These guidelines have been withdrawn

MOH clinical practice guidelines are considered withdrawn five years after publication unless otherwise specified in individual guidelines. Users should keep in mind that evidence-based guidelines are only as current as the evidence that supports them and new evidence can supersede recommendations made in the guidelines.

CLINICAL PRACTICE GUIDELINES

Colorectal Cancer

Ministry of Health

NMRC
National Medical Research Council

Feb 2004

MOH Clinical Practice Guidelines 2/2004

Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well-designed controlled study without randomisation.
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grades of recommendation

Grade	Recommendation
A (evidence levels Ia, Ib)	Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency, addressing the specific recommendation.
B (evidence levels IIa, IIb, III)	Requires availability of well conducted clinical studies, but no randomised clinical trials on the topic of recommendation.
C (evidence level IV)	Requires evidence obtained from expert committee reports or opinions, and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Colorectal Cancer

MOH Clinical Practice Guidelines 2/2004

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

Foreword

In Singapore, colorectal cancer is the second most commonly occurring cancer in men as well as in women after lung cancer and breast cancer respectively. Considering both sexes together, it is the cancer with the highest incidence and a significant contributor to mortality in Singapore.

These clinical practice guidelines provide extensive evidence-based recommendations on diagnosis, risk factors, surgery, chemotherapy, radiotherapy and prevention of colorectal cancer. The guidelines complement the recommendations on colorectal cancer screening in the MOH Health Screening Clinical Practice Guidelines. The guidelines are the work of a multidisciplinary workgroup, including colorectal surgeons, medical and radiation oncologists, and a general practitioner.

I hope that you will find the guidelines a useful reference in your own practice.

PROFESSOR TAN CHORH CHUAN
DIRECTOR OF MEDICAL SERVICES

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Diagnosis of Colorectal Cancer in a Patient with Symptoms

B In the presence of symptoms and signs suggestive of colorectal cancer or in the presence of unexplained iron deficiency anaemia, proctoscopy should be performed to identify an anorectal cause for symptoms. In the absence of an obvious cause, colonoscopy should be performed and is the investigation of choice. (pg 10)

Grade B, Level III

B Double contrast barium enema together with sigmoidoscopy is an alternative to colonoscopy in investigating patients with colorectal cancer. Barium enema should be performed if colonoscopy is incomplete. (pg 10)

Grade B, Level III

B Colonoscopy should be performed for persistent symptoms despite initial treatment for a presumptive diagnosis of a benign condition. (pg 10)

Grade B, Level III

Risk Factors for Colorectal Cancer

A Asymptomatic individuals above the age of 50 years should undergo screening for colorectal cancer. (pg 11)

Grade A, Level Ib

A A post-polypectomy surveillance programme is recommended for patients with a personal history of colorectal adenoma. (pg 11)

Grade A, Level Ia

A Asymptomatic individuals above the age of 50 years should undergo screening for colorectal cancer. This would include asymptomatic individuals with a family history limited to non-first degree relatives. The screening options would be faecal occult blood testing annually. (pg 12)

Grade A, Level Ia

B It is recommended that people at high risk of colorectal cancer be referred for colonoscopy at three-yearly intervals from age 45, or 10 years younger than the age of earliest diagnosis of colorectal cancer in the family, whichever is the younger age. (pg 12)

Grade B, Level IIb

B The first step in the management of familial adenomatous polyposis is the identification of the affected patient and his kindred. Detailed family history of individuals having colorectal cancer or polyps should be obtained. Genetic testing if available may be informative. (pg 13)

Grade B, Level IIb

B Screening of familial adenomatous polyposis kindred begins at the age of puberty with flexible sigmoidoscopy. Genetic testing should be considered and if the individual carries the mutation, these patients should be followed-up closely from puberty with possible proctocolectomy or total colectomy. (pg 13)

Grade B, Level IIb

B Colonoscopy rather than flexible sigmoidoscopy is recommended in kindred with a history of hereditary non-polyposis colorectal cancer as they are predisposed to right-sided colon cancer. (pg 14)

Grade B, Level IIb

B Surveillance colonoscopy with systematic biopsies should be considered for patients with extensive, longstanding ulcerative colitis. (pg 14)

Grade B, Level IIa

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A A single dose of appropriate antibiotics administered perioperatively is as effective as long term post-operative use in the prophylaxis against

wound infection following colorectal cancer surgery. Inappropriate postoperative use of antibiotics is associated with increased costs. (pg 15)

Grade A, Level Ib

A Randomized trials both locally and overseas have shown reduction in the risk of deep venous thrombosis with heparin prophylaxis. (pg 16)

Grade A, Level Ib

B Optimal care of patients undergoing stoma creation surgery would include pre-operative counselling and stoma siting. (pg 16)

Grade B, Level III

B The length of bowel resected for colon cancer will be dictated by the removal of the arterial supply of the colon which parallels the lymphatic drainage. At least 5 cm of normal bowel on either side of the tumour appears to be a minimum length to remove the paracolic lymph nodes and to minimize anastomotic recurrences. (pg 17)

Grade B, Level III

C Patients with multiple (i.e. two or more) colon cancers or those with hereditary nonpolyposis colorectal cancer should be considered for a total abdominal colectomy with ileorectal anastomosis. (pg 18)

Grade C, Level IV

C Patients with ulcerative colitis who develop a colorectal cancer should have a panproctocolectomy with or without restoration. (pg 18)

Grade C, Level IV

B The ideal bowel margin is 2 cm or more distally and 5 cm or more proximally, measured in the fresh, anatomically restored ex vivo condition from the tr±nsected full-thickness edge and does not include the tissue donuts from the endoluminal stapler. The minimal acceptable distal margin for tumours of the lower rectum (<5 cm from the anal verge) where sphincter preservation is an issue is 1cm. A 1 cm margin is not advised in cases of large, bulky tumours, or poorly differentiated tumours with lymphovascular or perineural invasion. (pg 22)

Grade B, Level III

B Total mesorectal excision is not required for tumours located in the upper rectum (10-15 cm from the anal verge), which can be resected including 5 cm of distal mesorectum. (pg 23)

Grade B, Level III

B 5-year survival in excess of 50-60% can be obtained by pelvic exenteration for selected patients with locally advanced rectal cancer operated with curative intent. The operative mortality should be less than 10% but morbidity of 25-50% can be expected. (pg 25)

Grade B, Level III

B Distal rectal washout (after distal occlusion) may have a benefit in reducing anastomotic recurrence in rectal cancer surgery. (pg 26)

Grade B, Level III

B En bloc resection of adjacent organs locally invaded by colorectal cancers can achieve survival rates similar to those of tumours that do not invade an adjacent organ. To achieve this, the tumour must not be transected at the site of adherence, and negative resection margins are required. (pg 26)

Grade B, Level III

B Metastatic tumor burden limited to one site and less extensive liver involvement select out a group of patients with stage IV colorectal cancer who can have resection of the asymptomatic colorectal primary tumour and expect substantial survival benefit over those never having resection. (pg 28)

Grade B, Level IIb

B Transanal excision of ultrasound staged T1 and ultrasound staged T2 rectal cancers together with adjuvant therapy may be an acceptable alternative in those not suitable for major resection surgery. (pg 31)

Grade B, Level IIa

A Synchronous liver metastases are those diagnosed within 6 months from diagnosis of the primary. The treatment of choice in this setting is resection of the metastases if there is no extrahepatic disease. (pg 32)

Grade A, Level Ib

Use of Tumour Markers

C Due to the low sensitivity and specificity, CEA cannot be recommended as a screening test for colorectal cancer. There are no data that CEA screening provides better survival, quality of life or lower costs in the population compared to no screening. (pg 35)

Grade C, Level IV

A It is recommended that CEA levels be monitored every 2 to 3 months in patients with stage II or III disease for at least 2 years after diagnosis. The benefit of monitoring decreases after 2 years. (pg 36)

Grade A, Level Ia

Follow-up after Primary Surgery

B The frequency of surveillance colonoscopy is not clear but has been recommended to between 3-5 yearly after an initial complete colonoscopic examination (without synchronous polyps or cancers) either preoperatively or within 6 weeks after surgery. Metachronous lesions and polyps are believed to occur less frequently than extraluminal recurrence. More frequent examination is suggested for certain high risk factors such as high grade dysplasia, multiplicity, flat rather than polypoid morphology and the size of greater than 1 cm in the resected polyp. (pg 37)

Grade B, Level IIb

Adjuvant Therapy for Colon Cancer

A 5-flourouracil based chemotherapy is recommended after surgery as it improves disease-free survival and overall survival for stage III* colon cancer.

Postoperative chemotherapy with 5-flourouracil/folinic acid (leucovorin) for 6 months is equivalent to 5-flourouracil/levamisole for 12 months. (pg 39)

* TNM staging system

Grade A, Level Ib

Adjuvant Therapy for Rectal Cancer

A If total mesorectal excision is not performed, post-operative radiotherapy can be recommended for improved local control and also recommended for improved survival when combined with chemotherapy. (pg 40)

Grade A, Level Ib

A Neoadjuvant, preoperative, short course radiotherapy improves local control and survival. Surgical complications may be increased, but not substantially. (pg 40)

Grade A, Level 1a

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A Chemotherapy prolongs survival and improves quality of life for patients with metastatic colorectal cancers. Even when there is no radiologically demonstrable shrinkage of tumour, stabilization of disease is often associated with prolongation of survival and decrease in tumour-related symptoms. (pg 42)

Grade A, Level Ia

B While studies have shown age-dependent toxicity associated with the use of cytotoxic agents, advanced age is not a reason to withhold chemotherapy. (pg 42)

Grade B, Level IIa

C Raltitrexed can be used when 5-fluorouracil is either not tolerated or inappropriate. (pg 43)

Grade C, Level IV

A Capecitabine or UFT plus folinic acid are acceptable as a first-line chemotherapy for advanced colorectal cancer. (pg 44)

Grade A, Level Ib

Prevention of Colorectal Cancer

B Case-control studies show a positive correlation between energy intake and colorectal cancer risk. Although fat intake may be a confounding factor in this relationship, it has been concluded that

replacing fat with other energy sources is unlikely to reduce colorectal cancer risk. There is sufficient evidence to recommend reducing energy intake to prevent colorectal cancer. (pg 51)

Grade B, Level III

B It is reasonable to recommend a high fibre intake as a possible measure to prevent colorectal cancer. (pg 52)

Grade B, Level III

B Calcium supplementation on current evidence may be beneficial in the prevention of colorectal cancer. (pg 52)

Grade B, Level III

B Physical activity is recommended as a preventive measure against colorectal cancer. (pg 53)

Grade B, Level IIa

B Stop smoking to avoid development of colorectal cancer. (pg 53)

Grade B, Level IIa

1 Introduction

1.1 Background information

Colorectal cancer is the cancer with the highest incidence in Singapore and accounts for a significant number of cancer deaths[1]. The risk increases with age and rises sharply from the age of 50 years. Colorectal cancer is most common among the Chinese in terms of ethnic distribution. It affects both sexes about equally. Significant progress in survival among colorectal cancer patients in Singapore has been observed. This has been the result of cancer control activities such as health promotion, early diagnosis and treatment.[2]

1.2 Objectives

These guidelines were developed with the intention of maintaining the positive trend towards better survival of patients with colorectal cancer in Singapore. They are intended for use by all medical practitioners and health care workers who require information about patients with colorectal cancer. The scope is wide covering the areas of diagnosis, risk factors, surgery, chemotherapy, radiotherapy and prevention. Guidelines for the screening for colorectal cancer have been covered in the MOH Clinical Practice Guidelines on Health Screening.[3]

1.3 Development of Guidelines

These guidelines have been produced by a committee of general practitioners, surgeons, medical oncologists and therapeutic radiologists appointed by the Ministry of Health. They were developed using the best available current evidence and expert opinion.

1.4 Review of Guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supercede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or if new evidence appears that requires substantive changes to the recommendations.

2 Diagnosis of Colorectal Cancer in a Patient with Symptoms

2.1 Introduction

Three main sets of clinical presentation may raise the possibility of colorectal cancer

a. primary symptoms arising from the bowel.

b. The secondary effect of the cancer producing iron-deficiency anaemia.

c. detectable masses on abdominal or rectal examination.

2.2 The patient with bowel symptoms.

The principal symptoms of colorectal cancer include

a. rectal bleeding without anal symptoms

b. a change in bowel habit, especially of recent onset.

c. abdominal pain, especially of recent onset.

Other symptoms include abdominal bloating, mucus in stools, tenesmus and weight loss. The symptoms of colorectal cancer may be confused with those due to common benign conditions such as irritable bowel syndrome and haemorrhoids, making the decision to investigate difficult.

A patient aged 40 years and over and with recent onset of symptoms should raise the suspicion of colorectal cancer.[4] Although less common under the age of 40 years, colorectal cancer should be considered in younger people with persistent symptoms and in the presence of risk factors (section 3).

2.3 Rectal Bleeding

The predictive value of rectal bleeding for colorectal cancer or adenoma in the primary care setting is in the region of 2% to 10% for cancer and 7% to 8% for adenoma.[4,5] Three variables in a patient with rectal bleeding have been found to be significantly predictive: age, a change in bowel habit and blood on or mixed with stool.[5]

2.4 Iron deficiency anaemia

In non-menstruating patients, gastrointestinal bleeding is the most common cause of iron deficiency anaemia.[6] The anaemia is usually occult. In non-menstruating patients over 40 years of age, colorectal cancer is a common cause.[7]

2.5 Abdominal and Rectal Masses

An abdominal mass is a sign of locally advanced colorectal cancer. Rectal examination is mandatory in patients with bowel symptoms. A rectal mass may indicate the presence of a cancer. Metastatic deposits may be palpable in the rectovesical or rectouterine pouch. The presence of altered blood is highly suggestive of a malignancy.

2.6 Investigation of symptoms

B In the presence of symptoms and signs suggestive of colorectal cancer or in the presence of unexplained iron deficiency anaemia, proctoscopy should be performed to identify an anorectal cause for symptoms. In the absence of an obvious cause, colonoscopy should be performed and is the investigation of choice.[4,5,6,7]

Grade B, Level III

B Double contrast barium enema together with sigmoidoscopy is an alternative to colonoscopy in investigating patients with colorectal cancer. Barium enema should be performed if colonoscopy is incomplete.[4,5,6,7]

Grade B, Level III

B Colonoscopy should be performed for persistent symptoms despite initial treatment for a presumptive diagnosis of a benign condition.[4,5,6,7]

Grade B, Level III

3 Risk Factors for Colorectal Cancer

Risk factors for colorectal cancer include

a. age of 50 years or older

b. a personal history of colorectal cancer or adenoma

c. a family history of colorectal cancer or adenoma

d. a history of ulcerative colitis

3.1 Age

The risk of colorectal cancer increases with age.[5] There is a sharp rise in incidence above the age of 50 years and the risk of colorectal cancer remains high till the age of 80 years where there appears to be a plateau in incidence. Age is a risk factor to be considered in the evaluation of a patient with bowel symptoms suggestive of colorectal cancer.

A Asymptomatic individuals above the age of 50 years should undergo screening for colorectal cancer.[3]

Grade A, Level Ib

3.2 Personal history of colorectal adenoma or cancer

The majority of colorectal cancers are believed to arise from adenomas.[8] The characteristics of adenomas associated with a higher frequency of carcinoma include larger size, villous architecture, severe dysplasia and multiplicity.[8,9] Removal of adenomas detected during colonoscopy reduces the risk of colorectal cancer.

A A post-polypectomy surveillance programme is recommended for patients with a personal history of colorectal adenoma.[10,11]

Grade A, Level Ia

The incidence of a synchronous cancer and adenomas at the time of initial diagnosis is between 2% to 6% and 25% to 40% respectively.[12,13]

Metachronous colorectal cancer and adenoma are reported in 3% to 8% and 25% to 40% respectively.[14,15] Total colonoscopy perioperatively and surveillance colonoscopy post-operatively targets the detection of synchronous and metachronous neoplasma (see section 6.5).

3.3 Family history of colorectal or cancer.

There is a predisposition towards colorectal cancer in some families.[16,17] Taking a history in patients with colorectal cancer should include a family history with the details of age of diagnosis of, relationship with and number of other affected family members. Based on this information it is possible to stratify the relative risk for a presently unaffected family member:

3.3.1 Those at average risk

A Asymptomatic individuals above the age of 50 years should undergo screening for colorectal cancer. This would include asymptomatic individuals with a family history limited to non-first degree relatives. The screening options would be faecal occult blood testing annually.[3]

Grade A, Level Ia

3.3.2 Those at high risk

These would include asymptomatic individuals who have

- one first degree relative diagnosed with colorectal cancer less than 45 years of age, or

- two first or second degree relatives from the same side of the family with colorectal cancer diagnosed at any age.[17,18,19] Relative risk in this group is increased three- to six-fold.

B It is recommended that people at high risk of colorectal cancer be referred for colonoscopy at three-yearly intervals from age 45, or 10 years younger than the age of earliest diagnosis of colorectal cancer in the family, whichever is the younger age.[20,21,22]

Grade B, Level IIb

3.3.3 Those at very high risk

Members of families with either familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (HNPCC) are at high risk of colorectal cancer.[23,24,25,26] Members of these families require surveillance and should be considered for genetic testing.

3.3.3.1 Familial Adenomatous Polyposis Coli

FAP is the result of germline mutation of the APC gene, a tumour suppressor gene. The lifetime risk of colorectal cancer is nearly 100%.

B The first step in the management of FAP is the identification of the affected patient and his kindred.[27] Detailed family history of individuals having colorectal cancer or polyps should be obtained. Genetic testing if available may be informative.

Grade B, Level IIb

B Screening of FAP kindred begins at the age of puberty with flexible sigmoidoscopy. Genetic testing should be considered and if the individual carries the mutation, these patients should be followed-up closely from puberty with possible proctocolectomy or total colectomy.[28,29]

Grade B, Level IIb

B Individuals from families where the genetic mutation for FAP has been identified but are tested negative themselves would require similar screening as the average risk population. For at risk individuals where the mutation has not been identified in the family or if genetic testing is not available, annual screening with flexible sigmoidoscopy is recommended from puberty. Genetic counselling is essential prior to genetic testing.[28,29]

Grade B, Level IIb

3.3.3.2 Hereditary Non-Polyposis Colorectal Cancer

The lifetime gastrointestinal cancer risk associated with HNPCC is variously reported as around 80% for colorectal cancer and 13-20% for gastric cancer in studies that have selected families by HNPCC criteria.

B Colonoscopy rather than flexible sigmoidoscopy is recommended in kindred with a history of HNPCC as they are predisposed to right-sided colon cancer.

Grade B, Level IIb

The ages when screening should begin and the interval of colonoscopy are not clear. More rigorous studies into this area is unlikely forthcoming given the high risk of cancer and the relative infrequency of HNPCC in affected individuals.[27]

3.4 History of longstanding ulcerative colitis

Colorectal cancer occurs more frequently in patients with longstanding ulcerative colitis. The factors increasing the likelihood of cancer formation in this group of patients include the extent of colitis, severity and time course of inflammation, the duration of disease and the age of onset.[30]

B Surveillance colonoscopy with systematic biopsies should be considered for patients with extensive, longstanding ulcerative colitis.[31]

Grade B, Level IIa

4 Surgery for Colorectal Cancer

4.1 Preoperative preparation

4.1.1 Mechanical bowel preparation

The presence of bowel contents within the colon during bowel surgery was believed to be significantly related to anastomotic dehiscence for many years. A meta-analysis.[32,33] involving 6 randomized prospective trials in elective colorectal surgery comparing any form of mechanical bowel preparation to without has shown no difference in the incidence of anastomotic leaks stratified for rectal and colonic anastomosis, mortality, re-operation, wound infection, infectious extraperitoneal complication, non-infectious extraperitoneal complication and overall surgical site infection. A similar RCT published recently had a similar conclusion.[34]

A Bowel preparation is not essential for colorectal resection[32,33,34] especially right-sided colon resections.[35]

Grade A, Level Ia

Most surgeons would generally agree that it is technically easier to operate on a mechanically cleansed colon.

4.1.2 Perioperative antibiotics

Perioperative antibiotics are effective in reducing the incidence of wound infection after colorectal surgery.[36,37] There is no significant difference between many regimes so long as the spectrum of organism coverage includes both aerobes and anaerobes, but certain regimes appear inadequate (e.g. metronidazole alone, doxycycline alone, piperacillin alone, oral neomycin plus erythromycin on the day before operation).

A A single dose of appropriate antibiotics administered perioperatively[38] is as effective as long term post-operative use in the prophylaxis against wound infection following colorectal cancer surgery. Inappropriate postoperative use of antibiotics is associated with increased costs.[39]

Grade A, Level Ib

4.1.3 Prophylaxis for DVT – anticoagulants, mechanical methods

The incidence of deep venous thrombosis and the consequential risk of pulmonary embolism is significant in patients undergoing colorectal cancer surgery. This may range from 3-7%[40] and as high as 41% in certain groups.[41] Any single method has been shown to reduce the incidence of deep venous thrombosis (with heparin being the most effective single agent) but a combination is more effective.[42]

A Randomized trials both locally and overseas have shown reduction in the risk of deep venous thrombosis with heparin prophylaxis.[43,44]

Grade A, Level Ib

4.1.4 Counselling, stoma nurse

A certain degree of anxiety exists in all patients undergoing stoma creation surgery.[45,46] Enterostomal therapy nurses have much to offer in preparing patients undergoing such surgery.[47]

Counselling patients as to what to expect after surgery as well as positioning of the site of the stoma alleviates anxiety and reduces complications.

B Optimal care of patients undergoing stoma creation surgery would include pre-operative counselling and stoma siting.

Grade B, Level III

4.2 Curative surgery for colon cancer

Colon cancer originates in the mucosa and initially spreads by direct invasion of the bowel wall. Lymphatic, peritoneal and blood borne metastases become more common as the cancer extends through the bowel wall. Direct extension to adjacent structures may also occur.

Surgical treatment of the disease involves wide resection of the tumour with its regional lymphatics. As the lymphatic supply of the colon passes along the arterial blood supply, treatment should be resection of the affected segment of colon along with its mesenteric blood supply to the level of the origin of the primary feeding arterial vessel. When the

primary tumour is equidistant from two feeding vessels, both vessels should be excised at their origins.

4.2.1 Extent of bowel resection and margins

4.2.1.1 Single tumour

B The length of bowel resected for colon cancer will be dictated by the removal of the arterial supply of the colon which parallels the lymphatic drainage. At least 5 cm of normal bowel on either side of the tumour appears to be a minimum length to remove the paracolic lymph nodes and to minimize anastomotic recurrences.[48]

Grade B, Level III

4.2.1.2 Multiple tumours

The extent of resection for patients with multiple tumours depends on the number and location of the lesions. Lesions that are confined to one side of the colon are easily dealt with by extending the length of the resection. For lesions at opposite ends of the bowel, like the rectosigmoid and the cecum, the decision is more difficult. Minimizing the number of anastomoses should be weighed against the impairment of bowel function with an extended resection.

A primary consideration is whether the intervening bowel is healthy or highly predisposed to malignant change. In the presence of multiple adenomatous polyps or a background of inflammatory bowel disease, an extended resection is preferable. The age, mobility, continence and general condition of the patient would also weigh on the decision.

B It is safe to perform double segmental bowel resections and synchronous anastomoses for multiple colonic cancers provided the anastomoses are technically good with adequate blood supply and lack of tension.[49]

Grade B, Level III

C Patients with multiple (i.e. two or more) colon cancers or those with hereditary nonpolyposis colorectal cancer should be considered for a total abdominal colectomy with ileorectal anastomosis.[50,51]

Grade C, Level IV

C Other suggested indications for subtotal/total colectomy include associated polyps (not removed/removable by colonoscopy), acute left-sided obstruction, associated complicated sigmoid diverticular disease, prior transverse colostomy for obstruction, young patient age under 50 years with a positive family history, and adherence of the sigmoid colon to a caecal carcinoma.[52]

Grade C, Level IV

4.2.1.3 Cancer in ulcerative colitis

The risk of malignant change in ulcerative colitis increases with time, severity of the disease and extent of bowel involvement. In general, this risk is low in the first decade of the onset of the disease. If a colorectal cancer is detected in a patient suffering from longstanding ulcerative colitis, complete excision of the whole colon and rectum is indicated as this not only deals with the malignancy, but also removes the risk of subsequent malignant change in the residual colon.

C Patients with ulcerative colitis who develop a colorectal cancer should have a panproctocolectomy with or without restoration.[50]

Grade C, Level IV

4.2.1.4 No-touch technique

The no-touch technique proposes mesenteric vascular ligation before tumour handling and mobilisation in the expectation that this decreases dislodgement of tumour emboli during resection of colorectal carcinomas. Turnbull et al.[53] demonstrated survival benefit but this was biased by more extended resections in the no-touch group. Subsequent studies have also not demonstrated consistent benefit. No

conclusive data demonstrate that the detachment and circulation of tumour cells increase in the mesenteric circulation during manipulation of colorectal cancers.[54,55]

A There is no survival advantage to support the routine use of the no-touch isolation technique in colon cancer surgery.[56]

Grade A, Level Ib

4.2.1.5 Location of cancers

a. Caecum or ascending colon

B In cases of caecal or ascending colon cancer in which the middle colic artery is not the main trunk artery, a right hemicolectomy with resection of only the right branch of the middle colic will usually suffice.[57]

Grade B, Level III

b. Hepatic flexure

As the right colic artery is absent or non-dominant in up to 80% of cases,[11] the primary feeding artery to a hepatic flexure cancer will be the right branch of the middle colic artery.

C Hepatic flexure cancer can be resected by an extended right hemicolectomy taking the middle colic artery at its origin. The length of ileum resected does not affect local recurrence and the shortest length of ileum needed to perform the procedure should be excised to prevent malabsorption syndromes.[50]

Grade C, Level IV

c. Transverse colon

The appropriate operation for a transverse colon carcinoma is controversial. The reason is the desire to fulfill the criteria for resection of the regional lymphatics, which depending on the portion of the transverse colon involved, may occur through the middle colic and/or right colic and possibly the left colic branches.

GPP For lesions near the hepatic flexure, an extended right hemicolectomy is recommended. For lesions near the splenic flexure, a left segmental colectomy with anastomosis of the transverse colon to the proximal sigmoid can be performed. For a lesion in the midtranverse colon, a transverse colectomy is in order.

GPP

d. Splenic flexure

Splenic flexure cancer is characterized by a higher risk of obstruction and the presence of distant metastases.[58] However, after curative resection, splenic flexure cancer has a similar outcome to colon cancer at other sites.[58,59]

B Splenic flexure cancer can be resected by left hemicolectomy or segmental resection of the transverse/ descending colon without routine extended resection comprising extended right hemicolectomy, splenectomy, and distal pancreatectomy.[60]

Grade B, Level III

e. Descending colon

Left hemicolectomy removes the entire left colon along with the origin of the inferior mesenteric artery and the dependent lymphatic territory. Left segmental colectomy removes a more restricted segment of the colon with its primary feeding vessels and leaves the origin of the inferior mesenteric artery intact.

For left colonic carcinoma, the survival after left segmental colectomy is equivalent to that of left hemicolectomy.[61]

A A limited resection can be performed for descending colon cancers without compromising oncologic outcome.

Grade A, Level Ib

B For obstructed left colonic carcinoma, there is no significant difference in bowel function or complications between extended right colectomy without colonic decompression and segmental left colectomy with intraoperative decompression.[62]

Grade B, Level III

f. Sigmoid colon

B Segmental resection of the sigmoid colon (with anastomosis of the descending colon to the upper rectum) is an effective cancer operation for carcinoma of the sigmoid colon, and has a lesser morbidity and mortality than a radical left hemicolectomy.[63,64]

Grade B, Level III

4.3 Curative surgery for rectal cancer

Anatomic definition of the rectum is highly variable. Both endoscopic and intraoperative criteria are used. Although it is universally agreed that the rectum is the portion between the sigmoid and the anorectal ring, its proximal limit has been variously defined at 12 cm[65,66] or 15 cm[67] measured from the anal verge.

For intraoperative description, the proximal limit of the rectum can be determined by the point where the taeniae coli coalesce, the pertioneal reflection or the sacral promontory.

Flexible sigmoidoscopy introduces variability in the level of the rectum due to technique.

C Rigid proctoscopy (in the left decubitus position) is thought to be a highly reproducible method of determining the level of the rectum and is less dependent on the operator or technique. The anal verge is the preferred anal landmark (over the anorectal junction) since it can be visualised simultaneously with the edge of the rectal tumour during rigid proctoscopy.[50]

The goals in the treatment of rectal cancer are to cure, avoid local failure and maintain quality of life, including bowel, bladder and sexual function.

4.3.1 Extent of bowel resection and margins

Proximal and distal margins are determined by the level of proximal vascular ligation and distal mesorectal clearance. A minimum 5 cm bowel margin is based on Grinnell's work on intramural extension,[68] but subsequent studies have shown that distal intramural spread is rare and seldom beyond 1 cm, with acceptable survival and local control with a distal bowel margin of 2 cm or more.[69,70]

B The ideal bowel margin is 2 cm or more distally and 5 cm or more proximally, measured in the fresh, anatomically restored ex vivo condition from the transected full-thickness edge and does not include the tissue donuts from the endoluminal stapler. The minimal acceptable distal margin for tumours of the lower rectum (<5 cm from the anal verge) where sphincter preservation is an issue is 1 cm.[71,72] A 1 cm margin is not advised in cases of large, bulky tumours, or poorly differentiated tumours with lymphovascular or perineural invasion.[70]

Grade B, Level III

B Intersphincteric dissection may be employed in sphincter preserving operations for some selected low rectal tumours.[73]

Grade B, Level III

C An intraoperative frozen section evaluation of the distal margin is recommended when this is 1-2 cm.[50]

Grade C, Level IV

4.3.2 Lymphovascular ligation

Extending the lymphatic clearance to the aorta does not appear to confer added benefits, as nodal metastases at this location are generally an indicator of widespread disease and a poor prognosis.[64]

High tie of the inferior mesenteric artery is division and ligation of the inferior mesenteric artery at its origin at the aorta. Low tie is division and ligation of the inferior mesenteric artery distal to the branching of the left colic artery.

B More accurate staging and prognosis may be obtained by high ligation of the inferior mesenteric artery but this has not been found to improve 5-year survival in patients with cancer of the rectum or rectosigmoid.[64,74,75]

Grade B, Level III

C All clinically suspicious lymph nodes beyond the origin of the feeding vessel should be biopsied or removed, or the level of resection should be extended to include the worrisome lymph nodes where technically feasible and safe.[50]

Grade C, Level IV

4.3.3 Mesorectal excision

The clinical significance of the mesorectum and of its surgical excision is supported by the demonstration of tumour deposits within the mesorectum remote from the primary tumour and by the demonstration of a strong correlation between the extent of the mesorectal spread and oncologic outcomes.[67] Mesorectal spread can occur by direct tumour extension, lymph nodes, perineural invasion or isolated mesorectal deposits.[76]

Total mesorectal excision (TME) is the complete excision of the intact visceral mesorectal tissue to the level of the levators by sharp dissection under direct visualization. Wide mesorectal excision (WME) is the precise perpendicular and circumferential excision of the mesorectum to the level of an appropriate distal resection margin.

B Total mesorectal excision (TME) is not required for tumours located in the upper rectum (10-15 cm from the anal verge), which can be resected including 5 cm of distal mesorectum.[77,78]

Grade B, Level III

B Wide mesorectal excision (WME) of at least 4 cm distal to the tumour is sufficient for mid-rectal tumours Total mesorectal excision (TME) is required for patients with tumours in the lower rectum.[79]

Grade B, Level III

B Circumferential margin involvement after mesorectal excision of rectal cancer with curative intent indicates advanced disease, not inadequate surgery. Patients with an involved margin may die from distant disease before local recurrence becomes apparent.[80]

Grade B, Level III

4.3.4 Reconstruction

Functional outcome after low anterior resection for rectal cancer is improved by colonic pouch reconstruction compared with straight anastomosis, although long-term function, especially evacuation, may militate against its routine use.

B Colonic J-pouch reconstruction is indicated when the distance of anastomosis from the anal verge is less than 8 cm, and it is essential when the distance is less than 4 cm.[81]

Grade B, Level III

A Reconstruction with a colonic J-pouch is associated with a lower incidence of anastomotic leakage and better clinical bowel function when compared with the traditional straight coloanal anastomosis. Functional superiority is especially evident during the first 2-6 months but diminishes at 2 years.[82,83]

Grade A, Level Ib

A A 5 cm colonic J-pouch is an optimum size that confers adequate reservoir function without compromising evacuation.[84]

Grade A, Level Ib

A Colonic pouches constructed from sigmoid or descending colon give similar bowel function after low anterior resection for rectal cancers.[84]

Grade A, Level Ib

B Coloplasty has similar functional outcome and pouch compliance compared with colonic J-pouch in low colorectal anastomosis. Coloplasty may provide an alternative method to the colonic J-pouch for a neorectal reservoir construction when reach or a narrow pelvis prohibits its formation. Technically a coloplasty may also be easier to construct.[84]

Grade B, Level IIb

4.3.5 Extended resections

En bloc resection to obtain negative margins is the ideal surgical method to manage locally advanced, adherent tumours. Consideration should be given to neoadjuvant chemoirradiation in these instances. (See section 8.2)

a. Pelvic exenteration

B 5-year survival in excess of 50-60% can be obtained by pelvic exenteration for selected patients with locally advanced rectal cancer operated with curative intent. The operative mortality should be less than 10% but morbidity of 25-50% can be expected.[85,86,87]

Grade B, Level III

b. Extended lateral pelvic lymph node dissection

The prognosis for patients with metastasis to the lateral lymph nodes is poor, and the improvement in survival rate from lateral lymph node dissection is minimal.

B Extended lateral pelvic lymph node dissection for rectal cancer in the absence of clinically suspicious nodes cannot be recommended.[88]

Grade B, Level III

C Clinically suspected lateral lymph node disease should be removed as is technically feasible and safe to do so. Biopsy of suspected lymph nodes beyond the surgical resection field (e.g. iliac lymph node) should be done for staging purposes.[50]

Grade C, Level IV

4.3.6 Stomas

Defunctioning stomas do not decrease the anastomotic leak rate but mitigate against the morbidity of an anastomotic leak.

GPP A defunctioning stoma is recommended after low anterior resection or coloanal anastomosis following total mesorectal excision

(TME), and in patients presenting for surgery after neoadjuvant chemoradiation. It should also be considered for patients on steroids, obstructed tumours, locally advanced cancers after difficult and/or extended resections, and where the tissue donuts after stapling are deficient or the air-leak test is positive.

GPP

A Loop ileostomy[89,90] and loop transverse colostomy[91,92] are variously preferred but are probably equivalent options for temporary faecal diversion.[93]

Grade A, Level Ib

4.3.7 Distal rectal washout

Exfoliated malignant cells that are viable and have the ability to proliferate and metastasize can be found in the effluent of resection margins, rectal stumps and on circular stapling devices.[94,95] Different chemical washout solutions, including normal saline, have been shown to eliminate these exfoliated cells.[96]

B Distal rectal washout (after distal occlusion) may have a benefit in reducing anastomotic recurrence in rectal cancer surgery.[97]

Grade B, Level III

4.4 Surgery for locally advanced cancers

The critical issue is that it cannot be determined reliably before resection whether tumour involvement of contiguous organs and structures is the result of an inflammatory or malignant process. En bloc resection of the tumour and adherent structures is hence the most appropriate surgical approach.

B En bloc resection of adjacent organs locally invaded by colorectal cancers can achieve survival rates similar to those of tumours that do not invade an adjacent organ. To achieve this, the tumour must not be transected at the site of adherence, and negative resection margins are required.[98,99]

Grade B, Level III

4.5 Rectal cancers: Endosonography and staging, neoadjuvant treatment

Accurate staging information is crucial in rectal cancers because there are more treatment options available. Some well-localised tumours are amenable to local resection while more advanced cancers allow a choice among sphincter-sparing low anterior resection, abdominoperineal resection or perioperative adjuvant chemoradiotherapy.

The major role for imaging in staging of rectal tumours is, first, to determine the extent of the tumour in or through the rectal wall; second, to recognise the presence of enlarged lymph nodes or distant metastases and third, to assess the distance between the distal tumour margin and the anorectal junction.

B Endosonography and magnetic resource imaging (MRI) are accurate and have become the primary imaging techniques in the locoregional staging of rectal cancers.[100,101]

Grade B, Level III

B Neoadjuvant therapy for adenocarcinoma of the rectum is well tolerated and can produce substantial down-staging and a high curative resection/sphincter preservation rate. Chemoradiation can achieve significant complete pathologic response rates, although toxicity during neoadjuvant therapy is greater than for radiation alone. Short-course radiation can also achieve down-staging of both T stage and N stage.[102]

Grade B, Level IIb

4.6 Defunctioning stoma before radiotherapy

GPP There is no evidence to support the routine creation of a stoma prior to radiotherapy in the absence of severe symptoms or impending obstruction.

GPP

4.7 Palliative resections

Surgical resection of primary colorectal cancer in patients with stage IV disease (that is irresectable for cure) at initial presentation remains

controversial. Although bowel resection to palliate symptoms such as bleeding, perforation, obstruction or pain has been advocated, management of asymptomatic patients has not been well defined.

Patient-dependent factors (performance status, co-morbid disease) and extent of distant metastases are among the considerations that impact on the decision to proceed with surgical management in asymptomatic stage IV disease.

B Metastatic tumor burden limited to one site and less extensive liver involvement select out a group of patients with stage IV colorectal cancer who can have resection of the asymptomatic colorectal primary tumour and expect substantial survival benefit over those never having resection.[103]

Grade B, Level IIb

B Resection of primary colon cancer in patients with incurable disease has a relatively high postoperative mortality and morbidity but is worthwhile where the tumour is not poorly differentiated and as long as hepatic metastases occupy less than 50% of liver volume.[104]

Grade B, Level IIb

GPP A segmental resection with primary bowel anastomosis, where technically feasible and safe, is preferable to a stoma.

GPP

4.8 Laparoscopic and laparoscopy-assisted resections

Laparoscopic and laparoscopy-assisted colonic resections is widely accepted for benign conditions and has been demonstrated in several series to be equally safe and effective as conventional open surgery by experienced surgeons.[105,106,107,108] However, this approach in the treatment of colorectal cancer is viewed with caution as no long term survival results are available from randomized prospective clinical trials.[109,110] Safety has been dampened by the increased incidence of port-site recurrence in many early case series but was not seen in later controlled trials.[111]

Compared to conventional open surgery, laparoscopic and laparoscopic-assisted resections can achieve similar extent of lymphovascular and tumour clearance. Less immune suppression from the stress response

during laparoscopy has been noted but the clinical benefits are not clear. Although case series have shown reduced post-operative pain with the laparoscopic approach, this has not necessarily been translated into a shorter length of stay.[112,113,114] Further results from randomized trials would provide more evidence on the survival benefits of this approach.

4.9 Obstructed Cancers

The presence of bowel obstruction has influence on the prognostic outcome. Examination of the data without considering tumor location disclosed that patients with bowel obstruction were at greater risk for treatment failure than those without obstruction. The effect of bowel obstruction was influenced by the location of the tumor. The occurrence of bowel obstruction in the right colon was associated with a significantly diminished disease-free survival, whereas obstruction in the left colon demonstrated no such effect. This phenomenon was independent of nodal status and tumor encirclement, the latter two factors proving to be of prognostic significance independent of tumor obstruction.[115,116,117]

In acutely obstructed colon from pathology in the left side, on-table irrigation compared to bowel decompression shows no difference in the rate of anastomotic complications. On-table irrigation tends to prolong operative time as more work needs to be performed. (See section 4.2.1.5 e). Segmental resection, with or without on-table irrigation, when compared with subtotal/total colectomy is not associated with increased operative mortality, anastomotic leak rates or intraabdominal sepsis.[118,119,120] Increased stool frequency is expected with subtotal/total colectomy but has the advantage of removing synchronous neoplasms in the proximal bowel.

B Segmental resection with intraoperative bowel decompression or irrigation and subtotal/total colectomy are alternatives for surgery of obstructed colonic cancers.

Grade B, Level III

B The use of intraluminal self-expanding metallic stents to decompress the acutely obstructed colon may defer surgery and provide effective palliation in very advanced disease.[121]

Grade B, Level IIb

Perforation,[122] stent migration, failure of deployment and obstruction are the main complications.[123,124,125]

There does not appear to be a difference in outcome between a staged surgical procedure and resection with a primary anastomosis for patients with obstructed colon cancers.[126,127] At present, the decision for either procedure is greatly influenced by the patient's co-morbid status.

A There is no advantage in a staged operation compared to primary resection for obstructed colonic cancers.[128]

Grade A, Level Ib

4.10 Perforated cancers

Perforated cancers are associated with significant mortality. Generalized colonic perforation is associated with disseminated disease[129] but resections with localized or intra-operative perforation may still be curative.[130]

B Inadvertent intraoperative perforation must be documented for more accurate survival data analysis. They should be considered as candidates for local radiotherapy and systemic chemotherapy. Primary anastomosis is not contraindicated in selected cases of colonic perforation.[131]

Grade B, Level III

4.11 Recurrent cancer

a. *Loco-regional recurrence*

Surgery is performed to palliate symptoms in disseminated intra-abdominal disease.

A Loco-regional recurrence if detected early is amenable to surgical resection with a possibility for improved survival.[132]

Grade A, Level Ia

b. *Distant recurrence*

Please refer to section on metastatic liver disease and palliative treatment. (see page 37)

c. Local and distant recurrence

C Resection of the local recurrence in the presence of metastatic disease is not contra-indicated but case selection is problematic.[129] Palliative resection may improve the quality of life in properly selected candidates.

Grade C, Level IV

4.12 Transanal local excision

Transanal local excision is a safe option for villous adenomas but remains controversial in the resection of ultrasound staged T1 (uT1) lesions.[133,134,135] The use of adjuvant treatment in conjunction with ultrasound staged T2 (uT2) lesion is also controversial. Local excision has the benefit of being less morbid than formal resections and also has the preservation of sphincter function in many instances. Other than the T-stage, recurrence after local excision is associated with poor histologic grade, presence of lymphovascular invasion and positive margins[136]. Preoperative staging is usually by digital examination and CT scan but currently should include endorectal ultrasonography. Effective salvage resections are possible in recurrence. There is a lack of randomized trials for the local treatment of uT1 and uT2 cancers. Case series report acceptable results especially when combined with adjuvant treatment.[137]

B Transanal excision of ultrasound staged T1 and ultrasound staged T2 rectal cancers together with adjuvant therapy may be an acceptable alternative in those not suitable for major resection surgery.

Grade B, Level IIa

4.13 Oophorectomy

A Bilateral oophorectomy is indicated in cancer metastasis.

Grade A, Level Ib

A There is no conclusive evidence in support of prophylactic oophorectomy if the ovaries are not macroscopically affected.[138,139]

Grade A, Level Ib

GPP HRT should be considered post-oophorectomy.

GPP

4.14 Surgical management of colorectal metastases to the liver

More than 50% of patients with curative resection of colorectal cancer will develop metastases in the course of the disease with up to 80% having disease in the liver.[140,141,142] Of these, up to half have disease confined to the liver only.[143]

4.14.1 Management of isolated synchronous liver metastases

A Synchronous liver metastases are those diagnosed within 6 months from diagnosis of the primary. The treatment of choice in this setting is resection of the metastases if there is no extrahepatic disease.[141,142]

Grade A, Level Ib

B The timing of resection of the liver metastases is controversial. There is no survival difference between synchronous versus delayed resection of the metastases.[144,145] A "test-of-time" approach by waiting 6 weeks to 3 months before resection of the liver metastases may select the patients with best outcome from surgery. The wait allows additional disease or extrahepatic disease to declare itself.

Grade B, Level III

C The role of chemotherapy in the setting of delayed resection is not proven but may be beneficial in allowing a measurable assessment of chemotherapy response as well as reducing the risk of tertiary metastases.[146]

Grade C, Level IV

4.14.2 Management of isolated metachronous liver metastases

Metachronous liver metastases are those that occur more than 6 months after diagnosis of the primary. The treatment of choice in this setting is

surgical resection with 5- and 10-year survivals of more than 45% and 25% respectively.[146,147,148]

B Surgical resection of isolated liver metastases offers the only potential for long-term survival and should be the treatment of choice.

Grade B, Level IIa

B Although a clear resection margin is important, the exact width of this margin has little effect on survival.[149,150]

Grade B, Level III

B The number of lesions is not a contraindication to resection provided a complete resection with clear margins can be obtained.[148]

Grade B, Level III

The use of adjuvant systemic chemotherapy and hepatic arterial infusion in combination may reduce recurrence but has conflicting effect on survival outcome. One randomized controlled trial shows reduction of recurrence only,[151] while another randomized controlled trial shows additional effect of prolonging survival.[152]

Neoadjuvant chemotherapy may significantly downstage inoperable liver metastases to an extent that curative resection is feasible in up to 13.5% to 38% of cases with survival results similar to that from resection at the first instance. (see section 9.3)

4.15 Surgical management of lung metastases

Unlike the liver which receives blood from the portal venous system, metastases to the lungs generally implies systemic dissemination of cancer. Occassionally isolated metastases to the lung may occur.

B Surgical treatment of resectable lung metastases may confer a survival benefit.[153]

Grade B, Level III

4.16 Postoperative notes documentation

GPP Proper documentation using standard prevailing nomenclature is essential in continuing patient care, recruitment for trials, audit and for the protection of the physician. Failure in adequate documentation has led to malpractice suits.[158]

GPP

5 Use of Tumour Markers

5.1 Carcinoembryonic antigen (CEA)

CEA is a serum glycoprotein which functions as an adhesion molecule promoting colorectal cancer cell aggregation. More than 90% of primary colorectal carcinomas produce CEA. An abnormal serum level is not specific for colorectal cancer as it can be elevated in smokers, alcoholic cirrhosis, cholangitis, bronchitis and other malignancies such as carcinomas of the breast, lung stomach, pancreas, cervix, bladder and kidney.

5.1.1 As a screening marker for colorectal cancer

Serum level of CEA may not be elevated at the time of diagnosis because CEA enters the portal circulation and is metabolized on first pass through the liver. An elevated level is associated with many non-malignant conditions including those listed above, 3% of the healthy population may have a serum CEA level above the normal range.

C Due to the low sensitivity and specificity, CEA cannot be recommended as a screening test for colorectal cancer. There are no data that CEA screening provides better survival, quality of life or lower costs in the population compared to no screening.[159]

Grade C, Level IV

5.1.2 As a marker of high risk factor

CEA may be ordered pre-operatively for patients with colorectal cancer to assist in staging and surgical treatment planning. Although an elevated pre-operative 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. Neither is there data to support the institution of systemic therapy for an elevated CEA on follow-up for presumed metastatic disease.

5.1.3 As a follow-up test after curative resection

CEA is generally regarded as the marker of choice for monitoring colorectal cancer. CEA is the most sensitive test for the detection of

recurrence[160] and has been found to be the most cost-effective approach to detecting potentially resectable metastases.[161,162]

Curative resection of recurrence is more often performed in patients who have routine CEA measurement.

A It is recommended that CEA levels be monitored every 2 to 3 months in patients with stage II or III disease for at least 2 years after diagnosis. The benefit of monitoring decreases after 2 years.

Grade A, Level Ia

5.1.4 As a marker of response to treatment

During chemotherapy for advanced colorectal cancer, CEA level may be used as a means of follow-up, with subsequent radiologic assessment to confirm the response indicated by the change in marker level. In addition, it can be used to aid the assessment of patients whose disease is not accurately measured by imaging studies.[163]

B Two sequential values above baseline are adequate to document progressive disease even in the absence of corroborating radiographs.[159]

Grade B, Level IIa

5.2 CA 19.9

GPP Present data are insufficient to support the use of CA 19.9 for screening, diagnosis, staging, surveillance, or monitoring treatment of patients with colorectal cancer.

GPP

6 Follow-up after Primary Surgery

Postoperative surveillance can be labour and cost intensive and is variable from country to country and from different institutions within the same country.[164,165] Earlier diagnosis of recurrence is believed to confer earlier appropriate treatment and better chance of disease remission.[166,167] Significant reduction in overall mortality of between 9-13% was found in the use of CT scans for extramural recurrence and frequent measurement of CEA levels.

Follow-up programme should comprise:

6.1 **GPP** History and physical examination 3-monthly for first 2 years, then 6-monthly for next 3 years.

GPP

6.2 CEA level

(See section 5.1.3)

6.3 Liver scan

GPP For patients whose pre-operative CEA level is normal, routine liver ultrasound scan or CT-scan may be appropriate for patients who are fit for surgery should they develop metastatic disease. Data is unavailable to determine the frequency of such investigations.

GPP

6.4 Chest X-ray

GPP Similarly, when pre-operative CEA level was normal, chest X-ray may be appropriate for patients who might be expected to benefit from surgery should they develop metastatic disease. Data is unavailable to determine the frequency of chest x-ray in this setting.

GPP

6.5 Colonoscopy

B The frequency of surveillance colonoscopy is not clear but has been recommended to between 3-5 yearly after an initial complete

colonoscopic examination (without synchronous polyps or cancers) either preoperatively or within 6 weeks after surgery.[166,167,168] Metachronous lesions and polyps are believed to occur less frequently than extraluminal recurrence. More frequent examination is suggested for certain high risk factors such as high grade dysplasia, multiplicity, flat rather than polypoid morphology and the size of greater than 1 cm in the resected polyp.

Grade B, Level IIb

7 Adjuvant Therapy for Colon Cancer

7.1 Any T with node positive (stage III)*

A 5FU based chemotherapy is recommended after surgery as it improves disease-free survival and overall survival for stage III colon cancer.

Postoperative chemotherapy with 5-fluorouracil/folinic acid (leucovorin) for 6 months is equivalent to 5-fluorouracil/levamisole for 12 months.[169,170,171,172,173]

Grade A, Level Ib

7.2 T3 or T4 and node negative (stage II)*

A Overall survival is not improved with postoperative chemotherapy. Adjuvant chemotherapy for stage II patients with colon cancer is not recommended.[174]

Grade A, Level Ia

Although features of perforation of the bowel wall, obstruction and elevated preoperative CEA may correlate with a poorer prognosis, adjuvant chemotherapy has not been demonstrated to improve survival in these patients.

* TNM staging system

8 Adjuvant Therapy for Rectal Cancer

8.1 T3, T4, node positive (stages II or III)*

Post-operative radiotherapy improves local control and when combined with chemotherapy improves survival.[175,176,177,178]

The data to support this are obtained from trials prior to the widespread adoption of total mesorectal excision as a surgical technique for rectal cancer.

A If total mesorectal excision is not performed, post-operative radiotherapy can be recommended for improved local control and also recommended for improved survival when combined with chemotherapy.

Grade A, Level Ib

A Infusional 5-fluorouracil concurrently administered with radiotherapy improves survival compared to bolus 5-fluorouracil.[179]

Grade A, Level Ib

* TNM staging system

8.2 Neoadjuvant therapy for rectal cancer

Operable disease

A Neoadjuvant, preoperative, short course radiotherapy improves local control and survival. Surgical complications may be increased, but not substantially.[180,181,182,183,184]

Grade A, Level Ia

B Neoadjuvant, preoperative, 5-fluorouracil based chemotherapy and radiotherapy in cases of low rectal cancer may improve the chance of sphincter preservation.[185,186,187]

Grade B, Level IIa

Inoperable/marginally operable

B Combined concurrent chemotherapy and radiotherapy can downstage inoperable and marginally operable cases making them suitable for resection.[188]

Grade B, Level IIa

9 Chemotherapy for Advanced Colorectal Cancer

9.1 Systemic chemotherapy

A Chemotherapy prolongs survival and improves quality of life for patients with metastatic colorectal cancers.[189,190] Even when there is no radiologically demonstrable shrinkage of tumour, stabilization of disease is often associated with prolongation of survival and decrease in tumour-related symptoms.

Grade A, Level Ia

B While studies have shown age-dependent toxicity associated with the use of cytotoxic agents,[191,192] advanced age is not a reason to withhold chemotherapy.[193]

Grade B, Level IIa

9.1.1 Cytotoxic agents

First-line chemotherapy

A 5-fluorouracil has been the mainstay for more than 4 decades. It is acceptable as standard chemotherapy, either as a single agent in an infusional schedule, or in combination with folinic acid.[193]

Grade A, Level Ia

Meta-analysis shows that biomodulation of 5-fluorouracil with folinic acid results in improved response rate and survival for patients with advanced colorectal cancer.[193]

A Compared to bolus injections, 5-fluorouracil given by infusional schedule improves the response rate and progression-free survival in patients with advanced colorectal cancer. In addition, there is also a lower haematologic toxicity.[194,195]

Grade A, Level Ia

New agents like irinotecan (CPT-11), oxaliplatin, capecitabine and raltitrexed (ZD 1694, Tomudex), have been introduced in the first-line treatment of advanced colorectal cancers.

Overall survival was also improved for patients receiving the 3-drug combination in the first-line setting.[196,197] Combinations of irinotecan with 5-fluoromacil plus folinic acid improve response rate, increase time to tumour progression and improve overall survival compared with 5-flourouracil plus folinic acid.

Combinations of irinotecan (CPT-11) with 5-fluorouracil plus folinic acid, and of oxaliplatin with 5-fluorouracil plus folinic acid have been tested in randomized trials. The results showed that the 3-drug combinations are superior to 5-fluorouracil plus folinic acid combination. There is improved response rate and a longer time to tumour progression.[198,199]

'Patient convenience' has been cited as a potential advantage of raltitrexed as it can be administered over 15 minutes on an outpatient basis. There will be a need to monitor patients more closely for toxicity and renal function when using this drug.

C Raltitrexed can be used when 5-fluorouracil is either not tolerated or inappropriate.[200]

Grade C, Level IV

Capecitabine, an oral cytotoxic drug, has activity similar to 5-fluorouracil plus folinic acid combinations. In one study, a blinded Independent Review Committee showed that patients treated with capecitabine had higher response rate compared with patients treated with bolus 5-fluorouracil plus folinic acid combinations.[201]

In another multicenter study using an identical chemotherapy protocol, patients treated with capecitabine had higher overall response.[202]

UFT, a combination of uracil plus tegafur, is another oral cytotoxic, usually administered with oral folinic acid. It has similar activity among patients with advanced colorectal cancers. In one study, the overall objective responses and median survival for the UFT plus folinic acid group were not different than in those treated with 5-fluorouracil plus folinic acid.[203] A similar study using slightly different schedule of bolus 5-fluorouracil and folinic acid, showed comparable responses. Median survival was better in the UFT treated group.[204] In both studies, UFT plus folinic acid was associated with significantly lower toxicities.

A Capecitabine or UFT plus folinic acid are acceptable as a first-line chemotherapy for advanced colorectal cancer.

Grade A, Level Ib

At the moment, there is no evidence to suggest that neither capecitabine nor UFT is superior to the other as first-line chemotherapy for advanced colorectal cancers.

9.1.2 Treatment of elderly patients with adjuvant chemotherapy

Elderly patients (more than 70 years of age) with Stage III colon cancer receive similar reductions in mortality odds with adjuvant 5-fluorouracil-based chemotherapy. Toxicities from treatment are similar to those experienced by younger patients.[205]

A Elderly patients with stage III colon cancer and without significant comorbidities should be offered adjuvant chemotherapy.

Grade A, Level Ia

Elderly patients with stage III rectal cancer experience similar benefits with combined 5-fluorouracil-based chemotherapy and radiotherapy, as do younger patients. It is unclear if stage II patients derive similar benefits with adjuvant treatment.[206]

B Elderly patients with stage III rectal cancer and without significant comorbidities should be offered adjuvant chemotherapy and radiotherapy.

Grade B, Level IIb

9.1.3 Second-line chemotherapy

Patients whose disease progress despite 5-fluorouracil and folinic acid combination as first-line chemotherapy, may respond to irinotecan, oxaliplatin, capecitabine, or infusional 5-fluorouracil.

A There is a survival advantage for patients with advanced colorectal cancer receiving irinotecan after failing first-line 5-fluorouracil and folinic acid chemotherapy.[198,199]

Grade A, Level Ib

9.1.4 Third-line Chemotherapy

There is no data to show that patients will benefit from third-line chemotherapy after failure of 2 different combinations.

9.1.5 Timing of Palliative Chemotherapy

In a randomized trial the Nordic Gastrointestinal Tumour Adjuvant Therapy Group showed that early treatment of asymptomatic metastatic colorectal cancer significantly prolongs the survival of patients. The median overall survival of the upfront chemotherapy group was 14 months, compared to 9 months when treatment was initiated only after appearance of symptoms.[207]

It should be noted that the chemotherapy regimens used in these studies are not considered optimum by today's standard.

There is insufficient data to suggest that early treatment of asymptomatic advanced disease with chemotherapy improves the outcome. The decision should be made after careful discussion between patients and primary physicians.

9.2 Regional Chemotherapy

Liver metastases derive their blood supply predominantly from the hepatic artery whereas normal hepatocytes derive theirs preferentially from the portal vein. Selective delivery of drug via hepatic artery optimizes tumour drug concentration, at the same time avoids excessive systemic exposure and toxicity. Floxuridine (FUDR) is the drug of choice for regional chemotherapy because of its high extraction ratio during the first hepatic pass (94-99%).

Hepatic artery infusion (HAI) chemotherapy has been most extensively investigated in untreated patients with liver-only metastases. Several meta-analyses[208,209] comparing hepatic intra-arterial FUDR with systemic chemotherapy have failed to show any clear survival difference despite a definite improvement in response rates. The failure to demonstrate a clear survival advantage may be due to a number of methodological limitations associated with these studies.

In a randomised 3-arm trial, patients were assigned to either systemic intravenous 5-fluorouracil plus folinic acid, HAI 5-fluorouracil plus folinic acid, or HAI FUDR. HAI chemotherapy produced a higher response rate compared to systemic therapy. Median time to disease progression and median survival were not significantly different among the three arms. Median survival of patients who were treated with HAI 5-fluorouracil plus folinic acid appeared to be better than the group treated with HAI FUDR. Patients treated with conventional systemic chemotherapy without HAI had a median survival intermediate between the two.[210] Although regional FUDR results in high local response rates, it may not provide adequate systemic control.

A HAI fluoropyrimidine-based chemotherapy cannot be recommended.[211]

Grade A, Level Ib

9.3 Neoadjuvant Chemotherapy

Neoadjuvant chemotherapy refers to the use of cytotoxic chemotherapy to reduce the tumour size prior to curative resection. It has been shown to improve resectability. Neoadjuvant chemotherapy allows the determination of tumour responsiveness to systemic chemotherapy for planning of adjuvant therapy after liver resection. It also allows observation time for as-yet undetected sites of metastases to declare themselves.

In addition, neoadjuvant chemotherapy has the theoretical advantage of eradicating systemic micrometastases.

Most of the neoadjuvant experiences reported have used oxaliplatin and 5-fluorouracil plus folinic acid combination. After several cycles of chemotherapy using chronomodulated schedule, 16% of patients who were diagnosed as having unresectable metastases underwent curative resection. Five-year survival after resection was 40%.[212]

In another retrospective analysis, patients with colorectal liver metastases, which were initially deemed unresectable, received the same 3-drug combination. The great majority of the patients (83%) received their treatment in a chronomodulated fashion. Half of the patients underwent surgery with the intent to cure, and 38% had all their disease

completely resected. The estimated five-year survival rate in the resected group was 58%.[213]

In a prospective follow-up study of patients with unresectable colorectal liver metastases treated with chronomodulated oxaliplatin, 5-fluorouracil plus folinic acid chemotherapy, 13.5% were rendered resectable on reevaluation. The overall five-year survival was 35% from the time of liver resection. For patients initially deemed unresectable because of large tumour size, the 5-year survival was 60% after resection.[214]

These are non-randomized studies. There is also no clear definition of unresectability and no quality control of hepatic resection. It would be ethically unacceptable to conduct a randomised trial comparing surgery versus no surgery after tumour reduction following systemic chemotherapy.[215]

B The use of neoadjuvant chemotherapy appears to be beneficial in a highly selected group of patients with potentially resectable hepatic metastases.

Grade B, Level IIb

B The concept of preoperative HAI therapy is appealing because of the high tumour response rate associated with intra-arterial delivery of drugs. Only a very small number of patients have been studied in retrospective series. There is no clear advantage in the use of HAI chemotherapy. Moreover, HAI therapy is associated with parenchymal and hemodynamic changes in the liver, rendering hepatectomy technically difficult and increases postoperative complications. HAI cannot be recommended as a neoadjuvant chemotherapy prior to planned resection of hepatic metastases.

Grade B, Level IIb

9.4 Adjuvant therapy after resection of metastases

Recurrence following resection of hepatic metastases from colorectal cancer is high. More than half of recurrences occur in the liver. Prospective randomized trials in patients with hepatic metastases have demonstrated significantly higher response rates for hepatic artery infusional (HAI) chemotherapy when compared to no treatment.

Although this did not necessarily confer a survival benefit, an earlier prospective trial randomly assigned patients after resection of hepatic metastases to either systemic chemotherapy using 5-fluorouracil plus folinic acid alone, or HAI chemotherapy. No significant difference was noted between both arms.

A In view of the increased toxicity, HAI chemotherapy cannot be recommended as a standard after resection of hepatic metastases.[216]

Grade A, Level Ib

There are no studies comparing adjuvant systemic chemotherapy with no therapy after resection of liver metastases.

B At this time, adjuvant systemic chemotherapy cannot be considered as a standard treatment after resection of liver metastases.

Grade B, Level IIb

10 Prevention of Colorectal Cancer

10.1 Chemoprevention

Cancer chemoprevention can be defined as pharmacologic intervention with specific nutrients or other chemicals to suppress or reverse carcinogenesis and to prevent the development of invasive cancer.

Carcinogenesis is a chronic, multistep process characterised by the accumulation of specific genetic and phenotypic alterations that can evolve over a 10-20 year period from the first initiating event. The premise of human chemoprevention is that one can intervene at many steps in the carcinogenic process and over many years.

It was also found that cancers at many epithelial sites have a wide surface area of carcinogenic tissue change that can be detected at the gross (adenomatous polyps in colon), microscopic (metaplasia and dysplasia) and molecular level (gene loss or amplification). Multifocal, genetically distinct premalignant lesions can progress over a broad tissue region.

Chemoprevention seeks to intervene within the multistep carcinogenic process and throughout a wide field.

10.2 Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)

The common pharmacologic action of NSAIDs is to inhibit cyclooxygenase (COX), the initial and rate-limiting enzymatic step in the metabolism of arachidonic acid into a complex group of signalling proteins known as prostaglandins. Prostaglandins modulate many functions within cells and across tissues. There is evidence to show that certain tumours may overproduce specific prostaglandins and thereby promote their own growth. The use of NSAIDs has been shown in experimental studies to suppress tumour development in animal models and cell cultures.

10.2.1 Aspirin

Several epidemiological studies have reported a reduction in colon cancer incidence associated with the use of aspirin. Among a group of

over 600,000 adults enrolled in an American Cancer Society study, mortality in regular users of aspirin was about 40% lower for cancers of the colon and rectum.[1-2]

In a study of over 11,000 men and women in Sweden with rheumatoid arthritis (and presumably ingesting NSAIDs), colon cancer incidence was 37% lower and rectal cancer was 28% lower than predicted from cancer registry data.[3] In a report from the Health Professionals Follow-up Study of 47,000 males, regular use of aspirin (at least 2 times per week) was associated with a 30% overall reduction in colorectal cancer including a 50% reduction in advanced cases.[217]

In the physician's Health Study a subsequent analysis over a 12-year period, analyses indicated that there was no association between the use of aspirin and the incidence of colorectal cancer.[218] The low dose of aspirin and the short treatment period may account for the negative findings.[6]

Two randomised controlled trials have demonstrated a chemopreventive effect on adenomas in the large bowel.[219]

Side effects of treatment included upper gastrointestinal haemorrhage and haemorrhagic stroke.

10.2.2 Sulindac

Several studies have demonstrated the effectiveness of sulindac in reducing the size and number of adenomas in familial polyposis.[220,221]

10.2.3 Celecoxib

In a randomized, double-blind, placebo-controlled study of patients with familial adenomatous polyposis, patients receiving 400 mg of celecoxib twice a day had a 28.0% reduction in the mean number of colorectal adenomas and a reduction in the polyp burden as compared with a placebo group. A group of patients receive 100 mg of celecoxib twice daily has a non significant response. The incidence of adverse events was similar among the groups.[222]

10.2.4 Piroxicam

The NSAID piroxicam, at a dose of 20 mg/day, reduced mean rectal prostaglandin concentration by 50% in individuals with a history of adenomas.[223]

The potential for the use of NSAIDs as a primary prevention measure is encouraging. Several unresolved issues mitigate against making general recommendations for their use. These include a paucity of knowledge about the proper dose and duration for these agents, and concern about whether the potential preventive benefits such as a reduction in the frequency or intensity of screening or surveillance could counterbalance such long-term risks as gastrointestinal ulceration and hemorrhagic stroke for the average risk individual.[224]

GPP While NSAIDS appear to be potential chemopreventive agents, routine use for primary prevention of colorectal cancer is not recommended presently.

GPP

10.3 Macronutrients

10.3.1 Energy intake

B Case-control studies show a positive correlation between energy intake and colorectal cancer risk.[225] Although fat intake may be a confounding factor in this relationship, it has been concluded that replacing fat with other energy sources is unlikely to reduce colorectal cancer risk.[226] There is sufficient evidence to recommend reducing energy intake to prevent colorectal cancer.

Grade B, Level III

10.3.2 Fat and Meat

Two randomised controlled trials have studied a reduced fat intake on adenoma recurrence in people with adenomas removed. The Toronto Polyp Study returned a negative result[227] whereas the Australian Polyp Prevention Project demonstrated a marginally significant result for low fat diets (<25% calories as fat).[228] A confounding factor in the relationship between dietary fact colorectal cancer is the possible beneficial effect of omega-3 fatty acids found in fish oil.[229] There also

appears to be no particular benefit regarding cancer prevention from reducing fat intake from vegetable sources.[230]

Similarly, it has been difficult to prospectively show an association of meat intake with the development of colorectal cancer.[231]

10.3.3 Fibre

The data on dietary fibre as protection against colorectal cancer has been conflicting. While eight of ten case-control or cohort studies show a reduction in risk of adenomas with higher communication of fibre,[232] prospective and intervention studies have not shown a protective effect against adenoma formation or colorectal cancer.[233,234] However recent observational studies have shown a reduction of both colorectal cancer[235] and adenoma[236] in people had high dietary fibre intakes.

B It is reasonable to recommend a high fibre intake as a possible measure to prevent colorectal cancer.

Grade B, Level III

10.4 Micronutrients

10.4.1 Calcium

Adenoma prevention trials suggest that calcium supplementation may reduce the risk of colorectal neoplasia.[237,238] Although contradictory data on the effect of calcium on the development of colorectal cancer is present,[239] recent studies show a modest reduction in risk of colorectal cancer in those who supplemented with calcium.[240,241]

B Calcium supplementation on current evidence may be beneficial in the prevention of colorectal cancer.

Grade B, Level III

10.5 Other Preventive Measure against Colorectal Cancer

10.5.1 Physical activity

There is strong evidence that physical activity protects against colon cancer. Multiple study designs have shown protection[242,243] against colon cancer. The data for rectal cancer is less consistent.[225,242,244]

B Physical activity is recommended as a preventive measure against colorectal cancer.

Grade B, Level IIa

10.5.2 Smoking

There is a 50% increased risk of colorectal cancer among smokers. The evidence is stronger for rectal cancer than colon cancer.[245]

B Stop smoking to avoid development of colorectal cancer.

Grade B, Level IIa

11 Clinical audit parameters

The following clinical audit parameters, based on recommendations in these guidelines are proposed:

1. Percentage of patients at average risk undergoing faecal occult blood testing annually from age 50 years. (see page 12)

2. Percentage of patients with single dose of appropriate perioperative antibiotics administered. (see page 15)

3. Percentage of patients receiving prophylaxis for DVT prior to any surgery for colorectal cancer. (see page 16)

4. Percentage of patients undergoing stoma creation surgery who receive pre-operative counselling and advice on stoma siting. (see page 16)

5. Percentage of patients with Stage II or III colorectal cancer with CEA levels being monitored every 2-3 months for a period of no less than 2 years after diagnosis. (see page 36)

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to "judge" your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose the right answer(s). There may be more than one answer for some questions.

1. A 60 year old woman was found on routine screening to have iron deficiency anaemia. Which one of the following is the most appropriate management of the patient.

   (a) prescribe an iron supplement
   (b) arrange for the patient to undergo colonoscopy
   (c) commence hormone replacement therapy
   (d) arrange for a bone marrow aspirate
   (e) prescribe Vitamin C

2. Which one of the following individuals is at highest risk of colorectal cancer:

   (a) a 40 year old man whose mother developed colon cancer at the age of 70 years
   (b) a 50 year old woman whose father developed colon cancer at the age of 45 years
   (c) a 40 year old man who was diagnosed to have ulcerative colitis two years previously
   (d) a 60 year old woman with a paternal aunt who developed rectal cancer at the age of 55 years
   (e) a 20 year old man whose uncle had a rectal cancer at the age of 60 years.

3. Which one of the following is indicated in an individual thought to be at high risk of colorectal cancer:

   (a) faecal occult blood testing
   (b) rigid sigmoidoscopy
   (c) MRI of the abdomen
   (d) colonoscopy
   (e) endoluminal ultrasound

4. Part of the peri-operative management of a patient with low rectal cancer would include

   (a) prophylactic antibiotics
   (b) albumin infusion
   (c) prophylaxis against deep vein thrombosis
   (d) stoma counselling
   (e) cardiac pacing

5. The "gold standard" surgical operation for low rectal cancer is:

   (a) Hartmann's procedure
   (b) anterior resection
   (c) total mesorectal excision
   (d) transverse colostomy
   (e) colonic J-pouch

6. In patients with Stage III colon cancer,

   (a) a referral should be made to an oncologist.
   (b) adjuvant radiotherapy is indicated.
   (c) PET scans can be used for routine follow-up.
   (d) CEA may be useful in monitoring the patients' progress.

7. In locally advanced rectal cancer,

   (a) a defunctioning ileostomy is the best option for treatment.
   (b) referral to a palliative care physician is appropriate.
   (c) 3rd line chemotherapy is indicated.
   (d) radiofrequency ablation is used.
   (e) combined concurrent chemotherapy and radiotherapy may be useful for downstaging the tumour.

8. The following may be useful in the prevention of colorectal cancer:

   (a) regular physical exercise
   (b) cessation of smoking
   (c) supplementation with calcium
   (d) regular alcohol consumption
   (e) moderating caloric intake

Answers

1. B
2. B
3. D
4. A, C, D
5. C
6. A, D
7. E
8. A, B, C, E

Workgroup

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MOH CLINICAL PRACTICE GUIDELINES 2/2004
Colorectal Cancer

Ministry of Health

NMRC National Medical Research Council

Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

Diagnosis of Colorectal Cancer in a Patient with Symptoms

B In the presence of symptoms and signs suggestive of colorectal cancer or in the presence of unexplained iron deficiency anaemia, proctoscopy should be performed to identify an anorectal cause for symptoms. In the absence of an obvious cause, colonoscopy should be performed and is the investigation of choice. (pg 10)

Grade B, Level III

B Double contrast barium enema together with sigmoidoscopy is an alternative to colonoscopy in investigating patients with colorectal cancer. Barium enema should be performed if colonoscopy is incomplete. (pg 10)

Grade B, Level III

B Colonoscopy should be performed for persistent symptoms despite initial treatment for a presumptive diagnosis of a benign condition. (pg 10)

Grade B, Level III

Risk Factors for Colorectal Cancer

A Asymptomatic individuals above the age of 50 years should undergo screening for colorectal cancer. (pg 11)

Grade A, Level Ib

A A post-polypectomy surveillance programme is recommended for patients with a personal history of colorectal adenoma. (pg 11)

Grade A, Level Ia

A Asymptomatic individuals above the age of 50 years should undergo screening for colorectal cancer. This would include asymptomatic individuals with a family history limited to non-first degree relatives. The screening options would be faecal occult blood testing annually. (pg 12)

Grade A, Level Ia

B It is recommended that people at high risk of colorectal cancer be referred for colonoscopy at three-yearly intervals from age 45, or 10 years younger than the age of earliest diagnosis of colorectal cancer in the family, whichever is the younger age. (pg 12)

Grade B, Level IIb

B The first step in the management of familial adenomatous polyposis (FAP) is the identification of the affected patient and his kindred. Detailed family history of individuals having colorectal cancer or polyps should be obtained. Genetic testing if available may be informative. (pg 13)

Grade B, Level IIb

B Screening of FAP kindred begins at the age of puberty with flexible sigmoidoscopy. Genetic testing should be considered and if the individual carries the mutation, these patients should be followed-up closely from puberty with possible proctocolectomy or total colectomy. (pg 13)

Grade B, Level IIb

B Colonoscopy rather than flexible sigmoidoscopy is recommended in kindred with a history of HNPCC as they are predisposed to right-sided colon cancer. (pg 14)

Grade B, Level IIb

B Surveillance colonoscopy with systematic biopsies should be considered for patients with extensive, longstanding ulcerative colitis. (pg 14)

Grade B, Level IIa

Surgery for Colorectal Cancer

A A single dose of appropriate antibiotics administered perioperatively is as effective as long term post-operative use in the prophylaxis against wound infection following colorectal cancer surgery. Inappropriate postoperative use of antibiotics is associated with increased costs. (pg 15)

Grade A, Level Ib

A Randomized trials both locally and overseas have shown reduction in the risk of deep venous thrombosis with heparin prophylaxis. (pg 16)

Grade A, Level Ib

B Optimal care of patients undergoing stoma creation surgery would include pre-operative counselling and stoma siting. (pg 16)

Grade B, Level III

B The length of bowel resected for colon cancer will be dictated by the removal of the arterial supply of the colon which parallels the lymphatic drainage. At least 5cm of normal bowel on either side of the tumour appears to be a minimum length to remove the paracolic lymph nodes and to minimize anastomotic recurrences. (pg 17)

Grade B, Level III

C Patients with multiple (i.e. two or more) colon cancers or those with hereditary nonpolyposis colorectal cancer should be considered for a total abdominal colectomy with ileorectal anastomosis. (pg 18)

Grade C, Level IV

C Patients with ulcerative colitis who develop a colorectal cancer should have a panproctocolectomy with or without restoration. (pg 18)

Grade C, Level IV

B The ideal bowel margin is 2 cm or more distally and 5 cm or more proximally, measured in the fresh, anatomically restored ex vivo condition from the transected full-thickness edge and does not include the tissue donuts from the endoluminal stapler. The minimal acceptable distal margin for tumours of the lower rectum (<5 cm from the anal verge) where sphincter preservation is an issue is 1cm. A 1cm margin is not advised in cases of large, bulky tumours, or poorly differentiated tumours with lymphovascular or perineural invasion. (pg 22)

Grade B, Level III

B Total mesorectal excision (TME) is not required for tumours located in the upper rectum (10-15 cm from the anal verge), which can be resected including 5 cm of distal mesorectum. (pg 23)

Grade B, Level III

B 5-year survival in excess of 50-60% can be obtained by pelvic exenteration for selected patients with locally advanced rectal cancer operated with curative intent. The operative mortality should be less than 10% but morbidity of 25-50% can be expected. (pg 25)

Grade B, Level III

B Distal rectal washout (after distal occlusion) and may have a benefit in reducing anastomotic recurrence in rectal cancer surgery. (pg 26)

Grade B, Level III

B En bloc resection of adjacent organs locally invaded by colorectal cancers can achieve survival rates similar to those of tumours that do not invade an adjacent organ. To achieve this, the tumour must not be transected at the site of adherence, and negative resection margins are required. (pg 26)

Grade B, Level III

B Metastatic tumor burden limited to one site and less extensive liver involvement select out a group of patients with stage IV colorectal cancer who can have resection of the asymptomatic colorectal primary tumour and expect substantial survival benefit over those never having resection. (pg 28)

Grade B, Level IIb

B Transanal excision of ultrasound staged T1 and ultrasound staged T2 rectal cancers together with adjuvant therapy may be an acceptable alternative in those not suitable for major resection surgery. (pg 31)

Grade B, Level IIa

A Synchronous liver metastases are those diagnosed within 6 months from diagnosis of the primary. The treatment of choice in this setting is resection of the metastases if there is no extrahepatic disease. (pg 32)

Grade A, Level Ib

Use of Tumour Markers

C Due to the low sensitivity and specificity, CEA cannot be recommended as a screening test for colorectal cancer. There are no data that CEA screening provides better survival, quality of life or lower costs in the population compared to no screening. (pg 35)

Grade C, Level IV

A It is recommended that CEA levels be monitored every 2 to 3 months in patients with stage II or III disease for at least 2 years after diagnosis. The benefit of monitoring decreases after 2 years. (pg 36)

Grade A, Level Ia

Follow-up after Primary Surgery

B The frequency of surveillance colonoscopy is not clear but has been recommended to between 3-5 yearly after an initial complete colonoscopic examination (without synchronous polyps or cancers) either preoperatively or within 6 weeks after surgery. Metachronous lesions and polyps are believed to occur less frequently than extraluminal recurrence. More frequent examination is suggested for certain high risk factors such as high grade dysplasia, multiplicity, flat rather than polypoid morphology and the size of greater than 1 cm in the resected polyp. (pg 37)

Grade B, Level IIb

Adjuvant Therapy for Colon Cancer

A 5FU based chemotherapy is recommended after surgery as it improves disease-free survival and overall survival for stage III* colon cancer.

Postoperative chemotherapy with 5-fluorouracil/folinic acid (leucovorin) for 6 months is equivalent to 5-fluorouracil/levamisole for 12 months. (pg 39)

* TNM staging system

Grade A, Level Ib

Adjuvant Therapy for Rectal Cancer

A If total mesorectal excision is not performed, post-operative radiotherapy can be recommended for improved local control and when combined with chemotherapy for improved survival. (pg 40)

Grade A, Level Ib

A Neoadjuvant, preoperative, short course radiotherapy improves local control and survival. Surgical complications may be increased, but not substantially. (pg 40)

Grade A, Level 1a

Chemotherapy for Advanced Colorectal Cancer

A Chemotherapy prolongs survival and improves quality of life for patients with metastatic colorectal cancers. Even when there is no radiologically demonstrable shrinkage of tumour, stabilization of disease is often associated with prolongation of survival and decrease in tumour-related symptoms. (pg 42)

Grade A, Level Ia

B While studies have shown age-dependent toxicity associated with the use of cytotoxic agents, advanced age is not a reason to withhold chemotherapy. (pg 42)

Grade B, Level IIa

C Raltitrexed can be used when 5-fluorouracil is either not tolerated or inappropriate. (pg 43)

Grade C, Level IV

A Capecitabine or UFT plus folinic acid are acceptable as a first-line chemotherapy for advanced colorectal cancer. (pg 44)

Grade A, Level Ib

Prevention of Colorectal Cancer

B Case-control studies show a positive correlation between energy intake and colorectal cancer risk. Although fat intake may be a confounding factor in this relationship, it has been concluded that replacing fat with other energy

sources is unlikely to reduce colorectal cancer risk. There is sufficient evidence to recommend reducing energy intake to prevent colorectal cancer. (pg 51)

Grade B, Level III

B It is reasonable to recommend a high fibre intake as a possible measure to prevent colorectal cancer. (pg 52)

Grade B, Level III

B Calcium supplementation on current evidence may be beneficial in the prevention of colorectal cancer. (pg 52)

Grade B, Level III

B Physical activity is recommended as a preventive measure against colorectal cancer. (pg 53)

Grade B, Level IIa

B Stop smoking to avoid development of colorectal cancer. (pg 53)

Grade B, Level IIa