
Surveillance report
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# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surveillance decision</td>
<td>3</td>
</tr>
<tr>
<td>Reason for the decision</td>
<td>3</td>
</tr>
<tr>
<td>Commentary on selected new evidence</td>
<td>6</td>
</tr>
<tr>
<td>Management of metastatic disease – positron emission tomography (PET) and PET-CT</td>
<td>6</td>
</tr>
<tr>
<td>Ongoing care and support – methods of follow-up</td>
<td>8</td>
</tr>
<tr>
<td>Multidisciplinary teams – surgeon and hospital surgical volume</td>
<td>10</td>
</tr>
<tr>
<td>How we made the decision</td>
<td>15</td>
</tr>
<tr>
<td>New evidence</td>
<td>15</td>
</tr>
<tr>
<td>Views of topic experts</td>
<td>16</td>
</tr>
<tr>
<td>Views of stakeholders</td>
<td>16</td>
</tr>
<tr>
<td>NICE Surveillance programme project team</td>
<td>16</td>
</tr>
</tbody>
</table>
Surveillance decision

We will plan an update of the guideline on colorectal cancer (NICE guideline CG131). An extension to the scope of NICE guideline CG131 will be needed to cover areas covered by the guidance on improving outcomes in colorectal cancer (NICE guideline CSG5) that have not been superseded by other NICE guidance.

We will withdraw NICE guideline CSG5 on publication of the update of the colorectal cancer guideline.

Reason for the decision

New evidence that could affect recommendations was identified. Topic experts, including those who helped to develop the guideline, advised us about whether the guidance should be updated.

Improving outcomes in colorectal cancer

For surveillance of NICE guideline CSG5, we looked only for studies about the effects of volume of colorectal cancer surgeries performed by surgeons or by hospitals and found 52 new studies. We also checked whether recommendations in NICE guideline CSG5 have been superseded by other NICE guidance.

Decision: The question about the volume of colorectal cancer surgeries should be included in an update of NICE guideline CG131. Much of CSG5 has been superseded by other NICE guidance. The remaining areas of NICE guideline CSG5 not covered in other NICE guidance should also be covered by the update of NICE guideline CG131. NICE guideline CSG5 should be withdrawn when the updated guidance is published.

Colorectal cancer

We found 329 new studies through surveillance of this guideline. The new evidence was thought to have a potential impact on the following sections of the guideline:

Investigation, diagnosis and staging

- What is the most effective diagnostic intervention for patients with suspected colorectal cancer to establish a diagnosis?
• For patients diagnosed with primary colorectal cancer, what is the most effective technique in order to accurately stage the disease (excluding pathology)?

Management of local disease

• For patients who have undergone local excision and diagnosed stage I colorectal cancer, including/or polyp cancer and with/without neoadjuvant treatment for low rectal tumours, can the use of prognostic factors determine the most effective curative treatment?

• In patients with clinical or pathological stage II and III rectal cancer what is the effectiveness of adjuvant chemotherapy following surgery?

Management of metastatic disease

• In patients with colorectal cancer presenting with overt synchronous metastatic disease, what is the effectiveness of treating metastatic disease before, after or at the same time as treating the primary tumour?

• In a patient with colorectal cancer metastasised to the liver which imaging modality most accurately determines the number and extent of metastases preoperatively?

• In a patient with colorectal cancer and extrahepatic metastases (for example, lung, brain, peritoneum), which imaging modality most accurately determines the extent of metastases?

• Capecitabine and tegafur with uracil.

Ongoing care and support

• In asymptomatic patients who have undergone treatment with curative intent for colorectal cancer, what is the optimal method, frequency and duration of follow-up?

Areas not currently covered by NICE guideline CG131

• What is the role of aspirin in primary and secondary prevention of colorectal cancer, including hereditary colorectal cancer?

• What surgical procedures, techniques, and perioperative interventions improve operative outcomes after surgery for colorectal cancer?

Other clinical areas

For any new evidence relating to published or ongoing NICE technology appraisals, the guideline surveillance review deferred to the technology appraisal decision.
Overall decision

After considering all the new evidence and views of topic experts, we decided that a full update of NICE guideline CG131 is necessary. For NICE guideline CSG5, the evidence relating to surgeon and hospital volumes of colorectal cancer surgeries was also thought to need an update. Checks showed that much of NICE guideline CSG5 has been superseded by other NICE guidance (mainly NICE guideline CG131). We decided that any areas of NICE guideline CSG5 that have not been covered in other guidance should be covered by the update of NICE guideline CG131, resulting in one new guideline.

See how we made the decision for further information.
Commentary on selected new evidence

With advice from topic experts we selected 3 studies for further commentary.

Management of metastatic disease – positron emission tomography (PET) and PET-CT

We selected the systematic review and meta-analysis by Maffione et al. (2015) for a full commentary because it adds useful new data to the evidence base reviewed for NICE guideline CG131, which could impact on current recommendations on imaging.

What the guideline recommends

NICE guideline CG131 recommends CT scanning as initial imaging for metastatic colorectal cancer and use of additional imaging is recommended depending on the site of the metastasis and treatment options, including:

- If the CT scan shows metastatic disease only in the liver and the patient has no contraindications to further treatment, a specialist hepatobiliary MDT should decide if further imaging to confirm surgery is suitable for the patient – or potentially suitable after further treatment – is needed.

- If the CT scan shows the patient may have extra-hepatic metastases that could be amenable to further radical surgery, an anatomical site-specific MDT should decide whether a PET-CT scan of the whole body is appropriate.

Methods

Maffione et al. (2015) reported a systematic review and meta-analysis of 18 studies (n=1059) of PET-CT (or PET) in staging of liver metastasis from colorectal cancer. The authors extracted data to 2x2 contingency tables and calculated the accuracy of PET-CT per patient and per lesion using pathology as the reference standard. The performance of PET-CT was then compared with other imaging methods and its effect on management was assessed.

Articles assessing PET-CT for initial staging or after chemotherapy were included. Articles about PET-CT used for restaging after surgery or in follow-up were excluded from the review.
Results

Overall, 4 studies reported patient-based analysis (n=484) and 4 studies reported lesion-based analysis (575 lesions). For patient based analysis, pooled sensitivity of PET-CT was 93% (95% confidence interval [CI] 88 to 96%) and pooled specificity was 93% (95% CI 84 to 98%). For lesion-based analysis the pooled sensitivity was 60% (95% CI 55 to 64%) and pooled specificity was 79% (95% CI 68 to 87%).

PET-CT was compared with other imaging modalities in 12 studies. In patient-based analysis, MRI had pooled sensitivity of 100% (3 studies) and CT had sensitivity of 95% and 100% (in 1 study each). Few studies reported specificity because many lesions considered to be benign were not resected. However, in the studies that did report patient-based specificity, it was 70% for both CT and MRI (1 study each). In lesion-based analysis, MRI had mean sensitivity of 89% (range 82–96%; 4 studies) and CT had sensitivity of 79% (range 69–98%; 3 studies). Specificity was 81% for MRI and 67% for CT (1 study each).

Compared with CT and MRI, PET-CT changed management in 9–42% of patients (mean 24%; 12 studies), and metastasis other than in the liver was detected in 0–68% of patients (14 studies). False-positive results for metastasis outside the liver occurred in 1–10% of patients (8 studies) and false-negative results occurred in 3–6% of patients (4 studies).

Strengths and limitations

Strengths

Strengths of this systematic review and meta-analysis included assessing the risk of bias of the included studies. Problems with the original data that restricted the possible analyses were reported clearly (for example, that few studies reported specificity).

Limitations

The reported problems with the original data available for analysis in the comparison of PET-CT and other imaging methods meant that robust meta-analysis was not possible. The type of analysis (patients or lesions) was not reported in 4 studies comparing PET with other imaging. In quality assessment, about half of studies had high risk of patient selection bias and about half were not clear how reference tests were performed or interpreted.

The search strategy for this systematic review and meta-analysis was limited because the authors searched only PubMed and Medline, which are interfaces of the same database.
Impact on guideline

Of the 12 included studies, 7 were published after the evidence review for the guideline. However, the finding of high sensitivity and specificity (both 93%) for PET-CT is fairly consistent with the evidence reviewed during development of the guideline.

During guideline development there was a lack of evidence around avoiding futile surgeries. The finding in this systematic review that management was changed in almost a quarter of cases, often a move from attempting curative surgery to palliative care, adds useful information.

Additionally, this study suggests that separate recommendations for people whose CT scan shows only liver metastasis or extra-hepatic metastasis may not be justified because PET may detect additional extra-hepatic disease.

Ongoing care and support – methods of follow-up

We selected the randomised controlled trial by Primrose et al. (2014) for a full commentary because it is a large UK-based clinical trial relevant to NICE guideline CG131 and the findings could impact on recommendations for follow-up.

What the guideline recommends

After treatment for colorectal cancer, NICE guideline CG131 recommends offering patients regular surveillance with:

- a minimum of 2 CTs of the chest, abdomen, and pelvis in the first 3 years and
- regular serum carcinoembryonic antigen (CEA) tests (at least every 6 months in the first 3 years).

Methods

Primrose et al. (2014) conducted a randomised controlled trial (n=1202) in 39 NHS hospitals in the UK assessing methods of follow-up for 5 years after curative treatment for colorectal cancer (stages 1–3). The primary outcome was surgical treatment for recurrence with curative intent after at least 3 years of follow-up. Secondary outcomes were mortality, time to detecting recurrence and survival after treatment with curative intent.

The methods assessed were:
• CEA follow-up every 3 months for 2 years (1 CT of the chest, abdomen and pelvis was allowed at 12–18 months if requested by the treating clinician at trial entry).
  - If a participant had CEA more than 7 micrograms/litre higher than their level at the start of the trial, a second test was done as soon as possible. If this test also crossed the threshold, the participant was referred urgently to the local hospital.

• CT follow-up of chest, abdomen and pelvis every 6 months for 2 years with colonoscopy at 2 years.

• Minimum follow-up (no scheduled follow-up although 1 CT of the chest, abdomen and pelvis was allowed at 12–18 months if requested by the treating clinician at trial entry).

Participants had 2 independent random allocations: to CEA follow-up or minimum follow-up; and to CT follow-up or minimum follow-up. This resulted in 4 groups: CEA follow-up (n=300), CT follow-up (n=299), CEA plus CT follow-up (n=302), and minimum follow-up (n=301). All participants were offered colonoscopy at 5 years.

Participants needed to be free of residual disease, including microscopically clear margins and no evidence of metastasis, with post-treatment blood CEA levels of 10 micrograms/litre or lower. Exclusion criteria included serious concurrent illness, hereditary colon cancer, or participating in a trial of primary treatment that had conflicting follow-up requirements. People younger than 50 years and those who had completed treatment more than 6 months from entering the trial were included if the chief surgical investigator agreed.

Results

During mean observation of 4.4 years, recurrence was seen in 16.6% (95% CI 14.5 to 18.7%) of participants. Recurrence was not detected significantly quicker in the active follow-up groups compared with minimum follow-up. Overall, 5.9% (95% CI 4.6 to 7.2%) of participants had further treatment with curative intent. A significantly smaller proportion of people in the minimum follow-up group had further treatment with curative intent (2.3%) than in the active follow-up groups (6.6–8.0%, p=0.02). In the minimum follow-up group, none of the recurrences detected after 2 years were treatable with curative intent. Recurrence was detected by follow-up in two-thirds of cases, the rest were found incidentally or because the participant had symptoms. There was no significant difference in total deaths in the groups having surveillance with CEA (18.7%), CT (20.1%) or CEA plus CT (15.9%) compared with minimum follow-up (15.9%, p=0.45). There was also no significant difference in deaths attributed to colorectal cancer in the groups having surveillance with CEA (10.7%), CT (11.7%) or CEA plus CT (8.9%) compared with minimum follow-up (9.3%, p=0.66).
Strengths and limitations

**Strengths**

The main strength of this study was that it clearly described the methods used and that it was at low risk of bias in randomisation or allocation concealment. It also clearly reported both intention-to-treat and per-protocol analyses.

**Limitations**

A limitation of the study was that it changed its primary outcome from overall survival to surgery with curative intent during the study when investigators noted that they would not be able to recruit enough patients to have statistical power to detect a difference in survival. Although this was clearly reported by the authors, being able to pick a new primary outcome during the trial introduces potential bias if results for that outcome were expected to be statistically significant.

Of the detected recurrences, 64% did not have curative treatment but the authors did not provide information on what palliative treatments, if any, were offered to those people.

**Impact on guideline**

Current guidance recommends less intensive follow-up than was studied in this trial, but uses the same main methods (CEA testing and CT). This study raises the possibility that detecting and treating recurrent cancer with curative intent may not have any effect on overall deaths or on deaths from colorectal cancer. Therefore, this study may have a potential impact on the guideline.

**Multidisciplinary teams – surgeon and hospital surgical volume**

We selected the Cochrane review by Archampong et al. (2012) for a full commentary because it covers a large number of relevant studies and looked at both surgeon volume and hospital volume, which are relevant to NICE guideline CSG5.

**What the guideline recommends**

NICE guideline CSG5 recommends that each surgeon in the multidisciplinary team should carry out a minimum of 20 colorectal resections with curative intent per annum.
Methods

Archampong et al. (2012) conducted a Cochrane review of 54 observational studies (n=943,728) assessing the effects of surgeon caseload and hospital volume on outcomes after surgery for colorectal cancer. Outcomes for colon and rectal cancers were analysed separately if possible. The primary outcomes were 5-year overall or cancer-specific survival and operative mortality rate. Studies conducted after 1990 only were included to represent modern surgical practices.

Results

Hospital volume

For studies that did not adjust for case-mix assessing 5 year survival:

- 5-year survival after colorectal cancer surgery was significantly greater in high-volume hospitals (hazard ratio [HR] for death= 0.88, 95% CI 0.80 to 0.98; 2 studies, n=36,858).

- 5-year survival after colon cancer surgery was not significantly greater in high volume hospitals (HR for death=0.94, 95% CI 0.84 to 1.04; 3 studies, n=22,464).

- 5-year survival after rectal cancer surgery was not significantly greater in high volume hospitals (HR for death=0.92, 95% CI 0.79 to 1.07; 7 studies, n=13,021).

- 5-year survival after colorectal, colon, and rectal surgery combined was not significantly greater in high volume hospitals (HR for death=0.92, 95% CI 0.81 to 1.04; 10 studies, n=72,343).

For studies that did adjust for case-mix assessing 5 year survival:

- 5-year survival after colorectal cancer surgery was significantly greater in high-volume hospitals (HR for death 0.90, 95% CI 0.84 to 0.95; 2 studies, n=36,858).

- 5-year survival after colon cancer surgery was not significantly greater in high volume hospitals (HR for death=0.97, 95% CI 0.77 to 1.22; 2 studies, n=5211).

- 5-year survival after rectal cancer surgery was significantly greater in high volume hospitals (HR for death =0.85, 95% CI 0.77 to 0.93; 4 studies, n=5100).

- 5 year survival after colorectal, colon, and rectal surgery combined was significantly greater in high volume hospitals (HR for death=0.90, 95% CI 0.85 to 0.96; 3 studies, n=55,169).

For studies that did not adjust for case-mix assessing operative mortality:
Operative mortality after colorectal cancer surgery was not significantly lower in high-volume hospitals (OR=0.74, 95% CI 0.55 to 1.00; 7 studies, n=113,795).

Operative mortality after colon cancer surgery was significantly lower in high-volume hospitals (OR=0.75, 95% CI 0.67 to 0.83; 14 studies, n=309,693).

Operative mortality after rectal cancer surgery was not significantly lower in high-volume hospitals (OR=0.75, 95% CI 0.54 to 1.05; 7 studies, n=18,383).

Operative mortality after colorectal, colon, and rectal surgery combined was not significantly lower in high-volume hospitals (OR=0.75, 95% CI 0.68 to 0.84; 28 studies, n=72,343).

For studies that did adjust for case-mix assessing operative mortality:

- Operative mortality after colorectal cancer surgery was not significantly lower in high-volume hospitals (OR=0.98, 95% CI 0.79 to 1.20; 3 studies, n=77,823).

- Operative mortality after colon cancer surgery was not significantly lower in high-volume hospitals (OR=0.90, 95% CI 0.79 to 1.03; 8 studies, n=302,978).

- Operative mortality after rectal cancer surgery was not significantly greater in high-volume hospitals (OR=1.07, 95% CI 0.76 to 1.50; 7 studies, n=33,747).

- Operative mortality after colorectal, colon, and rectal surgery combined was not significantly lower in high-volume hospitals (OR=0.95, 95% CI 0.85 to 1.05; 17 studies, n=414,548).

Surgeon volume

For studies that did not adjust for case-mix assessing 5 year survival:

- 5-year survival after colorectal cancer surgery was significantly greater with high-volume surgeons (HR for death=0.86, 95% CI 0.82 to 0.90; 2 studies, n=17,232).

- 5-year survival after colon cancer surgery was not significantly greater with high-volume surgeons (HR for death=0.85, 95% CI 0.71 to 1.02; 2 studies, n=3670).

- 5-year survival after rectal cancer surgery was significantly greater with high-volume surgeons (HR for death=0.85, 95% CI 0.78 to 0.94; 3 studies, n=3279).

- 5-year survival after colorectal, colon, and rectal surgery combined was significantly greater with high-volume surgeons (HR for death=0.85, 95% CI 0.81 to 0.90; 7 studies, n=24,181).
For studies that did adjust for case-mix assessing 5 year survival:

- 5-year survival after colorectal cancer surgery was significantly greater with high-volume surgeons (HR for death=0.87, 95% CI 0.82 to 0.92; 2 studies, n=17,232).

- 5-year survival after colon cancer surgery was significantly greater with high-volume surgeons (HR for death=0.84, 95% CI 0.76 to 0.93; 1 study, n=2907).

- 5-year survival after rectal cancer surgery was not significantly greater with high-volume surgeons (HR for death=0.99, 95% CI 0.86 to 1.14; 1 study, n=1903).

- 5-year survival after colorectal, colon, and rectal surgery combined was significantly greater with high-volume surgeons (HR for death=0.88, 95% CI 0.83 to 0.93; 3 studies, n=22,042).

For studies that did not adjust for case-mix assessing operative mortality:

- Operative mortality after colorectal cancer surgery was significantly lower with high-volume surgeons (OR=0.65, 95% CI 0.56 to 0.76; 5 studies, n=23,644).

- Operative mortality after colon cancer surgery was significantly lower with high-volume surgeons (OR=0.62, 95% CI 0.51 to 0.76; 7 studies, n=152,231).

- Operative mortality after rectal cancer surgery was significantly lower with high-volume surgeons (OR=0.73, 95% CI 0.53 to 0.98; 4 studies, n=5740).

- Operative mortality after colorectal, colon, and rectal surgery combined was significantly lower with high-volume surgeons (OR=0.65, 95% CI 0.57 to 0.75; 13 studies, n=181,615).

For studies that did adjust for case-mix assessing operative mortality:

- Operative mortality after colon cancer surgery was significantly lower with high-volume surgeons (OR=0.75, 95% CI 0.62 to 0.92; 4 studies, n=57,995).

- Operative mortality after rectal cancer surgery was not significantly lower with high-volume surgeons (OR=0.86, 95% CI 0.62 to 1.19; 2 studies, n=5537).

- Operative mortality after colon and rectal surgery combined was significantly lower with high-volume surgeons (0.77, 95% CI 0.66 to 0.91; 4 studies, n=63,532).
Strengths and limitations

Strengths

The study used Cochrane methodology and had little risk of bias in identifying or selecting studies or in analysing the data. The authors judged study design to be satisfactory because about half of the included studies were prospective and about 90% were population based.

Limitations

The main limitations of the study were related to the nature of the existing evidence. Of the included studies, the number and definition of volume categories varied across studies as did the definitions of clinical specialists. The authors noted that these issues meant that they could not make an overall judgement about minimum volume standards or specialist credentials. Additionally, many of the analyses had significant heterogeneity.

Impact on guideline

Much of the evidence assessed when developing the guideline is now quite old, for example 1 review included 13 studies from 1973 to 1998. There is now a substantial volume of evidence relevant to modern surgical practice. However, there is no agreement between studies about what constitutes high volume or low volume. This evidence suggests that the current recommendation of a minimum of 20 surgeries per surgeon per year should be re-evaluated.
How we made the decision

We check our guidelines regularly to ensure they remain up to date. We based the decision on surveillance 4 years after the publication of colorectal cancer (2011) NICE guideline CG131, and 12 years after the publication of improving outcomes in colorectal cancer (2004) NICE guideline CSG5.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

Previous surveillance update decisions for NICE guideline CG131 are on our website.

New evidence

Improving outcomes in colorectal cancer

We found 51 new studies in a search for studies addressing the effects of surgeon or hospital surgical volume on colorectal cancer outcomes published between 1 March 2003 and 4 May 2015. We had no restrictions on the type of study identified by searches. We also considered 1 additional study identified by topic experts who gave advice for this surveillance review.

From all sources, 52 studies were considered to be relevant to the guideline.

We also checked for relevant ongoing research relevant to this guideline.

See appendix A: decision matrix for summaries and references for all new evidence considered.

Colorectal cancer (NICE guideline CG131)

We found 312 new studies in a search for randomised controlled trials and systematic reviews published between 1 February 2011 and 15 January 2015. We also considered 5 additional studies identified by members of the Guideline Committee who originally worked on this guideline. A further study was identified through post-publication communications.

Evidence identified in previous surveillance 8 years after publication of NICE guideline CSG5 was also considered. This included 11 studies identified by search. NICE guideline CG131 was updated as a result of the 8-year surveillance of NICE guideline CSG5.

From all sources, 329 studies were considered to be relevant to the guideline.
We also checked for relevant ongoing research, which will be evaluated again at the next surveillance review of the guideline.

See appendix A: decision matrix for summaries and references for all new evidence considered.

**Views of topic experts**

We considered the views of topic experts, including those who helped to develop the guideline and other correspondence we have received since the publication of the guideline.

**Views of stakeholders**

Stakeholders are consulted only if we decide not to update the guideline following checks at 4 and 8 years after publication. Because this was a 4-year surveillance review of NICE guideline CG131 (and a 12-year surveillance review of NICE guideline CSG5), and the decision was to update, we did not consult on the decision.

See ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual' for more details on our consultation processes.

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