**Table 1: NHMRC Evidence Statement for clinical question: COLMNG3** What is the role for peritonectomy with or without PIC in the treatment recurrent as well as primary colorectal cancer with peritoneal involvement (not including appendiceal neoplasia)?

| **PICO Question COLMNG3:** *For patients diagnosed with colorectal cancer and peritoneal involvement or isolated peritoneal recurrence of colorectal cancer, does peritonectomy, with or without perioperative intraperitoneal chemotherapy (PIC), achieve better outcomes in terms of length and quality of life than usual care?* | | **Report body of evidence tables** |
|---|---|---|
| **1. Evidence base** *(number of studies (quantity), level of evidence and risk of bias in the included studies – see body of evidence tables in report)* | | |
| Two Level III studies compared the outcomes of cytoreductive surgery with or without perioperative intraperitoneal chemotherapy to usual care for colorectal cancer patients with peritoneal involvement in retrospective cohort studies. Chua et al. (2011) had a cohort of 294 patients while Cashin et al. (2012) had 151 patients. Patients were either histologically confirmed with peritoneal carcinomatosis (PC) or by means of multimodality imaging. Both studies reported overall median survival as their primary outcome. Other outcomes included 1-, 3- and 5-year survival. One study (Chua et al., 2011) had a median follow up at 17 months and the other was at 49 months (Cashin et al., 2012).<br><br>In Chua's 2011 study, the intervention group received cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy (PIC) along with neoadjuvant and/or adjuvant chemotherapy. PIC were either hyperthermic (HIPEC) or early preoperative intraperitoneal chemotherapy (EPIC). Chemotherapy regimens involved 5- fluorouracil and leucovorin (5FU-LV), FOLFOX, FILFIRI, capecitabin, oxaliplatin and iriniotecan. Patients in the comparator group were those who refused surgery or were unsuitable for aggressive surgical treatment. They received best supportive care, palliative surgery or systemic therapies. No attempts were made to cytoreduce peritoneal disease volume in palliative surgery.<br><br>In Cashin's 2012 study, the intervention group received CRS with or without PIC. PIC were either sequential perioperative intraperitoneal chemotherapy (SPIC) or HIPEC. Chemotherapy regimens included mitomycin, oxaliplatin, 5FU, calciumfolinate and irinotecan. Two patients underwent CRS only but data were not reported on this group. The comparator group in this study were open-and-close patients. | A | **One or more level I studies with a low risk of bias or several level II studies with a low risk of bias** |
| | B | **One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias** |
| | C | **One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias** |
| | D | **Level IV studies or Level I to III studies/SRs with a high risk of bias** |

| | | |
|---|---|---|
| Two Level II studies trialled cytoreductive surgeries with intraperitoneal chemotherapies against systemic chemotherapy only. The primary outcome from both trials was overall median survival with secondary outcomes including total treatment related mortality, cancer related deaths, total grade III-IV Morbidity, Grade 3-4 Morbidities and adverse events such as termination of treatment and secondary therapies. Some secondary outcomes were not comparable between the two arms.<br><br>Cashin (2016) reported a small trial of 48 patients with a median follow of 78 months and Verwaal (2008) reported a larger trial of 105 patients with a median follow up of 94 months. The intervention in one trial was peritonectomy with SPIC using 5-fluorouracil in combination with leucovorin (Cashin et al. 2016) compared to systemic chemotherapy only (involving fluorouracil, leucovorin and oxaliplatin). In Verwaal et al.'s (2008) trial, cytoreductive surgery with HIPEC using mitomycin C and post-operative adjuvant systemic chemotherapy was the intervention. The control arm received systemic chemotherapy only (5-fluourouracil in combination with leucovorin). Up to 17% of patients included had appendiceal involvement in these trials.<br><br>All studies were at risk of bias. The randomisation processes of Verwaal et al. (2008) was unclear which make it difficult to determine the true risk of bias of the trial. Cashin et al. (2016) particularly was an open-label study with no masking. Although there was cross over of patients in these studies, both trials continued with intention to treat analysis. In the Level III studies, patient characteristics were not comparable across cohorts and were not adjusted for. Cashin et al. (2012) did not report on the comparability of the cohort at all. In Chua et al.'s (2011) cohort, there were significant differences between groups due to the histology of tumours, staging by peritoneal surface disease severity score (PSDSS), sex and presence of peritoneal and liver metastases. The comparator cohort for Cashin et al.'s (2012) study were those who underwent open-and-close procedures and were likely to be extreme cases with already poor prognoses. This study had missing data for overall survival in one patient, who was excluded from the analysis.<br><br>**Grade D** | | |

| **2. Consistency** *(if only one study was available, rank this component as 'not applicable') See body of evidence tables in report – results and p value (95% CI)* | | |
|---|---|---|
| **Overall Survival**<br>Both cohort studies reported longer survival in patients receiving CRS with or without PIC. Patients in Chua et al.'s (2011) study reported a significant median survival of 36, 38 and 43 months overall (p<0.001) for those who received HIPEC, EPIC or both respectively in comparison to usual care patients at 9 months (95% CI 5.9-12.8). There was no significance between the differing therapies (p=0.715).<br><br>Patients in Cashin's (2012) study reported median survival of 34 months for HIPEC patients and 25 months for SPIC patients while open-and-close patients reported 6.5 months overall. When compared against open-and-close patients, SPIC patients held significantly greater median survival overall (p<0.001). This was also true of 1-, 3-, and 5-yr survival. The significance of HIPEC to open-and-close patients was not reported.<br><br>Likewise, Cashin (2016) reported longer median overall survival. The intervention arm reported 25 months median survival in comparison to the control arm at 18 months (HR=0.51, CI=0.27-0.96, p<0.04). One, three and five year survival was also higher for patients in the SPIC arm. 54% of SPIC patients were reported at actuarial 2-year survival against 38% of patients undergoing systemic chemotherapy (p=0.04).<br>**Grade A**<br><br>**Disease Specific Survival**<br>Disease specific survival was only reported by Verwaal 2008. In this trial, HIPEC patients showed longer median disease specific survival at 22.2 months while systemic chemotherapy patients were at 12.6 months (p=0.028). The same findings were reflected in 1-, 3- and 5-yr disease-specific survival although statistical analysis was not reported.<br>**Grade NA** | A | **All studies consistent** |
| | B | **Most studies consistent and inconsistency can be explained** |
| | C | **Some inconsistency, reflecting genuine uncertainty around question** |
| | D | **Evidence is inconsistent** |
| | NA | **Not applicable (one study only)** |

| | | |
|---|---|---|
| **Disease Free Survival**<br>Overall disease free survival was only reported by the Cashin 2012 study. In this study, participants receiving HIPEC had a median disease free survival of 15 months, compared to 10 months for those received SPIC (p=0.048).<br>**Grade NA**<br><br>**Total Deaths and Mortality**<br>No mortality occurred for 6 month treatment related Grade III-IV mortality in Cashin et al.'s (2016) trial. 79% of SPIC patient deaths were cancer related and all systemic chemotherapy patients passed due to cancer. Significance was not reported for either outcome.<br><br>Ninety-day treatment related mortality were reported in Cashin et al.'s (2012) study with patients receiving HIPEC at 4% and those receiving SPIC also at 4%. This could not be compared as it was not reported for the comparator patient group. Verwaal et al. (2008) also reported 7% of patients in the intervention arm for total deaths. Four percent of those deaths were related to the treatment. Again, these were not comparable outcomes as total deaths were not reported in the systemic chemotherapy arm. The significance of these were not reported either.<br>**Grade NA**<br><br>**Grade III-IV Morbidities and Adverse Events**<br>Fewer morbidities were reported for those in the SPIC arm of the Cashin et al. (2016) trial. Forty two percent of SPIC patients reported morbidities while 50% of those in the systemic chemotherapy arm experienced morbidities. Significance was not reported.<br><br>A further array of grade 3-4 morbidities were noted in each groups and across the two level II studies. Although significance was not reported, those that were comparable in Cashin et al. (2016) was Ileus in 8% of patients who underwent SPIC and 4% in patients who underwent systemic chemotherapy. Secondary therapy was required in fewer SPIC patients at 63% in contrast to 88% of systemic chemotherapy patients, although this was not a significant finding (p=0.09). | | |

| | | |
|---|---|---|
| Treatment was terminated in more SPIC patients than those in the systemic chemotherapy arm in Cashin et al.'s (2016) trial. It was reported in 67% of SPIC patients and 42% of systemic chemotherapy patients. This was prompted by various morbidities. These include tumour progression which occurred in 21% of SPIC patients and 50% of systemic chemotherapy patients whose treatment were terminated. The significance of these outcomes were not reported.<br><br>Likewise, in Verwaal et al.'s (2008) trial, tumour progression occurred in less HIPEC patients than those in the systemic chemotherapy arm. It was reported in 2% of SPIC patients and 24% of systemic chemotherapy patients overall. Consequently, treatment was terminated in these patients. Fewer HIPEC patients had treatment terminated with 7% terminating treatment in comparison to 86% of systemic chemotherapy patients. The significance of these were not reported.<br><br>**Grade C** | | |
| **3. Clinical impact** *See body of evidence tables in report - p value (95% CI), size of effect rating and relevance of evidence (Indicate in the space below if the study results varied according to some <u>unknown</u> factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined)* | | |
| **Overall median survival**<br>Patients who received CRS with or without PIC showed significantly longer overall survival. Regardless of which intraperitoneal therapy, Chua et al. (2011) found a strong advantage for the overall median survival of patients who underwent the intervention in comparison to usual care ($p<0.001$) as did Cashin et al. (2012) ($p<0.001$). However the clinical characteristics of cohort groups were not adjusted for and this may have exaggerated results. No further size of effects or significance were reported for other outcomes and groups.<br><br>Cashin et al.'s (2016) trial also showed a strong benefit for longer median overall survival (HR=0.51, p=0.04) with SPIC patients reporting 25 months and systemic chemotherapy patients at 18 months. This was also reflected at actuarial 2-year survival (p=0.04) and 5-year survival rates (p=0.02).<br>**Grade A** | A | **Very large** |
| | B | **Substantial** |
| | C | **Moderate** |
| | D | **Slight/Restricted** |

| | | |
|---|---|---|
| **Disease Specific Survival**<br>Significantly longer disease specific survival was observed in Verwaal et al.'s (2008) trial. Patients who underwent HIPEC reported 22.2 months and systemic chemotherapy patients reported 12.6 months (p=0.028). Although the significance was not reported for any further outcomes, this benefit was reflected in the 1-, 3- and 5-yr survival data.<br>**Grade D**<br><br>**Disease Free Survival (DFS)**<br>Disease free survival was not able to be compared between patients who received intraperitoneal chemotherapies in Cashin et al.'s (2012) cohort and the comparator cohort. This was not reported for the comparator cohort since open and close patients inevitably received no treatment and did not have their disease removed. Consequently, the significance of this was not investigated and the clinical impact unknown.<br>**Grade D**<br><br>**Total deaths and mortality**<br>Cashin et al. (2016) observed no treatment related mortality. Seventy nine percent of SPIC deaths were cancer related and all patients under systemic chemotherapy died due to cancer. The significance of these is not known as it was not reported.<br><br>The 90-day treatment related mortality in Cashin et al.'s (2012) study could not be compared between groups as it was not reported for comparator patients. This was the same in Verwaal et al.'s (2008) trial where total deaths were not reported in patients who received usual care. As the outcomes were not compared, significance was not reported and the relevance of these outcomes remain unknown.<br>**Grade D**<br><br>**Grade III-IV Morbidities and Adverse Events**<br>While the significance of these were not reported, SPIC patients in Cashin et al.'s (2016) trial experienced fewer treatment related Grade III-IV morbidities at 6 months. Both trials show fewer tumour progression for patients receiving the | | |

| | | |
|---|---|---|
| intervention and Cashin et al. (2016) reported fewer secondary therapies in patients who received SPIC although this was not a strong benefit (p=0.09).<br>**Grade D** | | |
| **4. Generalisability** *(How well does the body of evidence match the population and clinical settings being targeted by the Guideline?) For study population characteristics see table of study characteristics in report* | | |
| The studies were conducted in speciality hospitals within developed countries including Australia (Chua et al. 2011). As such the evidence is likely to be directly generalizable to clinical settings in Australia. It is evident that the procedures of CRS and PIC and usual care of the studies are also practiced in Australia (Chua et al. 2011).<br><br>Most patients in Chua et al.'s (2011) cohort were found with low (55.4%) to moderate (30.6%) PC and at PSDSS II (37.8%) or IV (40.5%). Differences in PSDSS across cohort groups were highly significant (p<0.001). Cashin et al.'s (2012) cohort were of mostly low (30%) to intermediate tumour grade (58%) overall. Demographics and clinical characteristics of patients between groups were not reported by Cashin et al. (2012). The comparator group was of open-and-close patients which may be exaggerating efficacy of CRS and PIC in comparison to usual care.<br><br>Most PC originated from colon cancer than rectal in Cashin et al.'s (2012) cohort as well as the two included randomised controlled trials. Primary colorectal cancer was not reported by Chua et al. (2011). It is not yet known whether this would affect the generalisability of the evidence as peritonectomy procedures for colorectal cancer has not been explored in depth.<br><br>For the majority of the studies included, there were more patients with synchronous PC than metachronous PC. Apart from Chua et al.'s (2011) study population where synchronous and metachronous PC patients were balanced approximately at 50:50, a large proportion of Cashin et al.'s (2012) and (2016) study population were diagnosed with PC after initial CRC treatment. While Cashin et al. (2012) have reported this as not significant (p=0.50), this was not explored in their (2016) study. Verwaal et al. (2008) did not report on the significance of their patient characteristics either with approximately 55% of their | A | **Evidence directly generalisable to target population** |
| | B | **Evidence directly generalisable to target population with some caveats** |
| | C | **Evidence not directly generalisable to the target population but could be sensibly applied** |
| | D | **Evidence not directly generalisable to target population and hard to judge whether it is sensible to apply** |

| | | |
|---|---|---|
| patient population with synchronous PC and approximately 45% with metachronous PC. As such it is unclear whether the evidence may be generalised specifically to a synchronous or metachronous patient.<br><br>In Australia, patient selection for CRS and PIC appears to be quite selective (Medical Services Advisory Committee (MSAC), March 2010, Peritonectomy with HIPEC, Review of Nationally Funded Centre Status. Accessed on 15 June 2016 from http://www.msac.gov.au/internet/msac/publishing.nsf/content/1FA6E935BAA0ECFECA257B2C000AD08F/$File/REPORT%20NFC%20Peritonectomy.pdf).<br>Types of peritoneal tumours can determine the response to treatment as they have varying prognoses and it has been noted that evidence in one patient group may not be transferable to others (MSAC, 2010).<br><br>Patients in Cashin et al.'s (2012) cohort were histologically confirmed with PC and free of appendiceal neoplasms. Chua et al.'s (2011) cohort is formed from Australian patients with histological diagnosis of CRC and evidence of peritoneal disease examined by multimodality imaging. However, there is no information about whether appendiceal patients were also included which may be a caveat when generalising to colorectal cancer patients. Both Level II studies had 15-17% appendiceal patients across their included population and the intervention in Verwaal et al.'s (2008) trial involved post-operative systemic chemotherapy in addition to HIPEC and a cytoreductive surgery. This may make it unclear as to whether benefits are due to cytoreductive surgery with or without HIPEC or whether the adjuvant systemic chemotherapy has provided an added advantage.<br>**Grade B** | | |
| **5. Applicability** *(Is the body of evidence relevant to the Australian healthcare context in terms of health services/delivery of care and cultural factors?)* | | |
| Around four specialist centres exist in Australia that perform PIC procedures and referrals for peritonectomy and HIPEC are increasing (MSAC, 2010). The proportion of these which are from colorectal patients are unknown. Evidence can still be applied as expert teams following international guidelines are | A | **Evidence directly applicable to Australian healthcare context** |
| | B | **Evidence applicable to Australian healthcare context with few caveats** |
| | C | **Evidence probably applicable to Australian healthcare context with some caveats** |

| | | |
|---|---|---|
| available to perform the procedure (MSAC, 2010) whether for colorectal patients or otherwise.<br><br>Peritonectomy and HIPEC in Australia is not nationally funded and without a dedicated heated chemotherapy pump (MSAC, 2010) which may pose a potential caveat. While services are also concentrated in major cities on the eastern coast of Australia, the learning curve would suggest that these centres have high concentration of expertise and experience (MSAC, 2010).<br><br>**Grade B** | D | **Evidence not applicable to Australian healthcare context** |

**Other factors** *(Indicate here any other factors that you took into account when assessing the evidence base (for example, issues that might cause the group to downgrade or upgrade the recommendation).*

The studies included did not report comparable data for 30-day mortality. Neither did these studies report on quality of life and colorectal cancer specific mortality. Cohort groups in the Level III studies were not comparable in clinical characteristics and were not adjusted for. This may have biased results favourably towards CRS with or without PIC. Only median overall survival had reported size of effects and/or significance from the Level III studies. No further size of effect and significance for remaining outcomes were reported. Significance and size of effects data were also mostly not reported in the included Level II trials. These trials had designs that were open to high risk of bias and included 15-17% of appendiceal patients in the patient population. Additionally, the intraperitoneal therapies included SPIC or EPIC procedures and these may differ in outcomes to HIPEC.

**EVIDENCE STATEMENT MATRIX**

*Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account.*

| Component | Rating | Description |
|---|---|---|
| 1. Evidence base | **D** | Two level III studies at high risk of bias. Two Level II studies at high risk of bias. |
| 2. Consistency | **A**<br>**NA**<br>**NA**<br>**NA**<br>**C** | Overall median survival<br>Disease Specific Survival<br>Disease Free Survival<br>Total deaths and mortality<br>Grade III-IV Morbidities and Adverse Events |

| | | |
|---|---|---|
| 3. Clinical impact | **A**<br>**D**<br>**D**<br>**D**<br>**D** | Grade A – Overall median survival<br>Grade D – Disease specific survival<br>Grade D – Disease Free Survival<br>Grade D – Total deaths and mortality<br>Grade D – Grade III-IV Morbidities and Adverse Events |
| 4. Generalisability | **B** | Directly generalizable to clinical setting with some caveats. |
| 5. Applicability | **B** | Evidence is directly applicable to the Australian context with the procedure performed by expert teams in specialised centres. However, lack of funding and technology may be limitations. |

**Evidence statements**

In patients with peritoneal metastases from colorectal cancer (synchronous or metachronous), cytoreduction surgery with intraperitoneal chemotherapy is associated with improved survival, compared with palliative surgery and systemic chemotherapy.

Cytoreduction surgery with perioperative intraperitoneal chemotherapy is associated with significant treatment morbidity.

**RECOMMENDATIONs**

*What recommendation(s) does the guideline development group draw from this evidence? Use action statements where possible.*

**Evidence-based Recommendation #1**

For patients with colorectal peritoneal metastases (either synchronous or metachronous to the primary), consider cytoreduction with perioperative intraperitoneal chemotherapy. Where this procedure is suitable, offer referral to a centre with the necessary expertise and infrastructure to perform this procedure.

**Grade D**

**Evidence-based Recommendation #2**

Cytoreduction surgery and perioperative intraperitoneal chemotherapy should only be offered after due consideration of, and discussion with the patient about, the potential treatment-related mortality and morbidity.

**Grade D**

**PRACTICE POINT (CONSENSUS-BASED RECOMMENDATION)**
*If there is no good quality evidence available but there is consensus among Guideline committee members, a consensus-based recommendation (practice point) can be given.*

Practice points:

- Patients with peritoneal carcinomatosis should be referred to a centre with expertise in the management of peritoneal surface malignancies and should be offered enrolment in a prospective trial, so as to allow further evaluation of cytoreduction and intraperitoneal chemotherapy.
- Prior to referral, treating clinicians should have an in-depth discussion with every patient about the potential survival advantage and potential treatment-related mortality or morbidity.
- All patients' cases should be discussed at a multidisciplinary team meeting with clinicians who have expertise in the management of peritoneal metastases, to review the relevant clinical information, previous histology (if applicable) and relevant imaging prior to offering patients cytoreductive surgery and intraperitoneal chemotherapy.
- All patients offered this procedure in established cytoreduction centres should be asked to give their consent for their patient records to be available for ongoing auditing of clinical outcomes. Patients should also be invited and encouraged to participate in research to enable collection of prospective longitudinal data for clinical and quality-of-life outcomes.

**CONSIDERATIONS**

Although available evidence is encouraging, there is currently insufficient evidence to recommend the widespread adoption of cytoreduction surgery and intraperitoneal chemotherapy for patients with colorectal peritoneal metastases. Further studies, with appropriate patient selection and outcomes, are needed before cytoreduction and intraperitoneal chemotherapy can be recommended.

**Table 2: Unresolved issues**

**UNRESOLVED ISSUES**
*If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up.*

| |
|---|
| Prognosis for patients with peritoneal carcinomatosis is poor. There is some suggestion that an elective relook may allow early diagnosis of peritoneal carcinomatosis, resulting in earlier treatment, and therefore lead to improved survival. However, it is unclear whether this is simply the result of lead time bias or whether this represents more effective treatment early in the diagnosis of peritoneal carcinomatosis. Data from long-term prospective RCTs are not currently available.<br><br>Cytoreduction surgery, with or without intraperitoneal chemotherapy, requires further prospective evaluation. At present, it is not clear if intraperitoneal chemotherapy is a necessary part of treatment in addition to cytoreduction. Furthermore, even if intraperitoneal chemotherapy is a necessary component of treatment, there is insufficient evidence to conclude which intraperitoneal chemotherapy regimen is most effective in terms of timing and mode of delivery as well as the chemotherapy agent used.<br><br>Quality-of-life outcomes have not been included in studies reporting outcomes in patients undergoing cytoreduction with or without intraperitoneal chemotherapy. These need to be evaluated as part of a prospective study. |

**Table 3: Implementation of recommendation**

| **IMPLEMENTATION OF RECOMMENDATION**<br>*Please indicate yes or no to the following questions. Where the answer is yes please provide explanatory information about this. This information will be used to develop the implementation plan for the guidelines.* | |
|---|---|
| Will this recommendation result in changes in usual care?<br>Cytoreduction surgery with perioperative intraperitoneal chemotherapy is a highly specialised treatment that is currently only offered at highly selected centres with the requisite expertise. The management of patients with peritoneal metastases requires a multidisciplinary team approach where the expertise is not restricted to surgical and medical oncology expertise alone.<br><br>With increasing evidence for the potential survival benefit of cytoreduction surgery and perioperative intraperitoneal chemotherapy, referrals to centres with the necessary expertise may increase. | **YES** |
| Are there any resource implications associated with implementing this recommendation?<br>The present recommendations would have only a minor effect on resourcing, because they would affect only referral centres with the necessary expertise and infrastructure to perform this procedure.<br><br>It is possible that there may be increased demand for cytoreduction surgery and perioperative intraperitoneal chemotherapy in the future, which may necessitate the development and establishment of more expert centres. | **YES** |
| Will the implementation of this recommendation require changes in the way care is currently organised? | **YES** |
| Are the guideline development group aware of any barriers to the implementation of this recommendation? | **NO** |

**Table 2: Unresolved issues**

| **UNRESOLVED ISSUES**<br><br>*If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up.* |
|---|
| Prognosis associated with peritoneal carcinomatosis is poor. There is some suggestion that an elective relook may allow early diagnosis of peritoneal carcinomatosis resulting in earlier treatment and therefore lead to improved survival. However, whether this is simply the result of lead time bias or whether this represents more effective treatment early in the diagnosis of peritoneal carcinomatosis is unclear. Long term prospective randomised data is not currently available.<br><br>Cytoreduction surgery with or without intra-peritoneal chemotherapy requires further prospective evaluation. At present, it is not clear if intraperitoneal chemotherapy is a necessary part of treatment in addition to cytoreduction. Furthermore, even if intraperitoneal chemotherapy is a necessary component of treatment, there is insufficient data to conclude which intraperitoneal chemotherapy regime is most effective in terms of timing and mode of delivery as well as the chemotherapy agent used.<br><br>Quality of life outcomes have not been studied in studies reporting outcomes in patients undergoing cytoreduction with or without intra-peritoneal chemotherapy and needs to be evaluated as part of a prospective study. |

**Table 3: Implementation of recommendation**

| **IMPLEMENTATION OF RECOMMENDATION**<br>*Please indicate yes or no to the following questions. Where the answer is yes please provide explanatory information about this. This information will be used to develop the implementation plan for the guidelines.* | |
|---|---|
| Will this recommendation result in changes in usual care? | **NO** |
| Are there any resource implications associated with implementing this recommendation?<br>The present recommendations would have only a minor effect on resourcing, because they would affect only referral centres with the necessary expertise and infrastructure to perform this procedure. | **YES** |
| Will the implementation of this recommendation require changes in the way care is currently organised? | **NO** |
| Are the guideline development group aware of any barriers to the implementation of this recommendation? | **NO** |