

SUMMARY AND GUIDELINES

Colorectal Cancer is a major health problem in the Australian community and one in twenty Australians are likely to develop the disease. The risk increases from the age of 40 years onwards but rises sharply and progressively from the age of 50 years.

These guidelines are intended for use by all practitioners and health workers who require information about management of patients with Colorectal Cancer. They are wide-ranging in scope, covering prevention, screening, diagnosis and psychosocial matters as well as the clinical aspects of surgery, radiotherapy and chemotherapy.

The guidelines have been produced by an exhaustive process of consultation and review encompassing all interested parties in Australia (see Appendix 2).

The guidelines are based on evidence obtained through an exhaustive literature review process. Individual studies have been rated as level I, II, III-1, III-2, III-3 or IV according to the National Health and Medical Research Council (NHMRC) scale (see below). Each recommendation has also been further evaluated according to the level, quality and statistical precision of the included studies (strength of evidence), and the overall size and clinical importance of the effect. The levels of evidence and strengths of recommendations are described in detail in Appendix 3. Detailed summations of the studies supporting each recommendation are included in the text of each chapter.

Guidelines to be used in the interpretation of tables

The following tables provide a list of the evidence-based recommendations detailed in the text of the document. Readers should refer to the appropriate chapters when considering application of these recommendations in the care and management of patients with Colorectal Cancer.

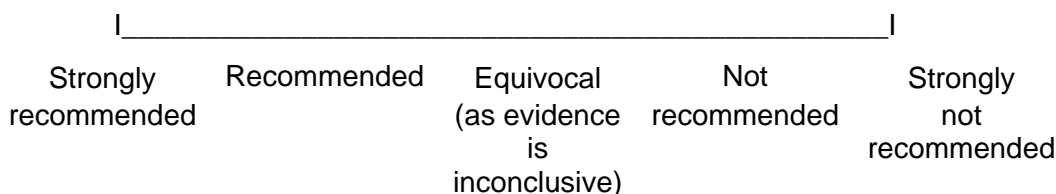
The clinical question is in bold. The recommendations of the advisory panel and working party follow in italics. These provide options for the clinician to discuss with the patient; they are not prescriptive but should be considered during the decision making process. The following columns provide the level of evidence (I-IV) of the key studies and the strength of the recommendation determined by the expert advisory panel taking into account the strength of the evidence from the included studies and the overall size and clinical importance of the effect. The key references that underpin the recommendation (included studies) are provided in the last column.

LEVELS OF EVIDENCE¹

- 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-1 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

STRENGTH OF RECOMMENDATIONS^{2,3}

The strength of recommendations are 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 are modified from The Canadian Task Force on the Periodic Health Examination and are explained in further detail in Appendix 3.



References

1. A guide to the development, implementation and evaluation of clinical practice guidelines. 1999. AGPS, Canberra, National Health & Medical Research Council (NHMRC).
2. Woolf SH, Battista RN, Anderson GM, Logan AG, Wang E. Assessing the clinical effectiveness of preventive manoeuvres: analytic principles and systematic methods in reviewing evidence and developing clinical practice recommendations. A report by the Canadian Task Force on the Periodic Health Examination. *J Clin Epidemiol* 1990; 43: 891-905.
3. Grimes DA, Schulz KF. An overview of clinical research: the lay of the land. *Lancet* 2002; 359: 57-61.

SECTION I: EARLY COLORECTAL CANCER

Chapter	Recommendations	Level of evidence		Practice recommendation		Refs
		Cancer	Adenoma	Cancer	Adenoma	
2	PRIMARY PREVENTION					
	<p>Should physical activity and weight control be advised to reduce the risk of Colorectal Cancer?</p> <p><i>“Engage in moderate to vigorous physical activity for 30–60 minutes/day, and avoid excessive weight gain.</i></p> <p><i>Weight should be maintained in the healthy weight range of BMI.”</i></p>	III-2 III-2	III-2 III-2	Recommended Recommended	Recommended Recommended	2,3,4,5,6,12 2,6,7,8,9,10,11,13
	<p>Should alcohol intake be restricted to reduce Colorectal Cancer risk?</p> <p><i>“Alcohol consumption should be limited or avoided. For people who do drink alcohol, recommended amounts for men are no more than 2 standard drinks per day and for women no more than one standard drink a day.”</i></p>	III-2	III-2	Strongly recommended	Recommended	9,14,17-20
	<p>Does smoking tobacco increase the risk of Colorectal Cancer?</p> <p><i>“Avoid tobacco smoking.”</i></p>	III-2	III-2	Recommended	Recommended	2,21-24
	<p>Should energy intake be restricted to reduce Colorectal Cancer risk?</p> <p><i>“Limit energy intake in most men to <2500 calories (10,480 kJ) per day and in most women to <2000 calories (8360 kJ) per day.”</i></p>	III-2	-	Strongly recommended	-	9,29,30
	<p>Should dietary fat be restricted to reduce Colorectal Cancer risk?</p> <p><i>“Reduce dietary fat to <25% of calories as fat.”</i></p>	III-2	II	Recommended		29,30,36-38,40,42,43

	<p>Should red meat intake be altered to reduce Colon Cancer risk?</p> <p><i>“Moderate intakes of lean red meat can be eaten as part of a mixed diet including carbohydrates (breads and cereals), vegetables and fruit, and dairy products. Charring of red meat is best avoided. Consumption of processed meats should be limited.”</i></p>	III-2	III-2	Equivocal	Equivocal	9,29, 36,41, 49, 50
	<p>Should fresh fruit and vegetable intake be increased to reduce Colorectal Cancer risk?</p> <p><i>“Eat five or more serves per day of a variety of vegetables. National nutrition guidelines also advise two serves of fruit daily (“Go for 2 and 5”).”</i></p>	III-2	-	Equivocal	-	32,36,41, 43,63,64, 68
	<p>Should cereal fibre be selected to reduce Colorectal Cancer risk?</p> <p><i>“Select poorly soluble cereal fibres (e.g. wheat bran), especially if at increased risk of Colorectal Cancer.”</i></p>	III-2	II	Equivocal	Equivocal	9,41,51,73-76
	<p>Does calcium supplementation reduce Colorectal Cancer risk?</p> <p><i>“Ensure a total calcium intake of 1000–1200 mg/day in keeping with general dietary guidelines.”</i></p>	III-2	II	Equivocal	Equivocal	83-87
	<p>Does selenium supplementation reduce Colorectal Cancer risk?</p> <p><i>“Selenium supplementation for chemoprevention is promising but requires confirmation.”</i></p>	II	-	Equivocal	Equivocal	106-109

	<p>Does antioxidant vitamin supplementation reduce Colorectal Cancer risk?</p> <p><i>“Antioxidant vitamin supplementation is not advised at present to protect against Colorectal Cancer.”</i></p>	II	II	Recommended	Recommended	41,77, 109,111, 112
	<p>Do anti-inflammatory drugs reduce Colorectal Cancer risk?</p> <p><i>“Aspirin should be considered as prophylaxis against further adenoma development in those with a previous removal of an adenoma.”</i></p>	II	II	Recommended	Recommended	113-119,124-126
	<p>Should hormone replacement therapy be recommended to reduce risk of Colorectal Cancer?</p> <p><i>“HRT cannot be recommended as prophylaxis against Colorectal Cancer because of its possible collateral risks, including breast cancer.”</i></p>	III-2	III-2	Equivocal	Equivocal	128-132
Chapter	Recommendations	Level of evidence		Levels of recommendations		Refs
3	SCREENING FOR COLORECTAL CANCER					
	<p>Should screening be recommended?</p> <p>Faecal Occult Blood Testing <i>“Organised screening with FOBT, performed at least once every two years, is recommended for the Australian population over 50 years of age.”</i></p> <p>Flexible Sigmoidoscopy <i>“Screening with flexible sigmoidoscopy on a five-yearly basis from the age of 50 years.”</i></p>	I		Strongly recommended		13
		III-2		Equivocal		38, 39

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
4	COMMUNICATION WITH THE PATIENT			
5	THE PATIENT WITH SYMPTOMS			
	<p>What investigations need to be included?</p> <p><i>"In symptomatic patients aged over 40 years, referral to a specialist should be considered and consideration of full examination of the colon with colonoscopy is recommended."</i></p>	III-3	Equivocal	4-8
6	FAMILY HISTORY OF COLORECTAL CANCER			
	<p>What recommendations are there for those at category 1 risk?</p> <p><i>"Faecal occult blood testing (FOBT) every second year from the age of 50 years."</i></p>	Refer to Chapter 3 & AHTAC recomms (Box 3.1)	Recommended	3-6, 21, 28-31
	<p><i>"Consider sigmoidoscopy (preferably flexible) every five years from the age of 50."</i></p>	Refer to Chapter 3 & AHTAC recomms III-3	Recommended	3-6, 21, 28-31
	<p>What recommendations are there for those at category 2 risk?</p> <p><i>"Offer colonoscopy every five years starting at age 50, or at an age 10 years younger than the age of first diagnosis of bowel cancer in the family, whichever comes first. Sigmoidoscopy plus double-contrast barium enema is an acceptable alternative for colonoscopy if the latter is unavailable."</i></p>	III-2	Recommended	4-6, 35, 36
7	HIGH RISK FAMILIAL COLORECTAL CANCER SYNDROMES			
	<p>How should genetic testing be undertaken for high risk CRC family syndromes?</p> <p><i>"After counselling, genetic testing should be undertaken under the supervision of a cancer genetics specialist."</i></p>	III-2	Recommended	14
	<p>What is the role of NSAIDs in the prevention of colorectal neoplasia?</p> <p><i>"The role of NSAIDs such as sulindac in the prevention of cancer in FAP is unclear. High dose celecoxib (400mg twice daily) has been shown to reduce polyp numbers and its use may facilitate the control of polyps, but carries significant cardiovascular morbidity."</i></p>	II	Equivocal	14, 32, 33, 35, 36

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>What is the surgical management of FAP?</p> <p><i>“The surgical management of FAP is by total colectomy and ileorectal anastomosis or restorative proctocolectomy.”</i></p>	III - 2	Recommended	14, 25
	<p>When should large bowel surveillance begin in FAP and what should be offered?</p> <p><i>“Surveillance in FAP is by sigmoidoscopy from 12-15 years of age (the later age is recommended), except in attenuated FAP where surveillance is based on colonoscopy.”</i></p>	III - 2	Recommended	1-3,19
	<p>Is duodenal surveillance recommended in FAP?</p> <p><i>“Duodenal surveillance in FAP is recommended, from 25 years of age or earlier should there be a family history of duodenal cancer at an earlier age.”</i></p>	III-2	Recommended	14, 26-31
	<p>How should FAP family members not carrying their family mutation be advised?</p> <p><i>Members of proven FAP families who test negatively for the family APC mutation are no longer at high risk.</i></p>	III - 2	Recommended	24
	<p>When should large bowel surveillance screening of at-risk members in proven HNPCC families be offered?</p> <p><i>“Screening of at-risk members of proven HNPCC families should be by annual or two yearly colonoscopy, commencing around the age of 25 years or five years before the earliest age of cancer diagnosis in the family, whichever comes first. Annual screening should be offered to individuals carrying a germline mutation and for clinically affected individuals in Amsterdam families where mutation status is unknown.”</i></p>	III-2	Recommended	4-6, 9, 14
	<p>What surveillance is recommended for extra-colonic cancers in HNPCC?</p> <p><i>Consideration should be given to screening extracolonic sites in HNPCC, especially in families with clusters of extracolonic cancers. Surveillance of uterus and ovaries should begin at around 30-35 years or five years earlier than the youngest relative affected with uterine or ovarian cancer, whichever comes first.</i></p>	III -3	Recommended	9

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>How should tumour testing (MSI and IHC) be used in affected individuals from families suspected to have HNPCC?</p> <p><i>“The Revised Bethesda Guidelines could be applied to the selection of cancers for microsatellite instability (MSI) testing and immunohistochemical staining.”</i></p>	III-2	Recommended	76
	<p>How should HNPCC family members not carrying their family mutation be advised?</p> <p><i>“Members of proven HNPCC families who test negatively for the family mismatch gene mutation do not have an additional risk associated with this mutation.”</i></p>	III-2	Recommended	14
	<p>What surveillance is recommended in hyperplastic polyposis and for MSI-variable cancers?</p> <p><i>“Affected subjects in familial clusters characterised by mixtures of MSI-H, MSI-L and MSS cancers and/or the finding of multiple/large hyperplastic polyps should be screened by colonoscopy according to HNPCC recommendations, though first degree relatives unaffected by cancer may be screened according to intermediate risk guidelines.”</i></p>	IV	Equivocal	92,93
8	DIAGNOSTIC TESTS AND PREOPERATIVE ASSESSMENT			
	<p>Who should be investigated?</p> <p><i>“All people with suspicious large bowel symptoms or rectal bleeding should be investigated, especially if other risk factors (such as older age or family history) are present, or in any patient over 40 years of age.</i></p> <p><i>People under 40 years of age should be investigated if there is a positive family history, if there is not an identified cause of symptoms, or if symptoms are persistent.”</i></p>	III-3	Equivocal	4-7
	<p>What are the investigations for symptoms of Colorectal Cancer?</p> <p><i>“Investigation should include a digital rectal examination, a rigid sigmoidoscopy and a colonoscopy. A double-contrast barium enema plus sigmoidoscopy or CT colonography may replace the colonoscopy if there are difficulties with local availability, expertise or an incomplete colonoscopy.”</i></p>	III-3	Equivocal	6, 9, 10, 13-16

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>What role does FDG-PET scan have in assessing recurrent Colorectal Cancer?</p> <p><i>“FDG-PET scan facilitates management of probable or proven recurrent Colorectal Cancer.”</i></p>	III-2	Recommended	10
9	MANAGEMENT OF EPITHELIAL POLYPS			
	<p>What is the management of epithelial polyps?</p> <p><i>“All polyps should be at least sampled, and preferably removed. Synchronous polyps should be sought and removed.”</i></p>	III-2	Recommended	25-34
	<p>What is the general management of all patients with colorectal neoplasia completely removed at colonoscopy?</p> <p><i>All patients with colorectal neoplasia completely removed at colonoscopy should then be considered for colonoscopic surveillance according to the following protocols.</i></p> <ul style="list-style-type: none"> <i>• Within a year following incomplete or possible inadequate examination, for example in a subject with multiple adenomas.</i> <i>• At three years for subjects with large adenomas (> 1 cm), adenomas with high grade dysplasia, villous change in adenomas, three or more adenomas, or aged 60 or more with a first degree with colorectal neoplasia</i> <i>• At four to six years in subjects without the risk factors outlined above.</i> 	<p>II</p> <p>II</p> <p>III-3</p>	<p>Recommended</p> <p>Recommended</p> <p>Equivocal</p>	45-48
	<p>What is the management of malignant adenomas?</p> <p><i>“Malignant adenomas may be managed safely by endoscopic polypectomy provided strict criteria for patient selection and histopathological assessment are adhered to. In particular, malignant adenomas should be well or moderately differentiated and excision should be complete.”</i></p>	III-2	Recommended	35-43
10	PREPARATION FOR SURGERY			
	<p>What is the role of the stomal therapist?</p> <p><i>“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.”</i></p>	III-2	Recommended	1

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>Should bowel preparation be given routinely preoperatively?</p> <p><i>“Bowel preparation is current standard practice prior to 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:</i></p> <p><i>mechanical bowel preparation is not indicated in elective colorectal operations unless there are anticipated problems with faecal loading which might create technical difficulties with the procedure. Eg. Laparoscopic surgery, low rectal cancers.”</i></p>	I	Not recommended	11
	<p>What happens if a blood transfusion is required perioperatively?</p> <p><i>“Perioperative blood transfusion is to be avoided whenever possible as there may be a detrimental association between transfusion and recurrence.”</i></p> <p><i>“If a transfusion is required, then autologous blood is preferable to allogeneic blood for reasons of infection control and resource use.”</i></p>	III-2	Recommended	27
	<p>Should thromboembolic prophylaxis be given?</p> <p><i>“All patients undergoing surgery for Colorectal Cancer should receive prophylaxis for thromboembolic disease.”</i></p> <p><i>“Unfractionated heparin, low molecular weight heparin, and intermittent calf compression are effective in reducing the incidence of thromboembolism. Low molecular weight heparin has not been shown to be superior to low dose heparin in colorectal surgical patients.”</i></p>	I II	Strongly recommended Strongly recommended	29 30
	<p>Should prophylactic antibiotics be given?</p> <p><i>“All patients undergoing Colorectal Cancer surgery require prophylactic antibiotics.”</i></p> <p><i>“A single preoperative dose of intravenous cephalosporin and metronidazole, or gentamicin and metronidazole is an effective regime.”</i></p>	II I	Recommended Strongly recommended	33 34
	<p>Should normal body temperature be maintained?</p> <p><i>“Perioperative normothermia should be maintained.”</i></p>	II	Recommended	36

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
11	ELECTIVE SURGERY FOR COLON CANCER			
	Does high ligation provide any benefit? <i>“High ligation of the lymphovascular pedicle does not confer any oncological benefit. Resection where feasible should extend to the origin of segmental vessels.”</i>	III - 3	Equivocal	4
	Does no-touch isolation technique have any benefit? <i>“No-touch isolation technique has no oncologic benefit.”</i>	II	Not recommended	5
	Is segmental and extended resection equivalent in outcome? <i>“Segmental resection is equivalent to extended resection in outcome.”</i>	II	Equivocal	7
	Do sutured and stapled anastomosis have equivalent outcomes? <i>“Sutured and stapled anastomosis have equivalent outcomes.”</i>	I	Strongly recommended	8, 9
	Does omental wrapping of intestinal anastomoses have any benefit? <i>“Omental wrapping of anastomosis has no benefit.”</i>	III-2	Strongly not recommended	11
	When should oophorectomy be performed in association with colectomy for colon cancer? <i>“Bilateral oophorectomy should be performed if there is obvious malignant disease of one or both ovaries.”</i> <i>“Prophylactic bilateral oophorectomy for colon cancer cannot be supported by the available evidence.”</i>	III-3 II	Recommended Not recommended	23, 24 26
	Is laparoscopic colonic surgery as effective as the conventional approach? <i>“In experienced hands, laparoscopic surgery for colon cancer has equivalent outcome to conventional surgery.”</i>	I	Recommended	36
12	ELECTIVE SURGERY FOR RECTAL CANCER			
	Who should perform elective rectal cancer surgery? <i>“Elective surgery for rectal cancer should be carried out by a surgeon who has undergone a period of special exposure to this form of surgery during surgical training and who has satisfactory experience in the surgical management of rectal cancer.”</i>	III-2	Recommended	1-7

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>When should local excision of rectal cancer be performed?</p> <p><i>“Local excision of T1 rectal cancer may be used in selected cancer patients according to the following guidelines.</i></p> <p><i>mobile tumour ≤ 3 cm</i></p> <ul style="list-style-type: none"> <i>T1 on endorectal ultrasound or MRI</i> <i>not poorly differentiated on histology (biopsy)”</i> 	III-3	Equivocal	8–12, 16–21
	<p>What is an adequate distal clearance of resection?</p> <p><i>“2 cm (fresh) and 1cm (fixed) of distal clearance is recommended in most instances.”</i></p>	III-2	Recommended	30–35
	<p>What factors influence sphincter preservation?</p> <p><i>“Sphincter saving operation is preferred to abdominoperineal resection except in the presence of:</i></p> <ul style="list-style-type: none"> <i>tumours such that adequate distal clearance (> 1 - 2 cm) cannot be achieved</i> <i>the sphincter mechanism is not adequate for continence</i> <i>access to the pelvis makes restoration technically impossible (rare).”</i> 	III - 3	Equivocal	10,22, 25–30
	<ul style="list-style-type: none"> What is recommended for the extent of mesorectal excision (TME)? <i>“For mid to low rectal tumours, the principles of extra fascial dissection and total mesorectal excision (TME) are recommended.”</i> 	III-2	Recommended	31,35, 43–55
	<p>Should a colonic reservoir be constructed?</p> <p><i>“Where technically feasible, a colonic reservoir is recommended for anastomosis within 2cm from ano-rectal junction.”</i></p>	II	Strongly recommended	56,57, 59,61, 65-67, 69-71, 74
	<p>Should drainage be considered?</p> <p><i>“Routine drainage should be considered only for rectal cancers.”</i></p>	II	Equivocal	76,77, 79–81
13	EMERGENCY SURGERY			
	<p>What surgery is recommended for bowel obstruction?</p> <p><i>“Primary resection of obstructing carcinoma is recommended unless the patient is moribund.”</i></p>	II	Recommended	14-21

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>When should primary anastomosis be considered?</p> <p><i>“Primary anastomosis should be considered as a colectomy, with an ileocolic or ileorectal anastomosis.”</i></p> <p><i>“Primary colonic and rectal anastomoses could be considered and may need to be preceded by on table colonic lavage.”</i></p>	<p>III - 2</p> <p>III - 2</p>	<p>Equivocal</p> <p>Equivocal</p>	<p>14, 15, 17-20</p> <p>18,19, 21</p>
14	STAGING AND REPORTING			
	<p>What staging data should be recorded?</p> <p><i>“TNM staging, ACPS staging and the data required to adequately prognose should all be recorded to allow national and international comparisons. (ACPS staging embodies the simplicity of Dukes).”</i></p>	III-3	Equivocal	9, 10
15	ADJUVANT THERAPY FOR COLON CANCER			
	<p>Who should be considered for adjuvant therapy?</p> <p><i>“People with resected Dukes C i.e. node positive colon cancer should be considered for adjuvant therapy.”</i></p>	I	Strongly recommended	3-5
	<p>What is the value of adjuvant therapy in Duke’s B colon cancer?</p> <p><i>“The value of adjuvant therapy in Dukes B colon cancer has not been demonstrated unequivocally. Adjuvant therapy in this group is not recommended except for patients with features of ‘poor prognosis’.”</i></p>	II	Recommended	46
16	ADJUVANT THERAPY FOR RECTAL CANCER			
	<p>When should adjuvant therapy be considered for rectal cancer?</p> <p><i>“Adjuvant preoperative or postoperative radiotherapy should be considered for the high-risk rectal cancer.”</i></p>	I	Strongly recommended	26
	<p>Does preoperative therapy reduce late morbidity compared with postoperative?</p> <p><i>“Preoperative therapy may lower the incidence of late morbidity.”</i></p>	II	Recommended	22, 34

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>What postoperative chemotherapy should be administered if radiotherapy is indicated?</p> <p><i>“Where postoperative radiotherapy is indicated, 5-FU based chemotherapy should be administered.”</i></p>	II	Recommended	6
17	<p>FOLLOW-UP AFTER CURATIVE RESECTION FOR COLORECTAL CANCER</p>			
	<p>What are the recommendations for follow up?</p> <p><i>“Intensive follow up for Colorectal Cancer should be considered for patients who have had potentially curable disease. Although future investigations and pathways are yet to be firmly established.”</i></p>	I	Recommended	12, 13
18	<p>PSYCHOSOCIAL CARE</p>			
	<p>How important is psychosocial care in patients with cancer?</p> <p><i>“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></p>	I	Strongly recommended	17, 22
SECTION II ADVANCED COLORECTAL CANCER				
19	<p>RECURRENT AND ADVANCED COLORECTAL CANCER: GENERAL APPROACH AND LOCAL MANAGMENT</p>			
	<p>What are the recommendations for recurrent and advanced rectal cancer?</p> <p><i>“Radiotherapy, generally combined with chemotherapy is recommended in rectal cancers fixed or tethered within the pelvis.”</i></p>	II	Recommended	2, 3
	<p>What are the recommendations for inoperable rectal cancer?</p> <p><i>“Radiotherapy alone or chemoradiation should be considered in patients with locally advanced rectal cancer not amenable to surgery.”</i></p>	IV	Recommended	6-9, 16
20	<p>THE ROLE OF SYSTEMIC CHEMOTHERAPY IN METASTATIC DISEASE</p>			
	<p>Should chemotherapy be offered to patients with metastatic disease?</p> <p><i>“First-line FU based chemotherapy prolongs life when compared to best supportive care and should be offered to patients with advanced Colorectal Cancer.”</i></p>	I	Strongly recommended	1

Chapter	Recommendations	Level of evidence	Practice recommendation	Refs
	<p>When is the optimal time to commence chemotherapy?</p> <p><i>“The optimal time to commence chemotherapy in patients that are initially asymptomatic is unclear.”</i></p>	II	Equivocal	6, 7
	<p>What is the response rate in regimes of 5-FU chemotherapy?</p> <p><i>“After failure of 5-FU therapy, second-line treatment with irinotecan prolongs life and improves quality of life when compared to either best supportive care or an alternative regimen of 5-FU.”</i></p>	II	Recommended	4,5
21	MANAGEMENT OF LIVER AND OTHER DISTANT METASTASES			
	<p>Should imaging controlled destruction be considered?</p> <p><i>“Radiofrequency ablation is an alternative to surgery in selected cases.”</i></p>	II	Equivocal	37
	<p>Should adjuvant chemotherapy be considered?</p> <p><i>“Adjuvant chemotherapy should be considered following resection of liver metastases.”</i></p>	II	Equivocal	27-30
	<p>Does combination systemic chemotherapy have any benefits?</p> <p><i>“Combination systemic chemotherapy regimens that incorporate irinotecan or oxaliplatin have response rates, survival outcomes and safety profiles that are superior to those achieved with hepatic artery infusion chemotherapy.”</i></p>	III-2	Recommended	48, 51-55
	<p>When should surgical resection of unresectable liver metastases be considered?</p> <p><i>“Patients with liver metastases that are initially considered unresectable and achieving a response to systemic chemotherapy could be reconsidered for surgical resection.”</i></p>	III-3	Equivocal	56
	<p>What is the role of cytoreductive surgery with hyperthermic intra-peritoneal chemotherapy?</p> <p><i>“Cytoreductive surgery with or without chemotherapy should be performed on an appropriate randomised controlled trial.”</i></p>	II	Equivocal	70-82