NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Centre for Clinical Practice

Review consultation document

Review of Clinical Guideline (CG75) – Metastatic spinal cord compression: diagnosis and management of adults at risk of and with metastatic spinal cord compression

1. Background information

Guideline issue date: 2008
4 year review: 2012
National Collaborating Centre: Cancer

2. Consideration of the evidence

Literature search

Through an assessment of abstracts from a high-level randomised control trial (RCT) search, new evidence was identified relating to the following clinical areas within the guideline:

- Treatment of spinal metastases and metastatic spinal cord compression:
    - Treatments for painful spinal metastases (bisphosphonates, radiotherapy, vertebroplasty and kyphoplasty)
    - Care of the threatened spinal cord in patients with metastatic spinal cord compression
    - Case selection for definitive treatment of metastatic spinal cord compression

    - Surgery for the definitive treatment of metastatic spinal cord compression
- Supportive care and rehabilitation

Through this stage of the process, a sufficient number of studies relevant to the above clinical areas were identified from the high level RCT search to allow an assessment for a proposed review decision and are summarised in Table 1 below.

From initial intelligence gathering, qualitative feedback from other NICE departments, the views expressed by the Guideline Development Group, as well as the high-level RCT search, an additional focused literature search was conducted for the following clinical area:

- Surgery for the definitive treatment of metastatic spinal cord compression (minimally invasive spinal fixation)

The results of the focused search are summarised in Table 2 below. All references identified through the high-level RCT search, initial intelligence gathering and the focused search can be viewed in Appendix 1.

Table 1: Summary of articles from the high level RCT search

Clinical area 1: Treatment for painful spinal metastases and prevention of metastatic spinal cord compression (bisphosphonates)		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: What is the effectiveness of Bisphosphonates at treating spinal pain and/or preventing spinal collapse and/or spinal cord compression? **Relevant section of the guideline and recommendations** Chapter 6 - Treatment for painful spinal metastases and prevention of metastatic spinal cord compression	Through an assessment of abstracts from the high-level RCT search, 19 studies relevant to the clinical question were identified. <u>Health economics (Four studies)</u> • One study was identified which assessed the cost-effectiveness of zoledronic acid in renal cell carcinoma patients with bone metastases.[1] The study concluded that zoledronic acid saves costs and increases QALYs compared to placebo although a larger trial is required to confirm the results. Similar results were obtained in another cost-effectiveness study which evaluated the use of zoledronic acid in patients with hormone refractory prostate cancer and bone metastases.[2] In addition, zoledronic acid was found to	This section of the guideline (Treatment for painful spinal metastases and prevention of metastatic spinal cord compression) will need to cross refer to a new technology appraisal that is expected to publish in June 2012 - Denosumab for the treatment of bone metastases from solid

(bisphosphonates).	be cost-effective compared with placebo in patients with non-small cell lung cancer who had bone metastases.[3] • One study was identified which compared the cost-effectiveness, from a US payer perspective, of denosumab (a human monoclonal antibody that reduces osteoclast-mediated bone destruction) with zoledronic acid in the treatment of bone metastases in men with hormone-refractory prostate cancer.[4] The study concluded that denosumab may be a costly alternative to zoledronic acid. <u>Bisphosphonates – systematic reviews (Two studies)</u> • A Cochrane systematic review evaluated the clinical role of bisphosphonates in multiple myeloma.[5] The review concluded that adding bisphosphonates to the treatment of multiple myeloma reduces pathological vertebral fractures and skeletal-related events although no bisphosphonate appeared to be superior to another. • A second Cochrane systematic review assessed the effect of	tumours and multiple myeloma.

	bisphosphonates on skeletal-related events and bone pain in women with breast cancer with bone metastases.[6] The results of the review indicated that bisphosphonates reduce the skeletal-related events rate and delay the time to skeletal-related events. <u>Intravenous bisphosphonate therapy versus denosumab (Two studies)</u> • One RCT was identified which compared subcutaneous denosumab with intravenous bisphosphonate therapy in patients with malignancy (prostate cancer, breast cancer or other neoplasms) and bone metastases.[7] The results of the study indicated that fewer patients receiving denosumab experienced skeletal-related events compared to those receiving intravenous bisphosphonate therapy. • The efficacy and safety of denosumab compared with intravenous bisphosphonate therapy in breast cancer patients with bone metastases was evaluated in an RCT.[8]	

	The results of the study suggested that both treatments reduced skeletal-related event risk to a similar extent. <u>Zoledronic acid versus denosumab (Three studies)</u> • One RCT compared denosumab with zoledronic acid for prevention of skeletal-related events in men with bone metastases from castration-resistant prostate cancer.[9] The study concluded that denosumab was better than zoledronic acid for prevention of skeletal-related events. • An RCT conducted in patients with advanced cancer and bone metastases (excluding breast and prostate) or myeloma concluded that denosumab was noninferior to zoledronic acid in preventing or delaying first on-study skeletal-related events in these populations.[10] • One RCT compared denosumab with zoledronic acid in delaying or preventing skeletal-related events in patients with breast cancer and bone metastases.[11] The results of the study indicated that denosumab was superior to zoledronic	

	acid in delaying or preventing skeletal-related events in this population. <u>Zoledronic acid versus clodronic acid (Two studies)</u> • One RCT was identified which aimed to determine whether bisphosphonates can affect clinical outcomes in patients with multiple myeloma.[12] Patients were randomised to zoledronic acid via infusion or oral clodronic acid daily. The results of the study indicated that zoledronic acid improved survival compared with clodronic acid in addition to having a beneficial effect on bone health. A follow-up of this RCT reported secondary outcomes relating to skeletal events and reported that zoledronic acid was associated with a lower risk of skeletal-related events whilst vertebral fractures were lower in the zoledronic acid group.[13] <u>Ibandroate versus placebo (Two studies)</u> • A placebo-controlled RCT evaluated the efficacy and safety	

	of ibandroate in patients with bone metastases from colorectal cancer.[14] Ibandroate significantly reduced the proportion of patients with skeletal events and prolonged time to progression of bone lesions although the authors suggest that larger studies are required to confirm the results. Similar results were obtained in an RCT evaluating the efficacy of ibandroate in patients with breast cancer and metastatic bone disease.[15] <u>Zoledronic acid versus placebo (One study)</u> • A placebo-controlled RCT was identified which evaluated the effect of zoledronic acid compared with placebo on skeletal-related events in patients with bone metastases from bladder cancer.[16] Zoledronic acid decreased the incidence of skeletal-related events in patients with bone metastases from bladder cancer. <u>Zoledronic acid versus observation (One study)</u>	

	• One RCT was identified which compared zoledronic acid with observation in patients with untreated, asymptomatic myeloma.[17] At disease progression, skeletal-related events were significantly lower in the zoledronic acid treated group. <u>Pamidronate 30mg versus pamidronate 90mg (One study)</u> • One RCT was identified which compared the effect of two doses of pamidronate (30mg versus 90mg) on skeletal morbidity in patients with newly diagnosed multiple myeloma.[18] The study concluded that a 30mg dose of pamidronate is preferable. <u>Clodronate, pamidronate and zoledronate versus placebo (One study)</u> • A systematic review was identified which compared the efficacy of clodronate, pamidronate and zoledronate with placebo in preventing skeletal-related events in metastatic bone disease originating from malignancy.[19] Each of the	

	three drugs were found to be more effective than placebo in preventing skeletal-related events in cancer patients with metastatic bone disease although no clear advantage of one drug over another was observed. **Summary** In general, the identified new literature relating to bisphosphonates indicated a beneficial effect compared with placebo or observation. One study which compared the efficacy of bisphosphonates (clodronate, pamidronate and zoledronate) with each other found no clear advantage of one drug over another. Conversely, a study comparing zoledronic acid with clodronic acid found that zoledronic acid improved survival compared with clodronic acid in addition to having a beneficial effect on bone health. One RCT assessed the efficacy of ibandroate in colorectal cancer however, this drug currently only has a licensed indication for prevention of skeletal related events in patients with breast cancer and bone metastases. In summary, this new evidence is unlikely to change the current	

	guideline recommendations which state: • Offer patients with vertebral involvement from myeloma or breast cancer bisphosphonates to reduce pain and the risk of vertebral fracture/collapse. • Offer patients with vertebral metastases from prostate cancer bisphosphonates to reduce pain only if conventional analgesia fails to control pain. • Bisphosphonates should not be used to treat spinal pain in patients with vertebral involvement from tumour types other than myeloma, breast cancer or prostate cancer (if conventional analgesia fails) or with the intention of preventing metastatic spinal cord compression, except as part of a randomised controlled trial. Several cost-effectiveness studies indicated that zoledronic acid saves costs and increases QALYs compared to placebo. However, it is unlikely that this new evidence will impact on the guideline recommendations as bisphosphonates are already recommended.	

	Several studies were identified comparing denosumab with bisphosphonates. The studies comparing denosumab with intravenous bisphosphonate therapy reported conflicting results. In addition, studies comparing denosumab with zoledronic acid found it was superior in delaying or preventing skeletal-related events in the specific populations evaluated. Denosumab is a new intervention not currently covered in the guideline however, there is a related Technology Appraisal due to publish in June 2012 entitled: Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma. As such, there needs to be consideration of cross-referral to this Technology Appraisal when it is published.	
Clinical area 2: Treatment for painful spinal metastases and prevention of metastatic spinal cord compression (radiotherapy)		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**

Q: What is the effectiveness of radiotherapy at treating spinal pain and/or preventing spinal collapse and/or spinal cord compression? **Relevant section of the guideline and recommendations** Chapter 6: Treatment for painful spinal metastases and prevention of metastatic spinal cord compression (radiotherapy).	Through an assessment of abstracts from the high-level RCT search, seven studies relevant to the clinical question were identified. *Radiotherapy (Three studies)* • A systematic review was identified which concluded that radiotherapy is a successful method to palliate pain and prevent the morbidity of bone metastases.[20] • The options and indications for radiotherapy for metastatic spinal disease were assessed in a systematic review.[21] The review concluded that there is moderate quality evidence for conventional fractionated radiotherapy as an appropriate initial therapy option for patients with spine metastases. • One systematic review was identified which aimed to determine the efficacy and safety of radioisotopes in patients with bone metastases.[22] The review concluded that radioisotopes may provide complete reduction in pain over a six month period although adverse effects are frequent.	No new evidence was identified which would invalidate current guideline recommendation(s).

	Three studies suggest a benefit of radiotherapy for bone and spinal metastases. As such, the identified new literature supports the current guideline recommendation which states: • Offer patients with spinal metastases causing non-mechanical spinal pain 8 Gy single fraction palliative radiotherapy even if they are completely paralysed. *Single versus multiple fraction schedules (Three studies)* • One RCT was identified which compared single (8 Gy in a single fraction) versus multiple fractions (30 Gy in 10 fractions) of palliative radiotherapy for management of painful bone metastases.[23] No significant difference in pain relief between the two treatments was observed. An additional RCT comparing single-fraction radiotherapy (8 Gy x 1) with multiple-fraction radiotherapy (3 Gy x 10) in patients with painful spinal metastases concluded that there were no differences between the two radiotherapy regimens in terms	

	of the rate of pathological fractures or spinal cord compressions. [24] • Single fraction versus multiple fraction schedules of palliative radiotherapy for bone metastases were compared in a systematic review.[25] No significant difference was observed in overall or complete response rates although higher retreatment rates occurred in those receiving single fractions. The identified new literature on radiotherapy indicated that single fraction and multiple fraction radiotherapy are equally effective for pain relief, rate of pathological fractures or spinal cord compressions. As such, the identified new literature supports the current guideline recommendation which states: • Offer patients with spinal metastases causing non-mechanical spinal pain 8 Gy single fraction palliative radiotherapy even if they are completely paralysed. *Radiotherapy combined with bisphosphonates (One study)*	

	• One RCT was identified which evaluated the effectiveness of a single dose of radiotherapy (8 Gy versus 6 Gy) plus zoledronic acid in cancer patients with bone metastases.[26] The higher dose in combination with zoledronic acid was associated with a longer period without skeletal related events although similar levels of pain control were observed in both groups. **<u>Summary</u>** In summary, three studies were identified which suggested a benefit of radiotherapy for bone and spinal metastases. In addition, the identified new literature on radiotherapy indicated that single fraction and multiple fraction radiotherapy are equally effective for pain relief, rate of pathological fractures or spinal cord compressions. As such, the identified new literature supports the current guideline recommendation which states: • Offer patients with spinal metastases causing non-mechanical spinal pain 8 Gy single fraction palliative	

	radiotherapy even if they are completely paralysed. One RCT was identified which evaluated the effectiveness of a single dose of radiotherapy plus zoledronic acid in cancer patients with bone metastases. However, there is currently insufficient data to consider this treatment option in the guideline and further research is required.	
Clinical area 3: Treatment for painful spinal metastases and prevention of metastatic spinal cord compression (vertebroplasty and kyphoplasty)		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: What is the effectiveness of vertebroplasty/kyphoplasty at treating spinal pain and/or preventing spinal collapse and/or spinal cord compression?	Through an assessment of abstracts from the high-level RCT search, five studies relevant to the clinical question were identified. *Vertebroplasty (Three studies)* • One systematic review evaluated the efficacy and complications associated with vertebroplasty in spinal	No new evidence was identified which would invalidate current guideline recommendation(s).

Relevant section of the guideline and recommendations Chapter 6: Treatment for painful spinal metastases and prevention of metastatic spinal cord compression (vertebroplasty and kyphoplasty).	metastases and myeloma.[27] The review concluded that there is a lack of good-quality literature on the use of percutaneous vertebroplasty in malignancy and that further research is required. • The use of percutaneous vertebroplasty for pathologic compression fractures in metastatic spinal disease was followed up in a retrospective case note review.[28] The results of the study indicated that immediate pain relief was observed after percutaneous vertebroplasty. In addition, the effect of percutaneous vertebroplasty was maintained without significant change at one year follow-up. • One RCT was identified which compared percutaneous vertebroplasty with percutaneous vertebroplasty combined with 125I seed implantation in patients with metastatic spinal tumours.[29] The results of the study indicated that there was no significant difference in overall clinical benefit rates between the two groups.	

	Kyphoplasty (Two studies) • One RCT evaluated the efficacy and safety of balloon kyphoplasty compared with non-surgical management for patients with cancer and vertebral compression fractures concluding that it rapidly reduces pain and improves function.[30] • A systematic review was identified which evaluated the role of kyphoplasty and vertebroplasty in patients with painful compression fractures associated with metastatic spine disease.[31] The review concluded that there is moderate evidence for vertebral augmentation being safe and effective in providing pain relief in patients with vertebral body fractures. **Summary** Three studies were identified related to vertebroplasty and two on kyphoplasty for vertebral metastases. However, due to heterogeneity in study methodology and reported results, there is	

	unlikely to be any impact on the current guideline recommendation which states:
	• Consider vertebroplasty or kyphoplasty for patients who have vertebral metastases and no evidence of metastatic spinal cord compression or spinal instability if they have:
	  ○ Mechanical pain resistant to conventional analgesia, or
	  ○ Vertebral body collapse	

Clinical area 4: Care of the threatened spinal cord in patients with metastatic spinal cord compression		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: For patients with known metastatic spinal cord compression does mobilisation give better outcomes than no mobilisation?	Through an assessment of abstracts from the high-level RCT search, one study relevant to the clinical question was identified. • A systematic review evaluated methods to assess spinal stability, the role of braces and mobilisation of patients.[32] The	No new evidence was identified which would invalidate current guideline recommendation(s).

Relevant section of the guideline and recommendations Chapter 6: Care of the threatened spinal cord in patients with metastatic spinal cord compression.	review concluded that evidence on spinal stability, bracing, patient mobilisation and positioning is limited and further research is required. **<u>Summary</u>** In summary, no new evidence was identified which would impact on the guideline recommendations relating to mobilisation.	
Clinical area 5: Case selection for definitive treatment of metastatic spinal cord compression		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Case selection for surgery or radiotherapy – For patients with an established diagnosis of metastatic spinal cord compression, what factors predict for successful outcomes	Through an assessment of abstracts from the high-level RCT search, three studies relevant to the clinical question were identified. • One study conducted a retrospective analysis of patients undergoing decompressive surgery for metastatic epidural	No new evidence was identified which would invalidate current guideline recommendation(s).

(mobility, continence, lack of pain, survival) following treatment? **Relevant section of the guideline and recommendations** Chapter 6: Case selection for definitive treatment of metastatic spinal cord compression.	spinal cord compression.[33] The results of the analysis indicated that more extensive surgery was required in preoperative nonambulatory patients whilst surgical site complications were higher in this group. In addition, preoperative ability to walk, symptoms present for less than 48 hours and postoperative radiotherapy increased the likelihood of ambulation at follow up. • Similarly, a systematic review evaluated prognostic factors predicting functional outcomes after primary decompressive surgery for metastatic spinal cord compression.[34] The review concluded that preoperative ambulation status, time to surgery, compression fracture and individual health status were the most relevant prognostic factors for ambulatory outcome. • Lastly, a post-hoc analysis of an RCT was identified which aimed to determine whether age affects outcomes from differing treatments (surgery compared with radiotherapy) in patients with spinal metastases.[35] However, as this study	

	involved secondary data analysis from a trial, further evidence is required to determine whether age should be used for case selection for definitive treatment of metastatic spinal cord compression. **Summary** In summary, the results of the identified studies indicated that preoperative ability to walk, time to surgery (for example, symptoms present for less than 48 hours) and postoperative radiotherapy increased the likelihood of ambulation at follow up following surgery. As such, the new evidence is unlikely to alter the current guideline recommendations: • Start definitive treatment, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of metastatic spinal cord compression.	
Clinical area 6: Surgery for the definitive treatment of metastatic spinal cord compression		
Clinical question	**Summary of evidence**	**Relevance to guideline**

		recommendations
Q: What surgical technique is the most effective in treating patients with known metastatic spinal cord compression? **Relevant section of the guideline and recommendations** Chapter 6: Surgery for the definitive treatment of metastatic spinal cord compression.	Through an assessment of abstracts from the high-level RCT search, two studies relevant to the clinical question were identified. • One systematic review evaluated the optimal treatment for patients with spinal cord compression secondary to solid metastases.[36] The review recommended that patients with cord compression due to solid tumour metastases should undergo surgical decompression with stabilisation followed by radiation therapy. • A second systematic review evaluated the efficacy of en bloc resection for primary and metastatic tumours of the spine.[37] The median time to recurrence for metastatic tumours was two years. **Summary** In summary, one study was identified which concluded that patients should undergo surgical decompression with stabilisation followed	No new evidence was identified which would invalidate current guideline recommendation(s).

	by radiation therapy. This study would not invalidate the current guideline recommendations which state: • If surgery is appropriate in patients with metastatic spinal cord compression, attempt to achieve both spinal cord decompression and durable spinal column stability. • Postoperative fractionated radiotherapy should be offered routinely to all patients with a satisfactory surgical outcome once the wound has healed. One study was identified focusing on en-bloc resection which indicated that the median time to recurrence for metastatic tumours was two years. However, currently there is insufficient new evidence to change the direction of the current guideline recommendation: • En bloc excisional surgery with the objective of curing the cancer should not be attempted, except in very rare circumstances (for example, confirmed solitary renal or thyroid metastasis following complete staging).	

Clinical area 7: Radiotherapy for the definitive treatment of metastatic spinal cord compression		
Summary of evidence	**Relevance to guideline recommendations**	
Q: In patients with known metastatic spinal cord compression referred for radiotherapy, what is the most effective and cost effective dose fractionation regimen? **Relevant section of the guideline and recommendations** Chapter 6: Radiotherapy for the definitive treatment of metastatic spinal cord compression.	Through an assessment of abstracts from the high-level RCT search, seven studies relevant to the clinical question were identified. *Radiotherapy and surgery (Three studies)* • A Cochrane systematic review evaluated the effectiveness and adverse effects of radiotherapy, surgery and corticosteroids in metastatic epidural spinal cord compression.[38] The review concluded that patients with stable spines retaining the ability to walk may be treated with radiotherapy. In addition, there is some evidence of benefit from decompressive surgery in ambulant patients with poor prognostic factors for radiotherapy. There was insufficient evidence about the role of corticosteroids. • A second systematic review aimed to determine the optimal	No new evidence was identified which would invalidate current guideline recommendation(s).

	timing of surgery and radiotherapy in patients surgically treated for spinal metastases.[39] A lack of relevant literature was identified however, the authors of the review suggested that optimal radiotherapy-surgery/surgery-radiotherapy time interval should be at least one week to minimise wound complications. • Lastly, one systematic review compared surgical decompression with or without radiation to radiation therapy alone in patients with metastatic spinal cord compression.[40] The results of the review suggested that surgical excision of the tumour and instrumented stabilisation may improve clinical outcomes compared with radiation therapy alone, although most of the data was obtained from observational studies which limited the ability to compare results of studies directly. *Single versus multiple fraction schedules (Two studies)* • One RCT compared 8 Gy single-dose radiotherapy with 8	

	Gy x 2 radiotherapy in patients with metastatic spinal cord compression and short life expectancy.[41] No difference in response was observed between the two radiotherapy schedules. • A systematic review concluded that single-fraction radiotherapy is as effective for pain relief of bone metastases as multi-fraction regimens.[42] However, the results of the review suggested that for metastatic spinal cord compression, 10 x 3 Gy may be preferable for patients with a favourable survival prognosis. *Short-course versus long-course radiotherapy (One study)* • A two-arm prospective nonrandomised study compared the effectiveness of short-course versus long-course radiotherapy for metastatic spinal cord compression.[43] The study concluded that both short-course and long-course radiotherapy resulted in similar functional outcomes and overall survival although long-course	

	radiotherapy significantly improved progression free survival and local control. *Additional treatment following radiotherapy (One study)* • A post-hoc analysis of two RCTs of radiotherapy for metastatic spinal cord compression concluded that reirradiation was safe and effective.[44] In particular, the effect of reirradiation on motor function was associated with walking capacity before reirradiation. **Summary** One systematic review concluded that patients with metastatic epidural spinal cord compression and stable spines retaining the ability to walk may be treated with radiotherapy which is unlikely to change the following recommendation: • Offer fractionated radiotherapy as the definitive treatment of choice to patients with epidural tumour without neurological impairment, mechanical pain or spinal	

	instability. Two studies compared single versus multiple fraction schedules for metastatic spinal cord compression. One study found no difference between single fraction and multiple fraction regimens however, the study was conducted in patients with short life expectancy. Conversely, the second study suggested that multiple fraction radiotherapy may be preferable for metastatic spinal cord compression patients with a favourable survival prognosis. Lastly, the results of one study indicated that long-course radiotherapy significantly improved progression free survival and local control in patients with metastatic spinal cord compression. Therefore, the identified new literature is unlikely to change the direction of the following guideline recommendation: • Offer a fractionated rather than a single fraction regimen to patients with a good prognosis who are having radiotherapy as their first-line treatment.	

	One study suggested that an optimal radiotherapy-surgery/surgery-radiotherapy time interval should be at least one week to minimise wound complications whilst a review concluded that that surgical excision of the tumour and instrumented stabilisation may improve clinical outcomes compared with radiation therapy alone. This new evidence is unlikely to impact on the current recommendation: • Postoperative fractionated radiotherapy should be offered routinely to all patients with a satisfactory surgical outcome once the wound has healed. One post-hoc analysis of two RCTs suggested that metastatic spinal cord compression reirradiation was safe and effective and is unlikely to change the direction of the current guideline recommendation which states: • Consider further radiotherapy or surgery for patients who have responded well to previous radiotherapy and develop recurrent symptoms after at least three months.	

Clinical area 8: Supportive care and rehabilitation		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Which patient factors will predict for beneficial outcomes from specialised services? **Relevant section of the guideline and recommendations** Chapter 7: Supportive care and rehabilitation.	Through an assessment of abstracts from the high-level RCT search, one study relevant to the clinical question was identified. • The aim of this review was to identify functional outcomes that could justify the need for a rehabilitation care programme for patients with metastatic epidural spinal cord compression.[45] The data showed a positive impact on pain and bladder and/or bowel dysfunction. **Summary** In summary, one study was identified. As the study suggests a potentially beneficial effect of rehabilitation on bladder and/or bowel function this would not have an impact on the current guideline recommendations relating to bladder and bowel continence	No new evidence was identified which would invalidate current guideline recommendation(s).

	management.	

Table 2: Summary of articles from the focused search

Clinical area 1: Surgery for the definitive treatment of metastatic spinal cord compression (minimally invasive spinal fixation)		
Clinical question	**Summary of evidence**	**Relevance to guideline recommendations**
Q: Is minimally invasive spinal fixation a safe and effective intervention in suspected/ confirmed metastatic spinal cord compression? **Relevant section of the guideline and recommendations** Chapter 6: Surgery for the definitive treatment of metastatic spinal cord compression (minimally	Through an assessment of abstracts from the focused search, seven studies relevant to the clinical question were identified. The identified studies were case series or case reports: • A case series was identified which described the use of minimally invasive posterolateral vertebrectomy and decompression in eight patients with metastatic disease of the spine.[46] Improvement (as measured by the Nurick scale) was observed in 62.5% of patients whilst two patients were able to ambulate independently immediately after surgery. • The safety of a minimally invasive approach for the	No new evidence was identified which would invalidate current guideline recommendation(s).

invasive spinal fixation).	resection of spinal neoplasms was evaluated in a retrospective case series.[47] The results of the study indicated that two patients developed postoperative complications, 68% of tumours were completely resected and postoperative improvement was observed in all but one patient at six months. • A case series was identified which examined the use of a minimally invasive thorascopic approach for surgical treatment of thoracic and thoracolumbar metastatic spinal cord compression.[48] The study included five people, all of whom had improvement in preoperative symptoms and neurological deficits. • Minimally invasive spine stabilisation with long implants was assessed in a case series of nine patients with thoracolumbar fractures.[49] The authors concluded that this technique could be an alternative surgical method for stabilisation of the spine in certain patients. • A case report described the use of a minimally invasive	

	surgical technique used in a patient with metastatic spinal cord compression.[50] The patient improved neurologically and remained neurologically intact at the nine-month follow-up. In addition, the patient was ambulatory on postoperative day one. • One case series was identified which assessed the feasibility and clinical improvement following minimally invasive surgery for metastatic epidural spinal cord compression.[51] The results of the study indicated that clinical remission of pain occurred in 96% of patients, improvement of neurological deficit was evident in 88% of patients and overall survival at one year was 43%. • One study evaluated long-term outcomes of a mini-open, lateral approach for thoracic spine tumour removal.[52] The approach was used to treat 21 patients with improvements in the visual analog scale and the Oswestry disability index.	

	Summary In summary, the identified new literature included small numbers of patients and did not include comparator groups. This new evidence may not be significant enough to warrant updating the guideline at this point. This area will be examined again in the next review of the guideline.	

Eight clinical trials (publication dates unknown) were identified focusing on:

- Bisphosphonates in treating painful spinal metastases
- Radiotherapy for treatment of metastatic spinal cord compression
- Surgical treatment of metastatic spinal cord compression

Guideline Development Group and National Collaborating Centre perspective

A questionnaire was distributed to GDG members and the National Collaborating Centre to consult them on the need for an update of the guideline. Seven responses were received with some respondents highlighting the publication of audits indicating experience of altered practice following publication of the guideline. One respondent suggested that minimally invasive spinal fixation is gaining popularity and may be useful in patients with metastatic spinal cord compression. This feedback contributed towards the development of the clinical question for the focused searches.

The majority of respondents felt that there is insufficient variation in current practice and minimal supporting evidence at this time to warrant an update of the current guideline.

Implementation and post publication feedback

In total 15 enquiries were received from post-publication feedback, most of which were routine.

Feedback from the NICE implementation team indicated that there has been an increase in the number of decompression of thoracic spinal cord procedures conducted in secondary care in England between 2003/04 and 2010/11.

No new evidence was identified through post publication enquiries or implementation feedback that would indicate a need to update the guideline.

Relationship to other NICE guidance

The following NICE guidance is related to CG75:

Guidance	Review date
IPG12: Percutaneous vertebroplasty, 2003.	Review date: TBC.
CG7: The use of pressure relieving devices for the prevention of pressure ulcers in primary and secondary care, 2003.	Review decision date: May 2011. The guideline will be amalgamated with the update of CG29 Pressure ulcers: the management of pressure ulcers in primary and secondary care, under a single scoping process.
CG29: The management of pressure ulcers in primary and secondary care, 2005.	Review decision date: May 2011. Following the recent review recommendation, an update of this guideline is currently in the process of being scheduled into the work programme.
NICE cancer service guidance: Improving supportive and palliative care for adults with cancer, 2004.	Review date: TBC.

CG23: Management of depression in primary and secondary care, 2004.	This guidance has been replaced by CG90 Depression in adults (update), 2009 which is currently under review (expected review decision date: October 2012).
IPG166: Balloon kyphoplasty for vertebral compression fractures, 2006.	Review date: TBC.
CG46: Venous thromboembolism (surgical), 2007.	This guidance has been replaced by CG92: Venous thromboembolism – reducing the risk, 2010.
CG49: The management of faecal incontinence in adults, 2007.	Next review date: June 2013.
CG58: Prostate cancer: diagnosis and treatment, 2008.	Review decision date: July 2011. Following the recent review recommendation, an update of this guideline is currently in the process of being scheduled into the work programme.
Related NICE guidance in progress	
Technology Appraisal: Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma.	Expected publication date: June 2012.

Anti-discrimination and equalities considerations

No evidence was identified to indicate that the guideline scope does not comply with anti-discrimination and equalities legislation. The original scope is

inclusive of adults with metastatic spinal disease at risk of developing metastatic spinal cord compression, adults with suspected and diagnosed spinal cord and nerve root compression due to metastatic malignant disease and adults with primary malignant tumours (for example, lung cancer, mesothelioma or plasmacytoma) and direct infiltration that threatens spinal cord function.

Conclusion

Through the process, new literature was identified focusing on the use of minimally invasive surgical techniques for metastatic spinal cord compression. However, as the identified trials were small with no comparator groups, this new evidence may not be significant enough to warrant updating the guideline at this point.

One ongoing related Technology Appraisal was also identified: Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma (expected date of issue: June 2012). Therefore, there needs to be consideration of cross-referral to this Technology Appraisal when it is published.

No additional areas were identified which would indicate a significant change in clinical practice. There are no factors described above which would invalidate or change the direction of current guideline recommendations. The Metastatic Spinal Cord Compression guideline should not be updated at this time.

3. Review recommendation

The guideline should not be considered for an update at this time.

The guideline should cross refer to the new Technology Appraisal: Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma (expected date of issue: June 2012) that was previously not mentioned in the guideline.

Centre for Clinical Practice
6 June 2012

Appendix I

1. Botteman MF, Meijboom M, Foley I et al. (2011) Cost-effectiveness of zoledronic acid in the prevention of skeletal-related events in patients with bone metastases secondary to advanced renal cell carcinoma: Application to France, Germany, and the United Kingdom. European Journal of Health Economics 12:575-588.

2. Carter JA, Joshi A, Kaura S et al. (2011) Cost effectiveness of zoledronic acid in the management of skeletal metastases in hormone-refractory prostate cancer patients in France, Germany, Portugal, and the Netherlands. Journal of Medical Economics 14:288-298.

3. Joshi AD, Carter JA, Botteman MF et al. (2011) Cost-effectiveness of zoledronic acid in the management of skeletal metastases in patients with lung cancer in France, Germany, Portugal, the Netherlands, and the United kingdom. Clinical Therapeutics 33:291-304.

4. Xie J, Namjoshi M, Wu EQ et al. (2011) Economic evaluation of denosumab compared with zoledronic acid in hormone-refractory prostate cancer patients with bone metastases. Journal of managed care pharmacy : JMCP 17:621-643.

5. Mhaskar R, Redzepovic J, Wheatley K et al. (2010) Bisphosphonates in multiple myeloma. Cochrane Database of Systematic Reviews CD003188.

6. Wong-Matthew HF, Stockler MR, and Pavlakis N. (2012) Bisphosphonates and other bone agents for breast cancer. Cochrane Database of Systematic Reviews .

7. Fizazi K, Lipton A, Mariette X et al. (2009) Randomized phase II trial of denosumab in patients with bone metastases from prostate cancer, breast cancer, or other neoplasms after intravenous bisphosphonates. Journal of Clinical Oncology 27:1564-1571.

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