NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE Guideline Colorectal cancer (update) Draft for consultation, August 2019

This guideline covers managing colorectal (bowel) cancer in people aged 18 and over. It aims to improve quality of life and survival for adults with colorectal cancer through management of local disease and management of secondary tumours (metastatic disease).

Who is it for?

- Health professionals working in secondary care
- Cancer Alliances and cancer clinical networks
- Commissioners of colorectal cancer preventative and treatment services (including Clinical Commissioning Groups and NHS England Specialised Commissioning)
- People with colorectal cancer, their families and carers

This guideline will update and replace NICE guidelines CG131 (published November 2011) and CSG5 (published June 2004).

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the recommendations and how they might affect practice and services
- the guideline context.

Information about how the guideline was developed is on the <u>guideline's page</u> on the NICE website. This includes the evidence reviews, the scope, and details of the committee and any declarations of interest.

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1 Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in <u>your care</u>.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

2 1.1 Prevention of colorectal cancer in people with Lynch 3 syndrome

4 1.1.1 Consider daily aspirin¹, to be taken for more than 2 years, to prevent colorectal cancer in people with Lynch syndrome.

To find out why the committee made the recommendation on prevention of colorectal cancer in people with Lynch syndrome and how it might affect practice, see <u>rationale and impact</u>.

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1.2 Information for people with colorectal cancer

Provide people with colorectal cancer information about their treatment (both written and spoken) in a sensitive and timely manner throughout their care, tailored to their needs and circumstances. Make sure the information is relevant to them, based on the treatment they might have and the possible side effects. Also see the NICE guidelines on patient experience in adult NHS services and decision-making and mental capacity.

A commonly used aspirin dose in current practice is either 150 mg or 300 mg.

¹ At the time of consultation (August 2019), aspirin does not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

1	1.2.2	Give people information on all treatment options for colorectal cancer available to them, including:
3 4 5 6		 surgery, radiotherapy, systemic anti-cancer therapy or palliative care the potential benefits, risks, side effects and implications of treatments, for example, possible effects on bowel and sexual function (see also recommendation 1.6.2), quality of life and independence.
7	1.2.3	Advise people with colorectal cancer of possible reasons why their
8		treatment plan might need to change during their care, including:
9		changes from laparoscopic to open surgery or curative to non-curative
0		treatment, and why this change may be the most suitable option for
11		them
2		 the likelihood of having a stoma, why it might be necessary and for how
13		long it might be needed.
14	1.2.4	If recovery protocols (such as 'enhanced recovery after surgery', ERAS)
15		are used, explain to people with colorectal cancer what these involve and
16		their value in improving their recovery after surgery.
17	1.2.5	Ensure that appropriate specialists discuss possible side effects with
8		people who have had surgery for colorectal cancer, including:
19		altered bowel and sexual function
20		 physical changes, including anal discharge or bleeding.
21		If relevant, have a trained stoma professional provide information on the
22		care and management of stomas and on learning to live with a stoma.
23	1.2.6	Emphasise to people the importance of monitoring and managing side
24		effects during non-surgical treatment to try to prevent permanent damage
25		(for example, monitoring prolonged sensory symptoms after platinum-
26		based chemotherapy treatment, which can be an indication to reduce
27		dosage to minimise future permanent peripheral neuropathy).

1	1.2.7	Give people who have had treatments for colorectal cancer information
2		about possible short-term, long-term, permanent and late side effects
3		which can affect quality of life, including:
4		pain or sexual dysfunction caused by radiotherapy or surgery
5		 nerve damage and neuropathy caused by chemotherapy
6		 mental and emotional changes, including anxiety, depression,
7		chemotherapy-related cognitive impairment, and changes to self-
8		perception and <u>social identity</u> .
9	1.2.8	Prepare people for discharge after treatment for colorectal cancer by
10		giving them advice on:
11		adapting physical activity to maintain their quality of life
12		diet, including advice on foods that can cause or contribute to bowel
13		problems such as diarrhoea, flatulence, incontinence and difficulty in
14		emptying the bowels
15		• weight management, physical activity and healthy lifestyle choices (for
16		example stopping smoking and reducing alcohol use)
17		how long their recovery might take
18		• how, when and where to seek help if side effects become problematic.
	To find o	out why the committee made the recommendations on information for

To find out why the committee made the recommendations on information for people with colorectal cancer and how they might affect practice, see <u>rationale and impact</u>.

1.3 Management of local disease

20 People with rectal cancer

- 21 Treatment for people with early rectal cancer (T1-T2, N0, M0)
- 22 1.3.1 Offer one of the treatments shown in table 1 to people with early rectal
 23 cancer (T1-T2, N0, M0) after discussing the implications of each treatment
 24 and reaching a shared decision with the person about the best option.

1 Table 1 Implications of treatments for early rectal cancer (<u>T1-T2, N0, M0</u>) based

2 on committee's expertise

	Transanal excision (TAE), including transanal minimally invasive surgery (TAMIS) and transanal endoscopic microsurgery (TEMS)	Endoscopic submucosal dissection (ESD)	Total mesorectal excision (TME)
Type of procedure	Endoscopic/Surgery	Endoscopic	Surgery
Minimally invasive	Yes	Yes	Possible
procedure			. 5555.5
Resection of bowel	No	No	Yes
(may have more impact on sexual and bowel function)			
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
Able to do a full thickness excision (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 include:	 Abdominal pain Bleeding Mild anal incontinence Perirectal abscess/sepsis and stricture (narrowing) Perforation 	 Abdominal pain Bleeding Bloating Perforation 	 Adhesions Anastomotic leak (leaking of bowel contents into the abdomen) Anastomotic stricture (narrowing at internal operation site)

Suture line dehiscence (wound reopening)Urinary retention	_, _	Bleeding Incisional hernia (hernia where the surgical incision
omary retemen	-	was made) Injury to neighbouring
	_	structures Pelvic abscess Urinary retention

Some of the potential complications shown in the table were identified from the evidence review.

To find out why the committee made the recommendation on treatment for people with early rectal cancer and how it might affect practice, see <u>rationale and impact</u>.

3 Preoperative treatment for people with rectal cancer

- 4 1.3.2 Do not offer preoperative radiotherapy to people with early rectal cancer (T1-T2 N0, M0), unless as part of a clinical trial.
- Offer preoperative radiotherapy or chemoradiotherapy to people with rectal cancer that is <u>T1-T2</u>, <u>N1-N2</u>, <u>M0</u>, or <u>T3-T4</u>, <u>any N, M0</u>.

To find out why the committee made the recommendations on preoperative treatment for people with rectal cancer and how they might affect practice, see rationale and impact.

8 Surgery for people with rectal cancer

- 9 1.3.4 Offer surgery to people with rectal cancer (<u>T1-T2, N1-N2, M0</u>, or <u>T3-T4</u>, 10 any N, M0) who have a resectable tumour. For those who choose to 11 defer, this should be in the context of a clinical trial or a national registry.
- 12 1.3.5 Inform people with a complete clinical and radiological response to 13 neoadjuvant treatment who wish to defer surgery that there are no 14 prognostic factors to guide selection for deferral of surgery.

To find out why the committee made the recommendations on deferral of surgery for people with rectal cancer and how they might affect practice, see <u>rationale and impact</u>.

1 Surgical technique for people with rectal cancer

- 2 1.3.6 Offer laparoscopic surgery for rectal cancer, in line with the NICE technology appraisal on <u>laparoscopic surgery for colorectal cancer</u>.
- 1.3.7 Consider open surgery if clinically indicated, for example by locally
 advanced tumours, multiple previous abdominal operations or previous
 pelvic surgery.
- 7 1.3.8 Only consider robotic surgery within established programmes that have appropriate audited outcomes.
- 9 1.3.9 Only consider transanal TME surgery within structured and supervised 10 programmes, and with the outcomes entered into the appropriate national 11 transanal TME registry.

To find out why the committee made the recommendations on surgical technique for people with rectal cancer and how they might affect practice, see <u>rationale and impact</u>.

12 People with locally advanced or recurrent rectal cancer

13 1.3.10 Consider referring people with locally advanced primary or recurrent rectal

14 cancer that might potentially need multi-visceral or <u>beyond-TME surgery</u>

15 to a specialist centre to discuss exenterative surgery.

To find out why the committee made the recommendation on locally advanced or recurrent rectal cancer and how it might affect practice, see <u>rationale and impact</u>.

Surgical volumes for rectal cancer surgeries

- 17 1.3.11 Hospitals performing <u>major resection for rectal cancer</u> should operate on at least 10 patients per year.
- 19 1.3.12 Individual surgeons performing <u>major resection for rectal cancer</u> should operate on at least 5 patients per year.

To find out why the committee made the recommendation on surgical volumes for rectal cancer surgeries and how it might affect services, see <u>rationale and impact</u>.

1 People with colon cancer

- 2 Preoperative treatment for people with colon cancer
- 3 1.3.13 Consider preoperative systemic anti-cancer therapy for people with $\underline{\mathsf{T4}}$
- 4 colon cancer.

To find out why the committee made the recommendation on preoperative treatment for people with colon cancer and how it might affect practice, see rationale and impact.

- 5 People with either colon or rectal cancer
- 6 Also see the NICE technology appraisal on laparoscopic surgery for colorectal
- 7 cancer.
- 8 Duration of adjuvant chemotherapy for people with colorectal cancer
- 9 Patients with rectal cancer treated with long-course chemoradiotherapy are not
- 10 covered by this recommendation.
- 11 1.3.14 For people with stage III colon cancer² (<u>T1-4, N1-2, M0</u>), or stage III rectal

 cancer³ (<u>T1-4, N1-2, M0</u>) treated with short-course radiotherapy or no
- preoperative treatment, offer:
 - capecitabine in combination with oxaliplatin (CAPOX) for 3 months, or if this is not suitable

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² Although use of capecitabine with oxaliplatin chemotherapy (CAPOX) is common in UK clinical practice, at the time of consultation (August 2019), oxaliplatin did not have UK marketing authorisation for use in combination with capecitabine and capecitabine did not have UK marketing authorisation for 3 months duration of adjuvant treatment in people with colon cancer. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

³ At the time of consultation (August 2019), capecitabine with oxaliplatin (CAPOX) and oxaliplatin with 5-fluorouracil and folinic acid (FOLFOX) did not have a UK marketing authorisations for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

1	 oxaliplatin in combination with 5-fluorouracil and folinic acid (FOLFOX)
2	for 3 to 6 months, or
3	 single-agent fluoropyrimidine (for example, capecitabine) for 6 months,
4	in line with NICE technology appraisal on capecitabine and oxaliplatin
5	in the adjuvant treatment of stage III (Dukes' C) colon cancer.
6	Base the choice on the person's histopathology (for example <u>T1-T3 and</u>
7	N1, and T4 and/or N2), performance status, any comorbidities, age and
8	personal preferences.
	To find out why the committee made the recommendation on duration of adjuvant
	chemotherapy for people with colorectal cancer and how it might affect practice,
	see rationale and impact.
9	Colonic stents in acute large bowel obstruction
10	1.3.15 Consider stenting for people presenting with acute left-sided large bowel

To find out why the committee made the recommendations on colonic stents in acute large bowel obstruction and how they might affect practice, see rationale

Offer either stenting or emergency surgery for people presenting with

acute left-sided large bowel obstruction if potentially curative treatment is

obstruction who are to be treated with palliative intent.

and impact.

1.4 15 Molecular biomarkers to guide systemic anti-cancer therapy 16

- Also see the NICE diagnostics guidance on molecular testing strategies for Lynch 17
- 18 syndrome in people with colorectal cancer.

suitable for them.

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1.4.1 19 Test all people with metastatic colorectal cancer suitable for systemic anti-20 cancer treatment for RAS and BRAF V600E mutations.

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To find out why the committee made the recommendation on molecular biomarkers to guide systemic anti-cancer therapy and how it might affect practice, see <u>rationale and impact</u>.

1.5 Management of metastatic disease

2 People with asymptomatic primary tumour

1.5.1 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. See table 2.

Table 2 Factors to take into account when considering resection of the

9 asymptomatic primary tumour

	Advantages	Disadvantages
Resection of the asymptomatic primary tumour	 Possible improvement in overall survival rate (based on low quality evidence from research) 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 from research) Systemic therapy still needed, and may be delayed if surgical complications occur
No resection (systemic anti- cancer 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 from research)

- Advantages and disadvantages in table 2 are based on committee expertise unless
- 11 otherwise indicated. Quality of evidence based on GRADE:
- 12 Moderate: True effect is probably close to the estimated effect.
- 13 Low: True effect might be markedly different from the estimated effect.

To find out why the committee made the recommendation on asymptomatic primary tumour and how it might affect practice, see <u>rationale and impact</u>.

1	Systemic	c anti-cancer therapy for people with metastatic colorectal cancer
2	1.5.2	For advice on systemic anti-cancer therapy for people with metastatic
3		cancer, see the following NICE technology appraisals:
4		Aflibercept in combination with irinotecan and fluorouracil-based
5		therapy for treating metastatic colorectal cancer that has progressed
6		following prior oxaliplatin-based chemotherapy
7		Bevacizumab and cetuximab for the treatment of metastatic colorectal
8		<u>cancer</u>
9		Bevacizumab in combination with oxaliplatin and either fluorouracil plus
10		folinic acid or capecitabine for the treatment of metastatic colorectal
11		<u>cancer</u>
12		Cetuximab and panitumumab for previously untreated metastatic
13		colorectal cancer
14		Cetuximab, bevacizumab and panitumumab for the treatment of
15		metastatic colorectal cancer after first-line chemotherapy: Cetuximab
16		(monotherapy or combination chemotherapy), bevacizumab (in
17		combination with non-oxaliplatin chemotherapy) and panitumumab
8		(monotherapy) for the treatment of metastatic colorectal cancer after
19		first-line chemotherapy
20		Guidance on the use of capecitabine and tegafur with uracil for
21		metastatic colorectal cancer
22		<u>Trifluridine-tipiracil for previously treated metastatic colorectal cancer</u>
	To find	out why the committee made the recommendation on systemic anti-cancer
	therapy	for people with metastatic cancer and how it might affect practice, see
	rationale	e and impact.
23	People v	vith metastatic colorectal cancer in the liver
24	1.5.3	Consider resection, either simultaneous or sequential, by a
25		multidisciplinary team (MDT) with expertise in resection of disease in all
26		sites.
7	151	Consider perioperative systemic anti-cancer therapy if liver resection is a

suitable treatment.

1 1.5.5 Consider chemotherapy with local ablative techniques for people with colorectal liver metastases that are unsuitable for liver resection after discussion in a specialist MDT.

1.5.6 Do not offer selective internal radiation therapy (SIRT) as first-line treatment for people with colorectal liver metastases that are unsuitable for local treatment.

To find out why the committee made the recommendations on metastatic colorectal cancer in the liver and how they might affect practice, see <u>rationale and impact</u>.

7 People with metastatic colorectal cancer in the lung

- Solution 1.5.7 Consider metastasectomy, ablation or stereotactic body radiation therapy for people with lung metastases that are suitable for local treatment, after discussion in a MDT that includes a thoracic surgeon and a specialist in non-surgical ablation.
- 12 1.5.8 Consider biopsy for people with a single lung lesion to exclude primary lung cancer.

To find out why the committee made the recommendations on metastatic colorectal cancer in the lung and how they might affect practice, see <u>rationale and impact.</u>

14 People with metastatic colorectal cancer in the peritoneum

- 15 1.5.9 For people with colorectal cancer metastases limited to the peritoneum:
- offer systemic anti-cancer therapy, and
- refer to a recognised specialist centre to consider cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC).

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To find out why the committee made the recommendation on metastatic colorectal cancer in the peritoneum and how it might affect practice, see <u>rationale and impact</u>.

1.6 Ongoing care and support

2 Follow-up for detection of local recurrence and distant metastases

1.6.1 For people who have had potentially curative surgical treatment for non metastatic colorectal cancer, offer follow-up for detection of local
 recurrence and distant metastases for the first 3 years that includes
 carcinoembryonic antigen (CEA) and CT.

To find out why the committee made the recommendation on follow-up for detection of local recurrence and distant metastases and how it might affect practice, see <u>rationale</u> and <u>impact</u>.

7 Management of low anterior resection syndrome

- 8 1.6.2 Give information on low anterior resection syndrome (LARS) to people
 9 who will potentially have sphincter-preserving surgery. Advise them to
 10 seek help from primary care if they think they have symptoms of LARS,
 11 such as:
- 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.
- 17 1.6.3 Assess people who present to primary care with symptoms of LARS using 18 a validated patient-administered questionnaire (for example, the LARS 19 score).
- 20 1.6.4 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.

To find out why the committee made the recommendations on management of low anterior resection syndrome and how they might affect practice, see <u>rationale and impact</u>.

3 Terms used in this guideline

4 Beyond-TME surgery

- 5 Beyond-TME surgery is when tumour extends beyond what is achievable to resect
- 6 by TME and requires more extensive surgery to achieve clear margins.

7 Major resection for rectal cancer

- 8 Major resection for rectal cancer means surgeries where part or whole of the rectum
- 9 are removed, including anterior resection and abdominoperineal resection.

10 Recovery protocols

- 11 Recovery protocols, such as 'enhanced recovery after surgery' or ERAS, are
- 12 perioperative care pathways designed to promote early recovery for patients
- undergoing major surgery by optimising the person's health before surgery and
- maintaining health and functioning after surgery.

15 **Social identity**

- 16 Social identity is about changes to people's concept of themselves as a result of
- 17 either their cancer, or the long-term side effects from treatment. For example, it could
- 18 cover changes from being a previously fit person to someone who has physical or
- mental problems, from being someone with the expectation of years to live to
- someone with a limited life expectancy, or the change from being a carer to
- 21 becoming cared for.

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TNM classification

- 23 This guideline uses the tumour, node, metastasis (TNM) classification developed by
- 24 the Union for Interventional Cancer Control (UICC) to describe the stage of the

- 1 cancer. Please refer to The TNM Classification of Malignant Tumours 8th Edition4
- 2 for further information. In this guideline early rectal cancer is defined as T1-2, N0,
- 3 M0.

4 Recommendations for research

- 5 The guideline committee has made the following recommendations for research.
- 6 Key recommendations for research
- 7 1 Treatment for metastatic colorectal cancer in the lung
- 8 What is the cost effectiveness and safety of non-surgical ablation and stereotactic
- 9 body radiotherapy compared to resection for people with metastatic colorectal
- 10 cancer in the lung amenable to local treatment?
- 11 To find out why the committee made the research recommendation on treatment for
- metastatic colorectal cancer in the lung see rationale and impact.
- 13 2 Management of lower anterior resection syndrome
- 14 What is the effectiveness and safety of sacral nerve stimulation and transanal
- irrigation compared to symptomatic treatment for people with major low anterior
- 16 resection syndrome?
- 17 To find out why the committee made the research recommendation on management
- 18 of lower anterior resection syndrome see rationale and impact.

19 Rationale and impact

- 20 These sections briefly explain why the committee made the recommendations and
- 21 how they might affect practice. They link to details of the evidence and a full
- 22 description of the committee's discussion.
- 23 Prevention of colorectal cancer in people with Lynch syndrome
- 24 Recommendation <u>1.1.1</u>

⁴ Brierley JD, Gospodarowicz MK, Wittekind C, eds. International Union Against Cancer (UICC). TNM Classification of Malignant Tumours, 8th edn. Oxford: Wiley Blackwell, 2017

1	Why the	committee	made the	recommendations
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- 2 There was evidence from a multi-country randomised controlled trial that taking daily
- 3 aspirin for more than 2 years reduces the risk of colorectal cancer in people with
- 4 Lynch syndrome, although this was only evident when restricting the analysis to
- 5 those who actually took aspirin as planned increasing the uncertainty around the
- 6 evidence. An observational study among people with Lynch syndrome also showed
- 7 a reduced risk of colorectal cancer in people who had taken aspirin in the long-term
- 8 compared to those who had not.
- 9 Potential harm of long-term aspirin use could be an increased bleeding risk but no
- 10 evidence was identified which compared adverse events, such as peptic ulcer,
- 11 gastrointestinal bleeding or cerebral haemorrhage, in people with Lynch syndrome
- who took aspirin on a long-term basis (compared to not taking aspirin at all), but the
- 13 committee agreed that the benefits are likely to outweigh any potential harms. The
- 14 committee recommended that the potential harms and benefits of long-term aspirin
- use should be discussed so that people are able to make an informed decision.
- 16 The optimal dose of aspirin that balances the benefits of aspirin as prevention of
- 17 colorectal cancer and the potential increased bleeding risk especially with higher
- 18 doses remains unclear and the committee was not able to recommend a dose.
- 19 though an ongoing trial is currently studying this. A commonly used dose in current
- 20 practice is either 150 mg or 300 mg.

21 How the recommendations might affect practice

- 22 Aspirin is already widely used for this indication and so the recommendation is not
- 23 expected to have a significant impact on practice.
- 24 Full details of the evidence and the committee's discussion are in evidence review
- 25 A1: Effectiveness of aspirin in the prevention of colorectal cancer in people with
- 26 Lynch syndrome.
- 27 Return to recommendations

28 Information needs

29 Recommendations 1.2.1 to 1.2.8

1 Why the committee made the recommendations

- 2 There was evidence that people having treatment for colorectal cancer need different
- 3 information at different stages of their care, and this was supported by the
- 4 committee's own clinical experience as well as NICE's guideline on patient
- 5 experience in adult NHS services.
- 6 The committee based their recommendations on qualitative evidence and their
- 7 clinical experience, which enabled the committee to identify areas where people
- 8 lacked understanding and issues that people would value information on. This
- 9 included explaining colorectal cancer and its treatments in depth, including non-
- 10 surgical treatment options and palliative care, as well as explaining how people can
- alter their diet to reduce bowel problems and manage their weight.
- 12 The committee also agreed it was important to prepare people for the fact that
- 13 changes to the agreed plan are sometimes needed during treatment, and to explain
- what these could be so that people feel ready for this possibility.

15 How the recommendations might affect practice

- 16 Current practice varies between hospitals, so these recommendations aim to reduce
- 17 variation and encourage best practice. There may be a cost to providing training to
- professionals but this is expected to be small and potentially recouped through
- 19 patients being better prepared for treatment and post-treatment.
- 20 Full details of the evidence and the committee's discussion are in evidence review
- 21 E3: Information needs of people prior, during and after treatment for colorectal
- 22 cancer.
- 23 Return to recommendations

24 Treatment for people with early rectal cancer

- 25 Recommendation <u>1.3.1</u>
- 26 Why the committee made the recommendations
- 27 The committee agreed that it was not possible to recommend one treatment over
- another because of the low quality of the evidence and the limited amount of
- 29 evidence available. The available evidence showed no clinically important

- 1 differences between treatments and, in addition, for many of the outcomes specified
- 2 in the protocol and a number of the comparisons, no evidence was identified at all.
- 3 However, based on their knowledge and experience, the committee noted that there
- 4 are risks and benefits associated with each treatment option. They highlighted that
- 5 while total mesorectal excision is a radical intervention and has more risks than the
- 6 others, it is the only way to accurately stage lymph nodes and, by doing so, allow
- 7 better treatment planning. Therefore, the committee recommended discussing the
- 8 implications of each intervention with the person before making a choice.

How the recommendations might affect practice

- 10 Currently, endoscopic submucosal dissection (ESD) is not widely available in the
- 11 UK. In centres where ESD is not already available, resources and time would be
- 12 needed to provide this service, including purchasing equipment and training staff
- 13 although this would be a short-term cost. After this initial investment there will be
- 14 minimal cost difference between ESD and alternatives. TAE (including TAMIS and
- 15 TEMS) and TME are current practice in the UK, so the recommendations will have a
- 16 minimal effect for these interventions. However, the recommendations will allow for
- an informed discussion with patients so they are fully aware of the risks and benefits
- 18 of each procedure.

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- 19 Full details of the evidence and the committee's discussion are in evidence review
- 20 C1: Treatment for early rectal cancer.
- 21 Return to recommendations

22 Preoperative treatment for people with rectal cancer

23 Recommendations 1.3.2 to 1.3.3

- 25 There was no evidence for the effectiveness of preoperative radiotherapy for people
- 26 with early rectal cancer, and based on their experience the committee would not
- 27 recommend preoperative radiotherapy. However, the ongoing STAR-TREC trial,
- which is a multicentre randomised controlled trial, compares radiotherapy to total
- 29 mesorectal excision for early rectal cancer. Because of this, the committee

- 1 recommended that preoperative radiotherapy for early rectal cancer could be
- 2 offered, but only in the context of a clinical trial.
- 3 For rectal cancer T1-T2, N1-N2, M0, or T3-T4, any N, M0, the evidence from several
- 4 RCTs shows that people who have preoperative radiotherapy or chemoradiotherapy
- 5 have less local recurrence and have better overall and disease-free survival
- 6 compared to people who did not have preoperative therapy. Although preoperative
- 7 therapy can potentially have adverse effects, from the evidence the committee did
- 8 not find a difference in quality of life or treatment-related mortality between those
- 9 who did or did not receive preoperative therapy.
- 10 The committee was not able to make a recommendation on the duration and type of
- 11 radiotherapy or chemoradiotherapy because the available evidence did not show a
- difference between short-course and long-course radiotherapy, chemoradiotherapy
- with or without induction chemotherapy, or internal radiotherapy with or without
- 14 external radiotherapy and external radiotherapy alone.

15 How the recommendations might affect practice

- 16 There is some variation in current practice among different multidisciplinary teams as
- to who is offered preoperative therapy. The aim of the recommendation is to
- standardise treatment across the country, so this might have a resource impact in
- areas where preoperative therapy is not currently offered and where more clinical
- 20 oncologists and radiotherapy equipment will be needed. There may be savings
- 21 downstream through reduced recurrence and increased disease-free survival
- 22 avoiding or delaying expensive further treatment.
- 23 The recommendation might increase the number of people offered preoperative
- 24 radiotherapy or chemoradiotherapy for lower-risk tumours (mainly cancers in the
- 25 upper and mid rectum). In current practice, people with cancer in the upper and mid
- 26 rectum might not have preoperative therapy because there is a lower risk of
- 27 recurrence in cancers in these locations compared to cancer in the low rectum.
- 28 Full details of the evidence and the committee's discussion are in evidence review
- 29 C1: Treatment for early rectal cancer and evidence review C2: Preoperative
- radiotherapy and chemoradiotherapy for rectal cancer.

1 Return to recommendations

2	Surgery	/ for	people	with	rectal	cancer
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3	Recommendations	13	4 to	13	5
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4 Why the committee made the recomme		wny the committee	₃ made	tne	recommendation	S
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- 5 Surgery is the preferred treatment for people with rectal cancer (T1-T2, N1-N2, M0,
- 6 or T3-T4, any N, M0) if the tumour is resectable. The committee acknowledged that
- 7 some people whose rectal cancer shows a complete clinical response to
- 8 neoadjuvant therapy choose to defer surgery and opt for an organ preserving 'watch-
- 9 and-wait' strategy instead. The committee agreed that those who choose to defer
- 10 surgery should be entered into a clinical trial or national registry because there was
- 11 no evidence about factors that predict the risk of recurrence. Clinical trials and
- 12 national registries could generate evidence to help a person decide whether to defer
- 13 surgery. Around one third of these people will experience local regrowth of their
- 14 tumour and need salvage surgery.
- 15 The committee were uncertain about how different definitions of complete clinical
- 16 response and different watch-and-wait surveillance protocols would impact risk of
- 17 recurrence. Because of the lack of evidence they recommended that people
- 18 considering deferral of surgery after a complete clinical and radiological response to
- 19 neoadjuvant treatment should be aware of the uncertainty about their outcome.

20 How the recommendations might affect practice

- 21 Deferral of surgery in people whose rectal cancer shows a complete clinical
- 22 response to neoadjuvant therapy is not standard practice in all centres. The watch-
- 23 and-wait approach requires repeated surveillance examinations and endoscopies to
- 24 monitor for tumour regrowth. In some cases, people choosing to defer surgery will
- 25 need to be referred to another centre that can provide the necessary watch-and-wait
- 26 surveillance programme. The recommendations are not expected to have a
- 27 significant impact on practice.
- 28 Full details of the evidence and the committee's discussion are in evidence review
- 29 C4: Deferral of surgery in people having neoadjuvant therapy for rectal cancer for
- 30 <u>rectal cancer.</u>

1 Return to recommendations

2	Surgical	techniqu	e for	people	with	rectal	cancer
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3 Recommendations <u>1.3.6 to 1.3.9</u>

4	Why the	committee	made the	recommendations
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- 5 The NICE technology appraisal on <u>laparoscopic surgery for colorectal cancer</u>
- 6 published in 2006 covers colorectal cancer in general, with evidence largely based
- 7 on mixed (colon and rectal cancer) populations or colon cancer populations. Over
- 8 time, the clinical community has started to treat surgery for colon and rectal cancer
- 9 as separate entities with rectal cancer surgery being considered more challenging. In
- 10 addition, robotic technique and transanal TME have been used in rectal cancer
- surgery. Therefore, it was considered important that new evidence on different
- 12 surgical techniques for rectal cancer specifically be reviewed.
- 13 The clinical evidence on the different surgical techniques for rectal cancer showed
- 14 that the short- and long-term outcomes of laparoscopic technique were similar or
- better than of the open technique and that there seemed to be no difference in
- 16 effectiveness between laparoscopic and robotic techniques. The committee agreed
- 17 that in addition to the clinical effectiveness it was important to consider the costs of
- these difference techniques in order to assess which technique is the most cost
- 19 effective approach in rectal cancer surgery, therefore, a health economic analysis
- was done.
- 21 The evidence showed that laparoscopic surgery is cost effective compared to open
- 22 surgery or robotic surgery. However, in some cases open surgery might be clinically
- 23 more appropriate and laparoscopic surgery might be less feasible, for example
- 24 because of scarring from previous surgeries or technically demanding resection of
- 25 adjacent organs or structures in locally advanced tumours.
- 26 Robotic surgery was not found to be cost effective; however, this technique could be
- 27 considered in centres that have already invested in a robot and have an established
- 28 programme. These programmes should collect outcome data in order to benchmark
- 29 the effectiveness and safety of this technique in clinical practice against other

- 1 centres and techniques. The techniques and equipment of robotic surgery develop
- 2 rapidly and more evidence on its cost effectiveness will be available in the future.
- 3 There is not enough clinical evidence on transanal TME to draw conclusions about
- 4 its safety and effectiveness. However, transanal TME could be considered in centres
- 5 that already have a structured and supervised programme. Outcome data should be
- 6 submitted to a national registry in order to assess the safety and effectiveness of this
- 7 technique in clinical practice. This is in line with NICE interventional procedures
- 8 guidance on <u>transanal total mesorectal excision of the rectum</u>.

9 How the recommendations might affect practice

- 10 There will be more laparoscopic surgery, while recognising that there is a role for
- open surgery in appropriately selected cases. Current robotic techniques were found
- 12 not to be cost effective, so there may be less investment in robotic techniques for
- this indication. However, the recommendation will not affect the use of robotic
- 14 surgery within established programmes. The recommendations are not expected to
- 15 have an impact on the use of transanal TME as these are largely performed within
- 16 structured and supervised programmes in current practice.
- 17 Full details of the evidence and the committee's discussion are in evidence review
- 18 C3: Optimal surgical technique for rectal cancer.
- 19 Return to recommendations

20 People with locally advanced or recurrent rectal cancer

- 21 Recommendation <u>1.3.10</u>
- 22 Why the committee made the recommendations
- 23 Based on their clinical experience, the committee acknowledged that many patients
- 24 are not currently referred to specialist centres and are only offered palliative care
- instead of potentially curative surgery. The committee also noted that pelvic
- 26 exenteration is a complex and invasive procedure.
- 27 However, there was some very low quality evidence that showed people who had
- 28 pelvic exenteration had similar quality of life scores to those who did not, and that the
- 29 procedure improved survival over 12 months. The committee agreed that evidence

- 1 from long-term follow-up of quality of life would help to inform the recommendation,
- 2 but there was no quality of life data available beyond 12 months of follow-up.
- 3 Therefore, the committee could not recommend referring everyone with locally
- 4 advanced or recurrent rectal cancer to have pelvic exenteration, but agreed that
- 5 people should have the opportunity to discuss pelvic exenteration as an option in a
- 6 specialist centre.

7 How the recommendations might affect practice

- 8 The recommendation could increase the number of referrals to specialist centres in
- 9 hospitals where this is not current practice. This would, in turn, increase demand for
- 10 specialist time and mean that more people may go on to have surgery. However, this
- 11 may improve quality of life and survival.
- 12 Full details of the evidence and the committee's discussion are in evidence review
- 13 <u>C5</u>: Effectiveness of exenterative surgery for locally advanced or recurrent rectal
- 14 cancer.

18

15 Return to recommendations

16 Surgical volumes for rectal cancer surgeries

17 Recommendations 1.3.11 to 1.3.12

- 19 Currently, there is uncertainty in the clinical community about optimal hospital and
- 20 surgeon volumes for rectal cancer outcomes, with some clinicians advocating for the
- 21 centralisation of services. There was evidence that when the threshold is set
- between 10 and 20 rectal cancer surgery patients per year, higher volume hospitals
- have better outcomes than lower volume hospitals in terms of overall survival, local
- 24 recurrence, permanent stoma rates and perioperative mortality. Similarly, there was
- evidence of benefit with a surgeon case volume threshold of between 5 and 10
- 26 cases per year in terms of resection margins, local recurrence and permanent stoma
- 27 rates.
- 28 The committee were cautious in their interpretation of the evidence: individual
- 29 studies had used different case volume thresholds and had not treated case volume

- 1 as a continuous outcome, and there were additional complexities with surgeon-level
- 2 data (that is, consultants may do more complex surgeries, but fewer of them, and a
- 3 consultant might be involved with other surgeries but not be the named surgeon) as
- 4 well as with hospital-level data (that is, some studies were old and from outside the
- 5 UK, with inconsistent staging across studies).
- 6 Given the uncertainties in the data, the committee agreed that the evidence was not
- 7 strong enough to recommend a minimum cut-off of 20 cases and instead decided to
- 8 recommend a more conservative cut-off of 10 cases a year.

How the recommendations might affect services

- 10 An audit of rectal cancer surgeries in the UK has indicated that most hospitals in the
- 11 UK perform at least 20 cases of rectal cancer surgery per year. Therefore, the
- 12 recommendation for a minimum threshold of 10 cases per year at hospital level will
- 13 not have a large impact on current practice. Based on their clinical knowledge, the
- committee were aware that some surgeons in the UK currently perform fewer than 5
- operations per year, so the recommendation could have an impact on these
- 16 surgeons. The centralisation of surgeons with fewer surgeons performing more
- 17 cases could have an impact on staffing, although as the overall number of surgeries
- will be the same the overall cost impact should be neutral. There may be an increase
- in the distance patients need to travel for surgery and this will have a cost impact on
- 20 the NHS where this is reimbursed. This cost will be offset by better surgical
- 21 outcomes reducing care-related costs later on and increasing quality of life.
- 22 Full details of the evidence and the committee's discussion are in evidence review
- 23 <u>F1: Surgical volumes and outcomes for rectal cancer.</u>
- 24 Return to recommendations

9

25 Preoperative treatment for people with colon cancer

- 26 Recommendation 1.3.13
- 27 Why the committee made the recommendations
- 28 The committee made the recommendation to consider chemotherapy preoperatively
- 29 for people with T4 colonic cancer based on evidence that it improved survival and

- 1 rates of clear resection margins in these patients. The committee was only able to
- 2 recommend preoperative chemotherapy as an option to consider because the
- 3 evidence was of low quality, despite the large sample size. There was no evidence
- 4 on the effectiveness of preoperative chemotherapy for people with colonic cancers at
- 5 other stages.
- 6 The committee also considered results from FOxTROT: a large international trial
- 7 comparing preoperative plus postoperative chemotherapy (with or without
- 8 panitumab) to standard postoperative chemotherapy in people with T3 or T4a
- 9 resectable tumours. The results showed that complete clinical response and tumour
- downstaging are more likely in those who receive preoperative chemotherapy,
- although follow-up is not yet long enough to show a difference in survival.

12 How the recommendations might affect practice

- 13 The current standard of care is surgical resection with postoperative chemotherapy,
- dependent on the organs or structures involved and the degree of involvement. The
- 15 committee was aware that some centres already give preoperative chemotherapy,
- but noted that this recommendation will affect practice and have a resource impact in
- 17 hospitals where this is not standard practice.
- 18 Full details of the evidence and the committee's discussion are in evidence review
- 19 C7: Preoperative chemotherapy for non-metastatic colon cancer.
- 20 Return to recommendations

21 Duration of adjuvant chemotherapy for people with colorectal

- 22 cancer
- 23 Recommendations 1.3.14

- 25 The benefits and risks of adjuvant chemotherapy can depend on several factors,
- 26 including the stage and characteristics of the cancer, and the person's performance
- 27 status, comorbidities and age.
- 28 Peripheral neuropathy is recognised as a major long-term side effect of oxaliplatin
- 29 chemotherapy and the risk of developing persistent neuropathy increases by

- 1 cumulative dose of treatment. The standard duration of chemotherapy has been 6
- 2 months, but a shorter 3-month course has been investigated.
- 3 There was good evidence that showed 3 months of CAPOX chemotherapy was at
- 4 least as beneficial for people with colon cancer as a 6-month course but caused
- 5 considerably less severe neuropathy and was cost saving. However, with FOLFOX
- 6 chemotherapy, disease-free survival was worse after a 3-month course compared
- 7 with the standard 6-month course, although the rate of severe neuropathy was again
- 8 considerably lower in the 3-month group.
- 9 A recent high quality health economic study found a 3-month course of FOLFOX to
- 10 be cost effective compared to a 6-month course, despite lower disease-free survival,
- as a result of a decrease in costs. Although this economic evidence was directly
- 12 applicable to the clinical question, and the study was included in the consideration of
- 13 the clinical evidence, the committee was concerned that basing recommendations
- solely in line with the economic evaluation (that is, CAPOX for 3 months or FOLFOX
- 15 for 3 months) might lead to people who would otherwise have received 6-month
- 16 FOLFOX to opt for 3-month CAPOX instead.
- 17 In the SCOT trial CAPOX was associated with a higher rate of severe diarrhoea than
- 18 FOLFOX. This was not looked at by the economic evaluation and the 'switching'
- 19 group would likely to be at higher risk of toxicity-related complications with worse
- 20 outcomes, increased treatment-related mortality and increased costs from the
- 21 treatment of severe adverse events than the trial population for 3-month CAPOX.
- 22 This would decrease the certainty of the conclusions of the economic evaluation.
- 23 Based on the balance of benefits and lower risk of long-term adverse effects, the
- 24 committee agreed CAPOX for 3 months should be the first choice of adjuvant
- 25 treatment. If CAPOX is not suitable, for example because of the person's higher risk
- of and lower tolerance for severe diarrhoea, FOLFOX should be offered. Having
- 27 considered the economic evaluation given the clinical concerns, it was decided that
- 28 there should be an individualised consideration for the duration of FOLFOX for those
- 29 who are not suitable for 3-month CAPOX chemotherapy, taking into account the
- 30 benefits and short- and long-term harms of both options, the person's comorbidities,
- 31 performance status and preference.

- 1 Single-agent capecitabine chemotherapy is also an effective adjuvant treatment and
- 2 can be more suitable for people who are older (for example over 70 years) or less fit,
- 3 as it is associated with fewer side effects than chemotherapy treatments that contain
- 4 oxaliplatin.
- 5 The available evidence is mainly for people with colon cancer. However, people with
- 6 rectal cancer who had received either short-course preoperative radiotherapy or no
- 7 preoperative therapy were also included in a large randomised trial and their
- 8 outcomes were similar to people with colon cancer, and therefore the committee
- 9 agreed the recommendation could also apply to this population.
- 10 No recommendations were made for people with rectal cancer who have been
- 11 treated with long-course chemotherapy or chemoradiotherapy because no evidence
- was identified in the available trials.

13 How the recommendations might affect practice

- 14 Halving the standard care from 6 months to 3 months (for people who can have
- 15 CAPOX) will reduce treatment time and costs, will mean people have chemotherapy
- side effects for a shorter time, and will lower the incidence of long-term toxicity
- 17 (neuropathy) and its consequences.
- 18 Full details of the evidence and the committee's discussion are in evidence review
- 19 C8: Optimal duration of adjuvant chemotherapy for colorectal cancer.
- 20 Return to recommendations

21 Colonic stents in acute large bowel obstruction

22 Recommendations <u>1.3.15 to 1.3.16</u>

- 24 In patients presenting with acute left-sided large bowel obstruction, evidence showed
- 25 that stoma rates were reduced in the stenting group compared to the emergency
- surgery group. There was no evidence of a difference in overall or disease-free
- 27 survival. Stenting also allows time to fully assess the patient and stabilise any
- 28 comorbidities before proceeding with potentially curative surgery. The committee

- 1 considered the yet to published results of the CREST trial shared with the committee
- 2 in confidence which were consistent with the published evidence.
- 3 The committee noted the evidence that stenting sometimes causes perforation and
- 4 is not always technically successful and so may not be appropriate in all cases for
- 5 the curative intent treatment group. For this reason they also recommended
- 6 emergency surgery as an option.

7 How the recommendations might affect practice

- 8 Stenting is established practice for patients presenting with acute left-sided large
- 9 bowel obstruction who are to be treated with palliative intent. Stenting is not
- 10 established practice in those to be treated with curative intent. Therefore, the
- 11 recommendation could lead to an increase in the provision of stenting and
- 12 associated costs. However, stenting allows patients to be assessed and become
- 13 stable before surgery, in turn reducing operative morbidity, the need for stoma and
- preventing expensive surgery in those people when it would not be appropriate, thus
- reducing downstream costs. Some patients might need to be transferred to another
- 16 unit in order to receive a stent.
- 17 Full details of the evidence and the committee's discussion are in evidence review
- 18 C9: Effectiveness of stenting for acute large bowel obstruction.
- 19 Return to recommendations

20 Molecular biomarkers to guideline systemic anti-cancer therapy

- 21 Recommendation <u>1.4.1</u>
- 22 Why the committee made the recommendations
- 23 The evidence showed that RAS and BRAF V600E mutations were predictive of
- 24 response to anti-EGFR targeted therapy in people with metastatic colorectal cancer.
- 25 People with RAS or BRAF V600E mutant metastatic colorectal cancer also had
- 26 poorer progression-free and overall survival than those without such mutations.
- 27 While RAS testing is already used to select those people with metastatic colorectal
- 28 cancer most likely to benefit from anti-EGFR targeted therapy, BRAF V600E testing
- 29 has the potential to further refine this group.

- 1 The committee noted evidence that testing for deficient DNA mismatch repair may
- 2 inform systemic therapy choices for those with non-metastatic colorectal cancer, but
- 3 NICE diagnostics guidance on molecular testing strategies for Lynch syndrome in
- 4 <u>people with colorectal cancer</u> already recommends such testing for all people with
- 5 colorectal cancer when first diagnosed. For this reason no further recommendations
- 6 were made about testing for deficient DNA mismatch repair.

7 How the recommendations might affect practice

- 8 RAS testing is current practice. BRAF V600E testing is not done routinely in current
- 9 practice. BRAF V600E test can be done from the extended colorectal cancer
- 10 molecular test panel which is part of the recommendations in NICE diagnostics
- 11 guidance on molecular testing strategies for Lynch syndrome in people with
- 12 <u>colorectal cancer</u>, so the recommendation should not have a large impact on
- 13 practice or costs.
- 14 Full details of the evidence and the committee's discussion are in evidence review
- 15 <u>B1: Use of molecular biomarkers to guide systemic therapy.</u>
- 16 Return to recommendations

17 **People with asymptomatic primary tumour**

- 18 Recommendation <u>1.5.1</u>
- 19 Why the committee made the recommendations
- 20 For people with incurable metastatic colorectal cancer whose primary tumour is
- 21 asymptomatic, there was some low quality evidence of better overall survival in
- 22 those who had resection of their primary tumour and chemotherapy compared with
- 23 chemotherapy alone.
- 24 Around a quarter of this group had postoperative complications and a small
- 25 proportion (around 5%) had severe postoperative complications which needed
- intervention or were life-threatening. However, resecting the tumour at this stage can
- 27 prevent symptoms from developing later: almost a fifth of people who did not have
- 28 the asymptomatic primary tumour resected went on to develop primary tumour-
- 29 related symptoms that needed surgical treatment which could often mean an

- 1 emergency operation that can have higher risks of complications and stoma.
- 2 Because of this, the committee agreed the implications should be discussed with the
- 3 person so they can make an informed decision.
- 4 How the recommendations might affect practice
- 5 There could be an increase in resections of asymptomatic primary tumours,
- 6 however, the population with metastatic colorectal cancer and asymptomatic primary
- 7 tumour is small so no major cost impact is expected.
- 8 Full details of the evidence and the committee's discussion are in evidence review
- 9 D1: Surgery for asymptomatic primary tumour.
- 10 Return to recommendations
- 11 Systemic anti-cancer therapy for people with metastatic colorectal
- 12 cancer
- 13 Recommendation 1.5.2
- 14 Why the committee made the recommendations
- 15 Guidance on systemic anti-cancer therapy for people with metastatic colorectal
- 16 cancer are covered by NICE technology appraisals and were not updated by this
- 17 guideline. The committee did not review the technology appraisals and merely refers
- to them without a suggestion of an order or hierarchy of treatment. The technology
- 19 appraisals should be used when appropriate to guide the choice of systemic anti-
- 20 cancer therapy.
- 21 How the recommendations might affect practice
- The recommendation reflects current practice and no change in practice is expected.
- 23 Return to recommendations
- 24 People with metastatic colorectal cancer in the liver
- 25 Recommendations 1.5.3 to 1.5.6

- 2 There was not enough evidence to show if simultaneous or sequential resection is
- 3 better. There was some poor quality evidence from retrospective cohort studies
- 4 showing that people who underwent sequential resection had better liver
- 5 progression-free survival. However, these results might be influenced by baseline
- 6 differences between the groups, and there was no difference in recurrence in other
- 7 parts of the body or in overall survival in several studies. There was no difference in
- 8 short-term adverse events and no evidence on quality of life was available. Based on
- 9 these findings and their experience, the committee agreed that a multidisciplinary
- 10 team with expertise in both colorectal and liver disease should consider if a
- simultaneous or a sequential resection is appropriate, taking into account the
- 12 person's preference.

- 13 Evidence from randomised trials suggested that chemotherapy in addition to liver
- 14 resection improves disease-free survival and may improve overall survival. The
- potential benefit on survival should be balanced with a higher rate of treatment-
- 16 related adverse events because of added chemotherapy. No quality of life evidence
- 17 was available.
- 18 The evidence on chemotherapy combined with radiofrequency ablation showed
- 19 better overall survival and progression-free survival compared to chemotherapy
- 20 alone. No difference was observed in treatment-related mortality and morbidity. The
- 21 evidence on quality of life was too limited for the committee to draw any conclusions.
- 22 The evidence on survival came from a single small study and the committee had
- 23 doubts about its relevance to current practice. Because of the uncertainties in the
- 24 evidence, the committee recommended considering chemotherapy with local
- 25 ablative techniques as an option for people whose liver metastases are determined
- 26 by the MDT to be unresectable but potentially curable. The evidence was on
- 27 radiofrequency ablation which is still used but in many centres has been largely
- 28 replaced by newer local ablative techniques, such as microwave ablation (see the
- 29 NICE interventional procedures guidance on microwave ablation for treating liver
- 30 metastases). Therefore, the committee agreed that it is more appropriate that local
- 31 ablative techniques, not only radiofrequency ablation, are considered.

- 1 Evidence from several randomised controlled trials did not show any benefit on
- 2 overall survival from SIRT as a first-line treatment for people with colorectal liver
- 3 metastases. Limited evidence was available on the effectiveness of SIRT for people
- 4 refractory or intolerant to standard chemotherapy and the committee was not able to
- 5 make a recommendation.

6 How the recommendations might affect practice

- 7 The recommendations largely reflect current practice and no substantial change in
- 8 practice is expected.
- 9 Full details of the evidence and the committee's discussion are in evidence review
- 10 D2a: Treatment for metastatic colorectal cancer in the liver amenable to treatment
- 11 with curative intent and evidence review D2b: Treatment for metastatic colorectal
- cancer in the liver not amenable to treatment with curative intent.
- 13 Return to recommendations

14 People with metastatic colorectal cancer in the lung

15 Recommendations 1.5.7 to 1.5.8

- 17 As there was limited evidence, the committee made recommendations based on
- 18 their clinical knowledge. There was not enough evidence to recommend one
- 19 treatment over another even though the current first choice is to perform surgery
- 20 over stereotactic body radiation therapy or ablation. Referring people to
- 21 multidisciplinary teams that specialise in primary lung disease may not be
- 22 appropriate as they do not specialise in the management of lung metastases from
- 23 colorectal cancer. Therefore, the committee agreed that the multidisciplinary team
- 24 should include a thoracic surgeon and a specialist in non-surgical ablation to ensure
- 25 that the appropriate specialist knowledge is available.
- 26 Based on their clinical knowledge, the committee recommended that biopsies should
- 27 be considered for patients with a single lung lesion to rule out primary lung cancer
- and guide treatment options even if surgical excision is not planned.

- 1 Because of the lack of clinical evidence, a randomised trial comparing surgical to
- 2 non-surgical treatment is needed to provide more high quality, comparative data, so
- 3 the committee made a research recommendation on this topic.

4 How the recommendations might affect practice

- 5 The recommendations are expected to increase the involvement of thoracic
- 6 surgeons in the management of metastatic colorectal cancer, however this additional
- 7 expertise would result in expensive treatments being more appropriately targeted.
- 8 While assessing fitness for surgery is common practice, the advice to also discuss
- 9 factors including disease-free interval, CEA level, number, size and site of
- metastases and other sites of disease should improve best practice across the NHS.
- 11 Full details of the evidence, the committee's discussion and the recommended
- 12 approach to research are in evidence review D3: Treatment for metastatic colorectal
- cancer in the lung amenable to local treatment.
- 14 Return to recommendations

15 People with metastatic colorectal cancer in the peritoneum

16 Recommendation 1.5.9

- 18 The committee made the recommendations based on both the evidence and their
- 19 clinical knowledge. The advice to offer chemotherapy and refer to a specialist
- 20 cytoreductive surgery centre is in the same recommendation because these
- 21 interventions should happen at the same time. That is, making a referral should not
- 22 wait until chemotherapy has been given, and chemotherapy could be started before
- the person is reviewed in the specialist centre.
- 24 It is standard practice to start all patients on a course of systemic anti-cancer therapy
- and the evidence supported this, showing greater overall survival compared to
- 26 supportive care. The evidence on the effectiveness of cytoreductive surgery and
- 27 HIPEC was mixed but, based on their clinical knowledge, the committee decided
- 28 they should be considered.

- 1 The committee agreed it was important to recommend referral to a specialist centre
- 2 so that more patients can have potentially curative treatment. However, they were
- 3 concerned that this might lead to more centres offering the service without having
- 4 the necessary training and resources, so referral to recognised specialist centres
- 5 was recommended instead. This recommendation is in line with the NICE
- 6 interventional procedure guidance on cytoreductive surgery followed by HIPEC for
- 7 peritoneal carcinomatosis.

8 How the recommendations might affect practice

- 9 It is standard practice for clinicians to initially offer chemotherapy to patients who are
- 10 fit, and if their cancer responds to systemic chemotherapy (that is, the person has
- 11 limited disease that has been stable over a period of time) cytoreductive surgery and
- 12 HIPEC might be suitable. Currently there are only 3 funded centres in England that
- 13 provide cytoreductive surgery and HIPEC. The recommendation could lead to an
- 14 increase in workload in these specialist centres as more patients would be referred
- to the currently funded centres and a proportion of those will be suitable for
- 16 cytoreductive surgery with HIPEC, although this would be offset by reductions at
- 17 other centres.
- 18 Full details of the evidence and the committee's discussion are in evidence review
- 19 D4: Local and systemic treatments for metastatic colorectal cancer isolated in the
- 20 peritoneum.
- 21 Return to recommendations

22 Follow-up for detection of local recurrence and distant metastases

23 Recommendation 1.6.1

- 25 Evidence showed that recurrent disease was more likely to be resectable when
- 26 patients received regular follow-up tests than with minimal or no follow-up. Evidence
- 27 also showed recurrent disease was more likely to be resectable when follow-up tests
- 28 included CEA and liver imaging. The 2011 NICE guideline on colorectal cancer
- 29 (updated and replaced by this guideline) recommended CEA and CT testing in the
- 30 first 3 years after treatment with curative intent, and the committee did not find

- 1 evidence to change this. Colonoscopic surveillance to detect metachronous
- 2 colorectal neoplasia was outside the scope of this guideline. The British Society of
- 3 Gastroenterology (BSG) and the Association of Coloproctology for Great Britain and
- 4 Ireland (ACPGBI) are currently updating guidance on this topic.
- 5 How the recommendations might affect practice
- 6 The recommendation reflects current practice so the committee agreed there should
- 7 be no change in practice.
- 8 Full details of the evidence and the committee's discussion are in evidence review
- 9 E1: Follow-up to detect recurrence after treatment for non-metastatic colorectal
- 10 cancer.
- 11 Return to recommendations
- 12 Management of low anterior resection syndrome
- 13 Recommendations <u>1.6.2 to 1.6.4</u>
- 14 Why the committee made the recommendations
- 15 Based on their experience, the committee agreed LARS can have a significant
- impact on a person's quality of life and daily functioning, so it is important to identify
- 17 and treat it quickly. Because LARS may only become apparent after discharge from
- hospital, it is important that LARS is identified in primary care and people who have
- 19 had sphincter-preserving surgery are aware of its symptoms.
- 20 LARS should be assessed using a validated tool, for example the LARS score, which
- 21 is a validated patient-administered questionnaire.
- 22 No comparative evidence on different treatments for LARS was available, so the
- 23 committee agreed based on their experience that people with LARS should be
- 24 offered symptomatic treatment in primary care. The committee also agreed that if
- 25 treatments offered in primary care have not helped within 6 months, advice should
- 26 be sought from secondary care to discuss further options and consider specialist
- 27 input.

- 1 Because of the lack of evidence on the effectiveness of treatments for LARS, a
- 2 research recommendation was made to compare sacral nerve stimulation and
- 3 transanal irrigation in people with LARS for whom conservative treatments have not
- 4 worked.

5 How the recommendations might affect practice

- 6 Primary care clinicians are not necessarily aware of LARS or how to assess it, and
- 7 administering the questionnaire might need extra work and time. However, it is
- 8 patient-administered and easy to score and no training should be needed. Bowel
- 9 dysfunction treatment for associated symptoms are commonly delivered in primary
- 10 care, therefore, the recommendation is not expected to have a large impact on
- 11 current practice except raising awareness of LARS.
- 12 Full details of the evidence, the committee's discussion and the recommended
- 13 approach to research are in evidence review E2: Optimal management of low
- 14 <u>anterior resection syndrome.</u>
- 15 Return to recommendations

16 Context

- 17 Colorectal cancer (cancer of the colon or rectum, or bowel cancer) is the fourth most
- 18 common cancer in the UK, with over 41,000 new cases diagnosed each year
- 19 according to Cancer Research UK. Risk factors include increasing age, genetics and
- 20 family history (particularly syndromes such as familial adenomatous polyposis and
- 21 Lynch syndrome), inflammatory bowel disease and other dietary and lifestyle factors.
- 22 Survival rates have improved over the years, with almost 60% of the people
- 23 diagnosed with colorectal cancer surviving for at least 5 years. Survival is linked to
- 24 disease stage at presentation, with better survival the earlier the disease is detected
- and treated.
- 26 People with Lynch syndrome have an increased risk of colorectal cancer, with
- 27 lifetime risk estimated to be between around 50 to 80%⁵. The main strategy to

Colorectal cancer (update): NICE guideline DRAFT (August 2019)

⁵ Kohlmann W, Gruber SB. Lynch Syndrome. 2004 (updated 2018). In: Adam MP, Ardinger HH, Pagon RA, et al., (eds). GeneReviews. University of Washington, Seattle, WA; 1993–2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1211/

- 1 prevent colorectal cancer in people with Lynch syndrome has been regular screening
- 2 with colonoscopy and polypectomy. Aspirin has been suggested as another potential
- 3 prevention strategy for colorectal cancer.
- 4 Diagnosis and staging of colorectal cancer are well established with histology and
- 5 appropriate imaging, and are not covered by this guideline.
- 6 Management of colorectal cancer has advanced over time with new treatment
- 7 methods and strategies being trialled and used. Management of local disease differs
- 8 depending on the site of the cancer. The standard practice for colon cancer is to
- 9 offer surgery for those who are fit for it. Recent trials have studied the effectiveness
- of preoperative systemic anti-cancer therapy for colon cancer to improve survival.
- 11 Treatment for rectal cancer is more complex. There is variation in current practice in
- the treatment for early rectal cancer, use of preoperative (chemo)radiotherapy,
- 13 surgical technique for rectal cancer surgery, and treatment for locally advanced or
- 14 recurrent rectal cancer. This guideline addresses all these issues. Until now, the
- 15 standard duration of adjuvant systemic therapy for colorectal cancer has been 6
- 16 months, which has been recently challenged by suggestion of a shorter duration in
- 17 order to lower toxicity caused by the treatment.
- 18 Metastatic colorectal cancer commonly affects the liver, lungs or peritoneum.
- 19 Treatment for metastatic colorectal cancer depends on, for example, the site and
- 20 number of the metastases and if the metastases are amenable to local treatment. In
- 21 addition, the role of molecular biomarkers in predicting effectiveness of systemic
- 22 anti-cancer therapy has been discussed more and more in recent years.
- 23 People who have been treated for colorectal cancer may have long-term side effects
- of their treatments. For example, low anterior resection syndrome can have major
- impact on quality of life and daily living and it affects around 40% of those who have
- 26 undergone sphincter-preserving surgery for rectal cancer. It is important that the
- 27 treatment options, their implications and potential consequences are discussed with
- 28 together with the person with colorectal cancer in order to enable shared decision
- 29 making.

1 Finding more information and resources

- 2 To find out what NICE has said on topics related to this guideline, see our web page
- 3 on colorectal cancer.

4 Update information

- 5 This guideline is an update of NICE guideline CG131 (published November 2011)
- 6 and NICE guideline CSG5 (published June 2004) and will replace them.
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