Colorectal cancer

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PRACTICE

GUIDELINES

Colorectal cancer: summary of NICE guidance

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What you need to know

- Long term use of aspirin may prevent colorectal cancer in people with Lynch syndrome, a group with a high risk of colorectal cancer
- Treatment options for early rectal cancer include endoscopic and surgical treatments
- A shorter duration of adjuvant chemotherapy for three months can be effective and with lower side effects compared with the standard six months for people with lymph node-positive colorectal cancer
- Colonic stenting is now an option for treatment with curative intent of acute left sided large bowel obstruction
- Low anterior resection syndrome (LARS) is a common long term side effect for people who have undergone sphincter-preserving surgery for colorectal cancer

Colorectal cancer (cancer of the colon, rectum, or bowel) is the fourth most common cancer in the UK, with over 42 000 new cases diagnosed each year.[1] Survival rates have improved, with a five year survival rate of almost 60% now.[2]

This article summarises recent recommendations from the update of the National Institute for Health and Care Excellence (NICE) guideline for the diagnosis and management of colorectal cancer.[3] The update focuses on the management of colorectal cancer, reflecting new research evidence in this area.

What's new in this guidance

- Aspirin is recommended for the prevention of colorectal cancer in people with Lynch syndrome
- Three months of adjuvant chemotherapy is recommended as an alternative to six months for people with stage III colon cancer (pT1-4, pN1-2, M0) or stage III rectal cancer (pT1-4, pN1-2, M0) treated with short course radiotherapy or no preoperative treatment
- Preoperative radiotherapy or chemoradiotherapy is recommended for people with rectal cancer that is cT1-T2, cN1-N2, M0 or cT3-T4, any cN, M0
- Treatment options are recommended for metastatic colorectal cancer in the lung, liver, or peritoneum
- Minimum case volumes are set for surgeons and institutions treating patients with rectal cancer
- Recognition and assessment of low anterior resection syndrome (LARS) is recommended in people with associated symptoms

Recommendations

NICE recommendations are based on systematic reviews of best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Committee's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in italic in square brackets.

Prevention of colorectal cancer in people with lynch syndrome

Lynch syndrome is a hereditary genetic condition caused by mutation in one of four DNA mismatch repair genes: MLH1, MSH2, MSH6, or PMS2.[4] People with Lynch syndrome have an estimated lifetime risk of colorectal cancer of 50-80%.[5] The main strategy to prevent it has been regular screening with colonoscopy and polypectomy, but there is now evidence from a randomised trial[6] to support aspirin as a prevention strategy.

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- Consider daily aspirin, to be taken for more than two years, to prevent colorectal cancer in people with Lynch syndrome. [*Based on low to moderate quality evidence*]

Management of local disease

The updated guideline has separated the management of colon and rectal cancer, where it differs. Standard practice for colon cancer is to offer surgery for those who are fit (see box 1). Treatment of rectal cancer has varied considerably in practice, and the guideline sets out surgical and endoscopic treatment options for preoperative (chemo)radiotherapy and surgical technique (see table 1).

Box 1: Treatment for people with colon cancer who are fit for surgery

Preoperative treatment

- Consider preoperative systemic anticancer therapy for people with cT4 colon cancer
  [*Based on very low quality evidence and the experience and opinion of the Guideline Committee (GC)*]

Surgical technique

In current practice, resection of the colonic tumour and nearby lymph nodes is performed via a laparoscopic or open technique. For advice on laparoscopic surgery in line with NICE technology appraisal guidance, see surgical techniques for colon cancer in the NICE Pathway on colorectal cancer.[7]

Treatment for people with early rectal cancer (cT1-T2, cN0, M0)

- Offer one of the treatments shown in table 1 to people with early rectal cancer (cT1-T2, cN0, M0—see box 2 for TNM classification) after discussing the implications of each treatment and reaching a shared decision with the person about the best option. [*Based on very low to low quality evidence and the experience and opinion of the GC*]

Box 2: TNM tumour classification

This guideline uses the tumour, node, metastasis (TNM) classification developed by the Union for International Cancer Control (UICC) to describe the stage of the cancer. Refer to the *TNM Classification of Malignant Tumours, 8th edition*[8] for further information. In this guideline early rectal cancer is defined as cT1-2, cN0, M0.

cTNM refers to clinical classification based on evidence acquired before treatment—for example, imaging, physical examination, and endoscopy.

pTNM refers to pathological classification based on histopathology

Preoperative treatment for people with rectal cancer

- Do not offer preoperative radiotherapy to people with early rectal cancer (cT1-T2 cN0, M0), unless as part of a clinical trial.
- Offer preoperative radiotherapy or chemoradiotherapy to people with rectal cancer that is cT1-T2, cN1-N2, M0 or cT3-T4, any cN, M0.

  [*Based on low to moderate quality evidence and the experience and opinion of the GC*]

Surgery for rectal cancer

- Offer surgery to people with rectal cancer (cT1-T2, cN1-N2, M0 or cT3-T4, any cN, M0) who have a resectable tumour.
- Inform people with a complete clinical and radiological response to neoadjuvant treatment who wish to defer surgery that there is a risk of recurrence and there are no prognostic factors to guide selection for deferral of surgery. For those who choose to defer, encourage their participation in a clinical trial and ensure that data are collected via a national registry.

  [*Based on very low to low quality evidence and the experience and opinion of the GC*]

Hospital and surgeon case volumes for people with rectal cancer

- Hospitals performing major resection for rectal cancer should perform at least 10 of these operations each year.
- Individual surgeons performing major resection for rectal cancer should perform at least five of these operations each year.

  [*Based on very low to high quality evidence and the experience and opinion of the GC*]

Surgical technique for people with rectal cancer

Laparoscopic surgery is the appropriate technique for most people being considered for surgery for rectal cancer. However, open surgery may be clinically indicated—for example, in locally advanced tumours or for people with multiple previous abdominal operations or previous pelvic surgery. Robotic surgery should be considered only within established robotic programmes. Transanal total mesorectal excision surgery should only be considered within structured and supervised programmes, and with data collected via the national registry in line with the NICE interventional procedures guidance.[9]

Duration of adjuvant chemotherapy for people with colorectal cancer

Until now, the standard duration of adjuvant systemic therapy for colorectal cancer has been six months, but new evidence has shown shorter duration to be as effective with lower treatment toxicity. Note that patients with rectal cancer treated with long course chemoradiotherapy are not covered by this recommendation.

- For people with stage III colon cancer (pT1-4, pN1-2, M0) or stage III rectal cancer (pT1-4, pN1-2, M0) treated with short course radiotherapy or no preoperative treatment, offer:
  - Capecitabine in combination with oxaliplatin (CAPOX or XELOX) for three months, or if this is not suitable
  - Oxaliplatin in combination with 5-fluorouracil and folinic acid (FOLFOX) for three to six months, or
  - Single agent fluoropyrimidine (such as capecitabine) for six months, in line with NICE technology appraisal guidance (see adjuvant treatment of stage III colon cancer in the NICE Pathway on colorectal cancer[7]).
  - Base the choice on the person's histopathology (for example, pT1-T3 and pN1, and pT4 and/or pN2), performance status, any comorbidities, age, and personal preferences.

  [*Based on low to high quality evidence and the experience and opinion of the GC*]

Colonic stents in acute large bowel obstruction

Over 20% of colorectal cancers present as an emergency with large bowel obstruction.[10] Emergency surgery is an option, but the patient may be at a higher risk of requiring a stoma (either

temporary or permanent) and of death with an emergency operation compared with an elective one. Stenting is an alternative and has the potential to convert bowel obstruction from an emergency condition to an elective situation, but it also comes with its own risks, including perforation.

- Consider stenting for people presenting with acute left sided large bowel obstruction who are to be treated with palliative intent.
- Offer either stenting or emergency surgery for people presenting with acute left sided large bowel obstruction if potentially curative treatment is suitable for them.

  [*Based on very low to moderate quality evidence and the experience and opinion of the GC*]

Management of metastatic disease

Metastatic colorectal cancer commonly affects the liver, lungs, or peritoneum. Treatment depends on, for example, the site and number of the metastases and involves discussion by a multidisciplinary team with expertise in treatment of disease in the involved sites.

People with metastatic disease and an asymptomatic primary tumour

Around 20% of people with colorectal cancer present with metastatic disease,[11] and in some cases the primary tumour is asymptomatic. Clinical practice varies over whether the asymptomatic primary tumour is resected in patients with incurable metastatic disease. Factors to consider are summarised in table 2.

- Consider surgical resection of the primary tumour for people with incurable metastatic colorectal cancer who are receiving systemic anticancer therapy and have an asymptomatic primary tumour. Discuss the implications of the treatment options with the person before making a shared decision. [*Based on very low to low quality evidence and the experience and opinion of the GC*]

People with metastatic colorectal cancer in the liver

- Consider resection, either simultaneous or sequential, after discussion by a multidisciplinary team with expertise in resection of disease in all involved sites.
- Consider perioperative systemic anticancer therapy if liver resection is a suitable treatment.
- Consider chemotherapy with local ablative techniques for colorectal liver metastases that are considered unsuitable for liver resection after discussion by a specialist multidisciplinary team.
- Do not offer selective internal radiation therapy (SIRT) as first line treatment for people with colorectal liver metastases that are unsuitable for local treatment. For advice on SIRT in line with the NICE interventional procedures guidance,[12] see managing liver metastases in the NICE Pathway on colorectal cancer.[7] This recommends that SIRT should only be offered:
  - With special arrangements for clinical governance, consent, and audit or research to people who are chemotherapy intolerant or who have liver metastases that are refractory to chemotherapy
  - In the context of research to people who can have chemotherapy.

  [*Based on very low to moderate quality evidence and the experience and opinion of the GC*]

People with metastatic colorectal cancer in the lung

- Consider metastasectomy, ablation, or stereotactic body radiation therapy for people with lung metastases that are suitable for local treatment, after discussion by a multidisciplinary team that includes a thoracic surgeon and a specialist in non-surgical ablation.
- Consider biopsy for people with a single lung lesion to exclude primary lung cancer.

  [*Based on very low quality evidence and the experience and opinion of the GC*]

People with metastatic colorectal cancer in the peritoneum

- For people with colorectal cancer metastases limited to the peritoneum:
  - offer systemic anticancer therapy, and
  - Discuss within a multidisciplinary team referral to a nationally commissioned specialist centre to consider cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC).

  [*Based on low to very low quality evidence and the experience and opinion of the GC*]

Low anterior resection syndrome (LARS)

LARS is a constellation of symptoms that may occur after sphincter-preserving surgery for rectal cancer, affecting around 40% of these patients. LARS can have a major impact on quality of life and daily living. Symptoms of LARS are described in box 3.

Box 3: Symptoms of low anterior resection syndrome (LARS)

- Symptoms of LARS may include some or all of:
  - Increased frequency of stool
  - Urgency with or without incontinence of stool
  - Feeling of incomplete emptying
  - Fragmentation of stool (passing small amounts little and often)
  - Difficulty in differentiating between gas and stool
- A LARS score is a validated, patient-administered questionnaire[13 14] which can be used to assess severity of LARS. It allocates points to the symptoms and allows differentiation into groups with major LARS, minor LARS, and no LARS

- Give information on LARS to people who will potentially have sphincter-preserving surgery. Advise them to seek help from primary care if they think they have symptoms of LARS (box 3).
- Assess people with symptoms of LARS using a validated patient-administered questionnaire (such as the LARS score, see box 3).
- Offer people with bowel dysfunction treatment for associated symptoms in primary care (such as dietary management, laxatives, anti-bulking agents, anti-diarrhoeal agents, or anti-spasmodic agents). Seek advice from secondary care if the treatment is not successful.

  [*Based on the experience and opinion of the GC*]

Challenges to implementation

Endoscopic submucosal dissection (ESD) is not widely available in the UK. In centres where ESD is not already available, resources and time will be needed to establish this service.

Preoperative therapy for rectal cancer is not currently offered to all patients: therefore, more clinical oncologists, radiotherapy equipment, and staff may be needed. The 2013 guideline recommended a magnetic resonance imaging-based stratification to guide preoperative therapy. The updated guideline does not do this as the evidence suggested potential survival benefit irrespective of local rectal cancer stage (excluding early rectal cancer). However, the Guideline Committee acknowledged that clinician and patient shared decision making will still be important in this setting, as preoperative (chemo)radiotherapy also has potential complications associated with its use.

Colonic stenting is not established practice in those to be treated with curative intent. Therefore, an increase in the provision of stenting and associated costs is possible and some patients might need to be transferred to another unit.

Primary care clinicians are not necessarily aware of LARS or how to assess it, so raising awareness about LARS and its assessment might increase their workload.

Future research

The Guideline Committee prioritised the following research recommendations:

- What is the cost effectiveness and safety of non-surgical ablation and stereotactic body radiotherapy compared with resection for people with metastatic colorectal cancer in the lung that is amenable to local treatment?
- What is the effectiveness and safety of sacral nerve stimulation and transanal irrigation compared with symptomatic treatment for people with major low anterior resection syndrome (LARS)?

How patients were involved in the creation of this article

Committee members involved in this guideline included two adults with experience as patients with colorectal cancer who contributed to the formulation of the recommendations summarised here.

Further information on the guidance

This guidance was developed by the National Guideline Alliance in accordance with NICE guideline methodology (www.nice.org.uk/media/default/about/what-we-do/our-programmes/developing-nice-guidelines-the-manual.pdf). A guideline committee (GC) was established by the National Guideline Alliance, which incorporated healthcare and allied healthcare professionals (two consultant colorectal cancer surgeons, two consultant clinical oncologists, two consultant radiologists, one consultant general and colorectal surgeon, one general practitioner, one head of nursing advisory service, one lead specialist nurse, one senior specialist dietitian, one gastroenterologist, one consultant thoracic surgeon, one hepatobiliary and pancreatic surgeon, one consultant medical oncologist, one molecular pathologist) and two lay members.

The GC identified relevant review questions and collected and appraised clinical and cost effectiveness evidence. Quality ratings of the evidence were based on GRADE methodology (www.gradeworkinggroup.org). These relate to the quality of the available evidence for assessed outcomes or themes rather than the quality of the study. The GC agreed recommendations for clinical practice based on the available evidence or, when evidence was not found, based on their experience and opinion using informal consensus methods.

The scope and the draft of the guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the GC took all comments into consideration when producing the final version of the guideline.

NICE will conduct regular reviews after publication of the guidance, to determine whether the evidence base has progressed significantly enough to alter the current guideline recommendations and require an update.

The members of the Guideline Committee were (shown alphabetically): Jay Bradbury, Michael Braun, Gemma Burgess, Cindy Chew, Justin Davies, Charlotte Dawson, Stephen Fenwick, Julie Hepburn, Peter Hoskin, Debby Lennard, Vivek Misra, Faheez Mohamed, Kevin Monahan, Richard Roope, Manuel Salto-Tellez, Michael Shackcloth, Baljit Singh, and Ratan Verma

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Tables

Table 1| Implications of treatments for early rectal cancer (cT1-T2, cN0, M0).

	Transanal excision*	Endoscopic submucosal dissection	Total mesorectal excision
Type of procedure	Endoscopic/surgery	Endoscopic	Surgery
Minimally invasive procedure	Yes	Yes	Possible
Resection of bowel (may have more impact on sexual and bowel function)	No	No	Yes
Stoma needed (a permanent or temporary opening in the abdomen for waste to pass through)	No	No	Possible
General anaesthetic needed (and the possibility of associated complications)	Yes	No, conscious sedation	Yes
Full thickness excision possible (better chance of removing cancerous cells and more accurate prediction of lymph node involvement)	Yes	No	Yes
Removal of lymph nodes (more accurate staging of the cancer so better chance of cure)	No	No	Yes
Conversion to more invasive surgery needed if complication	Possible	Possible	Possible
Further surgery needed depending on histology	Possible	Possible	Usually no
Usual hospital stay	1–2 days	1–2 days	5–7 days
External scarring	No	No	Yes
Possible complications (in alphabetical order):	• Abdominal pain • Bleeding • Mild anal incontinence • Perirectal abscess or sepsis and stricture (narrowing) • Perforation • Suture line dehiscence (wound reopening) • Urinary retention	• Abdominal pain • Bleeding • Bloating • Perforation	• Adhesions • Anastomotic leak (leaking of bowel contents into abdomen) • Anastomotic stricture (narrowing at internal operation site) • Bleeding • Incisional hernia (hernia where surgical incision was made) • Injury to neighbouring structures • Pelvic abscess • Urinary retention

* Transanal excision includes transanal minimally invasive surgery and transanal endoscopic microsurgery.

This table is based on the experience and opinion of the Guideline Committee or very low to low quality evidence and is intended to facilitate shared decision making about the best treatment option for the individual patient.

Table 2| Factors to take into account when considering resection of an asymptomatic primary tumour for people with incurable metastatic colorectal cancer who are receiving systemic anticancer therapy [*Based on the experience and opinion of the GC unless otherwise stated*]

Treatment	Advantages	Disadvantages
Resection of asymptomatic primary tumour	• Possible improvement in overall survival rate [*Based on low quality evidence*] • Avoidance of primary tumour-related symptoms such as obstruction, perforation, bleeding, and pain	• Around 5 in 100 people will have severe postoperative complications [*Based on moderate quality evidence*] • Systemic therapy still needed, and may be delayed if surgical complications occur
No resection (systemic anticancer therapy only)	• Avoids surgery and the potential for postoperative complications	• Around 20 in 100 people will develop primary tumour-related symptoms such as obstruction, perforation, bleeding, and pain that need surgery. [*Based on low quality evidence*]