practice before elective colorectal operations. However, recent randomised controlled trials have not demonstrated any conclusive benefit from this procedure. Accordingly, the previous guideline has been revised as follows: Mechanical bowel preparation is not indicated in elective colorectal operations unless there are anticipated problems with faecal loading that might create technical difficulties with the procedure, for example, laparoscopic surgery, low rectal cancers	I	Not recommended	
All patients undergoing surgery for colorectal cancer should receive prophylaxis for thromboembolic disease	I	Strongly recommended	
Unfractionated heparin, low molecular weight heparin, and intermittent calf compression are effective in reducing the incidence of thromboembolism	II	Strongly recommended	

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5 Preparation for surgery continued...

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Low molecular weight heparin has not been shown to be superior to low-dose heparin in colorectal surgical patients	II	Strongly recommended	
All patients undergoing colorectal cancer surgery require prophylactic antibiotics	II	Recommended	
A single preoperative dose of intravenous cephalosporin and metronidazole, or gentamicin and metronidazole, is an effective regimen	I	Strongly recommended	
Perioperative normothermia should be maintained	II	Recommended	

6 Elective surgery for colon cancer

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
High ligation of the lymphovascular pedicle does not confer any oncological benefit. Resection where feasible should extend to the origin of segmental vessels	III-3	Equivocal	
The no-touch isolation technique has no oncological benefit	II	Recommended	
Segmental resection is equivalent to extended resection in outcome	II	Equivocal	
Omental wrapping of anastomosis has no benefit	III-2	Strongly not recommended	
In experienced hands, laparoscopic surgery for colon cancer has equivalent outcomes to conventional surgery	I	Recommended	
Stapled functional end-to-end ileocolic anastomosis is recommended			A
Elective surgery for colon cancer should be performed by a surgeon with specific training and experience in colorectal surgery, and with sufficient caseload to maintain surgical skills			B

7 Elective surgery for rectal cancer

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Local excision of T1 rectal cancer may be used in selected cancer patients according to the following guidelines: • mobile tumour <3 cm • T1 on endorectal ultrasound • not poorly differentiated on histology (biopsy)	III-3	Equivocal	
A distal distance of 2 cm (fresh) is recommended in most instances, or 1 cm fixed	III-2	Recommended	
Sphincter-saving operations are preferred to abdominoperineal resection except in the presence of: • tumours such that adequate distal clearance (>2 cm) cannot be achieved • the sphincter mechanism is not adequate for continence • access to the pelvis makes restoration technically impossible (rare)	III-3	Equivocal	
For mid-to-low rectal tumours, the principles of extra fascial dissection and total mesorectal excision (TME) are recommended	III-2	Recommended	
Where technically feasible, the colonic reservoir is recommended for anastomosis within 2 cm from ano-rectal junction	II	Strongly recommended	
Routine drainage should only be considered for rectal cancers	II	Equivocal	
Elective surgery for rectal cancer should be carried out by a surgeon who has undergone a period of specialist exposure to this form of surgery during surgical training and who has maintained satisfactory experience in the surgical management of rectal cancer			B

8 Emergency surgery

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Primary anastomosis should be considered as a colectomy, with an ileocolic or ileorectal anastomosis	III-2	Equivocal	
Primary anastomosis could be considered for left-sided obstruction and may need to be preceded by on table colonic lavage	III-2	Equivocal	
Primary resection of obstructing carcinoma is recommended unless the patient is moribund			B
Colonic stenting for palliation of left-sided bowel obstruction in people with colorectal cancer is recommended, if endoscopic expertise can be readily accessed			B
Colonic stenting as a bridge to surgery for left-sided bowel obstruction in people with colorectal cancer may be considered for an individual, if endoscopic expertise can be readily accessed			C
People with colorectal cancer who have bowel obstruction and are being considered for colonic stenting should be invited to participate in randomised controlled trials, where these are available			✓

9 Adjuvant therapy for colon cancer

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
People with resected colon cancer should be considered for adjuvant therapy			✓
People with resected node positive colon cancer (Stage III) should be offered postoperative chemotherapy unless there is a particular contraindication, such as significant comorbidity or poor performance status			A
People with resected node negative colon cancer (Stage II) with poor prognostic features may be offered postoperative chemotherapy. Discussion of risks and benefits of treatment should include the potential but uncertain benefits of treatment and the potential side effects			C
For people with colon cancer who are to receive single agent postoperative chemotherapy, either capecitabine or bolus fluorouracil plus leucovorin are appropriate regimens			B
For people with resected node positive colon cancer (Stage III) who are to receive postoperative chemotherapy, combination chemotherapy with oxaliplatin and a fluoropyrimidine is recommended			A
Irinotecan should not be given as postoperative adjuvant chemotherapy for people with Stages I, II and III colon cancer Note: irinotecan is currently licensed in New Zealand for metastatic colorectal cancer only			A

10 Adjuvant therapy for rectal cancer

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Preoperative or postoperative adjuvant therapy should be considered by a multidisciplinary team for all people with rectal cancer			✓
Preoperative radiotherapy may lower the incidence of late morbidity compared to postoperative radiotherapy			C
For people with rectal cancer who are at risk of local recurrence, either preoperative short-course radiotherapy or preoperative long-course chemoradiation is recommended **Note:** Short-course radiotherapy – 25 Gy in 5 fractions; long-course radiotherapy – 45–50.4 Gy in 25–28 fractions			B
Preoperative long-course chemoradiation is recommended for people with rectal cancer who have a low rectal cancer or a threatened circumferential resection margin **Note:** Long-course radiotherapy – 45–50.4 Gy in 25–28 fractions			B
Where people are receiving long-course radiotherapy (preoperative or postoperative), concurrent chemotherapy should be considered			A

11 Follow-up after curative resection

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
All people who have undergone colorectal cancer resection should be followed up intensively			✓
All people who have undergone colorectal cancer resection and develop relevant symptoms should undergo clinical assessment			✓
For people with colon cancer at high risk of recurrence (Stages IIb and III), clinical assessment is recommended at least every six months for the first three years after initial surgery and then annually for a further two years or when symptoms occur			B
For people with colon cancer at lower risk of recurrence (Stages I and IIa) or for people with comorbidities restricting future surgery, clinical assessment is recommended when symptoms occur or by annual review for five years after initial surgery			B
All people with colorectal cancer should have a colonoscopy before surgery or within 12 months following initial surgery			B
For people with colon cancer at lower risk of recurrence (Stages I and IIa), follow-up colonoscopy every three to five years is recommended			B
For people with rectal cancer, digital rectal examination (DRE), proctoscopy or sigmoidoscopy should be undertaken at three months, six months, one year and two years after initial surgery. Thereafter colonoscopy should be undertaken at three- to five-yearly intervals			B
Follow-up should include physical examination and CEA			B

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11 Follow-up after curative resection continued...

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
All people with colorectal cancer Stages I to III should have liver imaging between years 1 and 3			B
The use of faecal occult blood testing as part of colorectal cancer follow-up is not recommended			B
Follow-up should be under the direction of the multidisciplinary team and may involve follow-up in primary care			✓
People with colorectal cancer should be given written information outlining planned follow-up (eg, discharge report) at discharge from treatment, including what they should expect regarding the components and the timing of follow-up assessments			✓

12 Synoptic reporting

Recommendations by chapter	Grading systems used		
	NHMRC level of evidence	NHMRC practice recommendation	NZGG grade
Pathology reporting of all colon and rectal cancer specimens should include structured (synoptic) reporting			C
Reporting of investigations and procedures (colonoscopy, radiology, operation notes, oncology treatment records) relating to colorectal cancer in a synoptic format is recommended			✓
TNM staging and the data required to stage the patient should all be recorded to allow national and international comparisons	III-3	Equivocal	

1 Introduction and guideline context

Colorectal cancer epidemiology

Colorectal cancer is an important public health problem; nearly one million new cases of colorectal cancer are diagnosed worldwide each year and half a million deaths.[4] Like most cancers, colorectal cancer is more common among older people. Men and women have similar rates of colon cancer, but men have considerably higher rates of rectal cancer.[5] In 2006, colorectal cancer was the most common cancer registered and the second most common cause of death from cancer in New Zealand, accounting for 14.8% of all cancer registrations and 14.7% of all deaths from cancer. Both registration and mortality rates fell between 1996 and 2006; male and female registration rates dropped 10.6% and 15.0% respectively, while mortality rates fell 28.9% for males and 16.8% for females.[6]

The age-standardised incidence rate in males is projected to fall to 71 per 100,000 (95% CI 53–94) by 2011, a decrease of 11% since 1996. However, the number of registrations among males is projected to increase from 1996 to 2011 by up to 29%, as the increasing population and ageing population offset the projected decrease in risk.[7] In females, the incidence rate is projected to fall by around 21% over the same period, and the number of registrations is projected to increase 16%. Despite the expected decline in mortality and incidence, colorectal cancer is predicted to rank second for incidence and third for cancer mortality among both genders in all age groups.[7]

Ethnic disparities and cultural issues

Disparities in health care outcomes and access exist between different ethnic groups in New Zealand. In 2006, colorectal cancer was the third most commonly registered cancer for Māori, and the third leading cause of death from cancer. For non-Māori, colorectal cancer was the most commonly registered and the second leading cause of death from cancer. Colorectal cancer is one of the few cancers for which Māori registration and mortality rates have historically been lower than non-Māori rates.[6,8] Māori are more likely to have distant disease than non-Māori (30.4% compared with 19.4%) and are more likely to have unknown stage at diagnosis than non-Māori (12.7% compared with 9.4%).[8] A study of Māori and non-Māori colorectal cancer deaths in New Zealand reported that Māori had significantly poorer cancer survival than non-Māori (HR 1.33, 95% CI 1.03–1.71) and noted that the primary contributory factors for Māori were patient comorbidity, smoking and markers of inequity in access to health care, which attributed one-third of the survival disparity.[9]

For non-Māori males, registration rates appear to have trended downwards. For Māori, however, rates for 2006 were very similar to those in 1996 (see Table 1.1). For females, the Māori registration rate increased markedly between 1996 and 2006, by 67.7% from 19.0 per 100,000 to 31.8 per 100,000. Conversely the registration rate of non-Māori females fell 16.9% over the same period, from 49.5 per 100,000 to 41.2 per 100,000.

Table 1.1 Colorectal cancer registrations per 100,000 from 1996 to 2006

	Males			Females		
	Total	Māori	Non-Māori	Total	Māori	Non-Māori
1996	61.6	41.3	62.9	47.8	19.0	49.5
1997	56.0	36.2	57.2	44.1	22.2	45.6
1998	56.8	47.6	57.7	45.2	25.5	46.4
1999	58.7	41.8	59.8	45.4	28.5	46.3
2000	54.2	35.6	55.4	46.5	25.3	48.0
2001	56.2	44.1	56.8	45.0	29.2	45.9
2002	55.2	42.8	55.9	42.5	27.9	43.4
2003	55.0	38.9	55.6	44.0	28.9	44.9
2004	53.6	34.9	54.6	44.6	26.6	45.5
2005	50.8	39.4	51.5	44.1	27.6	45.2
2006	55.1	42.5	55.8	40.6	31.8	41.2

Source: Cancer, new registrations and deaths 2006, Ministry of Health 2010.[6]

Mortality rates look to be decreasing for all groups except Māori females (see Table 1.2). In 2006, mortality rates for Māori males were 21.1% lower than in 1996 and for non-Māori males 29% lower than in 1996. The mortality rate for Māori females increased 49.2% over this time compared with a reduction in the mortality rate of 18.1% for non-Māori females.[6]

Table 1.2 Colorectal cancer mortality rates per 100,000 from 1996 to 2006

	Males			Females		
	Total	Māori	Non-Māori	Total	Māori	Non-Māori
1996	28.8	24.8	29.0	20.9	11.3	21.3
1997	26.8	23.4	27.0	18.4	12.9	18.7
1998	25.8	13.7	26.5	19.2	14.3	19.4
1999	26.0	24.4	26.0	19.3	9.7	19.7
2000	24.6	20.6	25.0	18.8	14.8	18.9
2001	25.5	20.5	25.7	18.4	13.2	18.6
2002	24.2	26.3	24.0	16.8	10.2	17.3
2003	22.2	20.8	22.1	17.0	11.2	17.2
2004	21.8	14.6	22.0	18.0	13.8	17.9
2005	22.6	21.9	22.6	17.7	11.4	18.0
2006	20.5	19.6	20.6	17.4	16.8	17.4

Source: Cancer, new registrations and deaths 2006, Ministry of Health 2010.[6]

Similarly to Māori, rates of registration and mortality for Pacific peoples with colorectal cancer are lower than the national averages.[10] Pacific males aged 65 years and over have below average mortality rates for colorectal cancer. Age-standardised rates of registration for Pacific males and females aged 65 years and under between 1996 and 2000 were less than 50 per 100,000 for both males and females. Age standardised rates for females aged 65 years and over were 100 per 100,000 and for males were 200 per 100,000. Registration rates for Pacific people of all ages were less than the national average.

Disparities in access to care

Ethnic disparities in colorectal cancer incidence and outcomes may be due in part to disparities in access to health care and services. While there is a lack of research examining the relationship between colorectal cancer outcomes and disparities in care in New Zealand, studies of access to cancer services in general suggest that similar ethnic disparities in access and outcomes are present.[11] Access to care includes the availability, affordability and appropriateness of services, information and health care workers, as well as the incorporation of philosophies and attitudes that facilitate the inclusion of different ethnic groups' concepts of health and wellbeing. Any barrier that prevents optimal access to care at any point on the patient's pathway has the potential to have an adverse impact on patient outcomes. Both the Māori[12] and Pacific[13] health strategies identify increasing access to care and services as one of the priority actions for improving health outcomes for Māori and Pacific peoples in New Zealand.

Multidimensional approaches to addressing disparities

Barriers to care can include geographic barriers such as the distance to travel for care because of the location of services or the lack of choice of provider; the financial costs of transport, child care, consultations or prescriptions; information and communication barriers; having to take time off work; feeling like a burden to others; and perceptions of the lack of cultural responsiveness of available health services to an individual's needs.[11]

The multidimensional nature of barriers to care requires a multidimensional approach to addressing these barriers. This approach may include addressing potential language barriers by providing information to patients and their families in a variety of forms and languages, providing interpreters to facilitate communication, providing outreach and community-based clinics to address the availability of services in rural areas, and addressing the financial costs of care, such as transport and child care costs. In addition, service providers should support health practitioners to receive training in culturally competent care. The effectiveness of strategies to improve access to care should be monitored through audit and the collection of quantitative data, as well as qualitative measures of patient experiences.

The integration of a patient-centred model that supports culturally competent care is of primary importance. Care is culturally competent when it integrates cultural practices, values and concepts in the provision of health services. Patient-centred care emphasises the importance of individual preferences, so that the wide diversity of health beliefs, values and care preferences within different ethnic groups are acknowledged and individual choice is respected.

Considerations for Māori with colorectal cancer

Traditionally, Māori tend to have a more holistic view of health than the majority of the New Zealand population, emphasising the inter-connectedness of physical, mental, spiritual, social and whānau aspects of wellbeing. Māori belief systems, such as views about the importance of whānau, individual mana, death and dying, and practices associated with tapu and noa continue to influence health behaviours and choices. These views may influence preferences for care, individual help-seeking behaviour and responses to health care providers.[14]

The *Māori Health Strategy, He Korowai Oranga (2002)*[12] aims to develop and support whānau ora, 'Māori families supported to achieve their maximum health and wellbeing', and recognises the central role of whānau in the individual and collective wellbeing of Māori in New Zealand.[15] Any model of service provision for Māori must incorporate a consideration of whānau, including extended family or wider community-based support people, and promote whānau inclusion and collective health and wellbeing. This will likely mean providing additional time and space for whānau to attend appointments and ensuring there are opportunities for discussion.

A study of Māori and non-Māori colorectal cancer deaths in New Zealand reported significant differences between Māori and non-Māori in terms of health service access.[9] Māori patients were less likely to be treated within the private sector and were more likely to be treated in secondary and smaller public health care facilities. Māori were four times more likely to live in rural areas compared with non-Māori and more likely to live in high deprivation areas. Given this, strategies to reduce disparities in access to care among Māori should address the location and accessibility of colorectal treatment and follow-up services as well as the financial cost of attending appointments for both the patient and their family/whānau.

Additional barriers to care revolve around the cultural fit of services and access to Māori-specific cancer services. A major factor in addressing these barriers is the development and support of the Māori cancer care workforce. Barriers to care will undoubtedly vary according to the specific context. In addition, there is a likelihood of significant overlap between different types of barriers and the impact of multiple barriers can be overwhelming for some of the most vulnerable groups.

Considerations for Pacific peoples with colorectal cancer

The term 'Pacific' describes a diverse group of people and increasingly includes multi-ethnic and New Zealand–born Pacific peoples, who identify with one or more of the Pacific cultures due to ancestry or heritage. While there is diversity in many aspects of culture and tradition between Pacific groups, there are some commonalities with regard to health and wellbeing.[16]

Traditionally, Pacific cultures are oriented towards the social group and concepts of holistic health care, which incorporate physical, spiritual, mental and community aspects of wellbeing. The role of the family is central and involving the family in the care process is important for Pacific peoples. Being aware of the diversity within Pacific cultures and respecting individual preferences for care will assist practitioners to understand the values and beliefs of a Pacific patient.

The priority outcomes and actions for Pacific health for 2010 to 2014 are outlined in the Ministry of Health document *'Ala mo'ui*.[13] *'Ala mo'ui* reinforces the importance of a holistic approach to Pacific health and wellbeing and of healthy, strong families and communities, and places priorities within the four guiding principles of:

- quality health care
- valuing family
- respecting Pacific culture
- working together.

Many Pacific peoples living in New Zealand use traditional methods of healing as well as Western medicine. Providing a non-judgmental approach to the use of traditional and alternative treatments will assist with patient rapport and compliance.

Language may be a barrier both to accessing information about services, including home help, for the patient and family and to open and effective communication between practitioner and patient. It can be difficult to determine whether there is a need for a professional interpreter, so this service should be offered to all patients in all clinical settings where there is any possibility of potential misunderstanding because of language differences between the practitioner and the patient. Non-professional interpreters, including other family members or friends, should be discouraged as some international evidence suggests this may lead to a poorer understanding of diagnosis and treatment options.[17,18] The use and choice of appropriate interpreters is an important part of cultural-competency training.

Limited information is available on Pacific peoples' access to care to inform the debate. However, Pacific peoples have been reported to experience similar access issues to Māori. Practical barriers to care (eg, cost, lack of time and difficulty obtaining an appointment) and cultural constraints (eg, discomfort with their health provider and a dislike of drugs) have been identified. Specific barriers to access that have been reported for Pacific peoples in New Zealand include language barriers, financial commitments taking priority over the need for health care, and a lack of understanding of the nature and/or need for an appointment.

NZGG recommendations

	Grade
A patient navigator, care coordinator or support person should be involved to support patients and their families/whānau following a diagnosis of colorectal cancer and to assist in guiding them along the patient care pathway	✓
Service providers should ensure that information about colorectal cancer care and support services meets the needs of different ethnic groups and their families/whānau	✓
Māori-specific and Pacific-specific cancer services or service components should be provided where a need is identified	✓
Health systems planners and service providers should improve access to services for ethnic groups, for example, by developing and supporting outreach and community-based clinics	✓
Health systems planners should support and develop Māori and Pacific participation in the colorectal cancer care workforce at all levels	✓
Service providers should collect and report accurate, high-quality ethnicity data at all stages of the patient pathway to ensure that the effectiveness of health services in reducing disparities can be monitored	✓
Service providers should monitor practice, including review of patient experiences, to foster culturally competent, patient-centred care	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Where this guidelines sits in the suite of New Zealand developed guidelines

Several guidelines and programmes have been developed to support health professionals to care for people with colorectal cancer in New Zealand. The guidelines, reports and programmes that follow have been published or are under way. For an overview of how this guideline fits within the context of other New Zealand guidance, see Figure 1.

Population screening

Ministry of Health Bowel Cancer Programme – screening

The Ministry of Health established a Bowel Cancer Programme in 2009, following a feasibility study of colorectal cancer screening and recommendations by an expert advisory group about whether New Zealand should have a national programme.[19] The programme's priority is to strengthen bowel cancer services across the country so they can effectively meet both the current demand and increased demand in the future. Part of this programme is to conduct a four-year bowel screening pilot that will begin by late 2011 to determine whether a bowel-screening programme should be rolled out nationally.[20]

People at increased risk of colorectal cancer

New Zealand Guidelines Group – *Surveillance and management of groups at increased risk of colorectal cancer*[21]

Following the 1998 report from the National Health Committee working party on population screening, the New Zealand Guidelines Group (NZGG) was commissioned to develop a guideline outlining groups that were at increased risk of colorectal cancer.[21] Recommendations were made for people with familial adenomatous polyposis (FAP); hereditary non-polyposis colorectal cancer (HNPCC); hamartomatous polyposis syndromes; hyperplastic polyposis syndrome; history of colorectal cancer; history of inflammatory bowel disease.

People presenting with symptoms

New Zealand Guidelines Group – *Suspected cancer in primary care*[22]

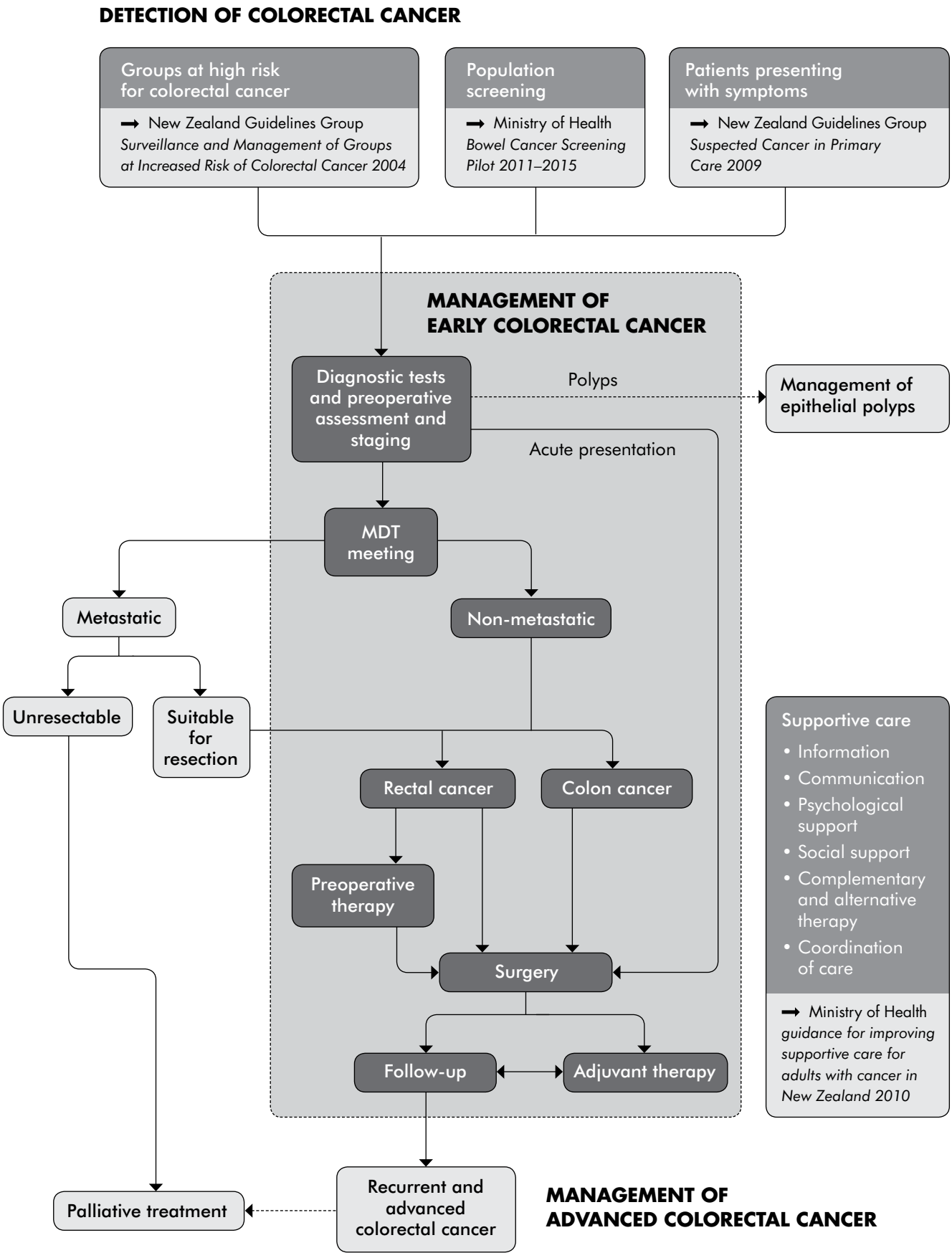
NZGG was commissioned to develop a primary care guideline for people presenting with symptoms suggestive of cancer. The guideline includes a chapter on colorectal cancers and presents recommendations for referral criteria and assessment and investigation in the primary care setting. The guideline covers the period from a person's first contact with a primary care practitioner with a sign or symptom suggestive of cancer through to their first specialist appointment.

Supportive care

Ministry of Health – *Guidelines for improving supportive care for adults with cancer in New Zealand*[23]

In July 2007, the Ministry of Health established an expert advisory group to oversee the development of supportive care guidance for adults affected by cancer. The guidance relied heavily on the UK-based National Institute for Health and Clinical Excellence (NICE) manual *Guidance on cancer services: Improving supportive and palliative care for adults with cancer*.[24] The aim of the New Zealand guidance document is to improve the quality of life for people affected by cancer by improving access to and the quality of supportive care in New Zealand. The guidance suggests best-practice service approaches that will help to ensure that adults with cancer and their families/whānau have access to the supportive care they need throughout the various stages of cancer, from diagnosis onwards.

Figure 1 Management of early colorectal cancer in the New Zealand context



Note: MDT=multidisciplinary team. See also Appendix 4, *Abbreviations and glossary*.

2 General principles of care

This chapter addresses general principles of care for people with colorectal cancer, including:

- the role of multidisciplinary teams (MDTs)
- supportive and rehabilitative care
- communication and information provision
- the timing of treatment.

Role of multidisciplinary teams

→ *Appendix 1 NHMRC*

Question development

The National Health and Medical Research Council (NHMRC) guideline discusses the principles of multidisciplinary care in general terms for Australians with colorectal cancer. The Guideline Development Team (GDT) felt that a specific question about the role of MDTs was an important consideration and needed additional clarification for the New Zealand context; a systematic review was undertaken to answer a new question on MDTs.

Clinical question: What is the role of multidisciplinary teams?

Body of evidence

Guidelines

Five clinical practice guidelines were identified that made recommendations for multidisciplinary teams for people with colon cancer.[25–29] Most guidelines were in agreement that a multidisciplinary team approach is necessary for treating and managing people with colorectal cancer. Recommendations focused on prompt, appropriate and seamless care. Some guidelines also recommended that a named member of the MDT should be the principal clinician (eg, the surgeon in the early stages of the disease, oncologist during adjuvant treatment, and oncologist or palliative care physician at later stages).

Systematic reviews

No systematic reviews were identified.

Primary studies

One historical case control study was identified that was considered to be of 'average' quality and reported on pathological outcomes.[30]

Four cohort studies were identified; two studies were considered to be of 'good' quality and reported on survival and treatment outcomes.[31,32] One retrospective cohort study was of average quality and evaluated the impact of MDT discussion of a preoperative magnetic resonance imaging (MRI) strategy on treatment-related outcomes.[33] One retrospective cohort study reporting on pathological outcomes could not be graded for quality due to lack of reported information.[34]

Other studies

One non-systematic review was identified that described practical barriers to the successful implementation of a working MDT.[35] The review found that despite an increase in the delivery of cancer services via this method, research showing the effectiveness of an MDT is scarce.

Summary of findings

Survival

A good-quality cohort study reviewed the effect of the implementation of the Calman-Hine recommendations for colorectal cancer patients (n=11,548) in the Yorkshire Cancer Regional Health Authority in the United Kingdom between 1995 and 2000.[32] These recommendations included the development of a formalised MDT discussion for colorectal cancer patients.[32] A 25% increase in a 'team score' (based on adherence to the Cancer Manual) was associated with a 3% reduction in the risk of death for all colorectal cancer patients (HR 0.97, 95% CI 0.94–0.99, p=0.01) and a 4% reduction for colon cancer alone (HR 0.96, 95% CI 0.93–0.99, p<0.01). A 1% (non-significant) decrease was observed for rectal cancer patients. The authors concluded that complete adherence to the Cancer Manual for implementation of an MDT may improve survival further. Uniformity of standards was felt to be essential for the maintenance of national standards. The use of a 'team score' is unclear in that it reports collaboration but not adherence to administrative standards.[32]

A good-quality cohort study compared three-year survival before (n=176) and after (n=134) the instigation of a colorectal MDT in patients undergoing colectomy for colorectal cancer (Dukes B or greater).[31] Three-year survival for Dukes C patients was 58% in the pre-MDT group and increased to 66% following the formation of the MDT (p=0.02). There was no significant difference in three-year survival in Dukes B patients before or after the formation of the MDT. MDT involvement in patient care was found to be an independent predictor of survival (HR 0.73, 95% CI 0.54–0.98, p=0.04) along with age (p=0.003) and Dukes stage (p=0.0002).[31]

Limited evidence indicates that the formation of an MDT and adherence to treatment standards may increase survival for patients with colon cancer. The outcomes for rectal cancer patients are unclear.

Pathology

An average-quality cohort study showed that MDT discussion of MRI and the implementation of a preoperative treatment strategy significantly reduced positive circumferential margins in patients with rectal cancer.[33] In potentially curative cases, 24% of patients proceeded to surgery without preoperative discussion of MRI results. The positive circumferential margin was 26% in those not discussed compared with 1% in those who were discussed by the MDT. One year after the introduction of a policy of mandatory MRI-based MDT discussion, the positive circumferential margin rate was reduced to 3%.[33]

An average-quality case control study reported a significant improvement in the harvesting of 12 or more lymph nodes following the formation of an MDT (67%) compared with a group of patients before the MDT was created (27%).[30]

An ungraded case series reported on a group of patients who had been discussed by an MDT and whose prognosis of positive circumferential margin had been predicted using an algorithm based on MRI and clinical findings.[34] Subsequent treatment was then based on these predictions. Of the 77 patients who were predicted to have a negative margin and received surgery alone, 15.5% were subsequently found to have a positive circumferential margin on the histological specimen. Those patients who were predicted to have threatened or involved margins were treated preoperatively with chemoradiation to downstage the disease. Of these, 38.4% were subsequently found to have positive margins on histological specimens. The study lacked any comparator, so the interpretation of the data is limited.

It appears that MDT discussion may produce more favourable outcomes than if no MDT discussion took place in terms of reducing the positive circumferential margin rate and improving the harvesting of lymph nodes.

Treatment

A good-quality cohort study reporting an evaluation of the Calman-Hine recommendations for MDT formation found that a 25% increase in the 'team score' was not associated with increased use of chemotherapy or preoperative radiotherapy; neither was any relationship found between adherence to the manual of cancer standards and the use of anterior resection.[32]

A good-quality cohort study noted that significantly more patients were prescribed adjuvant chemotherapy after the formation of an MDT (31.3%) compared with before formation (13%) ($p=0.0002$).[31]

Recommendation development

The GDT discussed the role of MDTs in New Zealand and shared its strategies for ensuring discussions take place with colleagues about patient care. The GDT discussed communication between health professionals and with patients, and it emerged that within the GDT different types of MDT meetings took place depending on the setting. For example, some hospitals held regular MDT meetings with all hospital staff involved in patient care, while other hospitals used less formal methods. The GDT was reluctant to stipulate the timing or frequency of MDT meetings because it may not be practical for different care settings (eg, smaller regional hospitals, larger urban hospitals) to function in the same way. The GDT agreed with the evidence that MDT discussion is likely to produce more favourable outcomes for patients than if no MDT discussion took place.

It was also noted that some confusion exists between MDT and Tumour Board meetings. Specifically, a Tumour Board comes together to discuss treatment planning for a patient with the staff directly responsible for administering the treatment, while MDTs offer a more holistic approach to the care of the patient and include staff from a wider variety of professions (see below). The GDT noted that both of the terms, MDT and Tumour Board, required definitions to clearly demonstrate the differences between them. The GDT decided to use the following definitions.

The **MDT** is a group of professionals from diverse disciplines who come together to provide comprehensive assessment and consultation (ie, a wider scope of participation and goals than those of a Tumour Board) and may include nursing staff, palliative care staff, general practitioners, research staff, occupational therapists, pharmacists and psychologists with the aim of using their skills and knowledge to conduct a comprehensive multidimensional assessment and plan to maintain the best physical, mental, emotional, functional and social status of the patient.[36,37]

The **Tumour Board** is a treatment planning approach in which doctors who are experts in different specialties or disciplines review and discuss the medical condition and treatment options for a patient. In cancer treatment, a Tumour Board may include a medical oncologist (who provides cancer treatment with drugs), a surgical oncologist (who provides cancer treatment with surgery), a radiologist, and a radiation oncologist (who provides cancer treatment with radiation).[38]

NZGG recommendations

	Grade
All people with colon cancer should be discussed at a Tumour Board meeting	B
All people with rectal cancer should be discussed at a Tumour Board meeting	B
Every health practitioner involved in colorectal cancer care should actively participate in a multidisciplinary team	✓
The Tumour Board and multidisciplinary team involved in colorectal cancer care should provide culturally appropriate and coordinated care, advice and support	✓
The outcomes of Tumour Board and multidisciplinary team meetings should be communicated to the person with colorectal cancer and his or her general practitioner, and should be clearly documented in the medical records	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Supportive and rehabilitative care

➞ *Chapter 18 NHMRC*

Question development

The NHMRC guideline reviewed the literature to investigate the importance of supportive and rehabilitative care. The GDT accepted the recommendation made by the NHMRC (below) but considered it important to narratively review the literature with special emphasis on the New Zealand context.

NHMRC recommendation

	Level of evidence	Practice recommendation
Psychosocial care is important. Psychological interventions should be a component of care as they can improve the quality of life for the patients with cancer	I	**Strongly recommended**

Levels of evidence

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one properly designed randomised controlled trial.

III-I Evidence obtained from well-designed pseudo randomised controlled trials (alternate allocation or some other method).

III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.

IV Evidence obtained from case series, either post-test or pre-test/post-test.

For more information please refer to chapter 18 of the NHMRC review (pp 207–211).

Supportive and rehabilitative care in New Zealand

Receiving a diagnosis of colorectal cancer is likely to be a significant and life-changing event for most people who are then faced with both emotionally and physically demanding treatment options. For patients to understand how they need to adapt their lifestyle to best cope with managing colorectal cancer, the right information needs to be delivered to them in a supportive environment where the psychological, social and physical aspects of care should be taken into account.

A recent Ministry of Health guideline for improving supportive care for adults with cancer in New Zealand aims to improve the quality of life for people affected by cancer, specifically by improving access to support and improving the quality of supportive care in New Zealand.[23] Supportive and rehabilitative care were defined as:

> The essential services required to meet a person's physical, social, cultural, emotional, nutritional, informational, psychological, spiritual and practical needs throughout their experience with cancer.

This definition was agreed by the GDT to be the most appropriate definition for use in this guideline. The guidance suggests that psychological support and services be available as a part of an integrated cancer service, and that there be prompt referral for patients who are significantly affected. A range of levels of service should be available as well as information about how to access them if the need for support arises at a later stage.[23]

Psychosocial factors are an important part of a patient's pathway of care, and support services and interventions aim both to help patients when difficulties and distress arise and to maintain quality of life, which has been shown to impact on survival in colorectal cancer patients.[3]

Quality of life

Distress can occur at any stage during diagnosis and/or treatment and can include clinical depression, anxiety and other disorders. Up to a third of people living with cancer experience clinically significant psychological distress or disturbance, and this proportion increases for patients with poorer outcomes and greater disease burden.[3,23] Groups of patients who tend to find it more difficult to adjust to diagnosis and treatment than others are those who are young; are female; have a stoma; have experience of cumulative losses; are socially isolated or socially deprived, widowed, separated or divorced; have a history of psychiatric disorder; or are in financial difficulty.[3,23]

Age, work and marital status can help predict people's ability to cope with colorectal cancer. One study reported that patients working at time of diagnosis reported better role functioning than those who were not working.[39] Another study (with two publications) reported that married patients tended to cope better with colorectal cancer than unmarried patients and that women coped better than men.[40,41] One study investigating quality of life reported similar scores between older patients (aged 70 to 81 years) with colorectal cancer and those without. However, patients aged under 60 years were more likely to report higher levels of distress than those of the same age without colorectal cancer.[39] A cancer diagnosis can also cause changes in health behaviour. One study reported that one year after diagnosis, patients in one study were more likely to be underweight and to have stopped smoking.[42]

Patients with colorectal cancer can also have different perceptions of risk and worry; one study reported that females and younger patients were more likely to think that their cancer would recur and experienced higher anxiety and tension.[43]

After surgery for colorectal cancer, patients are likely to experience physical limitations as a result. Sexual dysfunction, increased bowel movements, diarrhoea or constipation, flatus, odour and diet can interfere with quality of life and prove an ongoing problem for colorectal cancer survivors.[3] Patients who have a stoma have reported particular difficulty in social functioning (eg, problems with work, frequency of social contacts and quality of relationships).[39] Patients with stoma can also experience significant problems with the stoma such as leakage, odour and late complications.[3]

Psychosocial and other interventions

The NHMRC guideline reports that psychosocial care is important and recommends that psychological interventions should be a component of care as they can improve emotional adjustment, functional status, knowledge of disease and treatments, treatment and disease-related symptoms, and overall quality of life.[3] Meta-analyses have reported that psychological interventions are effective in managing distress in cancer patients[3,44] although the effect on survival remains unclear.[45,46] Psychological interventions are available, including psychotherapy, relaxation-based therapies, cognitive behavioural therapy, supportive-expressive therapy and telephone interventions.[3,42]

Physical interventions have also been shown to have an effect on quality of life for cancer patients. One study reported that higher levels of physical activity after diagnosis had a beneficial effect on survival outcomes with benefits increasing as the level of exercise increased.[47–49] Reducing fatigue was investigated in a meta-analysis where patients were educated about fatigue and were taught self-care or coping, and strategies for activity management. Studies using fatigue-specific interventions delivered by an oncology nurse during cancer treatment showed promising results for this type of therapy.[50] Diet is also an important aspect of post-treatment care for colorectal cancer patients. One study showed that dietary counselling by phone can improve diet in colorectal cancer patients and that interventions to improve both diet and exercise had beneficial effects on quality of life.[51]

Coordination of support

Cancer care services in New Zealand are delivered by a variety of providers, and some patients need to travel and spend time away from home to access these services. There is a general consensus among studies that reducing fragmented and poorly coordinated follow-up care is beneficial to cancer patients.[52]

The Ministry of Health suggests that a coordinator of continuity of care provision helps to support the patients through the treatment process and can help the family/whānau and carers know who to ask for advice. The coordination may be performed from within an MDT. For example, coordination may be undertaken by a specific member such as a social worker or patient navigator who is non-clinical but specifically trained (a system is being piloted in three centres in New Zealand[1*]) or some district health boards (DHBs) may use a hospital-based clinical nurse to liaise with primary health care and community-based services. The services that patients are referred to should be of high quality and appropriate to a patient's needs, including cultural needs. The coordinating care model needs to be culturally appropriate and improve access for Māori and Pacific peoples to services. Coordinating cancer care and support models require independent evaluation. People with cancer and their families may require forms of emotional, social and economic support. The need for these should be routinely, regularly and systematically assessed, and information about the range of services available and how to access them should be provided. In summary, there should be an integrated and coordinated system that involves the patient and their family/whānau, support agencies and health professionals and encompasses both the hospital and the community.[23]

NZGG recommendations

	Grade
Supportive and rehabilitative care should be available to all people with colorectal cancer	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Communication and information provision

➞ *Chapter 4 NHMRC*

Information resources

Many cancer patients and their families feel poorly informed.[23,53] Most would like to receive as much information as possible to help them understand how colorectal cancer may affect them, to anticipate challenges they may have to face and to plan.[53,54] The Ministry of Health suggests that health professionals have a responsibility to provide access to the available resources, and that these information resources should be high-quality, evidence-based, regularly updated and in a multimedia format. The resources should also be culturally and ethnically sensitive and relevant.[23]

A review of current clinical practice guidelines for the psychosocial care of cancer survivors suggests information should be provided for cancer patients in terms of planning for care, psychosocial needs and the resources available.[54] Care planning could include a description of follow-up care, recommended cancer screening and other tests and examinations, information about signs of recurrence and second tumours, possible late- and long-term treatment effects, and effective chemoprevention strategies for secondary prevention.

* See www.moh.govt.nz/moh.nsf/indexmh/cancercontrol-strategyandactionplan-bowelcancerscreening#absp

The psychosocial information that patients require could include the possible effects of cancer on marital or partner relationships, sexual function, parenting, financial status and employment status. Patients may also receive information about resources available in their community (eg, support groups sponsored by cancer service organisations) and websites designed specifically to assist post-treatment survivors.[54] There are many sources of information about the cancer journey for consumers; clinical teams should maintain a good working knowledge of consumer information resources available locally and nationally and ensure patients are offered the materials directly or have easy access to them.

Communication

Communicating effectively with patients is critical; as it helps patients to understand their options and make informed decisions. Guidance from the Ministry of Health suggests that all health professionals undertake communication skills training, including inter-cultural communication skills and that these skills should be updated periodically. Cultural advisors, trained patient advocates and interpreters should be available, but health professionals should be able and supported to communicate with all those affected by cancer, including Māori, Pacific peoples, people of other ethnicities and people with impairments. These communication skills also include ensuring that patients and carers understand the type, benefit and risks of treatments and procedures that are available.[23]

Patients prefer information based on their own medical records and situation, rather than general information about colorectal cancer. The Scottish Intercollegiate Guideline Network (SIGN) guideline recommends that health care professionals should consider giving written summaries or audio tapes of consultations to people who would like them, as this has been shown to help patients recall information and to feel satisfied with what they were told.[53] Patient diaries, or hand-held records, are a recent approach being trialled to improve communication between patients and practitioners. Patients are given copies of their diagnosis and the diary is updated with information on their diagnosis, treatment, appointment times and any other information about support they receive from any provider. The diary is beneficial to both clinicians and patients who can quickly and easily be brought up-to-date with treatment and support needs.

NZGG recommendations

	Grade
During consultation, practitioners should make available to people with colorectal cancer the level and amount of information that will be most effective in enabling them to understand their condition and treatment options	✓
People with colorectal cancer should be acknowledged as key partners in the decision-making about their cancer management	✓
Practitioners should provide people with colorectal cancer information about their diagnosis, treatment options (including risks and benefits) and support services	✓
Practitioners should give people with colorectal cancer information about managing bowel function, particularly diet, following surgery	
Practitioners should encourage people with colorectal cancer to take notes or record a consultation and have a support person present	
Practitioners should maintain a patient hand-held record, where available	✓
Service providers and practitioners should ensure that high-quality evidence-based information resources in a variety of formats and languages are available for people with colorectal cancer	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Timing

The GDT discussed the timing of investigations and treatment of colorectal cancer and recognised that there is no existing evidence (nationally or internationally) and no practice guidelines for secondary care. The GDT is aware that timing is resource-dependent and that it is important to get investigations started as soon as possible. National targets for radiotherapy state that treatment should be commenced within four weeks, but there is no known evidence to support this. It is understood that waiting for investigations and treatment is a particularly anxious time for patients. The GDT discussed the resource implications for putting timeframes on investigations and treatment but the team recognised that colorectal cancer management involves multiple stages and multiple disciplines. Investigations and treatment should be provided in a timely fashion and be under way as soon as is feasible.

3 Preoperative assessments

→ *Chapter 8 NHMRC*

This chapter addresses preoperative assessments for people with colorectal cancer, including:

- preoperative assessments for colon cancer
- preoperative assessments for rectal cancer.

Preoperative assessments include patients who have already been referred because of suspicious bowel symptoms or who have undergone some initial testing in primary care that has aroused suspicion.

Question development

Of the two National Health and Medical Research Council (NHMRC) clinical questions and recommendations for this chapter, one was deleted as it was outside the scope of this guideline and another was re-worded and a full review undertaken. One recommendation made by the NHMRC about fluorodeoxyglucose positron emission tomography (FDG-PET) scans for recurrent colorectal cancer is outside the scope of this guideline. The GDT identified one question about investigations for colorectal cancer, and decided it would be better re-worded as two questions and that these questions required updating. Systematic reviews were undertaken to answer these. The reworded questions asked by the GDT were:

- What preoperative investigations need to be done for colon cancer?
- What preoperative investigations need to be done for rectal cancer?

Where studies of preoperative assessments were identified that related to people with colorectal cancer with no separate analyses of colon or rectal cancer, these were considered under the subheading colon cancer.

Preoperative assessments for colon cancer

Clinical question:	What preoperative investigations need to be completed for colon cancer?

Body of evidence

Guidelines

Five clinical practice guidelines were identified that made recommendations for preoperative assessment for people with colon cancer.[26,29,55–57] Most guidelines were in agreement on preoperative assessments necessary to make an informed diagnosis, these included:

- clinical examination
- pathology review
- colonoscopy of the entire large bowel (ie, with postoperative repeat colonoscopy if proximal parts of the colon were not accessible preoperatively)

- complete blood count, platelets, chemistry profile, carcinoembryonic antigen (CEA)
- chest/abdominal/pelvic computed tomography (CT) scanning to assess cancer stage and metastatic spread
- liver and renal function tests (ultrasound imaging of the liver may be used to check for metastatic disease but negative findings may not be reliable).

Systematic reviews

Tumour markers

One systematic review was identified that examined the use of tumour markers in the preoperative investigation of colorectal cancer where there were no analyses of colon or rectal cancer patients separately.[58] This systematic review updated the American Society of Clinical Oncology (ASCO) guidelines, searching databases from 1999 to 2005 for markers that had previous recommendations and from 1966 to 2005 for new markers. For most of the markers, only case series were identified in the literature and this limited the recommendations that could be made regarding their use. Recommendations were as follows.

- CEA: Staging/treatment planning: CEA may be ordered preoperatively in patients with colorectal carcinoma if it would assist in staging and surgical treatment planning. Although elevated preoperative CEA may correlate with poorer prognosis, data are insufficient to support the use of CEA to determine whether to treat a patient with adjuvant therapy.
- CA 19-9 as a marker for colon cancer: Present data are insufficient to recommend CA 19-9 for staging patients with colorectal cancer.
- DNA ploidy or flow cytometric proliferation analysis as a marker for colon cancer: Neither flow cytometrically derived DNA ploidy (DNA index) nor DNA flow cytometric proliferation analysis (% S phase) should be used to determine prognosis of early-stage colorectal cancer.
- *p*53: Present data are insufficient to recommend the use of *p*53 expression or mutation for staging patients with colorectal cancer.
- Ras oncogene: Present data are insufficient to recommend the use of the ras oncogene for staging patients with colorectal cancer.
- TS, DPD and TP: Prognosis: none of the three markers – TS, DPD or TP – is recommended for use to determine the prognosis of colorectal carcinoma. There is insufficient evidence to recommend use of TS, DPD or TP as a predictor of response to therapy.
- MSI/hMSH2: Microsatellite instability (MSI) ascertained by PCR is not recommended at this time to determine the prognosis of operable colorectal cancer nor to predict the effectiveness of FU adjuvant chemotherapy.
- 18q-/DCC: Assaying for LOH on the long arm of chromosome 18 (18q) or DCC protein determination by immunohistochemistry should not be used to determine the prognosis of operable colorectal cancer, nor to predict response to therapy.

Imaging modalities

One systematic review reviewed the use of FDG-PET and dedicated PET scanners to evaluate 11 cancers, including gastrointestinal cancer.[59] The methodology of the systematic review was robust, but the authors noted that the overall quality of included studies was not high. Details regarding the characteristics of patients in included studies were omitted from the report, limiting the ability to draw conclusions about patient subgroups. The authors reported an overall sensitivity and specificity of FDG-PET for detecting hepatic metastases of greater than 85% in most studies, and suggested that FDG-PET is beneficial in addition to CT in the preoperative diagnostic work-up of patients with colorectal cancer with potentially resectable hepatic metastases.

Primary studies

No additional primary studies were identified.

Summary of findings

The evidence base for the use of preoperative investigations in colon cancer was small and limited by a lack of high-quality primary studies.

The review of tumour markers identified mainly case series and limited recommendations were made.[58] CEA was recommended as part of the preoperative workup but insufficient information was detected to recommend the use of any other markers.

The systematic review of imaging modalities suggested that FDG-PET is beneficial in addition to CT in the preoperative diagnostic workup of patients with colorectal cancer with potentially resectable hepatic metastases.[59]

Recommendation development

The GDT discussed the evidence base for this clinical question and concluded that the evidence is limited.

To assist in recommendation development, the GDT referred to an Australian study evaluating the role of FDG PET-CT in the management of primary rectal cancer rather than colon cancer.[60] Conventional imaging was compared to PET-CT and caused a change in stage from conventional imaging in 26 patients (31%); 14% were upstaged and 17% were downstaged. PET-CT also altered management intent in seven patients (8%) (curative to palliative six patients; palliative to curative one patient). The GDT felt that more robust evidence was required and it expects to see more published studies in the future.

The GDT discussed MSI/immunochemistry and noted the lack of high-level evidence on this issue. It appears that these methods may be useful in identifying gene mutations, but it is unclear whether MSI/immunochemistry influences outcomes due to lack of data, and there is a lack of clarity on their role in surgery.

The GDT discussed the evidence for CT and found no evidence to support routine chest CT. Although chest CT is included in some of the guideline recommendations, the GDT had concerns about recommending chest CT because of the number of incidental findings leading to subsequent investigations and possible harm as a result.

NZGG recommendations

	Grade
Preoperative assessment for colon cancer should include clinical examination, complete blood count, liver and renal function tests, carcinoembryonic antigen (CEA), chest x-ray and contrast-enhanced CT of the abdomen/pelvis/liver	C
Preoperative assessment should include colonoscopy of the entire large bowel. Where complete examination is not possible, imaging of the proximal colon with CT colonography (or with barium enema if CT colonography is not available) is recommended	C
If proximal parts of the colon are not directly visualised preoperatively, postoperative repeat colonoscopy should be undertaken within 12 months	C
In selected cases, preoperative microsatellite instability (MSI)/immunohistochemistry may be helpful in guiding surgical management	✓
PET-CT scanning is not recommended as part of routine preoperative assessment of non-metastatic colon cancer	C

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Preoperative assessments for rectal cancer

Clinical question: What preoperative investigations need to be completed for rectal cancer?

Body of evidence

Guidelines

Five clinical practice guidelines were identified and made recommendations for preoperative assessment for people with rectal cancer.[27–29,56,61] Most guidelines were in agreement on preoperative assessments.

Preoperative staging (derived from the guidelines) should consist of:

- complete history and physical examination
- complete blood count
- digital rectal examination and rigid proctosigmoidoscopy
- colonoscopy (pre- or post-)
- liver and renal function tests
- CEA
- chest, abdominal and pelvic CT
- CT or MRI or ultrasound of liver and abdomen
- endorectal ultrasound or endorectal or pelvic MRI.

Systematic reviews

Six systematic reviews and meta-analyses of varying quality were identified that examined the use of imaging techniques in the preoperative staging of rectal cancer. Three of the meta-analyses compared different modalities (MRI, CT and endorectal ultrasound [EUS]) while three others examined the performance of either MRI or CT.

Two systematic reviews completed meta-analyses comparing the diagnostic performance of MRI, CT and EUS in patients with rectal cancer.[62,63] Both reviews included studies that compared only preoperative imaging results with a histological reference standard and in which sufficient raw data to calculate sensitivity and specificity were provided.

One of these systematic reviews completed a high-quality review of 90 studies encompassing 299 data sets and reported pooled diagnostic performance for each of the modalities at different stages of disease.[62] For muscularis propria invasion, EUS and MRI had similar sensitivities; specificity of EUS (86%, 95% CI 80–90) was significantly higher than that of MRI (69%, 95% CI 52–82, p=0.02). For perirectal tissue invasion, sensitivity of EUS (90%, 95% CI 88–92) was significantly higher than that of CT (79%, 95% CI 74–84, p<0.001) and MRI (82%, 95% CI 74–87, p=0.003); specificities were comparable. For adjacent organ invasion and lymph node involvement, estimates for EUS, CT and MRI were comparable. The summary receiver operating curve (ROC) curve for EUS of perirectal tissue invasion showed better diagnostic accuracy than that of CT and MRI. Summary ROCs for lymph node involvement showed no differences in accuracy. Limited data were available for spiral CT or MRI for mesorectal fascia identification. The quality of included studies was moderate.

The other systematic review, of average quality, compared the ability of MRI, CT and EUS to detect circumferential resection margin (CRM) involvement and nodal status in the staging of rectal cancer.[63] Only seven studies of CRM involvement were identified, all of which used MRI, with sensitivity ranging from 60% to 88% and specificity ranging from 73% to 100%. The summary ROC, with a sensitivity of ~80%, suggested a false positive rate of ~20%. Eighty-four studies of nodal status were included (EUS=54, MRI=29, CT=18), with EUS having a better pooled diagnostic odds ratio (DOR=8.83) than CT (DOR=5.86) or MRI (DOR=6.53). When summary ROCs were compared, there was no significant difference in the performance of the three modalities in predicting nodal status. MRI was recommended as the only modality that detects CRM involvement with any accuracy. None of the three modalities performed well in predicting nodal status. No confidence intervals were reported for the odds ratios, making it difficult to assess the accuracy of the findings.

The diagnostic performance of MRI in predicting CRM involvement in rectal cancer patients was examined by one good-quality systematic review.[64] Nine studies were included with both pooled sensitivity (Se=94%, 95% CI 90–97%) and specificity (Sp=85%, 95% CI 81–89%) being relatively high. Subgroup analyses indicated that study quality, the type of magnet and coil used, and the number of interpreters of the imaging affected how well MRI predicted CRM involvement. However, the number of studies included in some subgroup analyses was small. The authors suggested that MRI should be used as the primary imaging modality in local staging of rectal cancer.

A systematic review of poor quality suggested that neither MRI nor EUS could successfully detect the depth of tumour invasion across all four tumour categories with EUS performing better than MRI in category T1 and T2 disease and both modalities performing equally well in category T3 and T4 disease.[65] Accuracy in nodal staging was relatively poor for both modalities.

The remaining meta-analyses were of good quality and examined only one imaging modality. When EUS was used to predict nodal status, one meta-analysis (n=35 studies) reported a pooled sensitivity of 73.2% (95% CI 70.6–75.6) and specificity of 75.8% (95% CI 73.5–78).[66] Two systematic reviews conducted meta-analyses of the ability of EUS to predict tumour stage and identified 42 studies of low to moderate quality, most of these being consecutive case series.[66,67] Pooled sensitivities ranged from ~80% to 95% and specificity from ~90% to 98% with EUS performing better at higher stages of disease (T3 and T4). The diagnostic odds ratios were high for T1, T3 and T4 disease.

Primary studies

No additional primary studies were identified.

Summary of findings

The included meta-analyses and systematic reviews were limited by a lack of high-quality studies to include in their analyses, most of which were case series without comparable control groups. Only two meta-analyses were able to compare the performance of two or more imaging modalities.

Depth of tumour invasion

Endorectal ultrasound as a good predictor of the depth of tumour invasion at early stages of disease was suggested by two reviews.[62,65] One review suggested that EUS and MRI are complementary imaging modalities, with EUS being a good initial diagnostic tool in preoperative investigations and MRI providing additional information regarding CRM involvement.

Circumferential resection margin involvement

One systematic review examined the ability of EUS, CT and MRI to detect CRM involvement and identified only seven studies, all of which used MRI.[63] MRI performed well in detecting CRM involvement, with a sensitivity of ~80% being associated with a false positive rate of ~20%. MRI was recommended as the only imaging modality that detects CRM involvement with any accuracy. One analysis reported a pooled sensitivity of 94% and specificity of 85% for MRI in detecting CRM involvement.[64]

Lymph node involvement

All of the included studies that examined the detection of lymph node status suggested that all three imaging modalities are equally poor at detecting lymph node involvement.[62,63,66]

Recommendation development

The GDT discussed the evidence and noted that all included secondary studies were limited by the lack of high-quality primary studies that researched preoperative investigations for rectal cancer. There was some disagreement between studies with regards to the best overall primary imaging modality to use in local staging of rectal cancer, but the GDT agreed that MRI appears to be the only imaging modality that can detect CRM involvement. Very little information regarding CT was available, with most studies recommending either EUS or MRI. Some authors suggested that EUS and MRI should be used as complementary modalities: EUS as a general diagnostic tool and MRI to detect CRM involvement. The GDT felt that although other guidelines suggest that EUS is suitable for investigating tumour (T) and node (N) stage, local experience in New Zealand is variable.

NZGG recommendations

	Grade
Preoperative assessment for rectal cancer should include clinical examination, complete blood count, liver and renal function tests, carcinoembryonic antigen (CEA), chest x-ray and contrast-enhanced CT of the abdomen/pelvis/liver	C
Preoperative assessments for rectal cancer should include MRI for identifying circumferential resection margin (CRM) involvement and local staging	B
Preoperative assessment of possible T1 rectal cancers may include endorectal ultrasound (EUS) for local staging, as an alternative to MRI of the pelvis	B
Endorectal ultrasound should not be used as the sole assessment to predict CRM involvement in people with rectal cancer	B

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

4 Management of epithelial polyps

→ *Chapter 9 NHMRC*

This chapter addresses the management of malignant epithelial polyps for people with colorectal cancer and includes a recommendation on the management of adenomas with focal malignancy.

Question development

The National Health and Medical Research Council (NHMRC) guideline answered three clinical questions in its chapter on epithelial polyps. Two of these clinical questions and subsequent recommendations were not included in this guideline as they were outside the scope of this guideline; specifically, non-cancerous polyps are not covered in the management of early colorectal cancer.

NHMRC recommendation

	Level of evidence	Practice recommendation
Adenomas with focal malignancy may be managed safely by endoscopic polypectomy provided strict criteria for patient selection and histopathological assessment are adhered to. In particular, adenomas with focal malignany should be well or moderately differentiated and excision should be complete	III-2	Recommended

Levels of evidence

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one properly designed randomised controlled trial.

III-I Evidence obtained from well-designed pseudo randomised controlled trials (alternate allocation or some other method).

III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.

IV Evidence obtained from case series, either post-test or pre-test/post-test.

For more information see chapter 8 of the NHMRC review (p 109).

5 Preparation for surgery

→ *Chapter 10 NHMRC*

This chapter addresses preparation for surgery for people with colorectal cancer, including:

- the role of the stomal therapist
- bowel preparation
- perioperative transfusion
- prophylaxis
- body temperature.

Question development

All but one of the clinical questions and recommendations from the National Health and Medical Research Council (NHMRC) guideline were considered acceptable by the GDT and adopted without change. One recommendation was deleted from the guideline (see Appendix 1, *Clinical questions*).

NHMRC recommendations

	Level of evidence	Practice recommendation
What is the role of the stomal therapist? All patients who have a reasonable chance of a postoperative stoma should be prepared for this possibility. This includes a visit, where possible, by the stomal therapy nurse	III-2	**Recommended**
Should bowel preparation be given routinely preoperatively? Bowel preparation is current standard practice before elective colorectal operations. However, recent randomised controlled trials have not demonstrated any conclusive benefit from this procedure. Accordingly, the previous guideline has been revised as follows: Mechanical bowel preparation is not indicated in elective colorectal operations unless there are anticipated problems with faecal loading that might create technical difficulties with the procedure, eg, laparoscopic surgery, low rectal cancers	I	**Not recommended**

continued over...

NHMRC recommendations continued...

	Level of evidence	Practice recommendation
Should thromboembolic prophylaxis be given?		
All patients undergoing surgery for colorectal cancer should receive prophylaxis for thromboembolic disease	I	**Strongly recommended**
Unfractionated heparin, low molecular weight heparin, and intermittent calf compression are effective in reducing the incidence of thromboembolism	II	**Strongly recommended**
Low molecular weight heparin has not been shown to be superior to low-dose heparin in colorectal surgical patients	II	**Strongly recommended**
Should prophylactic antibiotics be given?		
All patients undergoing colorectal cancer surgery require prophylactic antibiotics	II	**Recommended**
A single preoperative dose of intravenous cephalosporin and metronidazole, or gentamicin and metronidazole, is an effective regimen	I	**Strongly recommended**
Should normal body temperature be maintained?		
Perioperative normothermia should be maintained	II	**Recommended**

Levels of evidence

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one properly designed randomised controlled trial.

III-I Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.

IV Evidence obtained from case series, either post-test or pre-test/post-test.

For more information see chapter 10 of the NHMRC review (pp 117–124).

6 Elective surgery for colon cancer

→ *Chapter 11 NHMRC*

This chapter addresses elective surgery for people with colon or colorectal cancer, including:

- high ligation
- no-touch isolation
- segmental compared with extended resection
- anastomosis
- laparoscopic surgery
- who should perform colon cancer surgery
- where colon cancer surgery should be performed.

The term 'elective surgery' in this chapter refers to surgery that can be planned, rather than surgery carried out under urgent or emergency circumstances; it does not imply a lack of urgency.

Question development

Most of the National Health and Medical Research Council (NHMRC) clinical questions and recommendations for this chapter were considered acceptable by the GDT and adopted without change. One recommendation was deleted from the guideline (see Appendix 1, *Clinical questions*).

One recommendation made by the NHMRC about sutured and stapled anastomosis was known to be out of date; this question was reworded and updated. The new question was: *Do sutured and stapled anastomosis have equivalent outcomes*?

The GDT identified two additional questions and systematic reviews were undertaken to answer these. The additional clinical questions were:

- *Who should perform elective surgery for colon cancer?*
- *Where should surgery be performed for colon cancer?*

NHMRC recommendations

	Level of evidence	Practice recommendation
Does high ligation provide any benefit? High ligation of the lymphovascular pedicle does not confer any oncological benefit. Resection where feasible should extend to the origin of segmental vessels	III-3	Equivocal
Does no-touch isolation technique have any benefit? The no-touch isolation technique has no oncological benefit	II	Recommended
Is segmental and extended resection equivalent in outcome? Segmental resection is equivalent to extended resection in outcome	II	Equivocal
Does omental wrapping of intestinal anastomoses have any benefit? Omental wrapping of anastomosis has no benefit	III-2	Strongly not recommended
Is laparoscopic colonic surgery as effective as the conventional approach? In experienced hands, laparoscopic surgery for colon cancer has equivalent outcomes to conventional surgery	I	Recommended

Levels of evidence

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one properly designed randomised controlled trial.

III-I Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.

IV Evidence obtained from case series, either post-test or pre-test/post-test.

For more information see chapter 11 of the NHMRC review (pp 126–133).

Stapled compared with handsewn anastomosis

Clinical question:	What is the effectiveness of stapled compared with handsewn techniques for anastomosis?

Body of evidence

Guidelines

No guidelines addressing the clinical question were identified.

Systematic reviews

One good-quality systematic review was identified investigating outcomes for ileocolic anastomoses performed using stapling and handsewn techniques and included six trials with 955 ileocolic participants.[68] Stapled anastomosis was associated with significantly fewer anastomotic leaks compared with handsewn anastomosis (S=5/357 (1.4%), HS=36/598 (6%), OR 0.34, 95% CI 0.14–0.82, p=0.02). For the subgroup of 825 cancer patients in four studies, stapled anastomosis led to significantly fewer anastomotic leaks (S=4/300 (1.3%), HS=35/525 (6.7%), OR 0.28, 95% CI 0.10–0.75, p=0.01). There was no evidence of a significant difference between techniques for all other outcomes: stricture, anastomotic haemorrhage, anastomotic time, re-operation, mortality, intra-abdominal abscess, wound infection and length of stay.

Primary studies

No additional primary studies were identified.

Summary of findings

Stapled functional end-to-end ileocolic anastomosis is associated with fewer anastomotic leaks than is handsewn anastomosis.

Recommendation development

NZGG recommendation	
	Grade
Stapled functional end-to-end ileocolic anastomosis is recommended	A
Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.	

Horizon scanning

A randomised controlled trial presented at the conference of American Society of Colon and Rectal Surgeons in 2010 aimed to compare the results of side-to-side stapled and end-to-end handsewn methods for ileocolic anastomoses in laparoscopic colectomy.[69] Preliminary results were underpowered to detect important differences. However, no significant differences were found in terms of operative time, anastomostic dehiscence and other postoperative complications.

High-volume compared with low-volume surgeons and hospitals

Clinical questions:	• Who should perform elective surgery for colon cancer? • Where should surgery be performed for colon cancer?

Body of evidence

In Chapter 7, *Elective surgery for rectal cancer* the same clinical questions are asked of rectal cancer as those asked above of colon cancer. Some evidence identified reported outcomes for 'colorectal' cancer and they were not further differentiated into colon or rectal cancer. This evidence is reported in this chapter on colon cancer because of the higher incidence of colon cancer and the likelihood that the majority of patients in these studies represent colon cancer patients.

Guidelines

No guidelines addressing the clinical questions were identified.

Systematic reviews

Two good-quality systematic reviews were identified investigating provider case volume in patients with colorectal cancer; one review was published in two parts.[70–72] One good-quality systematic review investigated provider volume in patients with colorectal cancer where there were no further analyses of colon or rectal cancer patients separately.[73]

Colon cancer

A recent systematic review investigated the association between provider case volume and mortality in patients with gastrointestinal cancers. Nineteen publications reporting 17 observational studies were identified. Ten of the 17 studies reported that high-volume hospitals had significantly lower perioperative mortality rates. A consistent relationship between unadjusted mortality and hospital case volume was evident.[70]

All six (of the 17 studies) investigating surgeon volume reported a significant association with short- or long-term mortality or both. The authors stressed that there are clearly some low-volume providers who get good results, so referral to relatively low-volume providers should be supported if good outcomes can be demonstrated by process measures or by risk-adjusted outcomes or if there are compelling personal or medical reasons for the patient to be treated close to home.

A systematic review investigating the influence of hospital and surgical caseloads identified 20 observational studies reporting outcomes for colon cancer patients. High hospital caseload was strongly associated with reduction in postoperative mortality (nine studies, OR 0.64, 95% CI 0.55–0.73) and increased overall survival (three studies, OR 1.22, 95% CI 1.16–1.28). Limited evidence of associations between hospital volume and postoperative morbidity and cancer-free survival were found. High surgeon caseloads were strongly associated with reduced postoperative mortality (three studies, OR 0.50, 95% CI 0.39–0.64) and reduced morbidity. There was no evidence of association between surgeon volume and overall or disease-free survival.[71,72]

Colorectal cancer (not further defined)

Two systematic reviews investigated provider volume in patients with colorectal cancer, where there were no further analyses of colon or rectal cancer patients separately.

A good-quality systematic review investigating high provider volumes reported that, of 16 included studies, most showed a significant relationship between high hospital volume and improved outcome for colorectal cancer. Ten studies showed a significant relationship, two showed a significant relationship that did not remain significant when the individual surgeon was accounted for, and two showed no relationship. Of the studies that measured surgeon volume, three out of seven found a significant relationship with a reduction in risk-adjusted mortality between 0.5 and 0.64. One of the studies reporting a significant relationship did not remain significant when hospital volume was accounted for. Four studies showed no relationship. The review concluded that although significant relationships can be seen, the relative contribution of hospital and surgeon volume-associated outcomes is not clear. The authors stated that the magnitude of effect on mortality was variable, most likely in the region of 1–2%, which translates into a number needed to treat of 50 to 100 patients.[73]

A systematic review investigating the influence of hospital and surgical caseloads on outcomes for colorectal cancer patients identified ten observational studies. There were no associations between provider volumes and overall or disease-free survival. However, patients had significantly higher five-year cancer free survival when managed by a colorectal surgeon rather than a general surgeon. There were no associations between provider volumes and postoperative mortality, but in terms of morbidity, there were significantly more medical and surgical complications in hospitals with fewer than 20 operations per year compared with hospitals with more than 75 operations per year.[71,72]

Primary studies

Three cohort studies were identified that reported outcomes for colon cancer patients,[74–76] and two cohort studies were identified reporting outcomes for colorectal cancer patients where there were no further analyses of colon or rectal cancer patients separately.[77,78]

Colon cancer

Three cohort studies were identified that reported outcomes for colon cancer patients.[74–76] One study reported significant correlations between case volume, intra-operative problems, operating time, conversion rate, number of lymph nodes harvested, recovery of bowel function, complications and hospital stay in hospitals with higher caseloads.[74] Another study found that the number of resections that a surgeon performed was an independent predictor of overall and cancer-specific survival.[75] A third study found that mortality increased and survival decreased as hospital surgical volume decreased in patients with colon cancer.[76]

Colorectal cancer (not further defined)

Two cohort studies were identified investigating hospital and surgeon volumes in colorectal cancer patients. Two studies found better outcomes in higher-volume hospitals[77] and one study showed no difference in complications, recurrence or 30-day mortality and reported more frequent complications at high-volume hospitals.[78]

Other studies

Additional non-comparative studies were identified. Although these studies were not appraised for quality, they are included here.

Longitudinal studies have reported improved outcomes in hospitals where provider volumes are higher.[79,80] However, there are also hospitals that report that surgical proficiency can be maintained at low-volume hospitals.[81,82] A New Zealand study investigating the workload of a general surgeon with a colorectal subspecialty in Nelson found that outcomes were comparable with published results in terms of quality of care. The authors concluded that provincial management of colorectal cancer remains an important resource for patients living outside major centres.[82]

Summary of findings

High-volume hospitals

Two systematic reviews[70–72] report improved postoperative mortality in high-volume hospitals in patients with colon cancer; one review also reported increased overall survival.

For colorectal cancer patients (not further defined), one review and two cohort studies found a significant relationship between high hospital volume and improved outcome[73] and estimated a number needed to treat of 50–100 patients. Another review found no association.[71,72] One review found that significantly more medical and surgical complications occurred in hospitals with fewer than 20 operations per year compared with in hospitals with more than 75 operations per year.[71,72]

High-volume surgeons

Two systematic reviews[70–72] reported improved postoperative mortality in colon cancer patients treated by high-volume surgeons. There did not appear to be any association with either overall or disease-free survival.[71,72]

Evidence was not clear for associations between surgeon volumes and patients with colorectal cancer.[73] One review reported that patients had significantly higher five-year cancer-free survival when managed by a colorectal surgeon rather than a general surgeon.[73]

Recommendation development

The Guideline Development Team (GDT) noted that all systematic reviews were limited in that they reviewed poor-quality, heterogeneous observational studies; no randomised controlled trials were identified for any outcome.

One review article (that supported a correlation between higher provider volumes and improved outcomes), discussed the methodological limitations of reviewing evidence on this topic, and the GDT took into account some of these points when drafting the recommendations, specifically:

- mortality rates that are not corrected for comorbidities or stage at diagnosis may be poor markers for volume–outcome analysis
- higher-volume hospitals are far more likely to take a multidisciplinary approach to care (sub-specialised radiologists, radiation and medical oncologists, high dependency and intensive care units, cancer specialist nurses, psychologists and palliative care support)
- concerns about what happens when high volume becomes too high – stretched resources in a high-volume hospital may prove worse for patients than an absence of resources at a smaller hospital
- patient quality of life must also be taken into account.[80]

Despite these caveats, the GDT discussed the issue that many of the included primary studies utilised data from administrative hospital databases and in some cases contained tens of thousands of patients. The GDT acknowledged that there is no easy way to conduct a study assessing provider volume, so it is unlikely future evidence will be of vastly better quality; no recommendation could be made because of these difficulties. The GDT wished to also acknowledge that the general lack of quality data on the management of patients with colorectal cancer is of concern; the GDT showed its support for improved data collection and management systems to facilitate better patient care.

NZGG recommendation

	Grade
Elective surgery for colon cancer should be performed by a surgeon with specific training and experience in colorectal surgery and with sufficient caseload to maintain surgical skills	**B**

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

7 Elective surgery for rectal cancer

→ *Chapter 12 NHMRC*

This addresses elective surgery for people with rectal cancer, including:

- local excision
- distal clearance
- sphincter preservation
- colonic reservoirs
- drainage
- who should perform rectal cancer surgery
- where rectal cancer surgery should be performed.

The term 'elective surgery' in this chapter means surgery that can be planned rather than surgery carried out under urgent or emergency circumstances; it does not imply a lack of urgency.

Question development

The National Health and Medical Research Council (NHMRC) clinical questions and recommendations for this chapter were mostly considered acceptable by the Guideline Development Team (GDT) and adopted without change. They are listed below. The GDT identified one question requiring an update and one additional question. Systematic reviews were undertaken to answer these.

The question that needed to be updated was: *Who should perform elective surgery for rectal cancer*? The additional question was: *Where should surgery be performed for rectal cancer*?

NHMRC recommendations

	Level of evidence	Practice recommendation
When should local excision of rectal cancer be performed? Local excision of T1 rectal cancer may be used in selected cancer patients according to the following guidelines: • mobile tumour <3 cm • T1 on endorectal ultrasound • not poorly differentiated on histology (biopsy)	III-3	Equivocal
What is adequate distal clearance of resection? A distal distance of 2 cm (fresh) is recommended in most instances, or 1 cm fixed	III-2	Recommended
What factors influence sphincter preservation? Sphincter-saving operations are preferred to abdominoperineal resection except in the presence of: • tumours such that adequate distal clearance (>2 cm) cannot be achieved • the sphincter mechanism is not adequate for continence • access to the pelvis makes restoration technically impossible (rare)	III-3	Equivocal
What is recommended for the extent of total mesorectal excision (TME)? For mid-to-low rectal tumours, the principles of extra fascial dissection and TME are recommended	III-2	Recommended
Should a colonic reservoir be constructed? Where technically feasible, the colonic reservoir is recommended for anastomosis within 2 cm from ano-rectal junction	II	Strongly recommended
Drainage Routine drainage should only be considered for rectal cancers	II	Equivocal

Levels of evidence

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one properly designed randomised controlled trial.

III-I Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.

IV Evidence obtained from case series, either post-test or pre-test/post-test.

For more information see to chapter 12 of the NHMRC review (pp 135–149).

High-volume compared with low-volume surgeons and hospitals

Clinical questions:	• Who should perform elective surgery for rectal cancer? • Where should surgery be performed for rectal cancer?

Body of evidence

Guidelines

No guidelines addressing the clinical questions were identified.

Systematic reviews

Three systematic reviews investigating provider volume in patients with rectal cancer, one of which was in two parts, were identified.[70–72,83]

A recent good-quality systematic review investigated the association between provider case volume and mortality in patients with gastrointestinal cancers. Nineteen publications reporting 17 observational studies were identified. Of the studies investigating hospital volume, three of nine studies of rectal cancer reported a significant association between hospital volume and short- or long-term mortality or both, but this finding was not reported in the other studies. In studies investigating surgeon volume, two of four studies reported a significant association between surgeon volume and mortality. While a consistent relationship between unadjusted mortality and hospital case volume was evident for colon cancer and colorectal cancer, this was not the case for rectal cancer as results of the studies were inconsistent.[70]

One average-quality systematic review investigated whether hospital and surgeon volume influenced the type of surgery performed and outcomes of surgery for rectal cancer.[83] Eleven observational studies were identified, the majority of which were retrospective cohorts. The authors concluded that hospitals and surgeons with higher caseloads appeared to perform more sphincter-preserving surgeries and had lower postoperative mortality. However, there appeared to be little or no beneficial effect on leak and complication rates, local recurrence, overall survival and cancer-specific survival. The review suggested that the effect of hospital volume may be stronger for short-term outcomes; beyond the immediate recovery period, the effect of hospital and surgeon volume may be minimal.

A good-quality systematic review investigating the influence of hospital and surgical caseloads on outcomes for rectal cancer patients identified ten observational studies. Overall survival improved with increasing hospital caseload (OR 1.38, 95% CI 1.19–1.60) and the frequency of permanent stoma was significantly less. There were no associations between provider volumes and cancer-free survival, postoperative mortality, postoperative morbidity or anastomotic leak.[71,72]

Primary studies

Five cohort studies were identified that investigated outcomes for rectal cancer patients.[76,84–87] All studies had different objectives.

One good-quality study found that patients of very high-volume surgeons had the lowest postoperative procedural interventions and low odds of complications when compared with very low-volume surgeons.[84] Another good-quality study found that mortality increased and survival decreased as hospital surgical volume decreased in patients with rectal cancer.[76] One average-quality study found that treatment at a teaching hospital was associated with a lower risk of death than at a community hospital. Significant improvement was also seen for overall survival at 5 and 10 years.[85] One good-quality study found no differences in intra-operative complications, specific postoperative complications, postoperative mortality or intra-operative tumour perforation.[86] An average-quality Norwegian study assessed outcome in a low-volume hospital compared with the national average. The survival rate, local recurrence peri- and postoperative complications did not differ significantly from the national average. No consistent pattern was found when analysing survival by surgeon caseload.[87]

Other studies

An additional non-systematic review was identified. Although it was not appraised for quality it is included here.

A non-systematic review was identified that investigated whether the type of surgeon could be judged as a factor affecting prognosis of rectal cancer patients.[88] The review reported the conclusions of the 2006 Congress of the American College of Surgeons where it was stated that high-skill, high-volume surgeons undoubtedly perform more sphincter-preserving resections, have less local recurrence and have better survival rates.

Summary of findings

High-volume hospitals

The evidence for an association between high-volume hospitals and outcomes in patients with rectal cancer is not clear; one review reported lower postoperative mortality in high volume hospitals,[83] and one reported a beneficial effect in three of nine studies, with the remaining six studies showing no difference.[70] Another review did not find an association between postoperative mortality and hospital caseload or surgeon caseload at one year. Longer-term outcomes at two to five years showed that overall survival improved with increasing hospital caseload (OR 1.38, 95% CI 1.19–1.60) and the frequency of permanent stoma was significantly less.[71,72]

High-volume surgeons

The evidence for an association between high-volume surgeons and outcomes in rectal cancer patients is not clear. One review found significantly lower postoperative mortality with higher volume surgeons,[83] one review showed a significant association in two of four studies[70] and one review found no evidence of significant differences.[71,72] One review showed an improved rate of sphincter preservation in higher-volume surgeons.[83]

No associations were found for overall or disease-free survival, leak rate or local recurrence.[71,72,83]

Recommendation development

The GDT acknowledged that there is no easy way to conduct a study assessing provider volume, so it is unlikely future evidence will be of vastly better quality; no recommendation could be made because of these difficulties.

The GDT decided to accept the NHMRC recommendation on who should perform rectal cancer surgery. General consensus, both within the GDT and internationally, is that more experienced surgeons will produce better outcomes, particularly in terms of sphincter-preserving resections. Given the evidence presented, the GDT did not feel that a stronger recommendation could be made about rectal cancer surgery than the previous NHMRC recommendation, so the wording remains the same, although the grading reflects the new evidence identified.

NZGG recommendation

	Grade
Elective surgery for rectal cancer should be carried out by a surgeon who has undergone a period of specialist exposure to this form of surgery during surgical training and who has maintained satisfactory experience in the surgical management of rectal cancer	**B**

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

8 Emergency surgery

→ *Chapter 13 NHMRC*

This chapter addresses emergency surgery for surgery for people with colorectal cancer, specifically bowel obstruction, including:

- when to consider primary anastomosis
- stenting.

Question development

There were two National Health and Medical Research Council (NHMRC) clinical questions and recommendations for this chapter; one clinical question and two recommendations were considered acceptable by the Guideline Development Team (GDT) and adopted without change. The GDT decided that the second clinical question required updating: *What surgery is recommended for bowel obstruction?* A systematic review was undertaken to answer this question.

NHMRC recommendations

	Level of evidence	Practice recommendation
When should primary anastomosis be considered?		
Primary anastomosis should be considered as a colectomy, with an ileocolic or ileorectal anastomosis	**III-2**	**Equivocal**
Primary anastomosis could be considered for left-sided obstruction and may need to be preceded by on table colonic lavage	**III-2**	**Equivocal**

Levels of evidence

I Evidence obtained from a systematic review of all relevant randomised controlled trials.

II Evidence obtained from at least one properly designed randomised controlled trial.

III-I Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).

III-2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.

IV Evidence obtained from case series, either post-test or pre-test/post-test.

For more information see chapter 13 of the NHMRC review (pp 151–157).

Surgery for bowel obstruction

Clinical question: What surgery is recommended for bowel obstruction?

Body of evidence

Guidelines

Three guidelines were identified that made recommendations about surgery for bowel obstruction for people with colon cancer.[25,26,29] Most guidelines agreed that in patients with resectable colon cancer the insertion of an expanding stent should be considered where adequate local expertise exists. Stenting may be used either for palliation or as a bridge to surgery.

Systematic reviews

Six systematic reviews were identified that compared the use of stent insertion (often followed by elective surgery) with emergency surgery in patients with bowel obstruction.[89–94] Primary studies using stent insertion as palliative treatment in metastatic disease were excluded.

Two systematic reviews were considered to be of good quality.[92,94] One included 15 non-randomised studies, three of which compared stent insertion followed by elective surgery with emergency surgery.[94] The other included ten non-randomised studies in a meta-analysis, of which five reported on stent insertion as a bridge to surgery compared with emergency surgery.[92]

One systematic review was considered to be of average quality and included four case control studies.[89]

Three systematic reviews were considered to be of poor quality.[90,91,93] One review included two other systematic reviews, although the details of one were not described and the second systematic review was of metastatic disease. A historical case control study was also included.[91] The second systematic review[93] identified the same two systematic reviews as in the previous review[91] and identified one of the good-quality reviews reported above.[92] Three additional non-randomised trials were also identified.[93]

A third systematic review included only studies that considered stent placement for both palliation and as a bridge to surgery.[90] The author identified five non-randomised studies.[90]

Mortality and survival

Perioperative mortality in the stent group ranged from 0% to 13% and from 0% to 26% in the emergency surgery group.[89] A good-quality review reported post-procedural mortality of 5.7% in the stent group and 12.1% in the emergency surgery group (OR 0.45, 95% CI 0.22–0.91, $p=0.03$) (note that this is based on the inclusion of five palliative studies).[92] Another good-quality review reported that, based on a single historical case control study, 30-day mortality was greater in the emergency surgery group than the stent group ($p<0.001$), although the cause of death was not clarified.[94]

Two systematic reviews found no evidence of a benefit in long-term survival.[91,94] Both reviews identified one historical case control study ($n=84$) and reported no differences in survival at three to five years between stent and emergency surgery groups (50% compared with 48% and 44% compared with 40%, respectively).

Morbidity

An average-quality review reported that morbidity was not well defined in the four case control studies that were identified in the review.[89] Two of the studies reported no risk difference for morbidity between the stented and emergency surgery group, and two reported results favouring stent insertion.[89]

A poor-quality review reported on studies that included palliative as well as bridge to surgery procedures.[90] The most common complications following stent insertion were perforation (2.5%), stent migration (4.4%), pain and tenesmus (2.2%), stent occlusion and rectovescical fistula (0.8%).[90] A historical case control study that was identified by two systematic reviews reported significantly reduced wound infection (2% compared with 14%) and significantly reduced anastomotic leaks (3% compared with 11%) with stent insertion compared with emergency surgery.[89,91]

Post-procedural complications were reduced in the stent group compared with the emergency surgery group.[91,94] Patients undergoing stent insertion were also found to be at a lower risk of stoma formation (note that five out of eight studies were palliative) (OR 0.02, 95% CI 0.01–0.08, $p<0.001$), although this was associated with some heterogeneity.[92] A greater rate of primary anastomosis and a reduced colostomy rate was reported (figures not given) in the group undergoing stent insertion compared with an emergency surgery group.[94,93]

A reduced hospital stay of about eight days was reported in the stent group compared with the surgical group (note that five of the eight studies were palliative) (WMD -7.72, 95% CI -11.42 – -4.02, $p<0.001$).[92] Another systematic review also reported reduced hospital stay, although the review did not distinguish between palliative and bridge-to-surgery patients.[93] Intensive care bed use (one of four studies was palliative) was also reported as being reduced in the stent group (OR 0.07, 95% CI 0.01–0.31, $p<0.001$).[92]

Primary studies

No additional primary studies were identified.

Summary of findings

No randomised controlled were trials identified in any of the systematic reviews. The evidence is based on case control and historical case control studies.

Mortality and survival

Based on limited evidence, results suggest that endoscopic stent insertion may reduce mortality compared with emergency surgery and could have a role in decompression of acute malignant colonic obstruction. There is no evidence to support a benefit of long-term survival at three and five years following stent insertion compared with emergency surgery.

Morbidity

Morbidity appears to be reduced as a result of stent insertion compared with emergency surgery, although the studies lacked consistent definitions of complications. Stent insertion followed by elective surgery appears to be safe and effective and may mitigate the need for emergency surgery in some patients, thus converting an emergency situation into an elective one.

Recommendation development

The GDT discussed the type of surgery required for bowel obstruction and noted that no new evidence has become available since the NHMRC guideline was developed. The recommendation 'primary resection of obstructing carcinoma is recommended unless the patient is moribund' made by the NHMRC was accepted and graded according to the NZGG grading system.

The GDT considered the evidence presented and had extensive discussion about the availability of stents in New Zealand hospitals and the training of endoscopists. The GDT also considered the condition of the patient allowing transfer for stent, or having been operated on then requiring transfer to an intensive care unit. There was concern about a possible detrimental effect of a stent on curative situation. The GDT noted the poor quality of the available evidence, which based recommendations on systematic reviews of case control and historical case control studies. Three randomised trials are under way that will add to the evidence base, although no current trial answers this question directly. The effect of stenting on the outcomes for people with obstructing colon cancer is yet to be determined.

NZGG recommendations

	Grade
Primary resection of obstructing carcinoma is recommended unless the patient is moribund	B
Colonic stenting for palliation of left-sided bowel obstruction in people with colorectal cancer is recommended, if endoscopic expertise can be readily accessed	B
Colonic stenting as a bridge to surgery for left-sided bowel obstruction in people with colorectal cancer may be considered for an individual, if endoscopic expertise can be readily accessed	C
People with colorectal cancer who have bowel obstruction and are being considered for colonic stenting should be invited to participate in randomised controlled trials, where these are available	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Horizon scanning

No published randomised trials investigating stent insertion as a bridge to surgery compared with emergency surgery were identified.

One randomised trial is in process and aims to report on colonic stenting compared with emergency surgery in acute left-sided malignant obstruction.[95]

9 Adjuvant therapy for colon cancer

→ *Chapter 15 NHMRC*

This chapter addresses adjuvant therapy for people with colon cancer, including:

- who should be considered for adjuvant chemotherapy
- postoperative chemotherapy regimens
- postoperative fluoropyrimidine-based chemotherapy plus other cytotoxic agents.

Question development

The National Health and Medical Research Council (NHMRC) guideline asked two clinical questions for this chapter.

The first question was: *Who should be considered for adjuvant therapy?* The recommendation was 'People with resected Dukes C, that is, node positive colon cancer should be considered for adjuvant therapy'. The Guideline Development Team (GDT) discussed this question and resulting recommendation and decided that all people with colon cancer should be considered for adjuvant therapy on a case-by-case basis, not just those with node positive disease. The GDT changed the recommendation wording, but did not feel a full review was warranted. The new recommendation is 'People with resected colon cancer should be considered for adjuvant therapy'.

The second clinical question (*What is the value of adjuvant therapy in Dukes B colon cancer?*) and resulting recommendations were not considered acceptable by the GDT. The GDT formed two new questions and systematic reviews were undertaken to answer these.

- *In patients with completely resected colorectal cancer, what is the effect of postoperative chemotherapy on survival at five years?*
- *In patients with completely resected colorectal cancer, what is the effect of adding other cytotoxic agents to postoperative fluoropyrimidine-based chemotherapy on survival at five years?*

In this guideline, the term leucovorin (LV) appears several times; the GDT is aware that other terms for this drug are folinic acid and calcium folinate (the term used by PHARMAC). However, because LV is commonly used in clinical practice and in the included trials, this name was retained throughout the guideline.

Several chemotherapy regimens are also referred to in this chapter. The Roswell Park regimen and the de Gramont regimen both use different doses, timing and methods of administration of fluorouracil (5-FU) and leucovorin. Adding oxaliplatin to this combination is commonly known as FOLFOX (folinic acid (leucovorin) + fluorouracil (5-FU) + oxaliplatin) and different doses, timing and routes of administration have given rise to different FOLFOX regimens, including FLOX, FOLFOX-4 and FOLFOX-6.

Postoperative chemotherapy

Clinical question:	In patients with completely resected colorectal cancer, what is the effect of postoperative chemotherapy on survival at five years?

Body of evidence

Guidelines

Six clinical practice guidelines were identified that made recommendations for adjuvant therapy for people with colon cancer.[25,26,29,96–98] Most guidelines were in agreement on the adjuvant therapy offered.

Recommendations derived from the guidelines are as follows.

Stage II colon cancer

- Most guidelines did not recommend routine chemotherapy.
- Patients at higher risk should be offered chemotherapy with a similar regimen to Stage III patients.

Stage III colon cancer

- Patients fit enough to handle chemotherapy should be offered an oxaliplatin-based regimen (FOLFOX).
- Patients who are not appropriate candidates for FOLFOX can be offered oral capecitabine or 5-FU ± LV.
- All treatment decisions should be made by discussions between the patient and clinician.
- If appropriate, patients should be offered entry into clinical trials.

Systematic reviews

Five systematic reviews were identified that compared postoperative chemotherapy with surveillance after curative resection of colon cancer.[96,99–102]

Three reviews were rated as good-quality studies[99,100,102] and one was rated as an average-quality study.[101] One systematic review was identified[96] but is not included here because it is a subset of a larger review.[100]

Primary studies

Eight randomised controlled trials (RCTs) were identified.[103–110] One trial (X-ACT trial) has been reported in systematic reviews where more recent outcomes data were available, so is not included again here.[110] Only seven RCTs are referred to in this section.

There were five good-quality RCTs,[103,104,106,108,109] one average-quality RCT,[107] and one poor-quality RCT in which the influence of the sponsoring drug company could not be determined.[105] This trial was appraised and is included in Table 9.1, but not in the summary of results.[105]

Tables 9.1 and 9.2 overview the included studies. The included studies either compared chemotherapy with surgery alone in resectable colon cancer patients (Stage II or Stage III) or compared different types of chemotherapy head-to-head with respect to five-year survival outcomes. The studies are grouped as those that reported exclusively Stage II, Stage III, and combined Stages II and III.

Table 9.1 Postoperative chemotherapy

Study	Stage	Intervention	Comparison	Follow-up	Overall survival	Disease-free survival
Systematic reviews						
Figueredo 2008[99] 33 trials, 17 meta-analyses	II	5-FU + levamisole (lev) or leucovorin (LV) n=1256	Surgery only n=1270	5 years	RR=0.88 (95% CI 0.71–1.10)	No pooled data. Difference in percentage points between chemotherapy and observation: 5-FU + lev=6–20% for and 5-FU/LV=2–8%.
Figueredo 2004[100] 31 trials, 11 MA	II	5-FU/LV n=507	Surgery only n=509	Overall: 5-FU/LV trials median >3.0 years to 6.0 years MA used: 5.8 year median	5-year HR=0.86 (90% CI 0.68–1.07, p=0.06)	5-year event-free survival HR=0.83 (90% CI 0.72–1.07, p=0.06)
Gill 2005[101] 7 trials with FU/LV or FU + lev	II	5-FU + lev or 5-FU/LV n=1681	Surgery only n=1621	Varied by study. Maximum 8 years	HR=0.86 (p=0.11) (CI not reported)	HR=0.83 (p=0.05) (CI not reported)
	III				5-yr OS: (1–4 nodes): HR=0.66 (p <0.0001); (≥5 nodes): HR=0.65 (p=0.0031) (CI not reported)	5-year DFS: (1–4 nodes): HR=0.61 (p<0.0001); (≥5 nodes): HR=0.60 (p=0.0002) (CI not reported)
	II and III				HR=0.74 (95% CI 0.66–0.83, p <0.0001)	HR=0.70 (0.63–0.78, p<0.0001)

continued over...

Table 9.1 **Postoperative chemotherapy** continued...

Randomised controlled trials						
QUASAR[106]	II	5-FU/LV (generally low dose) n=1622	Surgery only n=1617	Median 5.5 years, maximum 10.6 years	RR=0.84 (95% CI 0.68–1.00, p=0.046) (time not stated)	RR recurrence= 0.78 (95% CI 0.66–0.93, p=0.004)
Schippinger 2007[107]	II	5-FU/LV n=252	Surgery only n=248	Median 8 years, maximum 12.4 years	HR=0.89 (95% CI 0.62–1.29, p=0.55)	Disease-free: HR=0.96 (95% CI 0.70–1.32, p=0.81) Relapse-free: HR=0.68 (95% CI 0.44–1.05, p=0.08) Cancer-specific: HR=0.82 (95% CI 0.51–1.30, p=0.39)
Glimelius 2005[103]	II III	5-FU + lev 5-FU/LV 5-FU/LV ± lev Stage II n=812 Stage III n=708	Surgery only Stage II n=401 Stage III n=364	Minimum 5 years	OS rates: 79 ± 2% for both chemotherapy and observation arms (p=0.81) Chemotherapy=55 ± 3%, Observation=48 ± 3% (p=0.15)	Not reported
NSABP C-01[108]	II and III	MeCCNU + vincristine + 5-FU n=379	Surgery alone n=394	5 years	RR=1.29 (95% CI 1.01–1.66, p=0.04)	5-year DFS: RR=1.29 (95% CI 1.03–1.61, p=0.03)
Dahl 2009	III	5-FU + lev	Surgery alone n=206	5 years	Not reported	5-FU + lev: 58% (95% CI 44–71) Surgery alone: 37% (95% CI 23–50)

continued over...

Table 9.1 **Postoperative chemotherapy** continued...

Randomised controlled trials continued...						
FOGT-1[104]	High risk Stages II and III	5-FU + lev + FA n=295 5-FU + lev + INF-α n=278	5-FU + lev n=282	Median 4.6 years, maximum 10 years	5-year OS rates: 5-FU + lev: 60.5% (95% CI 54.3–66.7) 5-FU + lev + FA: 72.0% (95% CI 66.5–77.5, p=0.004) 5-FU + lev + INF-α: 62.7% (95% CI 56.6–68.8, p=0.382)	5-year recurrence-free survival rates: 5-FU + lev: 52.3% (95% CI 46.2–58.5%) 5-FU + lev + FA: 61.6% (95% CI 55.7–67.4%, p=0.007) 5-FU + lev + INF-α: 56.3% (95% CI 50.1–62.5, p=0.137)
Sobrero 2005[109]	II and III	Methotrexate→ 5-FU/LV n=985	5-FU/LV n=960	Median 4.2 years, maximum 5 years	HR=1.07 (95% CI 0.96–1.19)	Stage-adjusted recurrence: HR=0.99 (95% CI 0.82–1.21)
X-ACT 2005[110]	III	Capecitabine n=1004	5-FU/LV n=983	Up to 4.4 years	3.8 years: HR=0.84 (95% CI 0.69–1.01) 4.4 years: HR=0.88 (95% CI 0.74– 1.05)	3.8 years: HR=0.87 (95% CI 0.75–1.00) 4.4 years: HR=0.87 (95% CI 0.76–1.00)
PETACC-1[105]	III	Raltitrexed n=952	5-FU/LV n=969	Median 4.1 years, maximum 9 years	HR=1.04 (90% CI 0.90–1.21)	HR=1.14 (90% CI 1.01–1.29)

Table developed by the New Zealand Guidelines Group.

Abbreviations: CI=confidence interval; DFS=disease-free survival; FA=folinic acid (also known as leucovorin); 5-FU=5 fluorouracil; HR=hazard ratio; INF-α=interferon alpha; lev=levamisole; LV=leucovorin; n=number; MA= meta-analyses; MeCCNU=semustine; OS=overall survival; RR=relative risk.

Summary of findings

Stage II colon cancer

Chemotherapy compared with surgery alone

Three systematic reviews compared chemotherapy with surgery alone in over 6500 Stage II patients.[99–101] Chemotherapy did not appear to offer any advantages over surgery alone in terms of overall survival. Two reviews showed no differences in disease-free survival outcomes; one review reported significant benefit for chemotherapy patients.

Four RCTs reported mixed results; three showed little or no difference between groups,[103,107,111] and one trial of over 3000 patients showed marginal benefit in patients receiving low dose 5-FU/LV for both overall and disease-free survival.[106]

Chemotherapy appears to offer limited, if any, survival benefit to patients with Stage II colon cancer.

Head-to-head comparisons of different types of chemotherapy

No head-to-head comparisons identified Stage II colon cancer patients.

Stage III colon cancer

Chemotherapy compared with surgery alone

One systematic review including over 3000 patients[101] and two RCTs[103,111] reported survival outcomes for Stage III colon cancer patients; all studies compared 5-FU and leucovorin and/or levamisole with surgery alone. The systematic review (including seven trials) reported significant benefits for chemotherapy patients, both for overall and disease-free survival. One RCT reported no difference between groups for overall survival. However, the 7% estimated difference between treatments was noted as clinically meaningful by the authors.[103] The other RCT reported significant benefits for chemotherapy patients both for disease-free survival and cancer-specific survival; further analysis showed that female patients benefited significantly from chemotherapy, while there was no difference between male patient groups.[111]

Chemotherapy appears to offer significant survival benefits to patients with Stage III colon cancer.

Head-to-head comparisons of different types of chemotherapy

One good-quality RCT[110] reported in a systematic review[102] presented survival outcomes for Stage III colon cancer patients where capecitabine was compared to 5-FU/LV. There did not appear to be any significant differences in survival for patients treated with capecitabine compared with 5-FU/LV. Further subgroup analyses by age reported no differences in effectiveness by age group and that oral capecitabine can be considered for use in all age groups, including patients aged over 70 years.[112]

Stages II and III colon cancer

Chemotherapy compared with surgery alone

One systematic review and one RCT reported outcomes for patients with Stages II and III colon cancer combined.[101,108] The systematic review and RCT both reported significant benefits for five-year overall and disease-free survival in chemotherapy patients.

Chemotherapy appears to offer a survival benefit in trials where outcomes are reported for both Stage II and III colon cancer patients combined. Given the above results in Stage II and Stage III patients separately, this is likely to reflect the Stage III patients in these groups.

Head-to-head comparisons of different types of chemotherapy

One RCT reported survival outcomes for patients with Stages II and III colon cancer combined where modulation of 5-FU with methotrexate was compared with FU/LV.[109] No significant differences were reported between MTX→FU and FU/LV. Toxicity profiles were similar.

The other RCT reported outcomes for both Stage III and high-risk Stage II patients where 5-FU + levamisole was modulated with interferon alpha (INF-α) compared with modulation with LV.[104] Modulating 5-FU + levamisole with LV significantly improved outcomes for high-risk Stage II and Stage III patients both for overall and disease-free survival. No advantages were reported for modulation with INF-α and toxicity was significantly increased with this regimen.[104]

Overall summary

Adjuvant chemotherapy following resection is of most benefit to Stage III colon cancer patients in terms of significant survival benefits. Chemotherapy appears to offer limited, if any, survival benefit to patients with Stage II colon cancer.

A limited number of studies reported head-to-head comparisons; no differences were reported between capecitabine and 5-FU/LV. Modulating 5-FU ± levamisole with LV may improve outcomes, but modulating with methotrexate or INF-α does not appear to improve survival.

Postoperative fluoropyrimidine-based chemotherapy plus other cytotoxic agents

Clinical question:	In patients with completely resected colorectal cancer, what is the effect of adding other cytotoxic agents to postoperative fluoropyrimidine-based chemotherapy on survival at five years?

Body of evidence

Guidelines

Six clinical practice guidelines were identified that made recommendations for adjuvant therapy for people with colon cancer.[25,26,29,96–98] Most guidelines were in agreement on the adjuvant therapy offered.

Recommendations derived from the guidelines are as follows.

Stage II colon cancer

- Most guidelines did not recommend routine chemotherapy.
- Patients at higher risk should be offered chemotherapy with a similar regimen to Stage III patients.

Stage III colon cancer

- Patients fit enough to handle chemotherapy should be offered an oxaliplatin-based regimen (FOLFOX).
- Patients who are not appropriate candidates for FOLFOX can be offered oral capecitabine or 5-FU ± LV.
- All treatment decisions should be made by discussions between the patient and clinician.
- If appropriate, patients should be offered entry into clinical trials.

Systematic reviews

One systematic review was identified that compared oxaliplatin and 5-FU/LV with 5-FU/LV alone after curative resection.[102] Although rated as good quality, the review has not been included here because more recent trial data are available; the most recent publications of both trials have been included below.

Primary studies

Six RCTs were identified that compared oxaliplatin and 5-FU/LV with 5-FU/LV after curative resection.[113–118] Five studies were rated as good quality and one was rated as poor quality.

Table 9.2 overviews the included studies. The included studies compared 5-FU/LV plus oxaliplatin or irinotecan to 5-FU/LV alone in patients with resectable colon cancer (Stage II or III).

Table 9.2 Postoperative fluoropyrimidine-based chemotherapy plus other cytotoxic agents

Study	Stage	Intervention	Comparison	Follow-up	Overall survival (five years)	Disease-free survival (five years)
Randomised controlled trials						
MOSAIC[113]	II	Oxaliplatin + de Gramont regimen (FOLFOX 4) n=1123	de Gramont regimen n=1123	Median 6.8 years	HR (6 years)=1.00 (0.70–1.41, p=0.986) Stage II high risk* HR (6 years)=0.94 (0.61–1.36, p=0.648)	HR=0.84 (0.62–1.14, p=0.258) Stage II high risk HR=0.72 (0.50–1.02, p=NR)
	III				HR=0.80 (0.65–0.97, p=0.023)	HR=0.78 (0.65–0.93, p=0.005)
	II and III				HR=0.84 (0.76–1.00, p=0.046)	HR=0.80 (0.68–0.93, p=0.003)
CALGB 89803[115]	IIIA, B, C	Irinotecan + Roswell Park regimen n=635	Roswell Park regimen n=629	Median 4.8 years	Survival rates: Irinotecan + 5-FU/LV=68% (64–72%) 5-FU/LV=71% (67–75%) p=0.74	Survival rates: Irinotecan + 5-FU/LV=59% (55–63%) 5-FU/LV=61% (57–65%) p=0.84
ACCORD-2 trial[117]	III	Irinotecan + de Gramont regimen n=200	de Gramont regimen n=200	Median 5.25 years	HR=1.00 (0.71–1.40, p=0.99)	HR (3-year)=0.98 (0.74–1.31, p=0.92)
NSABP C07[114]	II and III	Oxaliplatin + Roswell Park regimen (FLOX) n=1200	Roswell Park regimen n=1200	Median 3.5 years	NR	HR (4-year)=0.80 (0.69–0.83, p<0.004)

continued over...

Table 9.2 **Postoperative fluoropyrimidine-based chemotherapy plus other cytotoxic agents** continued...

Study	Stage	Intervention	Comparison	Follow-up	Overall survival (five years)	Disease-free survival (five years)
Randomised controlled trials continued...						
PETACC 3[116]	II	Irinotecan + de Gramont regimen n=1485	de Gramont regimen n=1497 or AIO regimen n=124	Median 5.5 years	Survival rate: Irinotecan + 5-FU/LV=90% 5-FU/LV=88.8%, p=0.344	HR=0.86 (0.61–1.08, p=0.158)
	III n=	or Irinotecan + AIO regimen n=135			Survival rate: Irinotecan + 5-FU/LV=73.6% 5-FU/LV=71.3%, p=0.094	HR=0.86 (0.76–0.98, p=0.021)
	II and III					HR=0.89 (0.79–1.00, p=0.045)

Table developed by the New Zealand Guidelines Group.

* High-risk Stage II patients were defined as having at least one of the following: T4, tumour perforation, bowel obstruction, poorly differentiated tumour, venous invasion, or less than 10 lymph nodes examined.

Abbreviations: AIO=Areitsgemeinschaft Internische Onkologie; 5-FU=5-fluorouracil; HR=hazard ratio; LV=leucovorin; n=number; NR=not relevant.

Summary of findings

Stage II colon cancer

One trial[113] compared the addition of oxaliplatin to 5-FU/LV to 5-FU/LV alone and reported outcomes at six years. Oxaliplatin did not provide further benefit when added to 5-FU/LV for patients with Stage II colon cancer or patients with high-risk Stage II colon cancer. Further analysis of high- and low-risk patients[119] and subgroups by age[120] did not markedly change the results. One trial compared the addition of irinotecan to 5-FU/LV but also did not find a survival benefit.[116]

Stage III colon cancer

One trial investigating the addition of oxaliplatin to 5-FU/LV (FOLFOX)[113] reported significantly improved survival in patients receiving FOLFOX compared with patients receiving 5-FU/LV alone in terms of both overall and disease-free survival.

Three trials reported outcomes for the addition of irinotecan to 5-FU/LV.[115–117] All three trials showed no significant differences between groups for overall survival. In terms of disease-free survival, three- and five-year data did not show a benefit for irinotecan-added regimens over 5-FU/LV alone except in one trial.[116] The Van Custem trial had double the number of participants than the other two trials combined.

Stages II and III colon cancer

Three trials reported survival outcomes for Stage II and Stage III patients combined; two adding oxaliplatin,[113,114] and one adding irinotecan to 5-FU/LV.[116] Only one trial reported overall survival in which the addition of oxaliplatin significantly improved outcomes compared with 5-FU/LV alone.[113] All trials reported significant improvements in disease-free survival when oxaliplatin or irinotecan was added.

A further poorer quality trial[118] investigated the addition of cis-diamminedichloroplatinum (CDDP) to fluourouracil in Stage II and Stage III patients. This trial included 51 patients and had substantial drop-outs and is not reported in the table because of low quality. The addition of CDDP did not improve outcomes for patients receiving 5-FU.

Recommendation development

The GDT discussed the evidence for high-risk Stage II patients and requested that NZGG investigate this group further. The included FOGT-1 trial[104] combined data for high-risk Stage II patients and Stage III patients, where 68 out of 855 (8%) were high-risk Stage II patients. Data were not reported separately for this group, so it is unclear how these patients contributed to results. The authors could not be contacted.

The American Society of Clinical Oncology extensively discussed the topic of high-risk Stage II patients in its 2004 recommendations.[96] It concluded that the use of adjuvant therapy outside clinical trials is not supported by the evidence. However, the methodological limitations of existing trials may give oncologists reason to consider adjuvant chemotherapy in high-risk Stage II patients. The GDT suggests that such decisions should balance the possible risks and benefits to individual patients.[96]

The GDT discussed the funding of oxaliplatin in New Zealand and agreed that node positive colon cancer patients should be offered combination therapy with oxaliplatin.

The GDT is aware of the possible benefits of XELOX (capecitabine + oxaliplatin) regimens, but no published RCTs report sufficient efficacy data on which to base recommendations.

NZGG recommendations

	Grade
People with resected colon cancer should be considered for adjuvant therapy	✓
People with resected node positive colon cancer (Stage III) should be offered postoperative chemotherapy unless there is a particular contraindication, such as significant comorbidity or poor performance status	A
People with resected node negative colon cancer (Stage II) with poor prognostic features may be offered postoperative chemotherapy. Discussion of risks and benefits of treatment should include the potential but uncertain benefits of treatment and the potential side effects	C
For people with colon cancer who are to receive single agent postoperative chemotherapy, either capecitabine or bolus fluorouracil plus leucovorin are appropriate regimens	B
For people with resected node positive colon cancer (Stage III) who are to receive postoperative chemotherapy, combination chemotherapy with oxaliplatin and a fluoropyrimidine is recommended	A
Irinotecan should not be given as postoperative adjuvant chemotherapy for people with Stages I, II and III colon cancer Note: irinotecan is currently licensed in New Zealand for metastatic colorectal cancer only	A

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Horizon scanning

The PETACC-8 trial is in progress.[121] This trial is comparing FOLFOX-4 + cetuximab with FOLFOX-4 alone in patients with curatively resected Stage III colon cancer.

The NSABP C-08 trial is investigating the addition of bevacizumab to oxaliplatin-based chemotherapy in Stages II and III colon cancer.[122] Three-year disease-free survival data have been presented at conference. The initial (one-year) improvement was not seen at three years.

The Intergroup/NCCTG N0147 trial is investigating a FOLFOX6 regimen with or without cetuximab, after curative resection in Stage III patients.[123] Interim results reported from the American Society of Clinical Oncology (ASCO) in 2010 indicated no benefit from the addition of cetuximab.

The French Intergroup R98 trial is comparing 5FU/LV alone or with irinotecan (CPT-11) in resected Stages II to III rectal cancers.[124] Interim efficacy analysis reported by ASCO 2010 indicated a trend in favour of 5FU/LV + CPT-11 although it is, as yet, underpowered to detect a significant difference.

A phase III trial is comparing capecitabine + oxaliplatin (XELOX) with 5-FU/LV in Stage III colon cancer patients.[125] Initial results presented at the ASCO conference in 2010 showed that, after a median follow-up of 57 months, disease-free survival was significantly greater in XELOX patients at 3, 4 and 5 years. No differences were found between patients aged <70 and ≥ 70 years. The authors conclude that XELOX is superior to bolus 5-FU/LV for disease-free survival as adjuvant treatment for stage III colon cancer. Overall survival data are currently immature; follow-up is ongoing and updates will be reported when available.

The AVANT trial is a phase III study evaluating the efficacy and safety of bevacizumab in combination with intermittent capecitabine and oxaliplatin (XELOX) or fluorouracil, leucovorin, and oxaliplatin (FOLFOX-4) versus FOLFOX-4 alone in the adjuvant treatment of patients with Stage III or high-risk Stage II colon cancer.[126] Interim safety analysis presented at the 2009 Joint European Cancer Organisation and European Society for Medical Oncology Multidisciplinary Congress indicated that bevacizumab plus the XELOX/FOLFOX combination is safe in the adjuvant treatment of colon cancer.

10 Adjuvant therapy for rectal cancer

→ *Chapter 16 NHMRC*

This chapter addresses adjuvant therapy for people with rectal cancer, including:

- when adjuvant therapy should be considered for rectal cancer
- preoperative compared with postoperative therapy
- the addition of chemotherapy to radiation therapy
- short-course compared with long-course radiation therapy.

Question development

There were three National Health and Medical Research Council (NHMRC) clinical questions and recommendations for this chapter.

The first question was: *When should adjuvant therapy be considered for rectal cancer*? The recommendation was 'Adjuvant preoperative or postoperative radiotherapy is recommended for high-risk (T3/4 or N1) rectal cancer'. The Guideline Development Team (GDT) discussed this question and the resulting recommendation and decided that all people with rectal cancer should be considered for adjuvant therapy on a case-by-case basis, not just those who are high risk. The GDT felt that treatment should be individualised for patients with rectal cancer and that the current NHMRC recommendation would exclude some people from treatment, specifically, those identified during surgery. The GDT also felt there were other indications for neoadjuvant treatment, for example, T2 patients who in New Zealand are considered for treatment. The GDT changed the recommendation wording, but did not feel a full review was warranted. The new recommendation is 'Preoperative or postoperative adjuvant therapy should be considered by a multidisciplinary team for all people with rectal cancer'.

The GDT felt the second clinical question (*Does preoperative therapy reduce late morbidity compared with postoperative?*) required updating and a systematic review was undertaken to answer this question.

The GDT decided that the third question (*What postoperative chemotherapy should be administered if radiotherapy is indicated?*) required updating, but also that the clinical question required amendment. The question was updated to: *In patients with locally advanced rectal cancer, what is the effect of adding chemotherapy to preoperative radiation treatment on patient outcomes?* A systematic review was undertaken to answer this question.

The GDT identified one additional question: *In patients with locally advanced rectal cancer, what is the effect of preoperative short-course radiation treatment compared with long-course perioperative chemoradiation on patient outcomes (local recurrence)?*

Body of evidence (for all questions)

Guidelines

Five clinical practice guidelines were identified that made recommendations for adjuvant therapy for people with rectal cancer.[25,27–29,127] Most guidelines were in agreement on the adjuvant therapy offered, except for short-course preoperative radiotherapy (RT) compared with chemoradiation (CRT).

The recommendations from the guidelines for adjuvant therapy for rectal cancer can be summarised as follows.

- The addition of RT to surgery for patients with rectal cancer is beneficial; whenever possible, preoperative treatment is preferred since it is more effective and less toxic than postoperative treatment.
- Some guidelines recommended short-course preoperative RT[25,28,29] while others recommended preoperative CRT.[27,127]
- Postoperative CRT is not recommended but could be used in high-risk patients (eg, those with positive circumferential margins or perforation in the tumour area) or in patients where preoperative RT was not given.
- Patients eligible for preoperative RT with or without chemotherapy should also be considered for adjuvant postoperative CRT.

Preoperative compared with postoperative therapy

Clinical question:	Does preoperative therapy reduce late morbidity compared with postoperative?

Body of evidence

Systematic reviews

One average quality systematic review comparing preoperative and postoperative CRT was identified.[128] Results reported no survival advantage with preoperative CRT. There were mixed results for sphincter-preservation advantage with preoperative and postoperative CRT. One of the studies identified a lower local recurrence with preoperative CRT ($p<0.01$). Preoperative CRT may enhance tumour response but increase acute toxicity.

An additional systematic review reported mortality and morbidity data for studies of adjuvant therapy for rectal cancer.[129] No differences were found in mortality rates. It was unclear whether preoperative or postoperative CRT produced more frequent adverse events, although postoperative complications (eg, bleeding, delayed wound healing, anastomotic leaks, small bowel obstruction and fistula formation) were not increased after preoperative CRT.

Primary studies

Two randomised controlled trials (RCTs) that compared preoperative and postoperative radiotherapy (with or without chemotherapy) were identified.[130,131] Both were average quality and had small sample sizes (<55).

One RCT compared preoperative CRT with postoperative CRT. No statistical differences were reported between the groups for overall survival, disease-free survival or local recurrence. However, the number of preoperative therapy patients alive in years three and four was higher, and for disease-free survival the rate was higher each year for the preoperative therapy patients. More patients in the postoperative therapy group had local recurrence. The authors concluded that preoperative radiotherapy is at least as effective as postoperative therapy, despite the small sample size.[130]

One RCT compared preoperative RT (± chemotherapy) with postoperative CRT. No statistical differences were reported between the groups for overall survival, disease-free survival or local recurrence.[131]

Summary of findings

Preoperative CRT offers no survival advantage over postoperative CRT. There remains uncertainty about whether preoperative CRT reduces late morbidity compared to postoperative CRT. Compared to preoperative RT alone, CRT enhances tumour response but causes an increase in acute toxicity and tumour downstaging did not always translate into an increase in sphincter preservation.

Adding chemotherapy to radiation therapy

Clinical question:	In patients with locally advanced rectal cancer, what is the effect of adding chemotherapy to preoperative radiation treatment on patient outcomes?

Body of evidence

Systematic reviews

Two systematic reviews were identified.[132,133]

A good-quality Cochrane review compared preoperative RT with preoperative CRT in patients with resectable Stage II and III rectal cancer.[132] This review included comparisons of different courses of RT. Another systematic review of average quality included patients with unresectable rectal cancer, so the results of the review are not reported here.[133] The results did not differ from the Cochrane review, and all the applicable primary trials from the review were included in the Cochrane review.

Primary studies

Six publications reporting three trials were included in a Cochrane review.[134–139] In terms of RT dose, three trials compared RT with chemotherapy added to the same RT dose. One trial compared 25 gray (Gy) in 5 fractions (fr) with 50.4 Gy in 28 fr + chemotherapy[140–142] (see Table 10.1). This trial better answered a subsequent clinical question (long compared with short RT). Therefore, where meta-analyses omitted this study, results of the meta-analysis are reported. Where meta-analyses included this trial, the individual studies are appraised and reported separately. Data for the three trials are presented in Table 10.1.

Table 10.1 Primary studies comparing preoperative radiotherapy with preoperative chemoradiation

	Patients	Location	Follow-up	Intervention	Comparison	Overall survival	Disease-free survival	Recurrence
Boulis-Wassif 1984[137]	247 T2, T3 and T4	≤15 cm from anal verge	7 years	34.5 Gy in 15 fr	34.5 Gy in 15 fr + 5-FU	HR=1.38 (95% CI 0.96–1.99)		HR=0.79 (95% CI 0.51–1.24)
Bosset 2004, 2005 and 2006[135,136,143] EORTC	1011 T3 or T4	≤15 cm from anal verge	5.4 years	45 Gy in 25 fr	45 Gy in 25 fr + 5-FU in weeks 1 and 5 ± postoperative chemotherapy	HR=1.02 (95% CI 0.83–1.26)	HR=0.84 (95% CI 0.78–1.13)	Preoperative RT 17.1% (95% CI 12.3–21.9) Preoperative CRT 8.7% (95% CI 4.9–12.6) Preoperative RT + postoperative chemotherapy 9.6% (95% CI 5.7–13.5) Preoperative CRT + postoperative chemotherapy 7.6% (95% CI 4.2–11.0) p=0.002 for the comparison between the group receiving preoperative RT alone and the other three groups
Gerard 2005 and 2006[138,139]	733 T3 or T4	Accessible by digital exam	6.75 years	45 Gy in 25 fr	45 Gy in 25 fr + 5-FU/FA	HR=0.96 (95% CI 0.73–1.27)	Progression-free survival HR=0.96 (95% CI 0.77–1.20)	RR=0.50 (95% CI 0.31–0.80, p=0.004)

Table developed by the New Zealand Guidelines Group.

Abbreviations: CI=confidence interval; cm=centimetres; CRT=chemoradiation; EORTC=European Organisation for Research and Treatment of Cancer; FA=folinic acid; 5-FU=5 fluorouracil; fr=fraction; Gy=gray; HR=hazard ratio; RR=relative risk; RT=radiotherapy.

A good-quality four-arm RCT conducted by the European Organisation for Research and Treatment of Cancer study group (EORTC 22921) investigated the addition of 5-fluorouracil plus leucovorin (5-FU/LV) to preoperative RT with or without postoperative chemotherapy. The addition of 5-FU/LV slightly increased the amount of acute toxicity; grade 2 acute diarrhoea occurred in 17.3% of patients having RT compared with and 34.3% having CRT ($p<0.005$). The other side effects remained unchanged or were only marginally increased. However, the compliance with the radiation protocol or the feasibility of surgery did not decrease.[143] Preliminary results indicated that the addition of chemotherapy to preoperative RT induces downsizing, downstaging and significant changes in histologic characteristics.[135] Longer-term outcomes concluded that adding fluorouracil-based chemotherapy preoperatively or postoperatively showed no significant effect on survival. However, regardless of timing, chemotherapy provided a significant benefit with respect to local control.[136]

The progression-free and overall survival curves in Bosset 2006[136] started to diverge at approximately two and five years after entry into the study, suggesting that a subset of patients of better prognosis who survive two to five years after the initiation of the first treatment might benefit from the adjuvant treatment in the long term. An exploratory analysis based on this noted that, although there was no statistically significant impact of adjuvant chemotherapy on disease-free survival for all patients ($p<0.5$), the treatment effect differed significantly between the ypT0–2 and the ypT3–4 patients (heterogeneity $p<0.009$); only the ypT0–2 patients seemed to benefit from adjuvant chemotherapy ($p<0.011$). The same pattern was observed for overall survival.

The authors suggested that only good-prognosis patients (ypT0–2) might benefit from adjuvant chemotherapy. This could explain why, in the whole group, the progression-free and overall survival diverged only after the poor-prognosis patients (ypT3–4) had experienced treatment failure. Patients in whom no downstaging was achieved did not benefit. It has been suggested that the same prognostic factors may drive both tumour sensitivity for the primary treatment and long-term clinical benefit from further adjuvant chemotherapy.[144]

A good-quality RCT evaluated whether concurrent CRT in a neoadjuvant schedule could increase overall survival compared with RT alone. Results were in agreement with the EORTC 22921 trial; they suggested that despite a moderate increase in acute toxicity in T3–4 resectable cancers of the lower and middle rectum, concurrent chemotherapy and RT should be considered standard. The authors also reported that in the long term, bowel and sexual function can be adversely affected by these preoperative regimens. Better selection could be considered to try to individualise the preoperative treatment, possibly using magnetic resonance imaging.[139]

A two-arm RCT evaluated preoperative RT with or without 5-FU in 247 patients between 1972 and 1976. RT alone produced better survival outcomes than did CRT (59% compared with 46%); five-year survival was marginally significant (HR 1.38, 95% CI 0.96–1.99). CRT patients experienced a higher incidence of side effects and postoperative deaths.[137]

Summary of findings

Survival

A Cochrane review found no evidence of differences in overall survival at five years (three studies, OR 0.95, 95% CI 0.79–1.14, p=0.58) or disease-free survival at five years (two studies, OR 1.11, 95% CI 0.92–1.34, p=0.27).

Local recurrence

A Cochrane review showed that the addition of chemotherapy demonstrated a significant reduction in the local recurrence rate at five years (three studies, OR 0.53, 95% CI 0.39–0.72, p<0.001).[99] In the RT group, 122 of 740 patients (16.5%) developed a local recurrence while in the CRT group this event was observed in 71 out of 754 patients (9.4%).

Toxicity

Two trials reported outcomes for grades III and IV toxicity.[136,139] Both trials reported grade III or IV treatment-related toxicity was significantly increased in patients receiving CRT compared with RT alone. One study reported that patients receiving CRT were almost twice as likely to report toxicity (OR 1.99, 95% CI 1.31–3.04)[136] while the other trial showed a six-fold increase (OR 6.14, 95% CI 3.08–12.24).[139]

Morbidity

Two trials reported outcomes for postoperative morbidity.[136,139] One trial showed no differences between patients receiving CRT compared with patients receiving RT alone (OR 0.98, 95% CI 0.73–1.32)[136] while the other trial reported better outcomes for patients receiving RT alone where 21% of patients reported morbidity compared with 27% of CRT patients (OR 0.72, 95% CI 0.51–1.01).[139]

Other outcomes

No differences were observed in any trials measuring sphincter-preservation rates, postoperative 30-day mortality rates or anastomotic leak.

Overall summary

Compared with preoperative RT alone, preoperative CRT enhances tumour response and reduces the rate of local recurrence. However, adding chemotherapy also causes an increase in acute toxicity. CRT does not appear to offer any survival benefits or influence morbidity, sphincter preservation, anastomotic leak or 30-day mortality.

Short-course compared with long-course therapy

Clinical question:	In patients with locally advanced rectal cancer, what is the effect of preoperative short-course radiation treatment compared with long-course pre/postoperative chemoradiation on patient outcomes?

Body of evidence

Systematic reviews

One average-quality systematic review reported mortality and morbidity data for studies of adjuvant therapy for rectal cancer.[129] Preoperative short-course RT caused less gastrointestinal toxicity, although an increase in the incidence of perineal wound infection and breakdown was reported compared with CRT. Increased cardiovascular events were also reported.

Primary studies

Three trials were identified comparing short-course preoperative radiotherapy with long-course preoperative or postoperative chemoradiation (see Table 10.2).[140–142,145,146]

Table 10.2 Primary studies comparing preoperative short-course radiotherapy with preoperative or postoperative long-course chemoradiation

	Patients	Location	Intervention	Comparison	Overall survival	Disease-free survival	Recurrence
Sebag-Montefiore 2009 MRC CR07[145]	n=1350 Stages I, II and III	<15 cm from anal verge	Preoperative 25 Gy in 5 fr	Postoperative 45 Gy in 2 5 fr + 5-FU	Short RT: 70.3% Long CRT: 67.9% 5-year HR=0.91 (95% CI 0.73–1.13)	Short RT: 73.6% Long CRT: 66.7% 5-year HR=0.76 (95% CI 0.62–0.94)	Short RT: 4.7% Long CRT: 11.5% 5-year HR=0.39 (95% CI 0.27–0.58) NNT=16 (95% CI 10.5–26.6)
Bujko 2004, 2005 and 2006[140–142]	n=312 T3 or T4	Inferior edge palpable on digital exam	Preoperative 25 Gy in 5 fr	Preoperative 50.4 Gy in 28 fr + 5-FU	Short RT: 67.2% CRT: 66.2% 4-year HR=1.01 (95% CI 0.69–1.48)	Short RT: 58.4% Long CRT: 55.6% 4-year HR=0.96 (0.69–1.35)	Local recurrence Short RT: 10.6% Long CRT: 15.6% HR=0.65 (95% CI 0.32–1.28)
Ngan (TROG) 2010[146]	n=326 T3	<12 cm from anal verge	Preoperative 25 Gy in 5 fr	Preoperative 50.4 Gy in 28 fr + 5-FU	Short RT: 74% Long CRT: 70% 5-year HR=0.89 (95% CI 0.60–1.32)		Distant recurrence Short RT: 72% Long CRT: 69% 5-year HR=0.96 (95% CI 0.64–1.45) Local recurrence Short course: 7.5% Long course: 4.4% 3-year difference: 3.1% (95% CI 2.0–8.3, p=0.24)

* Table developed by the New Zealand Guidelines Group.

Abbreviations: CI=confidence interval; cm=centimetres; CRT=chemoradiation; n=number of patients; Gy=gray; fr=fraction; 5-FU=5 fluorouracil; HR=hazard ratio; NNT=number needed to treat; RT=radiotherapy.

A good-quality RCT aimed to verify whether preoperative conventionally fractionated CRT offered an advantage in sphincter preservation compared with preoperative short-term irradiation. Despite significant downsizing, CRT did not result in an increased sphincter-preservation rate.[142] Further analyses showed no significant difference between arms in the numbers of patients with postoperative complications,[140] or survival, local control and late toxicity between short-course preoperative RT or long-course preoperative CRT.[141]

A good-quality RCT compared the effects of preoperative short-course RT with postoperative selective CRT.[145] Patients randomised to short-course RT experienced a 61% relative reduction in the risk of recurrence (HR 0.39, 95% CI 0.27–0.58, $p<0.0001$) and a 24% relative benefit in disease-free survival (HR 0.76, 95% CI 0.62–0.94, $p=0.013$). There was no significant difference between the treatment groups for overall survival.

A Trans-Tasman Radiation Oncology Group (TROG) multicentre randomised trial comparing long-course preoperative chemoradiation with short-course preoperative radiotherapy for patients with localised T3 rectal cancer recently completed recruiting patients.[146]

There was no clear evidence for a difference between short- and long-course therapy in terms of local recurrence at three years. Distant recurrence and overall survival rates were similar. Both short- and long-course therapy provided good local control. Late toxicity rates were not substantially different.

Summary of findings

The three included trials agree on one point; there do not appear to be any differences in overall survival between long- and short-course treatment groups.

Disease-free survival was reported by two trials. The MRC CR07 trial reported improved survival in patients receiving short-course preoperative RT.[145] The Polish trial reported no differences between groups.[140–142]

In terms of recurrence, no study found a significant difference between short- and long-course therapy. The MRC CR07 trial[145] reported improvements in recurrence rates in patients receiving short-course preoperative RT compared with long-course postoperative CRT, and the Polish trial[140–142] indicated that local recurrence is improved by short-course preoperative RT compared with long-course preoperative CRT, but the differences in both trials were not statistically significant. However, the TROG trial indicated the opposite, that local recurrence is improved in patients receiving long-course therapy, although this difference was not statistically significant.

Recommendations in published guidelines are divided; some guidelines recommend short-course preoperative RT, others recommend preoperative CRT.

Recommendation development

Preoperative versus postoperative therapy

The updated evidence for the effect of preoperative therapy on late morbidity was not thought to alter previous recommendations made by the NHMRC and the wording of this recommendation was agreed to by the GDT.

The GDT discussed the role of preoperative CRT in patients with threatened circumferential resection margin or low-lying tumours and agreed that there does not appear to be a survival benefit but preoperative CRT does show lower rates of local recurrence.

Adding chemotherapy to radiation therapy

Preoperative CRT improves local control over preoperative radiation alone but increases acute toxicity and offers no survival benefit. The GDT discussed different situations in which preoperative long-course RT was appropriate or not and felt that the decision about whether to administer this treatment should be taken on a case-by-case basis. The GDT noted that the evidence investigated only long-course CRT.

Short-course compared with long-course therapy

The GDT debated how long RT should be administered. This period varies in different parts of the world. There were differences between the two studies identified for this question, which made comparisons difficult, and the GDT noted that several factors influence the selection of patients for short- or long-course radiation; specifically, lower- risk patients may need only short-course radiation, while a longer course may be needed for T4 patients, for example, to shrink tumours. In sum, both approaches reduced local recurrence; either approach is valid, but there is debate around the selection of patients. The GDT also discussed the possibility of longer-course treatment providing more benefit for threatened circumferential margins on preoperative imaging.

The effect of the different comparator groups is unclear; the MRC CR07 trial comparator was postoperative CRT for selected patients, while both the Polish trial and TROG trial comparators were preoperative CRT. Results from the MRC CR07 trial indicated a number needed to treat (NNT) of 16 (95% CI 10.5–26.6), which suggests that 16 patients would need to be treated with short-course preoperative RT to prevent one local recurrence.* By comparison, the Polish trial included patients with local recurrence with or without distant metastases. Omitting patients with distant metastases would leave the RT group with recurrences of 2 out of 155 (1.4%) and the CRT group with 9 out of 157 (6.1%) ($p=0.0609$).*

The data for disease-free survival are less clear, and the calculation of NNTs is not possible for either trial.

* NZGG-calculated data.

Following the completion of the searches and appraisals for this topic, a new systematic review was identified that was completed during the same time as NZGG was conducting the reviews for this chapter.[147] NZGG appraised the review and concluded it was of a high quality but the findings had no implications for the recommendations that were developed by the GDT for this guideline. The review simply provided further supporting evidence for the recommendation that was developed.

NZGG recommendations

	Grade
Preoperative or postoperative adjuvant therapy should be considered by a multidisciplinary team for all people with rectal cancer	✓
Preoperative radiotherapy, with or without chemotherapy, may lower the incidence of late morbidity compared to postoperative chemoradiation	C
For people with rectal cancer who are at risk of local recurrence, either preoperative short-course radiotherapy or preoperative long-course chemoradiation is recommended Note: Short-course radiotherapy – 25 Gy in 5 fractions; long-course radiotherapy – 45–50.4 Gy in 25–28 fractions	B
Preoperative long-course chemoradiation is recommended for people with rectal cancer who have a low rectal cancer or a threatened circumferential resection margin Note: Long-course radiotherapy – 45–50.4 Gy in 25–28 fractions	B
Where people are receiving long-course radiotherapy (preoperative or postoperative), concurrent chemotherapy should be considered	A

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Horizon scanning

The Stockholm III trial of preoperative radiotherapy regimens for rectal cancer aims to address issues regarding the fractionation of RT and timing of surgery for rectal cancer. It is a multicentre trial randomising patients to preoperative short-course RT with two different intervals to surgery, or long-course RT with delayed surgery. Final data collection for primary outcomes is expected in December 2011 (see www.clinicaltrials.gov/ct2/show/NCT00904813?term=NCT00904813&rank=1).

11 Follow-up after curative resection

→ *Chapter 17 NHMRC*

This chapter addresses follow-up for people who have undergone curative resection, including:

- the components of follow-up
- who should perform the follow-up.

Question development

There was one National Health and Medical Research Council (NHMRC) clinical question and recommendation for this chapter. The clinical question *What are the recommendations for follow-up?* was discussed by the GDT and updated to two more-specific questions: *What components of follow-up are important?* and *Who should be doing follow-up?* Systematic reviews were undertaken to answer both questions.

Components of follow-up

Clinical question: What components of follow-up are important?

Body of evidence

Guidelines

Eight clinical practice guidelines were identified and made recommendations about follow-up for people with colon and rectal cancer.[25–29,148–150]

Most guidelines commented on the uncertainty about the effectiveness of different aspects and forms of follow-up. The relative importance of early assessment of symptoms versus screening tests in the diagnosis of resectable recurrence is unknown. Most guidelines also acknowledged the uncertainty of the timing of scheduled follow-up visits.

A broad summary of the recommendations derived from the guidelines for follow-up include the following:

- both colon and rectal cancer patients who did not undergo complete colonoscopy before surgery should be offered colonoscopy within six months of discharge
- intensive follow-up is likely to be more beneficial than less intensive follow-up
- clinical assessment should be undertaken yearly for suggestive symptoms of relapse
- high-risk patients should have a colonoscopy every six months to one year for the first three years, then yearly for at least five years
- low-risk patients should have a colonoscopy every three to five years
- clinical assessment for colon cancer patients should include CEA, chest, abdominal and pelvic CT scans, colonoscopy and liver ultrasound
- clinical assessment for rectal cancer patients should include CEA, chest, abdominal and pelvic CT scans, colonoscopy and proctoscopy or sigmoidoscopy.

Systematic reviews

Five systematic reviews were identified. All compared intensive with less intensive (conventional) follow-up strategies. A Cochrane systematic review[151] comparing different follow-up strategies in a meta-analysis was considered to be of good quality and two other systematic reviews, one of which comprised six RCTs[149,152] were also considered to be of good quality.

One meta-analysis[61] was considered to be of average quality. The review which formed the basis of the recommendations of the American Society of Clinical Oncology was also considered to be of average quality.[153]

Primary studies

Three primary studies were identified. An RCT of more frequent versus conventional colonoscopy[154] and a comparison of more intensive surveillance with standard postoperative surveillance with additional imaging[155] were both considered good quality. An RCT which added FDG-PET to a standard follow-up protocol was considered of average quality.[156]

Intensive versus conventional follow-up

All five of the systematic reviews/meta-analyses suggested a benefit in five-year overall survival of intensive follow-up when compared with conventional or less intensive follow-up.[149,151–153,157] This was reported in one study as an absolute risk difference of 7%.[153]

Intensive follow-up was associated with significantly earlier detection of recurrences ($p<0.001$), an increased detection rate for isolated local recurrences (RR 1.61, 95% CI 1.12–2.32; $p=0.01$)[152] and asymptomatic recurrences more frequently ($p<0.00001$) and 5.9 months earlier than less intensive interventions ($p<0.0001$).[157]

One good-quality systematic review found no evidence for an effect on the outcome of recurrences between different strategies although there was a significant effect on time to recurrence in favour of intensive follow-up (mean difference -6.8, 95% CI -11.06–-2.44; $p=0.002$) and for curative surgery attempted at the time of recurrence in favour of a more intensive strategy (OR 2.41, 95% CI 1.63–3.54; $p<0.00001$).[151] The review also reported an overall mortality benefit for more tests versus fewer tests (OR 0.64, 95% CI 0.49–0.85; $p=0.002$).[151] Curative re-operation rates were more likely to occur in the intensive follow-up groups (24.3% *vs* 9.9%, $p=0.0001$) compared with less intensive strategies.[157]

Two trials reported no differences in overall survival.[154,155] However, a more intensive strategy increased the proportion of resectable tumours and improved the prognosis of Stage II colon cancers and rectal tumours.[155]

One systematic review concluded that the observed reductions were in fact associated with the application of an investigation rather than more frequent performance of the investigations and cancer-related mortality was unaffected by the intensity of follow-up.[157] Another systematic review suggested that factors other than salvage may contribute to survival such as psychological wellbeing and/or improved treatment of coincidental disease.[152]

Investigations

Endoscopic surveillance

Trials using colonoscopy demonstrated a significant impact on overall survival (figures not reported, p=0.04);[157] however, there was no effect of more versus less colonoscopy. In contrast, another study found no evidence for a benefit in overall survival with a more intensive strategy.[154] Colonoscopy-detected tumour recurrence accounted for the highest resectability rate[155] and detection of asymptomatic recurrences.[154,157]

One RCT[154] recommended a conventional strategy of annual colonoscopy in postoperative years 1 and 2 and then three- to five-yearly, and a systematic review[149] recommended that all patients with resected cancer (Stage I, II, III) should undergo colonoscopy at follow-up if this had not been performed postoperatively. If high-risk polyps (villous/tubular >1cm) were present, these should be excised and annual colonoscopy performed until no longer found; otherwise colonoscopy every three to five years was recommended.

Colon and rectal cancer patients should have a preoperative or peri-operative documentation of cancer and polyp-free colon.[153] Colonoscopy was recommended after three years and then, if normal, five-yearly after that. Different recommendations were made for those with high-risk genetic syndromes as per the American Gastroenterological Association. For patients with rectal cancer, flexible sigmoidoscopy of the rectum was recommended every six months for five years.[153]

Serum CEA levels

Trials using serum CEA demonstrated a significant impact on overall survival (p=0.0002).[149,157] More frequent monitoring of CEA after curative surgery was the only test associated with a significant improvement in overall mortality (p=0.03). This resulted in a significantly higher detection of asymptomatic recurrence (p=0.007) and curative re-operation rate (p=0.0006).[157] CEA increased the detection of asymptomatic recurrence (p<0.00001).[157]

A guideline recommended that in patients at high risk of recurrence (Stage IIb/III), who are willing to undergo investigations and treatment if required, there should be clinical testing every six months for three years and then annually for five years. At these visits, the individual may undergo CEA testing, chest x-ray and liver ultrasound.[149] Another systematic review recommended postoperative serum CEA should be performed every three months in patients with Stage II or III disease for at least three years after diagnosis, if the patient is a candidate for surgery or systemic therapy.[153]

Analysis from a systematic review, limited to two RCTs, found no significant effect of CEA versus no CEA testing.[158]

Imaging

Trials which included liver imaging reported an overall survival benefit (RR 0.74, 95% CI 0.63–0.97, p=0.0004).[149] Mortality was reduced by 25% in patients undergoing liver imaging compared with non-imaging strategies. The benefit was thought to be derived from the usefulness of liver resections for metastatic cancer of limited extent.[153]

In contrast, imaging of the liver and CT of the abdomen and pelvis were not associated with any improvement in mortality.[157] Neither was there evidence of a benefit for chest x-ray as a follow-up modality.[153,157] Chest x-ray ($p < 0.00001$), liver ultrasound ($p = 0.009$) and CT scan ($p = 0.007$) increased the detection of asymptomatic recurrence.[157] However, increased frequency of testing had no additional benefit.[157]

The American Society of Clinical Oncology (ASCO) recommended that for those colon and rectal cancer patients at higher risk of recurrence and where curative intent was an option, CT imaging of the chest and abdomen should be undertaken annually for three years. A pelvic CT should be considered for rectal cancer surveillance, especially for those who had not received radiotherapy. There was an acknowledgment of the additional financial burden with more frequent imaging.[153]

Faecal occult blood (FOB) testing

Periodic testing of FOB was not recommended by one systematic review.[153]

PET

An RCT[156] examined the addition of FDT PET to routine follow-up procedures. This resulted in a higher number of curative surgical interventions being performed in the FDT PET group than in the conventional group. However, the authors noted that, as technology progresses, there is a need to evaluate the cost effectiveness and also the role of FDT PET CT.[156]

Scheduling of clinical visits

One systematic review[153] acknowledged the lack of efficacy testing for follow-up schedules. As a result of this review, the American Association of Clinical Oncology recommended a clinical visit every three to six months for the first three years after treatment, with decreased frequency thereafter for two years for colon cancer patients. After five years, follow-up may be left to physician discretion.[153]

Summary of findings

Intensive follow-up is likely to be more beneficial in terms of five-year survival when compared with conventional or less intensive follow-up. Follow-up strategies that include endoscopic surveillance, serum CEA and imaging may improve overall survival.

Recommendation development

The GDT noted that the definitions of 'intensive' and 'conventional' strategies are highly variable between the studies.[149,157] Many of the studies described within the systematic reviews pre-date adjuvant chemotherapy as a treatment and surgical interventions and imaging techniques have changed over time.[157,158] One guideline noted that it was unclear which test or combination of tests are optimal and there was a lack of formal testing of optimal scheduling.[149]

The GDT agreed that there is evidence to suggest improved survival in patients undergoing more intensive follow-up strategies and that the regular use of colonoscopy, liver imaging and CEA is supported by the literature. The use of chest x-ray and FOB testing is not supported by the literature.

The GDT also discussed side effects of follow-up investigations and noted that it is known that some side effects of cancer treatment may not become apparent until years have elapsed. A potential benefit of long-term follow-up is the opportunity to detect unanticipated side effects of new cancer treatments. Unanticipated events are inherently difficult to study and they are unlikely to be addressed by future research, so the GDT has made no recommendation on this issue.

NZGG recommendations

	Grade
All people who have undergone colorectal cancer resection should be followed up intensively	✓
All people who have undergone colorectal cancer resection and develop relevant symptoms should undergo clinical assessment	✓
For people with colon cancer at high risk of recurrence (Stages IIb and III), clinical assessment is recommended at least every six months for the first three years after initial surgery and then annually for a further two years or when symptoms occur	B
For people with colon cancer at lower risk of recurrence (Stages I and IIa) or for people with comorbidities restricting future surgery, clinical assessment is recommended when symptoms occur or by annual review for five years after initial surgery	B
All people with colorectal cancer should have a colonoscopy before surgery or within 12 months following initial surgery	B
For people with colon cancer at lower risk of recurrence (Stages I and IIa), follow-up colonoscopy every three to five years is recommended	B
For people with rectal cancer, digital rectal examination (DRE), proctoscopy or sigmoidoscopy should be undertaken at three months, six months, one year and two years after initial surgery. Thereafter colonoscopy should be undertaken at three- to five-yearly intervals	B
Follow-up should include physical examination and CEA	B
All people with colorectal cancer Stages I to III should have liver imaging between years 1 and 3	B
The use of faecal occult blood testing as part of colorectal cancer follow-up is not recommended	B

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Horizon scanning

Final results are expected from the GILDA trial, which compared intensive versus less intensive follow-up protocols.[159] The COLOFOL study (www.colofol.com) is randomising 2500 patients to a low or high frequency follow-up programme which includes serum CEA and chest and liver imaging.

Who should perform follow-up?

Clinical question: Who should be doing follow-up?

Body of evidence

Systematic reviews

One systematic review was identified which compared follow-up of all cancer patients in primary versus secondary care.[160] Both this review and a second systematic review[151] briefly include a reference to an RCT[161] which has been described in more detail below. Both systematic reviews were considered to be of good quality.

Primary studies

No additional primary studies were identified.

Summary of findings

Both systematic reviews[151,160] briefly described an Australian study comparing general practitioner (GP) or surgeon-led follow-up. The RCT[161] reported no differences in death rates (per 1000 months on trial), median survival (months), quality of life and time to recurrence after two years follow-up or levels of satisfaction for GPs versus surgeon-led follow-up. GPs were more likely to request faecal occult blood tests (FOBTs) (23.6% *vs* 9.8%, rate ratio 2.4, 95% CI 1.4–4.4) and surgeons were more likely to request ultrasound (18.4% *vs* 9.4%, rate ratio 0.5, 95% CI 0.3–1.0) or one or more colonoscopies (48.5% *vs* 32.4%, rate ratio 0.7, 95% CI 0.5–1.0).[151,160] However, the follow-up protocol (physical examination three-monthly for two years and then six-monthly for three years, annual FOBT and three-yearly colonoscopy) did not have to be adhered to and a high risk of contamination was expected.[161]

Recommendation development

The GDT discussed the limited evidence from one randomised controlled trial and noted that there do not appear to be any differences between GP and surgeon-led follow-up, with the exception of the type of investigations ordered. The study did not investigate the workforce or financial implications of moving follow-up from secondary to primary care. The GDT discussed the gaps in follow-up and the ways in which patients can be lost to follow-up. The accessibility of scanning and tests in a general care setting was discussed, as there are many instances where follow-up is more practical closer to home for patients who live far from main centres. Anecdotal evidence from smaller New Zealand centres suggests that follow-up is shared effectively between primary care and specialist care using an online system. It was agreed that the question of who should provide follow-up and where this should take place was really about access to scanning services. The group agreed that closing these gaps should be addressed by the team providing treatment.

NZGG recommendations

	Grade
Follow-up should be under the direction of the multidisciplinary team and may involve follow-up in primary care	✓
People with colorectal cancer should be given written information outlining planned follow-up (eg, discharge report) at discharge from treatment, including what they should expect regarding the components and the timing of follow-up assessments	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Horizon scanning

One protocol was identified for a randomised controlled trial comparing follow-up conducted by surgeons compared with general practitioners.[162]

The UK FACS trial aims to randomise 4890 patients to explore CEA testing in primary care and intensive hospital follow-up with CT and ultrasound scanning (www.facs.soton.ac.uk). The trial has now closed with recruitment of 1200 patients.

12 Synoptic reporting

→ *Chapter 14 NHMRC*

This chapter addresses synoptic reporting, including:

- what staging data should be recorded
- the minimum data set for synoptic reporting.

Question development

There was one NHMRC clinical question and recommendation in this section. The question was: *What staging data should be recorded?* The recommendation was 'TNM staging, ACPS (Australian Clinico-Pathological Staging System) staging and the data required to stage the patient should all be recorded to allow national and international comparisons (ACPS staging embodies the simplicity of Dukes)'. The GDT discussed this question and resulting recommendation and decided that the reference to ACPS was not appropriate, given that it is now largely out of date. The GDT made a change to the recommendation wording, but did not feel a full review was warranted. The new recommendation is 'TNM staging and the data required to stage the patient should all be recorded to allow national and international comparisons' (see Appendix 2, *TNM staging*).

The GDT identified an additional question: *What is the minimum data set for synoptic reporting?* A narrative review was undertaken to answer this question.

NHMRC recommendation

	Level of evidence	Practice recommendation
What staging data should be recorded? TNM staging and the data required to stage the patient should all be recorded to allow national and international comparisons	III-3	Equivocal

Levels of evidence

I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-I	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test/post-test.

For more information see chapter 15 of the NHMRC review (pp 159–170).

Minimum data set for synoptic reporting

Clinical question: What is the minimum data set for synoptic reporting?

Body of evidence

The GDT considered the recently published colorectal cancer structured reporting protocol from the Royal College of Pathologists of Australasia.[163] No further searching was undertaken for this question as the protocol was considered by the GDT to be an adequate synthesis of the available evidence. The following text is from this protocol.

> ### Pathological reporting
>
> Pathological reporting of resection specimens for colorectal cancer provides important information both for the clinical management of the affected patient and for the evaluation of health care systems as a whole. For the patient, it confirms the diagnosis and describes the variables that will affect prognosis, which will inform future clinical management. For health care evaluation, pathology reports provide information for cancer registries and clinical audit, for ensuring comparability of patient groups in clinical trials, and for assessing the accuracy of new diagnostic tests and preoperative staging techniques. In order to fulfil all of these functions, the information contained within the pathology report must be accurate and complete.
>
> ### Benefits of structured reporting
>
> Structured pathology reports with standardised definitions for each component have been shown to significantly improve the completeness and quality of data provided to clinicians, and have been recommended both in North America and the United Kingdom. Several studies have highlighted deficiencies in the content of colorectal cancer resection reports, including elements that are considered crucial for patient management. Many studies have shown that adherence to a checklist for colorectal cancer reporting significantly improves the rate of inclusion of these crucial features.

(A guide to colorectal cancer histopathology reporting derived from the colorectal cancer structured reporting protocol and colorectal cancer structured pathology reporting proforma is in Appendix 3: *Structured (synoptic) reporting*.)

Recommendation development

The GDT discussed the issue that synoptic reporting aids consistent adequate data collection through minimum data sets. There is no evidence that synoptic reporting makes a difference in terms of patient outcomes but a further consideration is what is done with the information in regard to patient management. The GDT discussed which health professionals should be using synoptic reporting – pathologists tend to already use reporting systems but other health professionals (eg, surgeons and radiologists) use reporting systems to a much lesser extent. The GDT considered that there may be differences in practice between the North and South Islands.

The recommendation relating to TNM staging was based on the NHMRC recommendation and has not been evaluated in this exercise. The GDT acknowledged that TNM staging has uses beyond national and international comparisons. A uniform staging system should be a vital part of any colorectal cancer screening programme's management, audit and quality control as well as part of the database of New Zealand's cancer registry. The GDT believes that the use of uniform staging systems for the major cancers including colorectal cancer is becoming accepted as good clinical practice.

NZGG recommendations

	Grade
Pathology reporting of all colon and rectal cancer specimens should include structured (synoptic) reporting	C
Reporting of investigations and procedures (colonoscopy, radiology, operation notes, oncology treatment records) relating to colorectal cancer in a synoptic format is recommended	✓

Grades indicate the strength of the supporting evidence, rather than the importance of the recommendations – refer to Appendix 1 for grading details.

Appendices

Appendix 1:
Guideline development

This appendix describes the guideline development process undertaken by the New Zealand Guidelines Group (NZGG), including:

- the contributors to the guideline (the Guideline Development Team [GDT] and NZGG team)
- the guideline development process, including:
  - scope
  - clinical questions
  - reviewing the literature and developing recommendations
  - the evidence and recommendation grading system.
- consultation.

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Declarations of competing interest

Professor Frank Frizelle received financial support from the American Society of Colon and Rectal Surgery to attend its annual meeting as a speaker in 2008 and received staff funding from Merck Sharp & Dome.

Adrian Balasingham is the director of the Christchurch Radiology Group and collaborated academically with Professor Frank Frizelle.

Teresa Lynch received financial support from the New Zealand Nurses Organisation to attend the Masters of Health Science in 2006 and from the Christchurch Gastro Day Unit to attend the Gastro Conference in 2004, 2005, 2006, 2007 and 2008 and is the bodytalk practitioner/trainee instructor for the Integrative Holistic Health System.

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Iain Ward received financial support from Roche to attend the American Society of Clinical Oncology Conference in 2007.

No other competing interests were noted.

Guideline development process

This section overviews the research methodology utilised during the development of this guideline. It describes how the clinical questions were developed, how the systematic and narrative reviews were undertaken, and the process by which the reviewed evidence was developed into recommendations.

Scope

The guideline aims to cover adults with early colorectal cancer clinically managed within secondary and tertiary healthcare settings. The issues of colorectal cancer screening in asymptomatic people or the prevention of colorectal cancer in the general population were excluded. The clinical management of people with advanced or metastatic disease, children or adolescents with colorectal cancer and high-risk familial colorectal cancer syndromes were also excluded from this guideline.

Clinical questions

The current strategic approach to the funding of the development of clinical guidance in New Zealand is to focus on the areas of highest priority for New Zealand practice for a given condition or setting. These priority areas are those where practice varies widely, and/or there are gaps between practice and current evidence, and the development of recommendations would likely improve outcomes. In some cases (such as in the case of this guideline), an existing guideline is identified as the starting point for developing guidance in these prioritised areas. In determining how best to use content from the existing guideline and reduce replication, a number of issues are considered. Firstly, there may be areas across that guideline where more recent evidence is available. However, a review of the evidence is not deemed critical if the recommended course of action is likely to remain the same as in the current guideline. Secondly, there may be questions that were never asked by the existing guideline. However, new questions might only be proposed if it is clear that developing new recommendations would have a major impact on significant patient outcomes. A consequence of this strategic approach is that the guideline panels are not always able to form recommendations in all areas. For the current guideline, NZGG and the panel were initially requested by the funding body to restrict the number of clinical questions reviewed to 15. The questions chosen for review followed the process outlined below.

NZGG convened the scoping Expert Advisory Group (EAG), comprising members nominated by the Ministry of Health. The Ministry of Health's Bowel Cancer Taskforce had previously requested that the guideline on the diagnosis and management of bowel cancer developed in Australia and endorsed by the National Health and Medical Research Council (NHMRC)[3] be adapted for use in New Zealand. The EAG was required to consider how best to utilise the content of this guideline to develop New Zealand guidance.

A one-day face-to-face meeting was held where the NHMRC clinical questions and recommendations were reviewed and EAG members agreed on which recommendations were acceptable in their current format and which needed updating either because new evidence had emerged or because the New Zealand context differed from the Australian. In addition, the EAG was asked to identify any new questions that were not currently answered by the NHMRC guideline.

One of four things happened to the clinical questions and recommendations from the NHMRC guideline.

1 The clinical questions and recommendations were accepted without change and are reported in this guideline in their original format and with their NHMRC grading without explanatory text.

2 The clinical questions and recommendations were deleted from this guideline (see *Deleted questions* on page 95 for explanations).

3 The NHMRC clinical question was adopted, and the recommendation was updated.

4 The NHMRC clinical question was amended, and the recommendation was updated.

In some instances, the NHMRC recommendations were mostly acceptable, but the EAG felt a wording change was necessary to enhance understanding of the recommendation. In these cases, permission was sought from the original NHMRC guideline members. The new questions identified by the EAG were based on important patient outcomes, areas of knowledge that are controversial or uncertain, and current practice gaps based on the experience of the group.

Following final agreement on the new clinical questions to be included, the research team prepared the questions in the PICO (Patient, Intervention, Comparison, Outcome) format, to ensure effective and focused searches and reviews could be undertaken.

New clinical questions

The new clinical questions include the following.

Chapter 2: General principles of care

- What is the role of multidisciplinary teams?

Participants: People with colorectal cancer pre- and post-surgery

Interventions: Multidisciplinary team

Comparison: Usual care

Outcomes: Mortality, morbidity, survival, compliance with recommendations, protocols and standard practice

Chapter 3: Preoperative assessments

- What preoperative investigations need to be completed for colon cancer?
- What preoperative investigations need to be completed for rectal cancer?

Participants: People with colorectal cancer pre-surgery

Interventions: Colonoscopy, sigmoidoscopy, haemoglobin, renal function, liver function, carcinoembryonic antigen, computed tomography (CT) scan, chest x-ray/CT (additional for rectal cancer: magnetic resonance imaging)

Comparison: No preoperative investigations, barium enema

Outcomes: Sensitivity, specificity, receiver operating curves, positive predictive value, negative predictive value, clinical value, harms

Chapter 6: Elective surgery for colon cancer

- Who should perform surgery for colon cancer?
- Where should surgery be performed for colon cancer?

Participants: People undergoing surgery for colorectal cancer

Interventions: High-volume surgeons and hospitals

Comparison: Low-volume surgeons and hospitals

Outcomes: Mortality, survival, perioperative deaths, morbidity, respiratory and cardiac outcomes, complications

Chapter 7: Elective surgery for rectal cancer

- Who should perform elective rectal cancer surgery?
- Where should surgery be performed for rectal cancer?

Participants: People undergoing surgery for colorectal cancer

Interventions: High-volume surgeons and hospitals

Comparison: Low-volume surgeons and hospitals

Outcomes: Mortality, survival, perioperative deaths, morbidity, respiratory and cardiac outcomes, complications

Chapter 8: Emergency surgery

- What surgery is recommended for bowel obstruction?

Participants: People with colorectal cancer and bowel obstruction

Interventions: Stent

Comparison: Surgery

Outcomes: Morbidity, survival

Chapter 9: Adjuvant therapy for colon cancer

- In patients with completely resected colorectal cancer, what is the effect of postoperative chemotherapy on survival at five years?

Participants: People with resected colon cancer

Interventions: Any postoperative chemotherapy regimen

Comparison: No postoperative chemotherapy/surveillance

Outcomes: Overall survival, disease-free survival, recurrence, adverse events

- In patients with completely resected colorectal cancer, what is the effect of adding other cytotoxic agents to postoperative fluoropyrimidine-based chemotherapy on survival at five years?

Participants: People with resected colon cancer

Interventions: 5-fluorouracil (5-FU) based chemotherapy (de Gramont or Roswell Park regimens: – 5-FU + leucovorin)

Comparison: 5-FU + oxaliplatin (FOLFOX) or irinotecan

Outcomes: Overall survival (five years), disease-free survival, recurrence, adverse events

Chapter 10: Adjuvant therapy for rectal cancer

- Does preoperative therapy reduce late morbidity compared with postoperative?

Participants: People with resected rectal cancer

Interventions: Any preoperative radiotherapy regimen, with or without chemotherapy

Comparison: Postoperative radiotherapy, with or without chemotherapy

Outcomes: Radiotherapy (RT) enteritis, RT cystitis, small bowel damage

- In patients with locally advanced rectal cancer, what is the effect of adding chemotherapy to preoperative radiation treatment on patient outcomes?

Participants: People with resected rectal cancer

Interventions: Preoperative RT + chemotherapy

Comparison: Preoperative RT

Outcomes: Local recurrence, overall survival, disease-free survival

- In patients with locally advanced rectal cancer, what is the effect of preoperative short-course radiation treatment compared with long-course pre- or postoperative chemoradiation on patient outcomes?

Participants: People with locally advanced rectal cancer

Interventions: Short-course preoperative radiotherapy regimen (25 Gy in 5 fractions)

Comparison: Long-course preoperative or postoperative chemoradiation (45–50 Gy in 25–28 fractions)

Outcomes: Local recurrence, overall survival, disease-free survival

Chapter 11: Follow-up after curative resection

- What components of follow-up are important?

Participants: People with locally advanced rectal cancer

Interventions: Clinical exam, blood tests, colonoscopy, ultrasound/CT scan

Comparison: No follow-up

Outcomes: Local recurrence, mortality

- Who should be doing follow-up?

Participants: People with locally advanced rectal cancer

Interventions: Hospital, specialist, nurse specialist

Comparison: General practitioner

Outcomes: Local recurrence, mortality

Other areas identified as needing New Zealand–specific content were narratively reviewed. These included epidemiological data for New Zealand, cultural disparities, supportive and rehabilitative care, and staging and reporting. In lieu of a formal systematic review, only good practice points were formulated for these sections.

Deleted questions

Some questions that were included in the NHMRC guideline were discussed during scoping meetings and, following agreement from the EAG, were excluded from the New Zealand guideline. These clinical questions and subsequent recommendations are listed below as well as reasons for their exclusion; the chapter numbers refer to the original NHMRC document, which can be accessed at www.nhmrc.gov.au/publications/synopses/cp106/cp106syn.htm

NHMRC Chapter 9: Management of epithelial polyps

This chapter of the NHMRC guideline straddled the New Zealand inclusion criteria. It was decided that the management of epithelial polyps fell outside the scope of management of early colorectal cancer. This topic is likely to be reviewed as part of the bowel screening project under way in New Zealand.

NHMRC clinical question	NHMRC recommendation
What is the management of epithelial polyps?	All polyps should be at least sampled, and preferably removed. Synchronous polyps should be sought and removed.
What is the general management of all patients with colorectal neoplasia completely removed at colonoscopy?	All patients with colorectal neoplasia completely removed at colonoscopy should then be considered for colonoscopic surveillance according to the following protocols. • Within a year following incomplete or possible inadequate examination, for example in a subject with multiple adenomas. • At least three years for subjects with large adenomas (>1 cm), adenomas with high-grade dysplasia, or villous change in adenomas or aged 60 or more with a first-degree relative with colorectal neoplasia. • At four to six years in subjects without the risk factors outlined above.

NHMRC Chapter 10: Preparation for surgery

There was much debate about the inclusion of the clinical question and recommendation in NHMRC chapter 10, and the GDT chose to consult a New Zealand-based transfusion medicine specialist. The specialist reported that although there is some evidence of increased postoperative infection following colorectal surgery, the evidence is incongruent and studies included in meta-analyses have been heterogeneous. The specialist concluded that the data supporting the recommendation were not in keeping with current understanding. As the question was not prioritised for an evidence review, the GDT agreed to delete this recommendation from the New Zealand guideline.

NHMRC clinical question	NHMRC recommendation
What happens if a blood transfusion is required perioperatively?	Perioperative blood transfusion is to be avoided whenever possible because there may be a detrimental association between transfusion and recurrence. If a transfusion is required, autologous blood is preferable to allogeneic blood for reasons of infection control and resource use.

NHMRC Chapter 11: Elective surgery for colon cancer

The GDT decided that the clinical question and recommendation in NHMRC Chapter 11 were outside the scope of the guideline, and outside the GDT's experience. The GDT preferred to delete it from the New Zealand guideline.

NHMRC clinical question	NHMRC recommendation
When should oophorectomy be performed in association with colectomy for colon cancer?	Bilateral oopherectomy should be performed if there is obvious malignant disease of one or both ovaries. Prophylactic bilateral oopherectomy for colon cancer cannot be supported by the available evidence.

NHMRC Chapter 13: Emergency surgery for colon cancer

The GDT decided that the clinical question and recommendation in NHMRC Chapter 13 were outside the scope of the guideline, and outside the GDT's experience. The GDT preferred to delete it from the New Zealand guideline.

NHMRC clinical question	NHMRC recommendation
When should primary anastomosis be considered?	Primary anastomosis could be considered for leftsided obstruction and may need to be preceded by on table colonic lavage.

Reviewing the literature and developing recommendations

Search strategy

Articles from 2004 onwards were sought to avoid overlap with articles already retrieved and appraised for the NHMRC guideline. Searches were completed in October 2009 and were re-run in October 2010.

The NZGG research team, in consultation with the GDT, set the inclusion and exclusion criteria for the searches. Systematic literature searches relating to each PICO question were designed in consultation with an information specialist and the search for each question was limited to:

- English-language systematic reviews, guidelines and Health Technology Assessments published since the publication of the NHMRC guideline (from 2004 onward)
- relevant English-language randomised controlled trials published after the latest systematic review, guideline and Health Technology Assessment (from 2004 onward) for each review question
- in addition, where the GDT identified earlier studies that it felt were of particular relevance to the New Zealand practice environment (and which the existing international guidelines or systematic reviews had not included), these were appraised and included for discussion by the GDT.

Studies investigating cost effectiveness were not included.

Search databases

The systematic review searches were conducted for the clinical questions noted above. The following bibliographic, Health Technology Assessment and guideline databases were included in the search:

- MEDLINE
- EMBASE
- CINAHL
- PsycINFO
- Cochrane Library
- National Guideline Clearinghouse (NCG) www.guideline.gov
- Turning Research into Practice (TRiP) www.tripdatabase.com
- Web of Science
- DARE Database
- HTA Database
- CCTR
- Current Controlled Trials
- ClinicalTrials.gov.

Evidence and recommendation grading system

Where NZGG identified existing guidelines, these were appraised for quality using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument[164] and are summarised at the beginning of each chapter. For all other studies, the three steps below were followed in appraising the evidence and grading the recommendations.

Step 1: Assign a level of evidence

Following the completion of searches, retrieved studies meeting the inclusion criteria for each clinical question were assigned a level of evidence. The level of evidence indicates how well the study eliminates bias based on its design. NZGG uses a published evidence hierarchy, designed by the NHMRC.[165] The levels of evidence are presented in Table A2.1.

Table A1.1 National Health and Medical Research Council of Australia levels of evidence

Level	Intervention	Diagnostic accuracy	Prognosis	Aetiology	Screening intervention
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive persons with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trail (ie, alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive persons with a defined clinical presentation	All or none	All or none	A pseudorandomised controlled trial (ie, alternate allocation or some other method)
III-2	A comparative study with concurrent controls: • non-randomised, experimental trial • cohort study • case-control study • interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for level II and III-1 evidence	Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: • non-randomised, experimental trial • cohort study • case-control study

continued over...

Table A1.1 **National Health and Medical Research Council of Australia levels of evidence** continued...

Level	Intervention	Diagnostic accuracy	Prognosis	Aetiology	Screening intervention
III-3	A comparative study without concurrent controls: • historical control study • two or more single arm study • interrupted time series without a parallel control group	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: • Historical control study • Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of persons at different stages of disease	A cross-sectional study or case series	Case series

Step 2: Appraise the quality of included studies

After assigning a level of evidence, all included studies were appraised using an adapted version of the Graphic Appraisal Tool for Epidemiology (GATE) checklists. These checklists assist researchers to assess the quality of each included study and are precise enough so that different reviewers can come to similar conclusions about each study. The checklists are available at www.fmhs.auckland.ac.nz/soph/depts/epi/epiq/ebp.aspx

For a full description of critical appraisal using GATE, see Jackson et al, 2006 (www.fmhs.auckland.ac.nz/soph/depts/epi/epiq/_docs/gateframe.pdf).

In brief, the GATE checklists are composed of slightly different criteria depending on the study design but all broadly address each part of the PICOT/PECOT framework for clinical questions. The case is slightly different for systematic reviews and meta-analyses where additional criteria are included to assess the appropriateness of combining and analysing multiple studies. In general, however, the checklists help the researcher to assess study quality in the three main areas of:

- study validity (steps made to minimise bias)
- study results (size and precision of the effect)
- study relevance (containing applicability and generalisability).

In the evaluation of each study, the researcher indicated whether the criteria for quality were met (+), unmet (x) or where there was not enough information to make a judgment (?) for each checklist item. Researchers then assigned the same quality criteria scoring to each of three overall summary sections that assess the validity, accuracy and relevance/applicability of the findings. For each of these summary sections, the researcher made judgments about the overall score by assessing the likelihood of major flaws within each category according to the answers obtained on the checklist items.

Finally, researchers assigned an overall assessment of the study quality based on a summary of all the checklist criteria:

- +: adequate
- X: not adequate, poor
- ?: unclear.

Scores for each of the three summary domains and the overall score have been presented as part of the evidence tables.

Following the appraisal of study quality using checklists, evidence tables were used to present the key characteristics of each of the included studies. Different forms of the template were used for each of the different study designs.

Evidence tables for this guideline are available from the NZGG (www.nzgg.org.nz).

Step 3: Grade recommendations

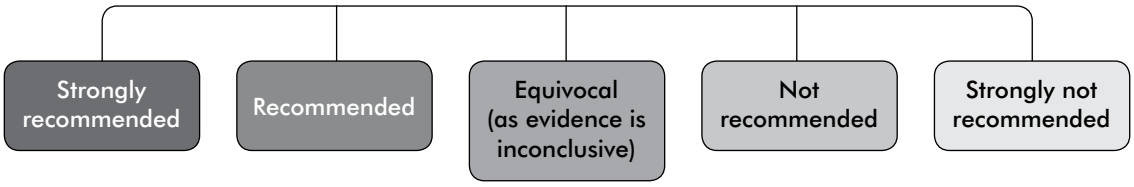
Where existing NHMRC recommendations were adopted without a review by NZGG, the NHMRC grading system was retained. Where new evidence was reviewed systematically or narratively by NZGG, recommendations were graded according to the NZGG system. Both grading systems are presented below.

NHMRC grading system

The system used by the NHMRC to grade recommendations was two-fold. Firstly, recommendations were assigned a level of evidence from I to IV. The level of evidence related to the key studies underpinning the recommendation, and is the same as the levels of evidence used by NZGG to assign levels to individual studies (see Table A1.1).

The strength of recommendations was determined by the Expert Advisory Panel taking into account the level of evidence, quality of studies, size of effect and clinical importance for all the included studies, and ranges from 'Strongly recommended' to 'Strongly not recommended'. These levels of recommendation were modified from work by the Canadian Task Force on the Periodic Health Examination.[166]

Figure A1.1 Strength of recommendations



NZGG grading system

Developing recommendations involves consideration of the whole evidence base for each of the clinical questions. The quality and consistency of the evidence base and the clinical implications of the evidence within a New Zealand context must be weighed up by all GDT members. Each recommendation was assigned a grade to indicate the overall strength of the evidence upon which it is based. Using their collective clinical judgment and experience, the GDT members discussed the relationship between the benefits and harms of the intervention and the applicability of the evidence within the context of New Zealand's clinical practice environment.

The recommendations were agreed by consensus during the meetings, but in some cases further research and discussion by teleconference with subgroups of the GDT were required. Recommendations that were drawn up outside the meetings were presented to the full GDT for agreement by consensus. A short summary of the process of recommendation development is presented in the text, highlighting particular issues that the GDT took into account while formulating the recommendations.

The NZGG grades of recommendations are as follows.

Recommendations

	Grade
The recommendation is supported by good evidence (based on a number of studies that are valid, consistent, applicable and clinically relevant)	A
The recommendation is supported by fair evidence (based on studies that are valid, but there are some concerns about the volume, consistency, applicability and clinical relevance of the evidence that may cause some uncertainty but are not likely to be overturned by other evidence)	B
The recommendation is supported by international expert opinion	C
The evidence is insufficient, evidence is lacking, of poor quality or opinions conflicting, the balance of benefits and harms cannot be determined	I
Good practice point – where no evidence is available, best practice recommendations are made based on the experience of the Guideline Development Team or feedback from consultation within New Zealand	✓

Grades indicate the strength of the supporting evidence rather than the importance of the evidence.

Consultation

A draft of this guideline was available from the NZGG website and circulated to 78 individuals and organisations for comment between 27 September and 8 November 2010. Comments were received from:

- Beat Bowel Cancer Aotearoa
- Cancer Society of New Zealand
- Colorectal Surgical Society of Australia and New Zealand
- David Barnes, Consumer
- Dr Andrew Moot
- Dr Nick Humpheries, Consultant Radiologist, Hutt Valley District Health Board
- Dr Bryan Parry, Colorectal Surgeon
- Dr Caroline Lintott, Central & Southern Regional Genetics Service
- Dr Susan Parry, Gastroentorologist, Southern Cancer Network
- Federation of New Zealand Ostomy Societies Incorporated
- Gastrointestinal Cancer Special Interest Group
- Hawke's Bay District Health Board
- Margaret Chavasse, General Practitioner
- Mark Fawcett-Thompson
- MidCentral District Health Board – Maria Stapleton
- Royal New Zealand College of General Practitioners
- Royal College of Pathologists
- Royal College of Pathologists of Australasia
- Southern Cancer Network
- University of Otago, Department of Surgery

Appendix 2:
TNM staging

→ *Chapter 14 NHMRC*

The most widely-used classification for colorectal carcinomas is the TNM classification. The T, N and M categories (tumour, nodes and metastases, respectively) are assessed by the combination of physical examination and imaging.

Table A2.1 TNM staging for colorectal cancer

Primary tumour (T)	
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
T_{is}	Carcinoma in situ: intraepithelial or invasion of lamina propria*
T1	Tumour invades submucosa
T2	Tumour invades musclaris propria
T3	Tumour invades through the muscularis propria into pericolorectal tissues
T4a	Tumour penetrates to the surface of the visceral peritoneum†
T4b	Tumour directly invades or is adherent to other organs or structures†‡
Regional lymph node (N)[Ω]	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1–3 regional lymph nodes
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2–3 regional lymph nodes
N1c	Tumour deposit(s) in the subserosa, mesentery, or non-peritonealised pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in 4 or more regional lymph nodes
N2a	Metastasis in 4–6 regional lymph nodes
N2b	Metastasis in 7 or more regional lymph nodes
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (eg, liver, lung, ovary, non-regional node)
M1b	Metastasis in more than one organ/site or the peritoneum

continued over...

Table A2.1 **TNM staging for colorectal cancer** continued...

Anatomic stage/prognostic groups§					
Stage	**T**	**N**	**M**	**Dukes¥**	**MAC¥**
0	T_{is}	N0	M0	–	–
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1–2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3–T4a	N1/N1c	M0	C	C2
	T2–T3	N2a	M0	C	C1/C2
	T1–T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3–T4a	N2b	M0	C	C2
	T4b	N1–N2	M0	C	C3
IVA	Any T	Any N	M1a	–	–
IVB	Any T	Any N	M1b	–	–

* T_{is} includes cancer cells confined within the glandular basement membrane (intraepithelial) or mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.

† Direct invasion in T4 includes invasion of other organs or other segments of the colorectum as a result of direct extension through the serosa, as confirmed on microscopic examination (for example, invasion of the sigmoid colon by a carcinoma of the cecum) or, for cancers in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria (ie, respectively, a tumour on the posterior wall of the descending colon invading the left kidney or lateral abdominal wall; or a mid or distal rectal cancer with invasion of prostate, seminal vesicles, cervix, or vagina).

‡ Tumour that is adherent to other organs or structures, grossly, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1–4a depending on the anatomical depth of wall invasion. The V and L classifications should be used to identify the presence or absence of vascular or lymphatic invasion whereas the PN site-specific factor should be used for perineural invasion.

Ω A satellite peritumoural nodule in the pericolorectal adipose tissue of a primary carcinoma without histologic evidence of residual lymph node in the nodule may represent discontinuous spread, venous invasion with extravascular spread (V1/2), or a totally replaced lymph node (N1/2). Replaced nodes should be counted separately as positive nodes in the N category, whereas discontinuous spread or venous invasion should be classified and counted in the site-specific factor category tumour deposits (TD).

§ cTNM is the clinical classification, pTNM is the pathologic classification. The y prefix is used for those cancers that are classified after neoadjuvant pre-treatment (eg, ypTNM). Patients who have a complete pathologic response are ypT0N0cm0 that may be similar to Stage Group 0 or I. The r prefix is to be used for those cancers that have recurred after a disease-free interval (rTNM).

¥ Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (any T N1 M0 and any T N2 M0). MAC is the modified Astler-Coller classification.

Source: Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual (7th edition), 2010, published by Springer New York, Inc.

Appendix 3:
Structured (synoptic) reporting

Figure A3.1 RCPA guide to Histopathology reporting

A guide to Colorectal Cancer Histopathology Reporting

Clinical details		
G1.02	Pathology accession number	Text
S1.02	**Principal clinician caring for the patient**	Text
S1.04	**Patient presentation at surgery**	
	Perforation	Absent Present Not stated
	If present, record the nature of perforation	See p3
	Obstruction	Absent Present Not stated
S1.05	**Tumour location** **For synchronous tumours indicate site**	See p3 Text
S1.06	**Distance from the anal verge (for rectal tumours only)**	___ cm Not stated
S1.07	**Type of operation**	See p3
S1.08	**Pre-operative radiotherapy**	Yes/No Not stated
	If yes, was it....	Short course Long course
S1.09	**Surgeon's opinion on the existence of local residual cancer postsurgery**	Text Not stated
S1.10	**Involvement of adjacent organs**	Text Not stated
S1.11	**Presence of distant metastases**	Yes/No Not stated
	If yes give details.	
G1.03	Any other relevant information	Text
Macroscopic findings		
G2.02	Images of the gross specimen	Include if avail.
S2.02	**Nature and site of blocks**	Text
S2.04	**Specimen length**	___ mm
S2.05	**Tumour site**	See p3
S2.06	**Maximum tumour diameter**	mm
S2.07	**Distance of tumour to the nearer proximal or distal 'cut end' margin**	___ mm
S2.08	**Distance of tumour to the nonperitonealised circumferential margin**	___ mm
S2.09	**Tumour perforation**	Absent Present
S2.10	**Relationship to anterior peritoneal reflection (rectal tumours)**	Entirely above Astride Entirely below
S2.11	**Intactness of mesorectum (rectal resections) (refer to p3 Notes)**	Incomplete Near complete Complete
S2.12	**Macroscopic comments**	Text
Microscopic findings		
S3.01	**Tumour type**	See p3
S3.02	**Histological grading**	Low grade High grade

Microscopic findings (cont.)		
S3.03	**Maximum degree of local invasion into or through the bowel wall**	pT1 pT2 pT3
	If pT4, indicate if 'a' or 'b'	pT4
S3.04	**Involvement of the proximal or distal resection margins**	Involved Not involved
	If involved, which margin?	Distal Proximal
	If not involved, what is clearance (if less than 10 mm)	___ mm
S3.05	**Minimum distance between tumour and the nonperitonealised circumferential margin (rectal tumours)**	___ mm
S3.06	**Minimum distance between tumour and the nonperitonealised circumferential margin (colon tumours)**	___ mm
S3.07	**Lymph nodes**	
	Total number	____
	Number positive	____
	Isolated extra-mural tumour deposits	Absent Present
G3.01	Status of apical node	Text
S3.08	**Venous and small vessel invasion**	
	Intramural vein invasion	Not identified Suspicious Present
	Extramural vein invasion	Not identified Suspicious Present
	Small vessel invasion	Not identified Suspicious Present Present,extensive
G3.02	Perineural invasion	Not identified Present Present,extensive
S3.09	**Distant metastases**	Absent Present
	If present,indicate..	Site(s)
S3.10	**Relevant coexistent pathological abnormalities**	See p3
S3.11	**Microscopic residual tumour status (completeness of resection)**	Text
S3.12	**Response to neoadjuvant therapy**	Text
	Indicate grade (refer to Notes p3)	Grade 0 Grade 1 Grade 2 Grade 3
G3.03	Microscopic comments	Text

V1.0 Guide derived from Colorectal Cancer Structured Reporting Protocol 1st Edition Page 1 of 3

Ancillary test findings

G4.01	Mismatch repair enzymes:	
	MLH-1	Not tested Normal staining Loss of staining
	PMS-2	Not tested Normal staining Loss of staining
	MSH-2	Not tested Normal staining Loss of staining
	MSH-6	Not tested Normal staining Loss of staining
	Comments	Text
	Microsatellite instability (MSI)	Unstable Stable Not tested
	Laboratory performing test and report number	Text
	Comments	Text
	BRAF (V600E mutation)	Mutated Wild type Not tested
	Laboratory performing test and report number	Text
	Comments	Text
G4.02	KRAS gene mutation (codons 12 and 13)	Mutated Wild type Not tested
	Laboratory performing test and report number	Text
	Comments	Text

Synthesis and overview

S5.01	**Tumour stage**	See p2
	Stage grouping	See p2
S5.02	**Residual tumour status**	See p2
G5.01	Diagnostic summary Include: a. specimen type (S1.01) b. tumour site (S2.05) c. tumour type (S3.01) d. tumour stage (S5.01) e. completeness of excision (S5.02)	Text
S5.03	**Comments**	Text

NOTES

S5.02 Residual tumour status**

R0: Complete resection, margins histologically negative, no residual tumour left after resection (primary tumour, regional nodes)

R1: Incomplete resection, margins histologically involved, microscopic tumour remains after resection of gross disease (primary tumour, regional nodes)

R2: Incomplete resection, margins macroscopically involved or gross disease remains after subtotal resection (eg primary tumour, regional nodes, or liver metastasis).

S5.01 Tumour stage**

T classification Primary tumour

TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria
T1	Tumour invades submucosa
T2	Tumour invades muscularis propria
T3	Tumour invades through the muscularis propria into pericolorectal tissues
T4a	Tumour penetrates to the surface of the visceral peritoneum
T4b	Tumour directly invades or is adherent to other organs or structures

N classification Regional lymph nodes

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional lymph nodes
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Tumour deposit(s) in the subserosa, mesentery, or nonperitonealised pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in 4 or more regional lymph nodes
N2a	Metastasis in 4-6 regional lymph nodes
N2b	Metastasis in 7 or more regional lymph nodes

M classification Distant metastasis

M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (e.g. liver, lung, ovary, nonregional node)
M1b	Metastases in more than one organ/site or the peritoneum

Stage Grouping

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
	T2	N0	M0
IIA	T3	N0	M0
IIB	T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T1-T2	N1/N1c	M0
	T1	N2a	M0
IIIB	T3-T4a	N1/N1c	M0
	T2-T3	N2a	M0
	T1-T2	N2b	M0
IIIC	T4a	N2a	M0
	T3-T4a	N2b	M0
	T4b	N1-N2	M0
IVA	Any T	Any N	M1a
IVB	Any T	Any N	M1b

A guide to Colorectal Cancer Histopathology Reporting

NOTES (Cont.)

S1.04 Patient presentation at surgery

Nature of perforation:

- Through tumour prior to surgery
- Through tumour during surgical mobilisation
- Away from tumour

S1.05 Tumour location
S2.05 Tumour site

- Caecum
- Ascending colon
- Hepatic flexure
- Transverse colon
- Splenic flexure
- Descending colon
- Sigmoid colon
- Rectosigmoid junction
- Rectum
- Not stated

S1.07 Type of operation

- Right hemicolectomy
- Extended right hemicolectomy
- Transverse colectomy
- Left hemicolectomy
- Anterior resection (High, Low, Ultralow)
- Abdominoperineal resection
- Proctocolectomy
- Total colectomy with ileorectal anastomosis
- Hartmann's procedure
- Other procedure(s)
- Not stated

S2.11 Intactness of mesorectum

Incomplete:

little bulk to the rectum, defects in the mesorectum down to the muscularis propria, after transverse sectioning the circumferential margin appears very irregular.

Nearly complete:

moderate bulk to the mesorectum, irregularity of the mesorectal surface with defects greater than 5 mm but none extending to the muscularis propria, no areas of visibility of the muscularis propria except at the insertion site of the levator ani muscles

Complete:

Intact bulky mesorectum with a smooth surface, only minor irregularities of the mesorectal surface, no surface defects greater than 5 mm in depth, no coning towards the distal margin of the specimen, after circumferential sectioning the circumferential margin appears smooth.

S3.01 Tumour type

- Adenocarcinoma
- Mucinous adenocarcinoma
- Signet-ring cell carcinoma
- Small cell carcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Medullary carcinoma
- Undifferentiated carcinoma

S3.10 Relevant coexistent pathological abnormalities

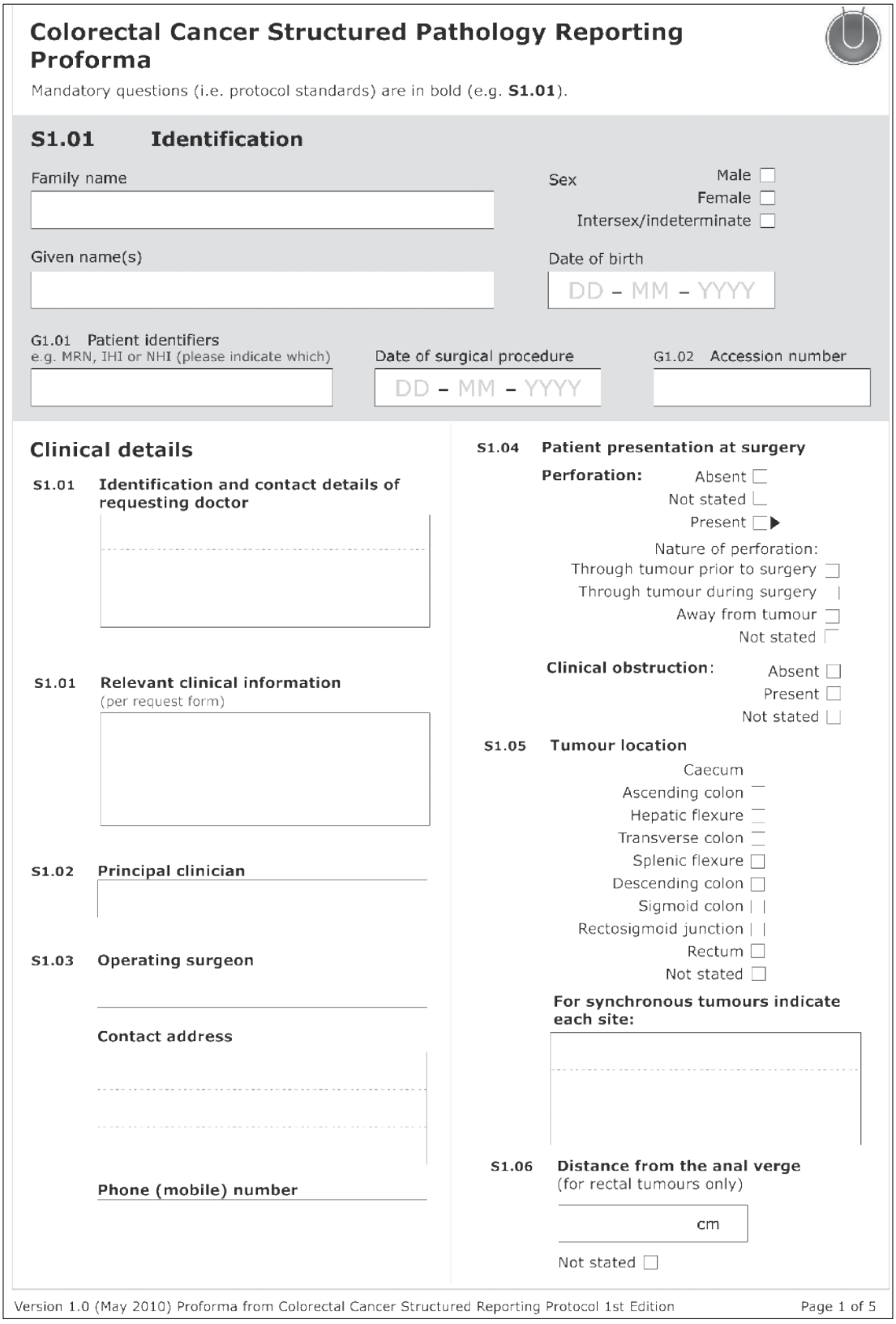
- Polyps (describe type, number, etc)
- Ulcerative colitis (with dysplasia/without dysplasia)
- Crohn's disease (with dysplasia/without dysplasia)
- Other

S3.12 Response to neoadjuvant therapy

Grade 0 (complete response)	No viable cancer cells
Grade 1 (moderate response)	Single cells or small groups of cancer cells
Grade 2 (minimal response)	Residual cancer outgrown by fibrosis
Grade 3 (poor response)	Minimal or no tumour kill; extensive residual cancer.

Citation: The Royal College of Pathologists of Australia (RCPA). A guide to colorectal cancer histopathology reporting: V1.2. (2010). Available from: http://www.rcpa.edu.au//static/File/Asset%20library/public%20documents/Publications/StructuredReporting/Colorectal%20guide%20V1.2.pdf

Figure A3.2 Structured (synoptic) reporting proforma



Colorectal Cancer Structured Pathology Reporting Proforma

Mandatory questions (i.e. protocol standards) are in bold (e.g. **S1.01**).

S1.01 Identification

Family name

Given name(s)

Sex: Male ☐ Female ☐ Intersex/indeterminate ☐

Date of birth: DD – MM – YYYY

G1.01 Patient identifiers
e.g. MRN, IHI or NHI (please indicate which)

Date of surgical procedure: DD – MM – YYYY

G1.02 Accession number

Clinical details

S1.01 Identification and contact details of requesting doctor

S1.01 Relevant clinical information
(per request form)

S1.02 Principal clinician

S1.03 Operating surgeon

Contact address

Phone (mobile) number

S1.04 Patient presentation at surgery

Perforation: Absent ☐ Not stated ☐ Present ☐ ▶

Nature of perforation:
Through tumour prior to surgery ☐
Through tumour during surgery ☐
Away from tumour ☐
Not stated ☐

Clinical obstruction: Absent ☐ Present ☐ Not stated ☐

S1.05 Tumour location

Caecum ☐
Ascending colon ☐
Hepatic flexure ☐
Transverse colon ☐
Splenic flexure ☐
Descending colon ☐
Sigmoid colon ☐
Rectosigmoid junction ☐
Rectum ☐
Not stated ☐

For synchronous tumours indicate each site:

S1.06 Distance from the anal verge
(for rectal tumours only)

cm

Not stated ☐

Version 1.0 (May 2010) Proforma from Colorectal Cancer Structured Reporting Protocol 1st Edition Page 1 of 5

S1.07 Type of operation

- Right hemicolectomy
- Extended right hemicolectomy
- Transverse colectomy
- Left hemicolectomy
- Anterior resection
  - High
  - Low
  - Ultralow
- Abdominoperineal resection
- Proctocolectomy
- Total colectomy with ileorectal anastomosis
- Hartmann's procedure
- Other procedure(s):
- Not stated

S1.08 Pre-operative radiotherapy

- No
- Yes
  - Short course
  - Long course
- Not stated

S1.09 Surgeon's opinion on the existence of local residual cancer postsurgery

Not stated

S1.10 Involvement of adjacent organs

Not stated

S1.11 Presence of distant metastases

- No
- Yes

Details:

Not stated

G1.03 Any other relevant information

Macroscopic findings

G2.02 Images of the gross specimen

S2.02 Nature and site of blocks

S2.04 Specimen length

mm

S2.05 Tumour site

- Caecum
- Ascending colon
- Hepatic flexure
- Transverse colon
- Splenic flexure
- Descending colon
- Sigmoid colon
- Rectosigmoid junction
- Rectum

S2.06 Maximum tumour diameter

mm

S2.07 Distance of tumour to the nearer proximal or distal 'cut end'

mm

S2.08 Distance of tumour to the nonperitonealised circumferential margin

mm

S2.09 Tumour perforation

- Absent
- Present

S2.10 Relationship to anterior peritoneal reflection (rectal tumours)

Entirely above ☐
Astride ☐
Entirely below ☐

S2.11 Intactness of mesorectum (rectal resections)

Incomplete ☐
Nearly complete ☐
Complete ☐

S2.12 Macroscopic comments

Microscopic findings

S3.01 Histological tumour type

Adenocarcinoma ☐
Mucinous adenocarcinoma ☐
Signet-ring cell carcinoma ☐
Small cell carcinoma ☐
Squamous cell carcinoma ☐
Adenosquamous carcinoma ☐
Medullary carcinoma ☐
Undifferentiated carcinoma ☐

S3.02 Histological grade

Low grade ☐
High grade ☐

S3.03 Maximum degree of local invasion into or through the bowel wall

pT1 ☐
pT2 ☐
pT3 ☐
pT4 ☐ ▶ a ☐
b ☐

S3.04 Involvement of the proximal or distal resection margins

Involved ☐ ▶
Distal ☐
Proximal ☐

Not involved ☐ ▶

Clearance (if the margin is less than 10 mm)

mm

S3.05 Minimum distance between tumour and the nonperitonealised circumferential margin (rectal tumours)

mm

S3.06 Minimum distance between tumour and the nonperitonealised circumferential margin (colon tumours)

mm

S3.07 Lymph nodes

Total number:

Number positive:

Isolated extra-mural tumour deposits:

Absent ☐
Present ☐

G3.01 Status of apical node

S3.08 Venous and small vessel invasion

Intramural vein invasion

Not identified ☐
Suspicious ☐
Present ☐

Extramural vein invasion

Not identified ☐
Suspicious ☐
Present ☐

Small vessel invasion

Not identified ☐
Suspicious ☐
Present ☐
Present and extensive ☐

G3.02 Perineural invasion

Not identified ☐
Present ☐
Present and extensive ☐

S3.09 Distant metastases

Absent ☐
Present ☐ ▶ Site(s):

Version 1.0 (May 2010) Proforma from Colorectal Cancer Structured Reporting Protocol 1st Edition Page 3 of 5

S3.10 Relevant coexistent pathological abnormalities

Polyps (describe type, number, etc)

Ulcerative colitis (with/without dysplasia)

Crohn's disease (with/without dysplasia)

Other

S3.11 Microscopic residual tumour status (completeness of resection)

S3.12 Response to neoadjuvant therapy

- **Grade 0 (complete response)** No viable cancer cells
- **Grade 1 (moderate response)** Single cells or small groups of cancer cells
- **Grade 2 (minimal response)** Residual cancer outgrown by fibrosis
- **Grade 3 (poor response)** Minimal or no tumour kill; extensive residual cancer

G3.03 Microscopic comments

Ancillary test findings

G4.01 Mismatch repair enzymes

	MLH-1	PMS-2	MSH-2	MSH-6
Not tested				
Normal staining				
Loss of staining				

Comments

Microsatellite instability (MSI):

Unstable ☐
Stable ☐
Not tested ☐

Lab performing test and report number:

Comments

BRAF (V600E mutation):

Mutated ☐
Wild type ☐
Not tested ☐

Lab performing test and report number:

Comments

G4.02 *KRAS* gene mutation (codons 12 and 13):

Mutated ☐
Wild type ☐
Not tested ☐

Lab performing test and report number:

Comments

Version 1.0 (May 2010) Proforma from Colorectal Cancer Structured Reporting Protocol 1st Edition Page 4 of 5

Synthesis and overview

S5.01 Tumour stage**

T

N

M

Stage grouping

S5.02 Residual tumour status

R0 ☐

R1 | |

R2 | |

G5.01 Diagnostic summary

specimen type, tumour site, tumour type, tumour stage, completeness of excision

S5.03 Comments

Worksheet prepared by:

On:

DD – MM – YYYY

TNM definitions**

T classification	Primary tumour
TX	Primary tumour cannot be assessed
T0	No evidence of primary tumour
Tis	Carcinoma in situ: intraepithelial or invasion of lamina propria
T1	Tumour invades submucosa
T2	Tumour invades muscularis propria
T3	Tumour invades through the muscularis propria into pericolorectal tissues
T4a	Tumour penetrates to the surface of the visceral peritoneum
T4b	Tumour directly invades or is adherent to other organs or structures

N classification	Regional lymph nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1-3 regional lymph nodes
N1a	Metastasis in one regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Tumour deposit(s) in the subserosa, mesentery, or nonperitonealised pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in 4 or more regional lymph nodes
N2a	Metastasis in 4-6 regional lymph nodes
N2b	Metastasis in 7 or more regional lymph nodes

M classification	Distant metastasis
M0	No distant metastasis
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (e.g., liver, lung, ovary, nonregional node)
M1b	Metastases in more than one organ/site or the peritoneum

Stage Grouping

Stage	T	N	M
0	Tis	N0	M0
I	T1	N0	M0
	T2	N0	M0
IIA	T3	N0	M0
IIB	T4a	N0	M0
IIC	T4b	N0	M0
IIIA	T1-T2	N1/N1c	M0
	T1	N2a	M0
IIIB	T3-T4a	N1/N1c	M0
	T2-T3	N2a	M0
	T1-T2	N2b	M0
IIIC	T4a	N2a	M0
	T3-T4a	N2b	M0
	T4b	N1-N2	M0
IVA	Any T	Any N	M1a
IVB	Any T	Any N	M1b

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Version 1.0 (May 2010) Proforma from Colorectal Cancer Structured Reporting Protocol 1st Edition Page 5 of 5

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Appendix 4:
Abbreviations and glossary

A4.1 Abbreviations

5-FU	5-fluorouracil
5-FU/LV	5-fluorouracil plus leucovorin
ACPS	Australian Clinico-Pathological Staging System
AIO	Arbeitsgemeinschaft Internische Onkologie
ASCO	American Society of Clinical Oncology
CDDP	cis-diamminedichloroplatinum
CEA	carcinoembryonic antigen
CI	confidence interval
CPT-11	irinotecan
CRM	circumferential resection margin
CRT	chemoradiation
CT	computed tomography
DCC	deleted in colon cancer
DFS	disease-free survival
DOR	diagnostic odds ratio
EAG	Expert Advisory Group
EORTC	European Organisation for Research and Treatment of Cancer
EUS	endorectal ultrasound
FA	folinic acid
FDG	fluorodeoxyglucose
FOBT	faecal occult blood testing
FOLFOX	folinic acid (leucovorin) + 5-fluorouracil + oxaliplatin
fr	fraction
FU	fluorouracil
GATE	Graphic Appraisal Tool for Epidemiology
GDT	Guideline Development Team

Gy	gray
HR	hazard ratio
INF-α	interferon alpha
LOH	loss of heterozygosity
LV	leucovorin (alson known as folinic acid)
M	metastasis
MDT	multidisciplinary team
MeCCNU	semustine, an alkylating nitrosourea compound
MRI	magnetic resonance imaging
MSI	microsatellite instability
MTX	mitoxantrone
N	nodes
NHMRC	National Health and Medical Research Council (Australia)
NNT	number needed to treat
NR	not relevant
NZGG	New Zealand Guidelines Group
OR	odds ratio
OS	overall survival
p	probablility
PCR	polymerase chain reaction
PET	positron emission tomography
RCPA	Royal College of Pathologists of Australasia
RCT	randomised controlled trial
ROC	receiver operating curve
RR	relative risk
RT	radiotherapy
T	tumour
TNM	A staging system based on the extent of the tumour (T), the extent of spread to the lymph nodes (N) and the presence of metastasis (M).
TROG	Trans-Tasman Radiation Oncology Group
WMD	Weighted mean difference

A4.2 Glossary

Adenoma	A benign tumour that develops from epithelial tissue.
Adjuvant therapy	Treatment following surgery designed to remove any microscopic traces of tumour that may have been left behind.
Anastomosis	An opening created by surgical, traumatic or pathological means between two normally separate spaces or organs.
Autologous	Blood drawn from one individual to be given back to that individual, or a very close blood match designee, as the need for transfusion arises.
Biopsy	The removal of a sample of tissue from the body to assist in the diagnosis of a disease.
Carcinoma	Most common type of cancer; malignant neoplasm (tumour) derived from epithelial cells, chiefly glandular (adenocarcinoma) or squamous (squamous cell carcinoma).
Chemotherapy	The use of medication (drugs) that is toxic to cancer cells. The drugs kill the cells or prevent or slow their growth.
Circumferential resection margin	Represents the retroperitoneal or peritoneal adventitial soft-tissue margin closest to the deepest penetration of the tumour.
Cognitive behavioural therapy	A type of psychological intervention used in the treatment of depression, anxiety and other mental disorders.
Colectomy	The surgical removal of the coloor part of the colon.
Computed tomography	A diagnostic imaging technique that uses x-rays and a computer to produce a detailed picture of a cross-section of the body.
Concurrent	Occurring at the same time.
Counselling	Encompasses supportive care delivered by a variety of health practitioners. Techniques are diverse and include supportive listening, the provision of practical information and education, instruction in relaxation therapies, assistance with communication and relationship problems, training in assertiveness and advice on problem-solving.
Cytotoxic	Toxic (harmful) to cells of the body.
De Gramont regimen	A regimen of a particular dose, timing and method of combined chemotherapy with 5-fluorouracil and leucovorin.
Dukes B, Dukes C	**B1**: tumor penetrates into, but not through the muscularis propria (the muscular layer) of the bowel wall. **B2**: tumor penetrates into and through the muscularis propria of the bowel wall. **C1**: tumor penetrates into, but not through, the muscularis propria of the bowel wall; there is pathologic evidence of colon cancer in the lymph nodes. **C2**: tumor penetrates into and through the muscularis propria of the bowel wall; there is pathologic evidence of colon cancer in the lymph nodes.

Elective surgery	Surgery that can be planned, rather than surgery carried out under urgent or emergency circumstances.
Endoscopic polypectomy	Surgical removal of a polyp.
Epithelial polyps	A focal, protruded lesion within the bowel.
Excision	The act of surgically removing or 'cutting out' tissue from the body.
False positive	A result that occurs when a test reports a positive result for a person who is disease-free.
Fistula	A permanent abnormal passageway between two organs of the body or between an organ and the exterior of the body.
Fraction	The radiation dose delivered in each treatment.
Grading	The degree of malignancy of a tumour, judged by its appearance under a microscope.
Heterogeneous	Having a large number of variants.
Histology	An examination of the cellular characteristics of a tissue.
Holistic care	Care that provides for the psychological as well as the physical requirements of the individual.
Immunohistochemistry	A technique that uses antibodies to identify specific proteins in tissues under a microscope.
Irradiation/radiation	Treatment with, or exposure to, any form of radiation.
Local recurrence	The return of the cancer in the affected site of the cancer.
Long-course radiotherapy	45–54 Gy in 1.8–2.0 Gy fractions.
Magnetic resonance imaging	A diagnostic imaging technique that uses powerful electromagnets, radio waves and a computer to produce well-defined images of the body's internal structures.
Mana	Power, respect, status, integrity.
Margins	The edge of the tissue removed.
Markers	Substances found in increased amounts in the blood, other body fluids or tissues that suggest that a certain type of cancer may be in the body.
Medical oncologist	A doctor who specialises in the treatment of cancer, using drugs as the main modality of treatment.
Metastases	The spread of cancer away from the primary site (origin) to somewhere else via the bloodstream or the lymphatic system.
Micrometastases	Metastases (cancer spread) that are too small to be seen without a microscope.
Morbidity	A diseased condition or state.
Mortality	Death.

Multidisciplinary team	A team with members from different health care professions (eg, surgery, oncology, pathology, radiology and nursing).
Neoadjuvant	Drug treatment given to people with cancer before surgery.
Neurotoxicity	Occurs when the exposure to natural or artificial toxic substances, which are called neurotoxins, alters the normal activity of the nervous system in such a way as to cause damage to nervous tissue.
Noa	Free from tapu or any other restriction.
Node negative	The absence of cancer in a lymph node or nodes.
Node positive	The presence of cancer in a lymph node or nodes.
Normothermia	Environmental temperature that does not cause increased or decreased activity of body cells.
Oncologist	A doctor who specialises in treating cancer.
Ora	Health, life, vitality.
Pathologist	A doctor who is laboratory based and carries out tests on tissues, cells, body fluids, urine, faeces and swabs to detect disease by identifying infectious organisms, biochemical, blood or immune system abnormalities as well as cancerous and pre-cancerous changes in tissues and cells.
Pathology	A branch of medicine concerned with disease, especially its structure and functional effects on the body.
Positron emission tomography	An imaging technique that produces a three-dimensional image or map of functional processes in the body.
Primary care	Services provided in community settings with which patients usually have first contact (eg, general practice).
Prognosis	A prediction of the likely outcome or course of a disease; the chance of recovery or recurrence.
Prognostic factors	Patient or disease characteristics (eg, age and disease stage) that influence the course of the disease under study.
Prophylactic	A medication or treatment designed and used to prevent a disease.
Psychotherapy	An interaction between a therapist and a patient that aims to decrease distress and increase morale, self-esteem and the ability to cope by increasing the patient's sense of mastery over the situation and helping them to overcome the practical challenges.
Radiation oncologist	A doctor who specialises in the treatment of cancer, using radiation as the main modality of treatment.
Radioisotopes	Isotopes extensively used in nuclear medicine to allow physicians to explore bodily structures and functions *in vivo* (in the living body) with a minimum of invasion to the patient.
Radiotherapy	A treatment for cancer to prevent cell growth that uses high energy-ionising radiation.

Recurrence	The relapse of the cancer in the same place or elsewhere in the body.
Regimen	A plan or regulated course of treatment.
Resectable	Capable of being removed by surgery.
Resection margins	The margins of tissue removed from the body by surgery.
Roswell Park regimen	A chemotherapy regimen named after the Roswell Park Memorial Institute, consisting of a particular dose, timing and method of combined chemotherapy with 5-fluorouracil and leucovorin.
Sensitivity	A measure of how likely it is for a test to pick up the presence of a disease in a person who has that disease.
Sequential	One treatment following another.
Short-course radiotherapy	25 Gy in 5 Gy fractions.
Specificity	A measure of how likely it is for a test to pick up the absence of a disease in a person who does not have the disease.
Staging	The clinical description of the size and extent of a patient's tumour, by its allocation into internationally agreed categories.
Stent	A tube made of metal or plastic that is inserted into a tubular structure such as a vessel or passage to keep the lumen open and prevent closure due to a stricture or external compression.
Stoma	An opening into the body from the outside created by a surgeon.
Systemic therapy/treatment	Treatment, usually given by mouth or injection, that reaches and affects tumour cells throughout the body rather than targeting one specific area.
Tapu	Sacred, taboo.
Toxicity	The quality of being poisonous, especially the degree of virulence of a toxic microbe or a poison.
Tumour Board	A treatment planning approach in which doctors who are experts in different specialties review and discuss the medical condition and treatment options for a patient.
Ultrasound	An imaging method in which high-frequency sound waves are used to outline a part of the body.
Whānau	Family, community.
Whānau ora	The health of an extended family or community of related families.

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