

Effective

Health Care

Bulletin on the effectiveness
of health service interventions
for decision makers

This bulletin summarises
the research evidence
that informed the update
of the guidance
'Improving Outcomes in
Colorectal Cancers'



The Management of Colorectal Cancers

- Colorectal (bowel) cancer is the second most common cause of cancer death in England and Wales. Early detection and good management result in improved survival rates.
- Flexible sigmoidoscopy is the most appropriate initial investigation for the majority of patients with left sided colon symptoms.
- There is a clear correlation between colonoscopy completion rates and the number and frequency of examinations performed.
- Nurses and GPs with appropriate training can perform endoscopy safely and accurately.
- Higher patient volumes and greater specialisation among surgeons are associated with better outcomes.
- Total mesorectal excision (TME) for patients with rectal cancer – is associated with reduced local recurrence and improved long term survival.
- Increasing the number of lymph nodes in a surgical specimen improves the accuracy of staging at histopathology.
- Colorectal stents are effective for temporary relief of acute intestinal obstruction, so avoiding emergency surgery. Expanding metal stents can provide good, and cost-effective, palliation.
- The use of chemoradiotherapy in the treatment of anal cancer has been shown to provide significant improvements in colostomy-free and disease-free survival.
- Follow-up is efficient and cost-effective if patients at higher risk of recurrence are followed up more intensively than those at lower risk.

A. Background

A.1 Incidence and mortality

Over 30,000 new cases of colorectal (bowel) cancer are diagnosed in England and Wales each year; of these, about half will have colorectal cancer registered as the underlying cause of death. The annual incidence rate per 100,000 (all ages) is 58.1 for men and 52.6 for women.¹

Incidence is age related. Between the ages of 45 and 55 the incidence is about 25 per 100,000, and among those aged 75 and above the rate is over 300 per 100,000 each year.²

A.2 People at raised risk

Two genetic syndromes cause colorectal cancer: Familial Adenomatous Polyposis (FAP) and Hereditary Nonpolyposis Colorectal Cancer (HNPCC), but clusters of cases also occur in families without either of these.

In addition to these rare genetic syndromes, close relatives of people diagnosed with colorectal cancer are at increased risk. The risk is greater the larger the number of relatives affected, the closer the family relationship, and the younger they are at the time of diagnosis (Fig. 1).^{3,4}

Around 5% of patients with colorectal cancer have identified genetic syndromes known to confer

very high risk. Colitis is also associated with increased risk of colorectal cancer and the risk rises with the duration of the condition.⁵ However, around 75% of patients have neither a clear family history nor any condition known to predispose them to developing colorectal cancer.

A.3 Early detection

There is evidence that the earlier colorectal cancer can be detected, the better the outcome for the patient. However, early detection is difficult as the most common presenting symptoms of colorectal cancer – change in bowel habit, rectal bleeding, abdominal pain and anaemia – are non-specific, occur relatively frequently in the population, and have a wide variety of causes.

In 2003 the government committed themselves to providing a colorectal cancer screening programme which would aim to identify and treat people with colorectal cancer at as early a stage as possible. Increased use of endoscopy in a screening programme would allow polyps, which can develop into cancer, to be removed from the lower gastrointestinal (GI) tract.⁶

A.4 Staging

Prognosis for patients depends on the spread of the cancer at diagnosis.

Historically, spread has been given in terms of modified Dukes' stage but this is being superseded by the more precise Tumour, Node, Metastases (TNM) classification system (Table 1).

Approximately 55% of patients in England and Wales present with advanced colorectal cancer (Stage III or IV; Dukes C or D),⁸ so even where surgical removal of the primary tumour is an option, accurate staging is essential for appropriate choice of treatment.

Survival rates vary between English health authorities, but the average is now around 45% at five years after diagnosis, and most of those who live this long are cured.¹

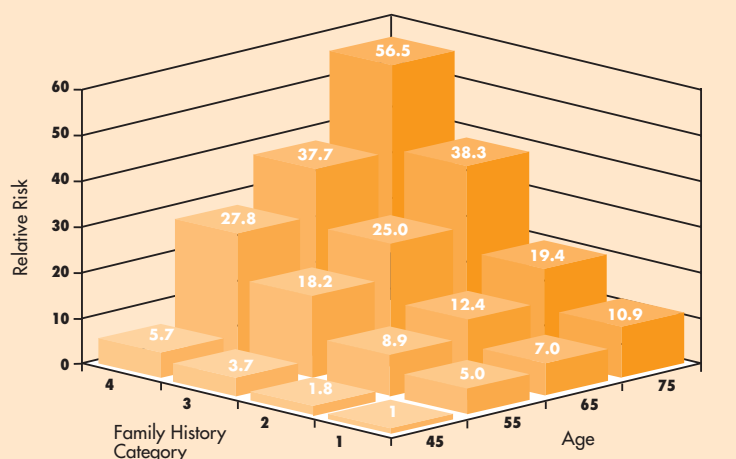
A.5 Guidance on commissioning cancer services

In 1997 the DoH's Clinical Outcomes Group (COG) produced service guidance for colorectal cancer.^{9,10} An update of this guidance has now been published by the National Institute for Clinical Excellence (NICE).^{11,12} The process of updating the original guidance involved identifying new issues to be addressed and also revising existing recommendations where new evidence had become available to inform the guidance. Systematic reviews of the research evidence in these areas were undertaken by the Centre for Reviews and Dissemination (CRD). A summary of these reviews along with brief details of the methodology used is given in *Improving Outcomes in Colorectal Cancers – Research Evidence for the Manual Update*.¹² This bulletin summarises the research evidence that informed the update of the guidance. Where the original guidance is still valid, this is referenced accordingly.

In addition to covering cancers of the colon and rectum, the update includes a section on anal cancer that was not covered in the original guidance.

B. Patient-centred care

Improving Supportive and Palliative Care for Adults with Cancer guidance



Family History Category

1. No family history
2. One affected first-degree relative, over 45 at diagnosis
3. One affected first-degree relative, under 45 at diagnosis
4. Two affected first-degree relatives

Fig.1 Risk of colorectal cancer by age and family history (relative to risk in 45 year olds with no family history)

has recently been published by NICE.¹³ This guidance provides recommendations on supportive and palliative care for cancer patients generally. It is intended to complement colorectal cancer specific guidance.

B.1 Information

Clear, accurate, timely and accessible information at each stage of the patient journey is important, for people at high risk, patients with colorectal cancer, and their carers.

A national survey of patients' experience, which included 15,891 patients with colorectal cancer, showed that although almost all patients were told of their diagnosis in person by a hospital doctor, less than a third were then given written information.¹⁴ While most understood the diagnosis, significant numbers did not understand the purpose of tests or understand the explanations about treatments or their possible side effects. There was wide variability between Trusts in whether patients' felt that they were treated with respect and dignity.

The Commission for Health Improvement (CHI)/Audit Commission investigation of cancer services in 2000/2001 reported that 28% of Trusts visited did not have a clinical nurse specialist for colorectal cancer and that 40% of clinical nurse specialists felt that they were not able to give sufficient time to patients with colorectal cancer.¹⁵

C. Access to appropriate services

C.1 Urgent referrals and the two-week guidelines

NHS referral guidance for colorectal cancer was introduced in July 2000, requiring patients who were suspected by their GP of having cancer to be seen by a specialist in secondary care within two weeks of their being referred.¹⁶ The evidence examining the two-week wait criteria is not extensive, but wide variations exist between services provided.¹⁷⁻²⁰

The CHI/Audit Commission report found that 18% of patients found to

Table 1 TNM and Dukes' Classifications.⁷

TNM Classification (American Joint Commission on Cancer)			Dukes' Classification	
Stages	T	N	Stages	
Stage 0	Tis	N0	M0	
Stage I	T1	N0	M0	A
	T2	N0	M0	B1
Stage II	T3	N0	M0	B2
	T4	N0	M0	B2
Stage III	T1, T2	N1 or N2	M0	C1
	T3, T4	N1 or N2	M0	C2
Stage IV	Any T	Any N	M1	D

have colorectal cancer were referred as 'not urgent', when adherence to national guidelines should have led to urgent referral.¹⁵ This study also found that at least half of those referred as urgent cases did not fit the criteria.

Between 1.7% and 14% of patients referred through fast-track services described in the evidence review were found to have cancer. It is not clear whether these clinics accepted referrals under all the criteria in the two-week guidelines; some hospitals have a different referral pathway for patients with anaemia.¹⁸⁻³⁴

Little information is available on patients referred by other routes, but there is some evidence that waiting times for patients referred as non-urgent cases may have increased after the introduction of the two-week wait services.¹⁸ However, in one study the establishment of a service to deal with patients referred under the two-week guidelines has meant that all patients – including those who are not referred as urgent – are now being seen more quickly.³⁵

C.2 Delays in diagnosis

There is evidence of delays between the onset of symptoms of colorectal cancer and diagnosis. This is due to patient delay in reporting symptoms and to inadequate investigation of symptoms, misdiagnosis, and false negative results of diagnostic tests.¹⁰

There is no clear relationship between length of delay and stage of cancer or outcome, but the situation is confounded by the fact that more advanced tumours (for which the outcome of treatment is poor) produce more obvious and alarming symptoms, so tend to be investigated relatively quickly.⁹

Delays associated with inadequate assessment of iron-deficiency anaemia are an issue because anaemia may be the only symptom of colon cancer. It appears that the majority of patients with anaemia of unknown cause are not referred for the relevant investigations.³⁶

C.3 Open-access and one-stop lower GI endoscopy services

The service available to patients in the UK is variable, with a wide range of clinic models and diagnostic algorithms in use.^{17-34,37-39}

Most open-access clinics for patients with bowel symptoms offer flexible sigmoidoscopy. The yield of cancers and polyps detected varies widely between clinics.^{17-34,37-39} Establishment of these services produced other benefits: one report noted that the waiting time for routine outpatient clinics fell from 16 weeks to eight,³⁵ whilst another noted improvements in the stage of cancers diagnosed.²⁴

Survey evidence suggests that managers of secondary care units believe they have limited room to restructure current services, a major constraint being the availability of appropriately trained staff.⁴⁰ Nurse endoscopy (predominantly flexible sigmoidoscopy) is not uncommon and levels of satisfaction among patients using nurse-led endoscopy clinics are consistently high.^{31-33,41} Primary care may have a role to play in expanding provision, but there are few GP endoscopists.⁴² Where accuracy of diagnosis is reported, GPs and nurses who have received appropriate training perform as well as surgeons and gastroenterologists.⁴³⁻⁵¹ Further information about achieving competency in endoscopy is given in Section E. Diagnosis.

D. Multi-disciplinary teams

There is general acceptance of the cancer guidance recommendation of management by multi-disciplinary teams (MDTs).

The following reforms have emerged as helpful:⁵²

- Appoint a co-ordinator to organise MDT meetings.
- Time meetings to allow all members to attend.
- Streamline referral systems.
- Develop a clear and efficient structure for the meeting.

Better organisation of meetings leads to more efficient use of time and allows more patients to be discussed. It also results in more patients being managed in accordance with guidelines.⁵³

D.1 Surgical specialisation and patient throughput

Six systematic reviews⁵⁴⁻⁵⁹ and a number of more recent primary studies were consistent in showing evidence that for rectal cancer at least, higher patient volumes and greater specialisation among surgeons were associated with much better outcomes; lower surgical complication rates,⁶⁰⁻⁶² decreased local recurrence,⁶³⁻⁶⁹ lower colostomy rates,^{70,71} and improved survival.^{53,61-65,67,68,70-78}

There is less evidence for colon cancer. Two studies found that increased volumes had no or little effect on mortality.^{76,79}

A single study of liver resection for metastatic colorectal cancer found a significant association between higher patient throughput and short-term survival.⁵³

E. Diagnosis

E.1 Diagnostic methods

In cases of suspected colorectal cancer, there are two main types of investigation: endoscopy (flexible sigmoidoscopy or colonoscopy) and imaging (barium enema, computed

tomography (CT) and CT colonography). Patients require bowel preparation for any of these investigations to produce accurate results. Each method has specific advantages and disadvantages that make it more or less appropriate for particular patients.

Endoscopy: Endoscopic investigation has the advantage of permitting biopsy and histopathological assessment of any suspicious lesion and removal of polyps. Colonoscopy involves little risk when carried out by experienced operators. However, it causes more adverse effects, such as perforation or bleeding, than flexible sigmoidoscopy or barium enema.

A prospective study of 13,580 colonoscopies carried out by surgeons in the US found that complication rates were very low.⁸⁰ Diagnostic colonoscopy caused perforation in 0.02% of cases. Therapeutic colonoscopy (colonoscopy with polypectomy) caused bleeding in 0.19% of cases and perforation in 0.15%. One death was reported, in a man with multiple co-morbidities.

A survey of 164 endoscopy units in the UK revealed that the median number of colonoscopies performed was 375 per 250,000 population per year.⁴⁰ A shortage of endoscopists and a lack of nursing support and theatre time prevented additional weekly endoscopy sessions. The Department of Health has made a specific commitment to expansion and development of lower GI endoscopy services, linked to the introduction of a screening service.

Imaging: Barium enema is well established in the NHS and staff are experienced in its use. It has the advantages of safety, availability, and no need for sedation.

A systematic review of studies of the accuracy of double contrast barium enema and colonoscopy found that colonoscopy is significantly more sensitive than barium enema for the detection of both colorectal cancer and polyps, but barium enema is associated with a much lower risk of complications.⁸¹ A large retrospective study from a UK teaching hospital came to similar conclusions.⁸²

CT colonography (also known as 'virtual colonoscopy') is a relatively

new diagnostic technology requiring expertise in its use.⁸³ Patients with abnormal findings may require a subsequent colonoscopy to biopsy or remove suspicious lesions. A systematic review of studies comparing CT colonography with colonoscopy, found that CT colonography was capable of correctly identifying most polyps over 10 mm in size.⁸⁴

E.2 Choice of diagnostic method

Decisions about which form of investigation should be used at any point in the diagnostic process should depend on the patient's symptoms, age, family history, other risk factors such as colitis or Crohn's disease, as well as their general condition and ability to tolerate any preparation and the test itself. The local availability of facilities, equipment and skilled staff will inevitably influence the choice of investigation used.

Flexible sigmoidoscopy is relatively quick and virtually risk-free, and is therefore the most appropriate initial investigation for the majority of patients with symptoms that suggest possible lesions in the left (descending or distal) colon, sigmoid or rectum. There is evidence to suggest that for patients who present with symptoms alone (usually rectal bleeding, changed bowel habit or pain), further investigation after a negative flexible sigmoidoscopy is rarely necessary.⁸⁵

Diagnostic colonoscopy is usually appropriate for patients with right-sided symptoms, except for those with palpable masses, for whom imaging (barium enema or CT) is likely to be more suitable. If a complete colonoscopy is not achieved and clinical doubt remains, imaging is necessary.

When patients present with iron deficiency anaemia, investigation should continue until the cause is found.

E.3 Achieving competence in endoscopy

The reliable diagnosis of colon cancer by colonoscopy requires a skilled colonoscopist who can achieve a high rate of completion (when the whole of the colon is inspected, all the way to the caecum). Two research studies and a

UK hospital audit found a clear correlation between completion rates and the number and frequency of examinations performed.^{80,86,87} The total number of colonoscopies carried out by endoscopists was also important. Improvement continues with experience, up to a level of 200 cases.^{80,86}

Traditionally, endoscopy has been carried out by hospital doctors. However, there is accumulating evidence that both flexible sigmoidoscopy and diagnostic colonoscopy can be carried out safely by appropriately trained nurses and GPs. A survey found that nurses carried out endoscopy, predominantly diagnostic flexible sigmoidoscopy, in 43% of 176 units.⁴¹ A number of studies comparing endoscopy results achieved by doctors and nurses showed equally good outcomes for both groups.^{48-50,88,89} Complications were not reported upon in any of these studies.

A survey of 27 NHS primary care endoscopy providers, of which 21 provided lower GI endoscopy, found that GPs could perform endoscopy safely.⁴² Of 12,260 lower GI investigations (including 1,386 colonoscopies), six led to hospital admission and there was one death. Average waiting times were 1.2 weeks for urgent cases and 3.4 weeks for routine referrals. 98% of patients said the service was very good or excellent.

E.4 Pre-operative staging

Patients diagnosed with colorectal cancer should undergo further investigation to provide information on cancer stage, unless the findings are unlikely to influence management. Accurate staging is essential for appropriate choice of treatment.

Pre-operative staging of liver: A number of imaging techniques are available to identify liver metastases – ultrasound (US), CT scanning, and Magnetic Resonance Imaging (MRI).

Studies of the diagnostic accuracy of pre-operative liver imaging suggest that overall, CT is slightly better than US.⁹⁰⁻⁹² However, there have been few direct comparisons between CT and US in this situation, and the studies that were identified

have serious methodological flaws. In general where abdominal US identifies a metastasis, it is likely to be accurate, but up to half of patients with negative US scans do in fact have cancer in the liver.⁹⁰⁻⁹²

One study (n=73) reported sensitivity figures for contrast-enhanced CT of 94%⁹⁰ with a specificity of 92%. However a smaller study (n=44) reported a much lower figure for the sensitivity of CT: 37.5% with a specificity of 97%.⁹³

Local staging of rectal cancer: MRI appears to be better than CT in locally staging primary rectal cancer.⁹⁴⁻¹⁰⁴ A systematic review found that MRI was superior to CT for the assessment of bowel wall penetration and the identification of metastatic lymph nodes.⁹⁴ Of several primary studies not included in the systematic review only one compared imaging techniques directly,⁹⁵ the others used histopathology findings alone as a reference standard.^{96-100,105-107} These studies found that MRI using a body coil^{99,100} or endorectal coil^{95,105-107} was superior to CT⁹⁵⁻⁹⁸ for correctly staging rectal cancer. For the assessment of metastatic lymph nodes, MRI using the body coil^{99,100} was found to be superior to CT.⁹⁵⁻⁹⁸

Good quality, comparative research studies are required, particularly as the technology used in these studies may now be considered out-of-date.

Rectal endosonography and endoscopic ultrasonography are used to demonstrate the extent of tumour invasion into the layers of the muscle wall. A systematic review found a sensitivity of 93% and specificity of 81% for rectal endosonography or endoscopic ultrasonography for differentiating benign tumours and early rectal cancers.⁹⁴ Other primary studies have reported levels of sensitivity varying from 0%^{104,108} to 100%,^{95,109-111} and specificity from 80%⁹⁵ to 98%.^{104,108-111}

The systematic review also found that when compared with CT and MRI, rectal endosonography was the most accurate way of assessing tumour penetration.⁹⁴ However, CT and MRI provide more staging information and are more widely available.

F. Surgery and histopathology

Surgery with curative intent aims to remove the whole tumour; if it succeeds, the patient may be rendered free from cancer. When curative surgery is not possible, patients may benefit from palliative interventions.

The surgical approaches for the lower two-thirds of the rectum are the traditional practice of manual blunt dissection or total mesorectal excision (TME). TME is precision surgery involving meticulous dissection.¹¹² Surgery should be undertaken by specialist colorectal cancer surgeons who are members of colorectal cancer MDTs.^{9,113} Good surgery – in particular, TME for patients with rectal cancer – is associated with reduced local recurrence and improved long term survival.¹¹⁴⁻¹¹⁷

F.1 Emergency surgery

About a third of colon cancer patients and a tenth of rectal cancer patients are admitted as emergencies. Over 20% of patients with colorectal cancer who undergo emergency surgery for intestinal obstruction die within a month,¹¹⁸ mainly due to poor physical status at admission. Patients admitted as emergencies require a high level of expertise and should always be managed by MDT members.⁹ Holding procedures should be used to stabilize patients until they can be seen by MDT members, unless delaying surgery would increase the risk of death. Improving systems for managing these patients is likely to reduce peri-operative death rates.

F.2 Colorectal stents

Colorectal stents may be used to provide temporary relief of acute intestinal obstruction so that emergency surgery can be avoided.¹¹⁹⁻¹²⁷ This allows surgery to be done electively, with tumour staging and adequate surgical preparation, which may prevent peri-operative death in patients with high levels of co-morbidity. The use of a stent can avoid the need for a stoma.^{119,120,127-130}

Expanding metal stents usually remain effective for more than a

year, and in many cases, provide good palliation until death.^{119-123,129,131-}

¹³³ Reported complications include death, perforation, migration and re-occlusion.

The cost of intestinal stenting may be balanced by reduced intensive care costs.^{123,134}

F.3 Histopathology

Local recurrence of rectal cancer is associated with tumour involvement in the surgical margins, and accurate staging requires information on lymph node status.¹⁰ Histopathology reporting should include information on the size, stage, type, grade and appearance of the tumour, depth of invasion, number of lymph nodes excised and number affected, and tumour involvement at surgical margins, including circumferential plane involvement or clearance in rectal cancer.^{9,135} Such detailed information can lead to improvements in the quality of surgery (through feedback to surgeons on the results they achieve), and provide better information on which decisions on adjuvant therapy may be based.¹³⁵

F.4 Lymph nodes

The removal and identification of lymph nodes containing tumour is crucial both to reduce the risk of recurrence and to the decision-making on adjuvant therapy.¹³⁵

There is no consensus on the optimum number of lymph nodes that should be examined,¹³⁶⁻¹⁴⁴ but there is evidence that removing 10 or more improves the accuracy of staging.^{141,145,146} Patients classed as node negative on the basis of fewer nodes have been shown to have significantly poorer recurrence and survival rates than those classed as node negative on more nodes.^{140,145-147} A study carried out using cancer registry data from 1988-1991 reports that 14% of patients treated in the UK had 12 or more nodes examined.¹⁴⁸

F.5 Local recurrence after surgery for rectal cancer

Local recurrence is a serious problem after surgery for rectal cancer, and usually leads to death after severe pain and distressing symptoms. Reported recurrence rates vary from less than 10%^{149,150} to over 40%.^{151,152}

TME is associated with about half the rate of local recurrence, compared with blunt dissection surgery for cancer in the lower two thirds of the rectum.^{115-117,153} Long-term survival rates are significantly higher after TME.^{114,115,150-156}

F.6 Laparoscopic surgery

NICE guidance, published in 2000, recommends that open resection should be used in preference to laparoscopic surgery.¹⁵⁷ This guidance is under review and randomised controlled trials (RCTs) currently in progress are expected to clarify the situation.

F.7 Preparation for surgery

Antibiotic prophylaxis, usually given at the time of anaesthesia for colorectal surgery, significantly reduces the risk of wound and other infections.¹⁵⁸ However the 2002 Report of the National Confidential Enquiry into Perioperative Deaths indicates that routine procedures for appropriate preoperative management of patients may be neglected in some cases.¹⁵⁹

There is reliable evidence for the effectiveness of thromboprophylaxis with anti-platelet therapy.¹⁶⁰

G. Radiotherapy in primary disease

Comparison between radiotherapy combined with blunt dissection surgery with surgery alone for rectal cancer shows that the addition of radiotherapy significantly reduces local recurrence rates.¹⁶¹⁻¹⁶³ Pre-operative radiotherapy at a biological equivalent dose (BED) $\geq 30\text{Gy}$, produces a greater proportional reduction in local recurrence when compared to no radiotherapy, than post-operative radiotherapy (57% and 37% respectively).¹⁶² Pre-operative radiotherapy also leads to a significant reduction in mortality rates among patients who receive a BED of 30Gy or more.¹⁶²

Modern treatment methods, using megavoltage equipment with a planned volume technique to deliver

radiotherapy to smaller volumes of tissue, reduce the toxicity of treatment. However, even this form of radiotherapy is likely to cause long-term problems with bowel function.¹⁶⁴

Radiotherapy given before TME reduces local recurrence, from 8.2% to 2.4% ($p < 0.001$), but no reduction in mortality has been shown at a median of two years after surgery.¹⁶⁵ Two RCTs currently in progress are expected to throw further light on the issue of whether radiotherapy is worthwhile for patients who undergo TME.^{166,167}

A small RCT (70 patients) found that the addition of chemotherapy to long course pre-operative radiotherapy (chemoradiotherapy, CRT) for non-resectable rectal cancer produced significant reductions in local recurrence, but CRT caused more acute toxicity than radiotherapy alone.¹⁶⁸ The numbers surviving after five years were too small for differences between groups to achieve statistical significance. The results of two larger trials are expected shortly.^{169,170}

H. Adjuvant chemotherapy

A meta-analysis of individual patient data was undertaken and reported in the original colorectal cancer guidance.¹⁰ This analysis has recently been updated but information regarding the results of the update is not yet available. No relevant systematic reviews were identified.

The original meta-analysis found that over a quarter of patients present with Stage III cancers. There is evidence that protracted systemic chemotherapy can improve survival in this group of patients, although the precise size of the benefit remains uncertain. While some uncertainty remains about agents other than 5-fluorouracil and folinic acid (FUFA), it is now clear that treatment for six months is as effective as longer durations of up to a year.

There is no clear evidence on the effectiveness of chemotherapy for patients with Stage II colorectal cancer. However, when the tumour has adverse features such as

vascular invasion, peritoneal involvement or perforation, or if the surgical margins are inflamed or contain tumour, patients have a higher disease-related mortality rate and therefore may be more likely to benefit from chemotherapy.^{171,172}

I. Anal cancer

Anal cancer is a rare disease and the guidance update recommends that all patients should be referred to multidisciplinary anal cancer teams to optimise their outcomes.

Two large RCTs comparing radiotherapy (RT) alone with CRT have demonstrated a highly statistically significant reduction in local failure.^{173,174} Both saw improvements in colostomy-free survival and reduction in deaths from anal cancer with CRT. Neither showed any significant effect on overall survival. A third RCT tested the benefit of adding mitomycin C to 5-fluorouracil (5FU) and radiotherapy.¹⁷⁵ This also demonstrated statistically significant improvements in colostomy-free and disease-free survival. Other forms of treatment, such as surgical excision, may be considered by anal cancer MDTs, but surgery is usually reserved for salvage.

ACT2, a current National Cancer Research Network (NCRN) phase III RCT is comparing two CRT schedules (mitomycin C, 5FU, and RT versus cisplatin, 5FU, and RT) and post-CRT adjuvant chemotherapy (cisplatin/5FU x2 versus control).¹⁷⁶ The radiotherapy fields used in this trial are designed to improve outcomes and reduce acute toxicity.

J. Follow-up

The results of two recently conducted systematic reviews showed that intensive follow-up that included liver imaging was associated with a decrease in mortality owing to any cause.^{177,178} However, it was not clear which elements of the intensive follow-up programme were important.

There is some evidence to suggest that CT scanning as part of a routine

follow-up programme may be useful.¹⁷⁷⁻¹⁸²

One RCT demonstrated that follow-up is efficient and cost-effective if patients at higher risk are followed up more intensively than those at lower risk.¹⁸³ Patients at greatest risk are those with more advanced tumours at the time of resection – particularly Stage III cancers.

Two studies looked at prognostic factors likely to identify patients who could develop liver metastases.^{184,185} In the first study, the only factor that remained significant after adjusting for all other covariates was the presence of multiple as opposed to single lesions.¹⁸⁴ The other study showed that alcohol consumption and blood vessel invasion are independent risk factors for liver metastases.¹⁸⁵

The NCRN is currently investigating follow up after colorectal cancer in the FACS trial.¹⁸⁶

J.1 Cost-effectiveness of follow-up in the NHS

The relative cost-effectiveness of intensive and conventional follow-up strategies has been estimated using figures for NHS costs in 2002 and life expectancy data for the UK. Based on data from a four-study meta-analysis,¹⁷⁸ which included only those trials in which surveillance was designed to detect extraluminal recurrence, costs per patient were calculated to be £4,758 for intensive follow-up and £2,279 for conventional follow-up.¹⁸⁷ This represents an incremental cost per life-year gained by intensive follow-up of £3,007. Similar calculations based on the five-study meta-analysis produced a cost per life-year gained of £3,042. These results suggest that the cost-effectiveness of intensive follow-up after surgery for colorectal cancer compares favourably with that of other interventions that are currently widely used in the NHS.

K. Treatment of recurrent and advanced disease

K.1 Palliative stents

In addition to use in patients with obstruction (see section F. Surgery), colorectal stents can provide effective and cost-effective palliation in advanced colorectal cancer, obviating the need for a stoma or resection, often until death.^{119,120,127-130}

K.2 Surgery for liver and lung metastases

Curative surgery is sometimes possible when metastases are small and localised. Case series reports suggest 5-year survival rates of 30-35% in selected patients.¹⁰ However, few patients can be treated successfully in this way.

K.3 Chemotherapy

Two meta-analyses demonstrate significantly lower mortality rates with palliative chemotherapy for patients with metastatic colorectal cancer.^{188,189} Quality of life was found to be either similar or better in patients who received chemotherapy than in those who did not.

There have been two recent NICE appraisals of newer chemotherapeutic agents for advanced and metastatic disease.^{8,190} The evidence on which these appraisals were based is summarised on the NICE website.

Chemotherapy given early in the course of metastatic disease produces better outcomes than chemotherapy given after symptoms have become severe, increasing survival by 3-6 months without increasing adverse effects on quality of life.^{188,189}

K.4 Palliative radiotherapy

External radiotherapy used alone eases pain in a high proportion of patients with locally advanced rectal cancer. In some patients, tumours have gone into complete remission or regressed sufficiently to permit curative surgery after prolonged fractionated radiotherapy of 45 to 50Gy.^{161,163} Around 4-7% of patients

develop bone metastases, for which palliative radiotherapy has been shown to be effective.¹⁰

L. Palliative care

NICE has recently published guidance on *Improving Supportive and Palliative Care for Adults with Cancer*.¹³

Most patients with advanced colorectal cancer are cared for at home by GPs and district nurses. Specialist pain control is particularly important for patients with locally recurrent rectal cancer, in whom pain can be very severe and difficult to manage. However, a postal survey showed that some GPs were unwilling to define patients as needing palliative care, although an unambiguous diagnosis of incurable malignancy had been made.¹⁹¹ At the same time, the GPs expressed dissatisfaction with the promptness, clarity about treatment, future management, and the adequacy of information provided by the hospital.

M. Implications

In the manual update,¹¹ the following key recommendations are identified as priorities for the NHS, which, if implemented would make a major contribution to improving outcomes in colorectal cancer.

- Action should be taken to improve recognition of potential symptoms of colorectal cancer in primary care and in the community. Efficient systems should be set up to ensure that patients who may have colorectal cancer are rapidly referred for endoscopy.
- There is an urgent need for substantial expansion of lower GI endoscopy services. Access to both flexible sigmoidoscopy and colonoscopy should be improved and the focus of diagnostic effort should move from barium enema to endoscopy. (Note - This will be crucial for screening services when they are introduced.)
- Cancer Networks and Trusts should review the composition

and function of colorectal cancer MDTs and make sure that each MDT has a co-ordinator. They should:

- Establish systems within Trusts to ensure that all patients with suspected or newly diagnosed colorectal cancer are promptly referred to, and managed by, a colorectal cancer MDT.
- Review operational links with hepatobiliary (HPB) services and the relevant clinical teams to ensure that patients with potentially resectable liver metastases are referred to specialist MDTs for assessment.
- Identify specialist MDTs which will manage patients with anal cancer.
- Emergency patients (particularly those with intestinal obstruction) should be managed by colorectal cancer MDTs. This may require the development of emergency teams and transfers of patients between neighbouring hospitals.
- Patients with rectal cancer should be managed by teams trained in all aspects of TME, including pre and post-operative assessment, surgical technique, and the role of clinical oncology.
- All aspects of patient-centred care should be re-assessed in the light of recommendations in this manual update. In particular, Trusts should:
 - Improve the provision of appropriately trained staff and resources.
 - Ensure that patients receive all the information they want at all times.
 - Arrange ongoing support for patients and carers from a clinical nurse specialist who is encouraged to play an active part in MDT discussions.

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Effective Health Care

This bulletin is based on a series of systematic reviews, carried out by the Centre for Reviews and Dissemination to inform the update of the 1997 service guidance for colorectal cancer. Full details are provided in *Improving Outcomes in Colorectal Cancers - The Manual Update* and *The Research Evidence for the Manual Update* published by NICE. These may be obtained free of charge by calling the NHS Response Line on 0870 1555 455.

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