Metastatic spinal cord compression:

Diagnosis and management of patients at risk of or with metastatic spinal cord compression

Full Guideline

November 2008

Developed for NICE by the National Collaborating Centre for Cancer

Update information
September 2023: NICE guideline CG75 (November 2008) has been updated and replaced by NICE guideline NG234. This document preserves the evidence and committee's discussion for areas of the guideline not updated in 2023. See https://www.nice.org.uk/guidance/ng234 for all current recommendations and the evidence behind them.

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Foreword

This Guideline is published in recognition that patients with metastatic spinal cord compression (MSCC) sometimes suffer delays and avoidable disability. It considers the available evidence and makes recommendations (to ensure that facilities are available and treatment is co-ordinated) to promote best practice and whenever possible to prevent paralysis from adversely affecting the quality of life for people with metastatic cancer.

For most it is reasonable to achieve referral, investigation, planning and treatment within a one week timescale. For many with early symptoms there is little urgency and it is important not to overwhelm the pathway with inappropriate demands. For some who present late, decompression surgery may be an out-of-hours emergency and it is important that the pathway is able to respond appropriately.

For all those affected by MSCC (including family and carers) it is important to recognise the impact of this diagnosis and the wide ranging needs and support required throughout this period of care.

Mr Barrie White
GDG Chair

Key priorities

1. Every cancer network should ensure that appropriate services are commissioned and in place for the efficient and effective diagnosis, treatment, rehabilitation and ongoing care of patients with MSCC. These services should be monitored regularly through prospective audit of the care pathway.

2. Inform patients at high risk of developing bone metastases, patients with diagnosed bone metastases, or patients with cancer who present with spinal pain about the symptoms of MSCC. Offer information (for example, in the form of a leaflet; see appendix 2) to patients and their families and carers which explains the symptoms of MSCC, and advises them (and their healthcare professionals) what to do if they develop these symptoms.

3. Contact the MSCC coordinator urgently (within 24 hours) to discuss the care of patients with cancer and any of the following symptoms suggestive of spinal metastases:
   - pain in the middle (thoracic) or upper (cervical) spine
   - progressive lower (lumbar) spinal pain
   - severe unremitting lower spinal pain
   - spinal pain aggravated by straining (for example, at stool, or when coughing or sneezing)
   - localised spinal tenderness
   - nocturnal spinal pain preventing sleep.

4. Contact the MSCC coordinator immediately to discuss the care of patients with cancer and symptoms suggestive of spinal metastases who have any of the following neurological symptoms or signs suggestive of MSCC, and view them as an oncological emergency:
   - neurological symptoms including radicular pain, any limb weakness, difficulty in walking, sensory loss or bladder or bowel dysfunction
   - neurological signs of spinal cord or cauda equina compression.

5. Perform MRI of the whole spine in patients with suspected MSCC, unless there is a specific contraindication. This should be done in time to allow definitive treatment to be planned within 1 week of the suspected diagnosis in the case of spinal pain suggestive of spinal meta-stases, and within 24 hours in the case of spinal pain suggestive of spinal metastases and neurological symptoms or signs suggestive of MSCC, and occasionally sooner if there is a pressing clinical need for emergency surgery.

6. Patients with severe mechanical pain suggestive of spinal instability, or any neurological symptoms or signs suggestive of MSCC, should be nursed flat with neutral spine alignment (including 'log rolling' or turning beds, with use of a slipper pan for toilet) until bony and neurological stability are ensured and cautious remobilisation may begin.

7. Start definitive treatment, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of MSCC.

8. Carefully plan surgery to maximise the probability of preserving spinal cord function without undue risk to the patient, taking into account their overall fitness, prognosis and preferences.

9. Ensure urgent (within 24 hours) access to and availability of radiotherapy and simulator facilities in daytime sessions, 7 days a week for patients with MSCC requiring definitive treatment or who are unsuitable for surgery.

10. Discharge planning and ongoing care, including rehabilitation for patients with MSCC, should start on admission and be led by a named individual from within the responsible clinical team. It should involve the patient and their families and carers, their primary oncology site team, rehabilitation team and community support, including primary care and specialist palliative care, as required.

Key research recommendations

1. Further research should be undertaken into the reasons why patients with MSCC present late. Although it is clear from the existing evidence that many patients with MSCC present late, often with established and irreversible neurological problems or a long preceding history of symptoms, the reasons for this are not understood.
2. The use of radiotherapy to prevent the development of MSCC in patients with identified spinal metastases but no pain should be investigated in prospective randomised controlled trials. There is currently no reliable evidence to indicate whether the use of prophylactic radiotherapy can prevent the development of MSCC in patients with known metastases in the spine but no pain.
3. The use of vertebroplasty and kyphoplasty in preventing MSCC in patients with vertebral metastases should be investigated in prospective comparative studies. These procedures have been investigated in observational studies without comparators and largely in patients with osteoporotic vertebral collapse. There is limited evidence about their use in patients with MSCC.
4. The use of surgery to prevent the development of MSCC in patients with identified spinal metastases but no pain should be investigated in prospective randomised controlled trials. There is currently no reliable evidence to indicate whether the use of prophylactic surgery can prevent the development of MSCC in patients with known metastases in the spine but no pain.
5. Further research should investigate what are the most clinically and cost-effective regimens of radiotherapy to treat patients with established MSCC and investigate the use of new techniques, such as intensity modulated radiation therapy. Currently there is insufficient high-quality evidence of the effect of different regimens of radiotherapy to treat patients with established MSCC. In order to evaluate the effects of different regimens of radiotherapy, more randomised controlled trials are required. There is no evidence that evaluates new techniques, such as intensity-modulated radiation therapy, in patients with MSCC.

Recommendations

Chapter 2: Service configuration and urgency of treatment

- Every cancer network should have a clear care pathway for the diagnosis, treatment, rehabilitation and ongoing care of patients with metastatic spinal cord compression (MSCC).
- Every cancer network should ensure that appropriate services are commissioned and in place for the efficient and effective diagnosis, treatment, rehabilitation and ongoing care of patients with MSCC. These services should be monitored regularly through prospective audit of the care pathway.
- Cancer networks should ensure that there is local access to urgent magnetic resonance imaging (MRI) within 24 hours for all patients with suspected MSCC. This service should be available outside normal working hours and with 24-hour capability in centres treating patients with MSCC.
- Every cancer network should have a network site specific group for MSCC. The group should include representatives from primary, secondary and tertiary care and should have strong links to network site specific groups for primary tumours.
- The cancer network should appoint a network lead for MSCC whose responsibilities include:
  - advising the cancer network, commissioners and providers about the provision and organisation of relevant clinical services
  - ensuring that the local care pathway for diagnosis and management are documented, agreed and consistent across the network
  - ensuring that there are appropriate points of telephone contact for the role of an MSCC coordinator and senior clinical advisers
  - maintaining a network-wide audit of the incidence, timeliness of management, and outcomes of patients with MSCC using nationally agreed measures
  - arranging and chairing twice-yearly meetings of the network site specific group for MSCC, at which patient outcomes will be reported and the local care pathway reviewed and amended if necessary.
- Every secondary or tertiary care centre should have an identified lead healthcare professional for MSCC (who is usually, but not necessarily, medical) whose responsibilities include:
  - representing the hospital at network level in the development of care pathways
  - implementing the care pathway and disseminating information about the diagnosis and appropriate management of patients with known or suspected MSCC
  - ensuring timely and effective communication between all relevant healthcare professionals involved in the care of patients with MSCC, including primary care and palliative care
  - raising and maintaining the awareness and understanding of treatments for MSCC among all clinical staff across the locality
  - contributing to regular network audits of the care of patients with MSCC
  - attending and contributing to the twice-yearly network site specific group meeting.
- Commissioners should establish a joint approach with councils responsible for local social services to ensure efficient provision of equipment and support, including nursing and rehabilitation services, to meet the individual needs of patients with MSCC and their families and carers.

MSCC coordinator and senior clinical adviser – roles and responsibilities

- Each centre treating patients with MSCC should identify or appoint individuals responsible for performing the role of MSCC coordinator and ensure its availability at all times.
- Each centre treating patients with MSCC should have a single point of contact to access the MSCC coordinator who should provide advice to clinicians and coordinate the care pathway at all times.
- The MSCC coordinator should:
  - provide the first point of contact for clinicians who suspect that a patient may be developing spinal metastases or MSCC
  - perform an initial telephone triage by assessing requirement for, and urgency of, investigations, transfer, and treatment
  - advise on the immediate care of the spinal cord and spine and seek senior clinical advice, as necessary
  - gather baseline information to aid decision-making and collate data for audit purposes
  - identify the appropriate place for timely investigations and admission if required
  - liaise with the acute receiving team and organise admission and mode of transport.
- The optimal care of patients with MSCC should be determined by senior clinical advisers (these include clinical oncologists, spinal surgeons and radiologists with experience and expertise in treating patients with MSCC), taking into account the patient's preferences and all aspects of their condition, with advice from primary tumour site clinicians or other experts, as required.
- Every centre treating patients with MSCC should ensure 24-hour availability of senior clinical advisers to give advice and support to the MSCC coordinator and other clinicians, inform the decision-making process and undertake treatment where necessary.

Chapter 3: The patient's experience of MSCC

Supporting patient decisions

- Ensure that communication with patients with known or suspected MSCC is clear and consistent, and that the patients, their families and carers are fully informed and involved in all decisions about treatment.

Emotional and family support

- Offer patients with MSCC and their families and carers specialist psychological and/or spiritual support appropriate to their needs at diagnosis, at other key points during treatment and on discharge from hospital.
- Provide information to patients with MSCC in an appropriate language and format that explains how to access psychological and/or spiritual support services when needed.
- Offer bereavement support services to patients' families based on the three component model outlined in 'Improving supportive and palliative care for adults with cancer' (NICE cancer service guidance CSGSP).

Chapter 4: Early detection

Communicating symptoms and risks

- Inform patients at high risk of developing bone metastases, patients with diagnosed bone metastases, or patients with cancer who present with spinal pain about the symptoms of MSCC. Offer information (for example, in the form of a leaflet; see appendix 2) to patients and their families and carers which explains the symptoms of MSCC, and advises them (and their healthcare professionals) what to do if they develop these symptoms.
- Ensure that patients with MSCC and their families and carers know who to contact if their symptoms progress while they are waiting for urgent investigation of suspected MSCC.

Early symptoms and signs

- Contact the MSCC coordinator urgently (within 24 hours) to discuss the care of patients with cancer and any of the following symptoms suggestive of spinal metastases:
  - pain in the middle (thoracic) or upper (cervical) spine
  - progressive lower (lumbar) spinal pain
  - severe unremitting lower spinal pain
  - spinal pain aggravated by straining (for example, at stool, or when coughing or sneezing)
  - localised spinal tenderness
  - nocturnal spinal pain preventing sleep.
- Contact the MSCC coordinator immediately to discuss the care of patients with cancer and symptoms suggestive of spinal metastases who have any of the following neurological symptoms or signs suggestive of MSCC, and view them as an oncological emergency:
  - neurological symptoms including radicular pain, any limb weakness, difficulty in walking, sensory loss or bladder or bowel dysfunction
  - neurological signs of spinal cord or cauda equina compression.
- Perform frequent clinical reviews of patients with cancer who develop lower spinal pain that is clinically thought to be of non-specific origin (that is, it is not progressive, severe or aggravated by straining and has no accompanying neurological symptoms). In particular, look for:
  - development of progressive pain or other symptoms suggestive of spinal metastases (contact the MSCC coordinator within 24 hours), or
  - development of neurological symptoms or signs suggestive of MSCC (contact the MSCC coordinator immediately).
- Perform frequent clinical reviews of patients without a prior diagnosis of cancer who develop suspicious spinal pain with or without neurological symptoms. Treat or refer patients with stable and mild symptoms by normal non-specific spinal pathways, or refer by cancer pathway if concerned. In particular, look for.
- development of progressive pain or other symptoms suggestive of spinal metastases (contact the MSCC coordinator within 24 hours), or
- development of neurological symptoms or signs suggestive of MSCC (contact the MSCC coordinator immediately).

Chapter 5: Imaging

Choice of imaging modality

- MRI of the spine in patients with suspected MSCC should be supervised and reported by a radiologist and should include sagittal T1 and/or short T1 inversion recovery (STIR) sequences of the whole spine, to prove or exclude the presence of spinal metastases. Sagittal T2 weighted sequences should also be performed to show the level and degree of compression of the cord or cauda equina by a soft tissue mass and to detect lesions within the cord itself. Supplementary axial imaging should be performed through any significant abnormality noted on the sagittal scan.
- Contact the MSCC coordinator to determine the most appropriate method of imaging for patients with suspected MSCC in whom MRI is contraindicated and where this should be carried out.
- Consider targeted computerised tomography (CT) scan with three-plane reconstruction to assess spinal stability and plan vertebroplasty, kyphoplasty or spinal surgery in patients with MSCC.
- Consider myelography if other imaging modalities are contraindicated or inadequate. Myelography should only be undertaken at a neuroscience or spinal surgical centre because of the technical expertise required and because patients with MSCC may deteriorate following myelography and require urgent decompression.
- Do not perform plain radiographs of the spine either to make or to exclude the diagnosis of spinal metastases or MSCC.

Routine MRI and early detection of MSCC

- In patients with a previous diagnosis of malignancy, routine imaging of the spine is not recommended if they are asymptomatic.
- Serial imaging of the spine in asymptomatic patients with cancer who are at high risk of developing spinal metastases should only be performed as part of a randomised controlled trial.

Timing of MRI assessment

- Imaging departments should configure MRI lists to permit time for examination of patients with suspected MSCC at short notice during existing or extended sessions (by moving routine cases into ad hoc overtime or to alternative sessions, if overtime is not possible).
- If MRI is not available at the referring hospital, transfer patients with suspected MSCC to a unit with 24-hour capability for MRI and definitive treatment of MSCC.
- Perform MRI of the whole spine in patients with suspected MSCC, unless there is a specific contraindication. This should be done in time to allow definitive treatment to be planned within 1 week of the suspected diagnosis in the case of spinal pain suggestive of spinal metastases, and within 24 hours in the case of spinal pain suggestive of spinal metastases and neurological symptoms or signs suggestive of MSCC, and occasionally sooner if there is a pressing clinical need for emergency surgery.
- Out of hours MRI should only be performed in clinical circumstances where there is an emergency need and intention to proceed immediately to treatment, if appropriate.

Chapter 6: Treatment of spinal metastases and MSCC

Treatments for painful spinal metastases and prevention of MSCC

Analgesia

- Offer conventional analgesia (including NSAIDs, non-opiate and opiate medication) as required to patients with painful spinal metastases in escalating doses as described by the WHO three-step pain relief ladder[1].
- Consider referral for specialist pain care including invasive procedures (such as epidural or intrathecal analgesia) and neurosurgical interventions for patients with intractable pain from spinal metastases.

Bisphosphonates

- 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 MSCC, except as part of a randomised controlled trial.

Radiotherapy

- Offer patients with spinal metastases causing non-mechanical spinal pain 8 Gy single fraction palliative radiotherapy even if they are completely paralysed.
- Patients with asymptomatic spinal metastases should not be offered radiotherapy with the intention of preventing MSCC except as part of a randomised controlled trial.

[1] See www.who.int/cancer/palliative/painladder/en

Vertebroplasty and kyphoplasty

- Consider vertebroplasty[2] or kyphoplasty[3] for patients who have vertebral metastases and no evidence of MSCC or spinal instability if they have:
  - mechanical pain resistant to conventional analgesia, or
  - vertebral body collapse.
- Vertebroplasty or kyphoplasty for spinal metastases should only be performed after agreement between appropriate specialists (including an oncologist, interventional radiologist, and spinal surgeon), with full involvement of the patient and in facilities where there is good access to spinal surgery.

Surgery

- Urgently consider patients with spinal metastases and imaging evidence of structural spinal failure with spinal instability for surgery to stabilise the spine and prevent MSCC.
- Consider patients with spinal metastases and mechanical pain resistant to conventional analgesia for spinal stabilisation surgery even if completely paralysed.
- Consider patients with MSCC who have severe mechanical pain and/or imaging evidence of spinal instability, but who are unsuitable for surgery, for external spinal support (for example, a halo vest or cervico-thoraco-lumbar orthosis).
- Patients with spinal metastases without pain or instability should not be offered surgery with the intention of preventing MSCC except as part of a randomised controlled trial.

Treatment options

- All decisions on the most appropriate combinations of treatment for pain or preventing paralysis caused by MSCC should be made by relevant spinal specialists in consultation with primary tumour site clinicians and with the full involvement of the patient.

Care of the threatened spinal cord in patients with MSCC

Mobilisation

- Patients with severe mechanical pain suggestive of spinal instability, or any neurological symptoms or signs suggestive of MSCC, should be nursed flat with neutral spine alignment (including 'log rolling' or turning beds, with use of a slipper pan for toilet) until bony and neurological stability are ensured and cautious remobilisation may begin.
- For patients with MSCC, once any spinal shock has settled and neurology is stable, carry out close monitoring and interval assessment during gradual sitting from supine to 60 degrees over a period of 3–4 hours.
- When patients with MSCC begin gradual sitting, if their blood pressure remains stable and no significant increase in pain or neurological symptoms occurs, continue to unsupported sitting, transfers and mobilisation as symptoms allow.
- If a significant increase in pain or neurological symptoms occurs when patients with MSCC begin gradual sitting and mobilisation, return them to a position where these changes reverse and reassess the stability of their spine.
- After a full discussion of the risks, patients who are not suitable for definitive treatment should be helped to position themselves and mobilise as symptoms permit with the aid of orthoses and/or specialist seating to stabilise the spine, if appropriate.

Corticosteroids

- Unless contraindicated (including a significant suspicion of lymphoma) offer all patients with MSCC a loading dose of at least 16 mg of dexamethasone as soon as possible after assessment, followed by a short course of 16 mg dexamethasone daily while treatment is being planned.

[2] 'Percutaneous vertebroplasty' (NICE interventional procedure guidance 12). The Medicines and Healthcare Products Regulatory Agency has issued safety notices relating to this procedure (reference MDA/2003/021).

[3] 'Balloon kyphoplasty for vertebral compression fractures' (NICE interventional procedure guidance 166).

- Continue dexamethasone 16 mg daily in patients awaiting surgery or radiotherapy for MSCC. After surgery or the start of radiotherapy the dose should be reduced gradually over 5-7 days and stopped. If neurological function deteriorates at any time the dose should be increased temporarily.
- Reduce gradually and stop dexamethasone 16 mg daily in patients with MSCC who do not proceed to surgery or radiotherapy after planning. If neurological function deteriorates at any time the dose should be reconsidered.
- Monitor blood glucose levels in all patients receiving corticosteroids.

Case selection for definitive treatment of MSCC

- Start definitive treatment, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of MSCC.

Nature of metastases

- Attempt to establish the primary histology of spinal metastases (including by tumour biopsy, if necessary) when planning definitive treatment.
- Stage the tumours of patients with MSCC to determine the number, anatomical sites and extent of spinal and visceral metastases when planning definitive treatment.

Functional ability, general fitness, previous treatments and fitness for anaesthesia

- Take into account the preferences of patients with MSCC as well as their neurological ability, functional status, general health and fitness, previous treatments, magnitude of surgery, likelihood of complications, fitness for general anaesthesia and overall prognosis when planning treatment.
- Patients with suspected MSCC, a poor performance status and widespread metastatic disease should wherever possible be discussed with their primary tumour site clinician and spinal senior clinical adviser before any urgent imaging or hospital transfer.
- Patients with suspected MSCC who have been completely paraplegic or tetraplegic for more than 24 hours should wherever possible be discussed urgently with their primary tumour site clinician and spinal senior clinical adviser before any imaging or hospital transfer.
- Patients who are too frail or unfit for specialist treatment for MSCC should not be transferred unnecessarily.

Age

- Patients with MSCC should not be denied either surgery (if fit enough) or radiotherapy on the basis of age alone.

The role of scoring systems

- When deciding whether surgery is appropriate, and if so its type and extent, use recognised prognostic factors including the revised Tokuhashi scoring system[4], and American Society of Anaesthetists (ASA) grading. Systematically record and take into account relevant comorbidities.
- Only consider major surgical treatments for patients expected to survive longer than 3 months.

Surgery for the definitive treatment of MSCC

General principles

- If surgery is appropriate in patients with MSCC, attempt to achieve both spinal cord decompression and durable spinal column stability.

[4] Tokuhashi Y et al. (2005) A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. Spine 30 (19): 2186–91.

Neurological ability

- Patients with MSCC who are suitable for surgery should have surgery before they lose the ability to walk.
- Patients with MSCC who have residual distal sensory or motor function and a good prognosis should be offered surgery in an attempt to recover useful function, regardless of their ability to walk.
- Patients with MSCC who have been completely paraplegic or tetraplegic for more than 24 hours should only be offered surgery if spinal stabilisation is required for pain relief.

Timing

- Consider the speed of onset, duration, degree and site of origin of neurological symptoms and signs (cord or cauda equina) when assessing the urgency of surgery.

Technical factors

- Carefully plan surgery to maximise the probability of preserving spinal cord function without undue risk to the patient, taking into account their overall fitness, prognosis and preferences.
- Posterior decompression alone should not be performed in patients with MSCC except in the rare circumstances of isolated epidural tumour or neural arch metastases without bony instability.
- If spinal metastases involve the vertebral body or threaten spinal stability, posterior decompression should always be accompanied by internal fixation with or without bone grafting.
- Consider vertebral body reinforcement with cement for patients with MSCC and vertebral body involvement who are suitable for instrumented decompression but are expected to survive for less than 1 year.
- Consider vertebral body reconstruction with anterior bone graft for patients with MSCC and vertebral body involvement who are suitable for instrumented decompression, are expected to survive for 1 year or longer and who are fit to undergo a more prolonged procedure.
- 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).

Radiotherapy for the definitive treatment of MSCC

- Ensure urgent (within 24 hours) access to and availability of radiotherapy and simulator facilities in daytime sessions, 7 days a week for patients with MSCC requiring definitive treatment or who are unsuitable for surgery.
- Offer fractionated radiotherapy as the definitive treatment of choice to patients with epidural tumour without neurological impairment, mechanical pain or spinal instability.
- Offer a fractionated rather than a single fraction regimen to patients with a good prognosis who are having radiotherapy as their first-line treatment.
- Preoperative radiotherapy should not be carried out on patients with MSCC if surgery is planned.
- Postoperative fractionated radiotherapy should be offered routinely to all patients with a satisfactory surgical outcome once the wound has healed.
- Offer urgent radiotherapy (within 24 hours) to all patients with MSCC who are not suitable for spinal surgery unless:
  - they have had complete tetraplegia or paraplegia for more than 24 hours and their pain is well controlled; or
  - their overall prognosis is judged to be too poor.

Selection of treatment following previous radiotherapy

- Consider further radiotherapy or surgery for patients who have responded well to previous radiotherapy and develop recurrent symptoms after at least 3 months.

- If patients have further radiotherapy, the total dose should be below a biologically equivalent dose of 100 Gy_2 where possible. Discuss the possible benefits and risks with the patient before agreeing a treatment plan.

Chapter 7: Supportive care and rehabilitation

Interventions for thromboprophylaxis

- Offer all patients who are on bed rest with suspected MSCC thigh-length graduated compression/anti-embolism stockings unless contraindicated, and/or intermittent pneumatic compression or foot impulse devices.
- Offer patients with MSCC who are at high risk of venous thromboembolism (including those treated surgically and judged safe for anticoagulation) subcutaneous thromboprophylactic low molecular weight heparin in addition to mechanical thromboprophylaxis[5].
- For patients with MSCC, individually assess the duration of thromboprophylactic treatment, based on the presence of ongoing risk factors, overall clinical condition and return to mobility.

Management of pressure ulcers

- Undertake and document a risk assessment for pressure ulcers (using a recognised assessment tool) at the beginning of an episode of care for patients with MSCC. Repeat this assessment every time the patient is turned while on bed rest and at least daily thereafter.
- While patients with MSCC are on bed rest, turn them using a log rolling technique at least every 2–3 hours. Encourage patients who are not on bed rest to mobilise regularly (every few hours). Encourage and assist those who are unable to stand or walk to perform pressure relieving activities such as forward/sideways leaning at least hourly when they are sitting out.
- Promptly provide pressure relieving devices to patients with MSCC appropriate to their pressure risk assessment score. Offer patients with restricted mobility or reduced sensation cushions and/or mattresses with very high-grade pressure-relieving properties.
- When caring for patients with MSCC, adhere to the pressure sore assessment, prevention and healing protocols recommended in 'The use of pressure-relieving devices for prevention of pressure ulcers' (NICE clinical guideline 7) and 'The management of pressure ulcers in primary and secondary care' (NICE clinical guideline 29).

Bladder and bowel continence management

- Assess bowel and bladder function in all patients with MSCC on initial presentation and start a plan of care.
- Monitor patients with MSCC who are continent and without urinary retention or disturbed bowel function at least daily for changes in bladder and bowel function.
- Manage bladder dysfunction in patients with MSCC initially by a urinary catheter on free drainage. If long-term catheterisation is required, consider intermittent catheterisation or suprapubic catheters.
- Offer a neurological bowel management programme to patients with MSCC and disturbed bowel habit as recommended in 'Faecal incontinence' (NICE clinical guideline 49). Take account of patient preferences when offering diet modification, faecal softeners, oral or rectal laxatives and/or constipating agents as required. Digital stimulation, manual evacuation, rectal irrigation and surgical treatment may be offered, as required.

Maintaining circulatory and respiratory functioning

- Include heart rate and blood pressure measurement, respiratory rate and pulse oximetry in the initial assessment and routine monitoring of all patients with MSCC.
- Symptomatic postural hypotension in patients with MSCC should be managed initially by patient positioning and devices to improve venous return (such as foot pumps and graduated

[5] See 'Venous thromboembolism' (NICE clinical guideline 46) for information on reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing spinal surgery.

compression/anti-embolism stockings). Avoid overhydration which can provoke pulmonary oedema.

- Include clearing of lung secretions by breathing exercises, assisted coughing and suctioning as needed in the prophylactic respiratory management of patients with MSCC. Treat retained secretions and the consequences by deep breathing and positioning supplemented by bi-phasic positive airway pressure and intermittent positive pressure ventilation if necessary.

Access to specialist rehabilitation and transition to care at home

- Ensure that all patients admitted to hospital with MSCC have access to a full range of health-care professional support services for assessment, advice and rehabilitation.
- Focus the rehabilitation of patients with MSCC on their goals and desired outcomes, which could include promoting functional independence, participation in normal activities of daily life and aspects related to their quality of life.
- Offer admission to a specialist rehabilitation unit to those patients with MSCC who are most likely to benefit, for example, those with a good prognosis, a high activity tolerance and strong rehabilitation potential.
- Discharge planning and ongoing care, including rehabilitation for patients with MSCC, should start on admission and be led by a named individual from within the responsible clinical team. It should involve the patient and their families and carers, their primary oncology site team, rehabilitation team and community support, including primary care and specialist palliative care, as required.
- Ensure that community-based rehabilitation and supportive care services are available to people with MSCC following their return home, in order to maximise their quality of life and continued involvement in activities that they value.
- Ensure that people with MSCC are provided with the equipment and care they require in a timely fashion to maximise their quality of life at home.
- Offer the families and carers of patients with MSCC relevant support and training before discharge home.
- Clear pathways should be established between hospitals and community-based healthcare and social services teams to ensure that equipment and support for people with MSCC returning home and their carers and families are arranged in an efficient and coordinated manner.

Methodology

Introduction

What is a clinical guideline?

Guidelines are recommendations for the care of individuals in specific clinical conditions or circumstances – from prevention and self-care through to primary and secondary care and onto more specialised services. NICE clinical guidelines are based on the best available evidence of clinical and cost effectiveness, and are produced to help healthcare professionals and patients make informed choices about appropriate healthcare. While guidelines assist the practice of healthcare professionals, they do not replace their knowledge and skills.

Clinical guidelines for the NHS in England, Wales and Northern Ireland are produced as a response to a request from the Department of Health (DH). They approve topics for guideline development and before deciding whether to refer a particular topic to the National Institute for Health and Clinical Excellence (NICE) they consult with the relevant patient bodies, professional organisations and companies. Once a topic is referred, NICE then commissions one of seven National Collaborating Centres (NCCs) to produce a guideline. The Collaborating Centres are independent of government and comprise partnerships between a variety of academic institutions, health profession bodies and patient groups. The National Collaborating Centre for Cancer (NCC-C) was referred the topic of metastatic spinal cord compression in January 2006 as part of NICE's 12th wave work programme. However the guideline development process began officially on 19th September 2006 when sufficient capacity became available at the NCC-C.

Who is the guideline intended for?

This guideline does not include recommendations covering every detail of the diagnosis and treatment of metastatic spinal cord compression. Instead we have tried to focus on those areas of clinical practice that are (i) known to be controversial or uncertain; (ii) where there is identifiable practice variation; (iii) where there is a lack of high quality evidence; or (iv) where NICE guidelines are likely to have most impact. More detail on how this was achieved is presented later in the section on 'Developing Clinical Evidence Based Questions'.

The guideline is relevant to all healthcare professionals who come into contact with patients with metastatic spinal cord compression, as well as to the patients themselves and their carers. It is also expected that the guideline will be of value to those involved in clinical governance in both primary and secondary care to help ensure that arrangements are in place to deliver appropriate care to this group of patients.

The remit of the guideline

Guideline topics selected by the DH identify the main areas to be covered by the guideline in a specific remit. The following remit for this guideline was received as part of NICE's 12th wave programme of work:

To develop a guideline on: 'Diagnosis and management of patients with metastatic spinal cord compression, including service delivery where appropriate.'

What the guideline covers – the scope

The remit was then translated into a scope document by the Guideline Development Group (GDG) Chair and Clinical Lead and staff at the NCC-C. The purpose of the scope was to:

- provide an overview of what the guideline would include and exclude
- identify the key aspects of care that must be included
- set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC-C and the remit
- inform the development of the clinical questions and search strategy
- inform professionals and the public about the expected content of the guideline.

Prior to the start of the guideline development process, the scope was subject to a four week stakeholder consultation in accordance with processes established by NICE in the 'NICE guidelines manual' (NICE, 2005, NICE 2006, NICE 2007). The full scope is shown in Appendix 7. During the consultation period, the scope was posted on the NICE website (www.nice.org.uk). Comments were invited from registered stakeholder organisations, the NICE Guideline Review Panel (GRP) and the Patient and Public Involvement Programme (PPIP) at NICE. Further information about the GRP can also be found on the NICE website. The NCC-C and NICE reviewed the scope in light of comments received, and the revised scope was signed off by the GRP; signed off by NICE and posted on the NICE website.

Involvement of stakeholders

Key to the development of all NICE guidance are the relevant professional and patient/carer organisations that register as stakeholders. Details of this process can be found on the NICE website or in the 'NICE guidelines manual' (NICE 2007). In brief, their contribution involves commenting on the draft scope, submitting relevant evidence and commenting on the draft version of the guideline during the end consultation period. A full list of all stakeholder organisations who registered for the metastatic spinal cord compression cancer guideline can be found in Appendix 9.2.

Needs assessment

As part of the guideline development process the NCC-C invited Specialist Registrars from Velindre NHS Trust in Cardiff to undertake a needs assessment. The needs assessment aims to describe the burden of disease and current service provision for people with metastatic spinal cord compression in England and Wales, which informed the development of the guideline. This document forms a supplement to the full guideline and will also appear on an accompanying CD-ROM when the guideline is published.

Assessment of the effectiveness of interventions is not included in the needs assessment, and was undertaken separately by researchers in the NCC-C as part of the guideline development process.

The information included in the needs assessment document was presented to the GDG. Most of the information was presented in the early stages of guideline development, and other information was included to meet the evolving information needs of the GDG during the course of guideline development.

The process of guideline development – who develops the guideline?

Overview

The development of this guideline was based upon methods outlined by the 'NICE guidelines manual' (NICE 2007). A team of health professionals, lay representatives and technical experts known as the GDG (see appendix 9.1), with support from the NCC-C staff, undertook the development of this clinical guideline. The basic steps in the process of developing a guideline are listed and discussed below:

- using the remit, define the scope which sets the parameters of the guideline

- forming the guideline development group (GDG)
- developing clinical questions
- systematically searching for the evidence
- critically appraising the evidence
- incorporating health economic evidence
- distilling and synthesising the evidence and writing recommendations
- agreeing the recommendations
- structuring and writing the guideline
- updating the guideline.

The Guideline Development Group (GDG)

The metastatic spinal cord compression GDG was recruited in line with the existing NICE protocol as set out in the 'NICE guidelines manual' (NICE 2007). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and candidates were informally interviewed prior to being offered the role. The NCC-C Director, GDG Chair and Lead Clinician identified a list of specialties that needed to be represented on the GDG. Requests for nominations were sent to the main stakeholder organisations and patient organisations/charities (Appendix 9.2). Individual GDG members were selected by the NCC-C Director, GDG Chair and Lead Clinician, based on their application forms, following nomination from their respective stakeholder organisation. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to drafting the guideline. At the start of the guideline development process all GDG members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new, arising conflicts of interest which were always recorded (see Appendix 9.1).

Guideline Development Group meetings

Thirteen GDG meetings were held between 19 September 2006 and 21 April 2008. During each GDG meeting (either held over one day or two days) clinical questions and clinical and economic evidence were reviewed and assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed as part of a standing agenda item.

NCC-C project managers divided the GDG workload by allocating specific topics, relevant to their area of clinical practice, to small sub-groups of the GDG in order to simplify and speed up the guideline development process. These groups considered the evidence, as reviewed by the systematic reviewer, and synthesised it into draft recommendations prior to presenting it to the GDG as a whole. Each topic group was led by a GDG member with expert knowledge of the topic area (usually one of the healthcare professionals). The GDG sub-groups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/carer representatives

Individuals with direct experience of MSCC services gave an integral user focus to the GDG and the guideline development process. The GDG included two patient/carer representatives. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GDG.

Expert advisers

During the development phase of the guideline the GDG identified areas where there was a requirement for expert input on particular specialist topic areas. The topics were addressed by either the production of a position paper or a formal presentation by a recognised expert

(Appendix 9.4) who had been identified via the relevant registered stakeholder organisation. All relevant position papers are presented as part of the evidence review.

Developing clinical evidence-based questions

Background

The scope, as described in Appendix 7, needs to be very clear about which patient groups are included and which areas of clinical care should be considered. But within these boundaries it does not usually specify which topics that are considered a priority.

It was recognised by the NCC-C at an early stage that in order to complete the guideline development work to an appropriate standard the GDG needed to restrict its work to approximately 30 clinical questions. Previously this prioritisation would have been carried out by the GDG at its first two meetings but it was clear from some guidelines already published that this approach had resulted in a much larger number of questions than 30 being addressed.

Clinical guidelines should be aimed at changing clinical practice and should avoid ending up as 'evidence-based textbooks' or making recommendations on topics where there is already good clinical practice. It was therefore felt important that the 30 clinical questions should be prioritised into areas that were known to be controversial or uncertain, where there was identifiable practice variation, or where NICE guidelines were likely to have most impact

Method

An extensive list of potential topics for the guideline to investigate was complied by the NCC-C Director and GDG Chair and Clinical Lead. This list was incorporated into a questionnaire which asked respondents to rate each topic on a five point Likert scale ranging from 0 (not a priority) to 5 (very high priority). It was made clear that respondents would be rating the priority for each topic to be included in a clinical guideline to be published in two years' time. The questionnaire also asked respondents to suggest any additional topics they would like to see included with an equivalent assessment of their priority.

Questionnaires were subsequently sent to all members of the MSCC GDG in advance of the first GDG meeting.

The scores from each completed questionnaire was aggregated by NCC-C staff and ranked. These results together with information on identifiable practice variation (see needs assessment) were presented to the GDG at its first meeting. The list of prioritised topics produced via the questionnaire survey was in no way definitive and the GDG used these results to agree their final priorities for the clinical questions.

For clinical questions about interventions, the PICO framework was used. This structured approach divides each question into four components: the patients (the population under study – P), the interventions (what is being done – I), the comparisons (other main treatment options – C) and the outcomes (the measures of how effective the interventions have been – O). Where appropriate, the clinical questions were refined once the evidence had been searched and, where necessary, sub-questions were generated.

The final list of clinical questions can be found in Appendix 8 of the evidence review.

Care pathway

Early in the development process the GDG designed an outline care pathway (or algorithm) in order to explore how people with metastatic spinal cord compression might access and be dealt with by the NHS.

Review of clinical literature

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national or international) produced by other groups or institutions. Additionally, stakeholder organisations were invited to submit evidence for consideration by the GDG, provided it was relevant to the agreed list of clinical questions.

In order to answer each question the NCC-C information specialist developed a search strategy to identify relevant published evidence for both clinical and cost effectiveness. Key words and terms for the search were agreed in collaboration with the GDG. When required, the health economist searched for supplemental papers to inform detailed health economic work, for example modelling (see section on 'Incorporating Health Economic Evidence').

Papers that were published or accepted for publication in peer-reviewed journals were considered as evidence. Search filters, such as those to identify systematic reviews (SRs) and randomised controlled trials (RCTs) were applied to the search strategies when necessary. No language restrictions were applied to the search; however, foreign language papers were not requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1950 onwards
- Excerpta Medica (Embase) 1980 onwards
- Cumulative Index to Nursing and Allied Health Literature (Cinahl) 1982 onwards
- Allied & Complementary Medicine (AMED) 1985 onwards
- British Nursing Index (BNI) 1994 onwards
- Psychinfo 1806 onwards
- Web of Science1970 onwards. [specifically Science Citation Index Expanded (SCI-EXPANDED) and Social Sciences Citation Index (SSCI)]
- System for Information on Grey Literature In Europe (SIGLE) 1980–2005
- Biomed Central 1997 onwards
- National Research Register (NRR)
- Current Controlled Trials

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

Searches were updated and re-run 6–8 weeks before the stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, 18 April 2008 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review (and will also appear on the accompanying CD-ROM to this guideline).

Critical appraisal and evidence grading

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision. The researcher then individually applied the inclusion/exclusion criteria to determine which studies would be relevant for inclusion and subsequent appraisal. Lists of excluded papers were generated for each question and the rationale for the exclusion was presented to the GDG when required.

The researcher then critically appraised the full papers. Critical appraisal checklists were compiled for each paper and one researcher undertook the critical appraisal and data extraction.

The researcher assessed the quality of eligible studies by referring to the SIGN quality checklist for systematic reviews/meta-analyses and randomised control trials (Table A). Evidence relating to clinical effectiveness was classified using this established hierarchical system. However this checklist is less appropriate for studies reporting diagnostic tests of accuracy. In the absence of a validated hierarchy for this type of test, NICE suggests levels of evidence that take into account the factors likely to affect the validity of these studies[1].

[1] National Institute for Health and Clinical Excellence (April 2007) The guidelines manual. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk

Table A Levels of evidence for intervention studies

Level	Source of evidence
1++	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs) or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1−	Meta-analyses, systematic reviews of RCTs or RCTs with a high risk of bias
2++	High-quality systematic reviews of case–control or cohort studies; high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2+	Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2−	Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies (for example, case reports, case series)
4	Expert opinion, formal consensus

For all the relevant appraised studies for a particular question, data on the type of population, intervention, comparator and outcomes (PICO) was recorded in evidence tables and an accompanying evidence summary prepared for the GDG (see evidence review). All the evidence was considered carefully by the GDG for accuracy and completeness.

All procedures were fully compliant with NICE methodology as detailed in the 'NICE guidelines manual' (NICE 2007).

In general, no formal contact was made with authors, however, there were ad hoc occasions when this was required in order to clarify specific details.

Incorporating health economics evidence

The aim of the economic input into the guideline was to inform the GDG of potential economic issues relating to metastatic spinal cord compression. It is important to investigate whether health services are both clinically effective and cost effective, i.e. are they 'value for money'.

The health economist helped the GDG by identifying priority topics within the guideline that might benefit from economic analysis, reviewing the available economic evidence and, where necessary, conducting economic analysis. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence wherever possible.

In order to assess the cost-effectiveness of each priority topic, a comprehensive systematic review of the economic literature was conducted. For those clinical areas reviewed, the information specialists used a similar search strategy as used for the review of clinical evidence but with the inclusion of a health economics and quality of life filter.

Each search strategy was designed to find any applied study estimating the cost or cost effectiveness of the topic under consideration. A health economist reviewed abstracts and relevant papers were ordered for appraisal.

Published economic evidence was obtained from a variety of sources:

- Medline 1966 onwards
- Embase 1980 onwards
- NHS Economic Evaluations Database (NHS EED)
- EconLit 1969 onwards

Economic modelling

In addition to the review of the relevant clinical evidence, the GDG were required to determine whether or not the cost-effectiveness of each of the individual clinical questions should be investigated. After the clinical questions were decided, the GDG agreed which topics were

an 'economic priority' for modelling. These 'economic priority' topics were chosen on the basis of the following criteria, in broad accordance with the NICE guidelines manual:

Overall relevance of the topic

- *The number of patients affected*: interventions affecting relatively large numbers of patients were given a higher economic priority than those affecting fewer patients
- *The health benefits to the patient*: interventions that that were considered to have a potentially significant impact on both survival and quality of life were given a higher economic priority
- *The per patient cost*: interventions with potentially high financial (cost/savings) implications were given high priority compared to interventions expected to have lower financial implications
- *Likelihood of changing clinical practice:* priority was given to topics that were considered likely to represent a significant change to existing clinical practice.

Uncertainty

- *High level of existing uncertainty*: higher economic priority was given to clinical questions in which further economic analysis was considered likely to reduce current uncertainty over cost-effectiveness. Low priority was given to clinical questions when the current literature implied a clearly 'attractive' or 'unattractive' incremental cost-effectiveness ratio, which was regarded as generalisable to a UK healthcare setting
- *Likelihood of reducing uncertainty with further analyses (feasibility issues)*: when there was poor evidence for the clinical effectiveness of an intervention, then there was considered to be less justification for an economic analysis to be undertaken.

Once the economic priority topics had been chosen, the next task was to perform a systematic review of the cost-effectiveness literature. When relevant published evidence was identified and considered to be of sufficient quality, this information was used to inform the recommendation for that specific clinical question. When no relevant cost-effectiveness evidence was identified, or when it was not considered to be of reasonable quality, consideration was given to building a de novo economic model. This decision was made by the GDG based on an assessment of the available evidence required to populate a potential economic model.

For those clinical questions where an economic model was required, the information specialist performed supplemental literature searches to obtain additional data for modelling. Assumptions and designs of the models were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

The clinical questions in this guideline selected for modelling were chosen because at the time it was considered likely that the recommendations under consideration could substantially change clinical practice in the NHS and have important consequences for resource use. The details of the model are presented in the evidence review (Appendices 1 and 4). During the modelling process the following general principles were adhered to:

- the GDG Chair and Clinicial Lead were consulted during the construction and interpretation of the model
- the model was based on the best evidence from the systematic review.
- model assumptions were reported fully and transparently
- the results were subject to thorough sensitivity analysis and limitations discussed
- costs were calculated from a health services perspective.

Agreeing the recommendations

For each clinical question the GDG were presented with a summary of the clinical evidence, and where appropriate economic evidence, derived from the studies reviewed and appraised. From this information the GDG were able to derive the guideline recommendations. The link between the evidence and the view of the GDG in making each recommendation is made explicit in the accompanying qualifying statement.

Qualifying statements

As clinical guidelines are currently formatted, there is limited scope for expressing how and why a GDG made a particular recommendation from the evidence of clinical and cost-effectiveness. To make this process more transparent to the reader, the NCC-C felt the need for an explicit, easily understood and consistent way of expressing the reasons for making each recommendation.

The way we have chosen to do this is by writing a 'qualifying statement' to accompany every recommendation and will usually cover:

- the strength of evidence about benefits and harms for the intervention being considered
- the degree of consensus within the GDG
- the costs and cost-effectiveness (if formally assessed by the health economics team).

Where evidence was weak or lacking the GDG agreed the final recommendations through informal consensus. Shortly before the consultation period, ten key priorities and five key research recommendations were selected by the GDG for implementation and the patient algorithms were agreed (see pages 32–36 for algorithms). To avoid giving the impression that higher grade recommendations are of higher priority for implementation, NICE no longer assigns grades to recommendations.

Consultation and validation of the guideline

The draft of the guideline was prepared by NCC-C staff in partnership with the GDG Chair and Lead Clinician. This was then discussed and agreed with the GDG and subsequently forwarded to NICE for consultation with stakeholders.

Registered stakeholders (see Appendix 9.2) had one opportunity to comment on the draft guideline and this was posted on the NICE website between 23rd May 2008 and 18th July 2008. The GRP also reviewed the guideline and checked that stakeholder comments had been addressed.

Following the consultation period the GDG will finalised the recommendations and the NCC-C will provide the final document. This was then be submitted to NICE for approval and publication on their website. The other versions of the guideline (see below) will also be discussed and approved by the GDG and published at the same time.

Other versions of the guideline

This full version of the guideline will be available to download free of charge from the NICE website (www.nice.org.uk) and the NCC-C website (www.wales.nhs.uk/nccc) when published.

NICE also produces three versions of the metastatic spinal cord compression guideline which will be available from the NICE website:

- the NICE guideline, which is a shorter version of this guideline, containing the key priorities, key research recommendations and all other recommendations
- the Quick Reference Guide (QRG), which is a summary of the main recommendations in the NICE guideline
- Understanding NICE Guidance (UNG), which describes the guideline using non-technical language. It is written chiefly for patients but may also be useful for family members, advocates or those who care for patients with metastatic spinal cord compression.

Updating the guideline

Literature searches were repeated for all of the clinical questions at the end of the GDG development process, allowing any relevant papers published before 18 April 2008 to be considered. Future guideline updates will consider evidence published after this cut-off date.

Two years after publication of the guideline, NICE will commission a National Collaborating Centre to determine whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an early update. If not, the guideline will be updated approximately 4 years after publication.

Funding

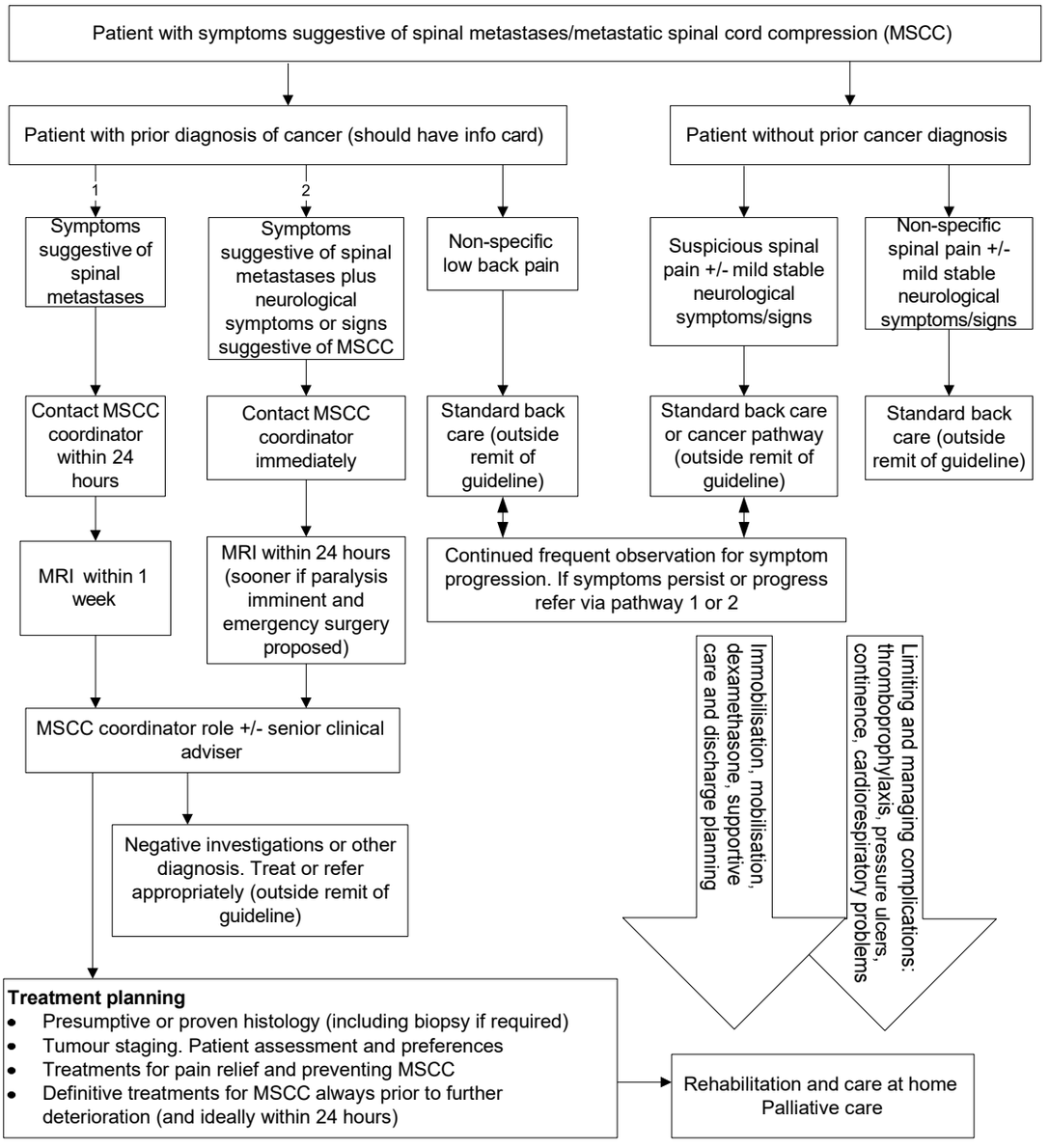
The National Collaborating Centre for Cancer was commissioned by NICE to develop this guideline

Disclaimer

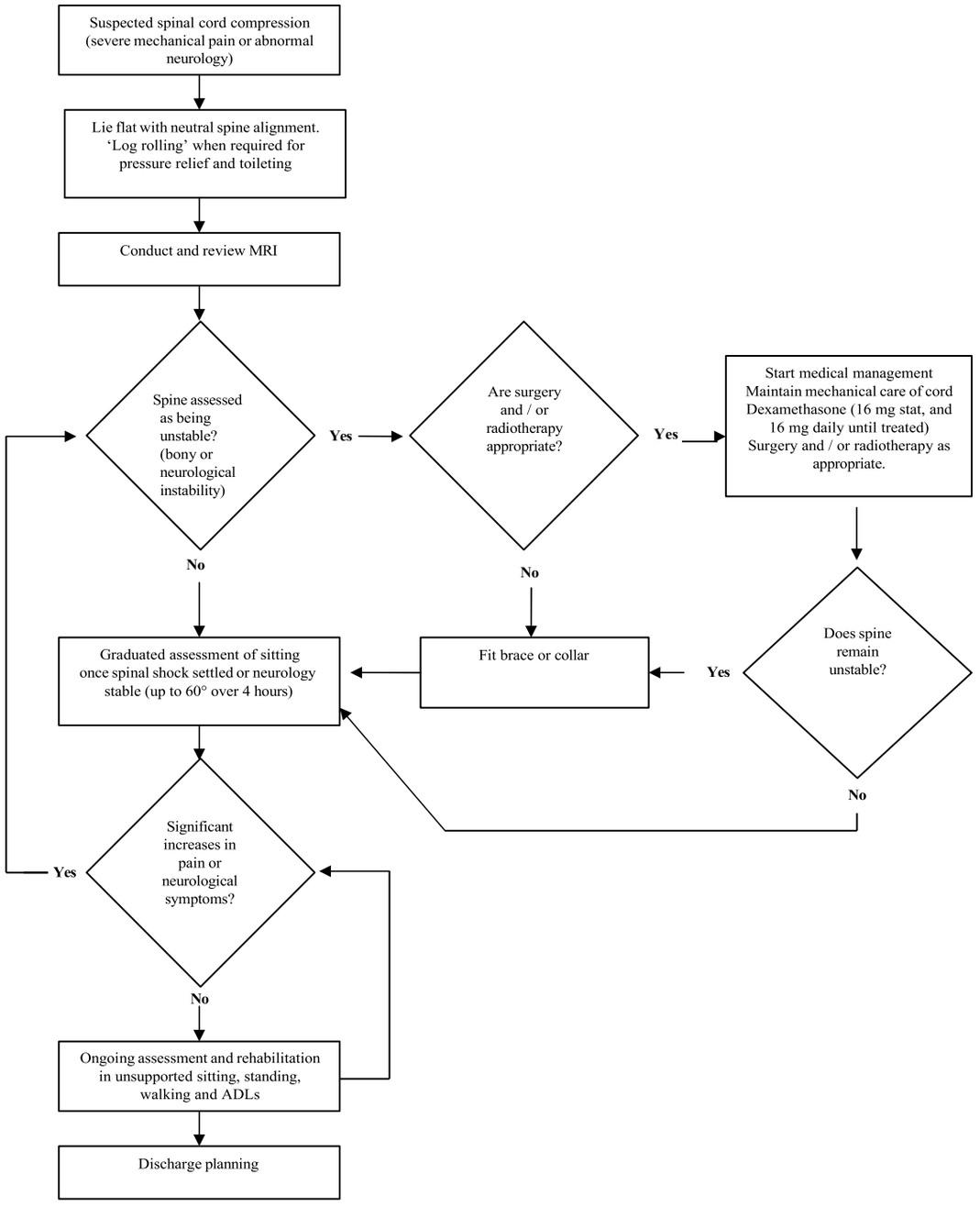
The GDG assumes that healthcare providers will use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply these guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioner in light of individual patient circumstances, the wishes of the patient and clinical expertise.

The NCC-C disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

Algorithms


Patient with symptoms suggestive of spinal metastases/metastatic spinal cord compression (MSCC)
Patient with prior diagnosis of cancer (should have info card)
Patient without prior cancer diagnosis
1
2
Symptoms suggestive of spinal metastases
Symptoms suggestive of spinal metastases plus neurological symptoms or signs suggestive of MSCC
Non-specific low back pain
Suspicious spinal pain +/- mild stable neurological symptoms/signs
Non-specific spinal pain +/- mild stable neurological symptoms/signs
Contact MSCC coordinator within 24 hours
Contact MSCC coordinator immediately
Standard back care (outside remit of guideline)
Standard back care or cancer pathway (outside remit of guideline)
Standard back care (outside remit of guideline)
MRI within 1 week
MRI within 24 hours (sooner if paralysis imminent and emergency surgery proposed)
Continued frequent observation for symptom progression. If symptoms persist or progress refer via pathway 1 or 2
MSCC coordinator role +/- senior clinical adviser
Negative investigations or other diagnosis. Treat or refer appropriately (outside remit of guideline)
Immobilisation, mobilisation, dexamethasone, supportive care and discharge planning
Limiting and managing complications: thromboprophylaxis, pressure ulcers, continence, cardiorespiratory problems
Treatment planning
Presumptive or proven histology (including biopsy if required)
Tumour staging. Patient assessment and preferences
Treatments for pain relief and preventing MSCC
Definitive treatments for MSCC always prior to further deterioration (and ideally within 24 hours)
Rehabilitation and care at home
Palliative care

Flow chart for decisions about the timing and safety of mobilisation once MSCC is suspected



1 Epidemiology

1.1 Introduction

Metastatic spinal cord compression (MSCC) is a well recognised complication of cancer and is usually an oncological emergency. MSCC was first described by Spiller in 1925 as progressive paraplegia in cancer patients (Loblaw *et al.* 2003).

Metastases to the spinal column occur in 3–5% of all patients with cancer (most commonly those with breast cancer, prostate cancer and lung cancer, in whom the incidence may be as high as 19%) and may cause pain, vertebral collapse and MSCC.

Patients with breast, lung and prostate cancer account for more than 50% of MSCC cases but it can be caused by any solid tumour. Patients who present with widespread malignancy and those with known spinal metastases are also at higher risk. The risk of MSCC is also proportionally related to the duration of disease and therefore, as cancer survival times increase, so too might the incidence of MSCC.

MSCC occurs when there is pathological vertebral body collapse or direct tumour growth causing compression of the spinal cord or cauda equina. Irreversible neurological damage ensues with resulting paraplegia (Levack *et al.* 2002). Early diagnosis and treatment is essential to prevent neurological damage and to achieve this, early recognition and reporting of symptoms, simple and rapid referral pathways, urgent and appropriate investigations and prompt treatment are needed.

Therefore it is important that the patient and all health care professionals are aware of the early symptoms and signs of MSCC (Loblaw *et al.* 2003, Levack *et al.* 2002, Husband 1998, Bucholtz 1999). Unfortunately, the symptoms and signs that are usually taught are those of established MSCC such as weakness of the limbs, bladder and bowel dysfunction and sensory loss.

There is a significant association between the ability to walk at the time of diagnosis and the ability to walk following treatment (Brown *et al.* 1999, Hacking *et al.* 1993, Huddart *et al.* 1997, Kim *et al.* 1990). Furthermore, data from the Clinical Resource Audit Group (CRAG audit) (Levack *et al.* 2001), suggest that the ability to walk at the time of diagnosis is a statistically significant predictor of outcome in terms of survival.

Once paraplegia develops it is usually irreversible. and can affect the quality of life of both the patient and their carers. These patients often need 24 hour nursing care either in hospital or in the community setting, which has major resource implications on the National Health Service (NHS).

The key investigation for the diagnosis of MSCC is magnetic resonance imaging (MRI) of the whole spine (Levack *et al.* 2001, Cook *et al.* 1998). Once a diagnosis of MSCC has been made, the treatment goals include pain relief, restoration of neurological status, prevention of further neurological damage and stabilisation of the spine (Husband 1998, Held & Peahota 1993, Royal College of Radiologists 2006).

When deciding the most appropriate treatment option for a patient it is important to consider quality of life (QOL) issues. Although there have been many studies that have assessed QOL in patients with advanced cancer, few have been on patients with MSCC (Levack *et al.* 2001).

1.2 Incidence

The true incidence of MSCC is unknown, post mortem evidence indicates that it is present in 5–10% of patients with advanced cancer. Levack *et al.* (2001) have also estimated similar figures in terms of incidence. In their report of a population based study from Ontario Canada, Loblaw *et al.* (2003) described a cumulative probability of experiencing at least one episode of MSCC in the 5 years preceding death from cancer of 2.5% overall with a 40-fold variation in the cumulative incidence of MSCC among different types of cancer. The authors acknowledged that they may have underestimated the true incidence by at least 15%, as the detection rate depended on admission to hospital, correct diagnosis, and entry into coding systems (Loblaw *et al.* 2003). One of the main reasons for the uncertain incidence of MSCC in the UK is the lack of a recognised coding system for the diagnosis. It is likely that the incidence of MSCC will increase in the future with improving cancer treatments resulting in better survival and outcomes.

The median age at time of MSCC diagnosis is 65 years (Loblaw *et al.* 2003, Levack *et al.* 2001). Data from the Levack *et al.* audit (2001) suggest that 77% of patients diagnosed with MSCC had an established diagnosis of cancer whereas 23% presented with MSCC as the first presentation of malignancy.

1.3 Aetiology and pathophysiology

Loblaw *et al.* (2003) define MSCC as compression of the dural sac and its contents, namely the spinal cord and cauda equina, by an extradural mass. Lung, breast and prostate cancers are the commonest malignancies causing MSCC and account for over 50% of cases (Loblaw *et al.* 2003, Levack *et al.* 2001). In 7% of patients the site of primary tumour may remain unidentified (Levack *et al.* 2002, Levack *et al.* 2001).

Three mechanisms are responsible for MSCC, the commonest being haematogenous spread to the vertebral spine causing collapse and compression, accounting for over 85% of cases (Bucholtz 1999, Levack *et al.* 2001). Less commonly it occurs secondary to direct tumour extension into the vertebral column or by direct deposition of tumour cells (Bucholtz 1999).

The cause of damage to the spinal cord from compression is complex and multifactorial. Direct compression results in oedema, venous congestion and demyelination. If the compression is gradual and of recent onset with some preservation of neurological function, the effects are often reversible. With prolonged compression, vascular injury ensues causing infarction of the spinal cord. After this type of injury any meaningful recovery is unlikely (Patchell *et al.* 2005). Paradoxically, slow onset compression (with an accompanying gradual neurological deficit) permits a degree of cord adaptation and usually predicts a better outcome than sudden onset compression and neurological loss.

1.4 Clinical symptoms and signs

Back pain is the most frequent first symptom occurring in 95% of patients for prolonged periods and usually precedes signs related to MSCC (Levack *et al.* 2001, Portenoy 1997, Byrne 1992, Quinn & DeAngelis 2000). The pain is described either as localised,spinal pain or neurogenic, radicular pain. Localised spinal pain is defined as pain in and around the spinal column area in distinction to neurogenic radicular pain, which is spinal cord or nerve root pain affecting one or both sides of the body (Levack *et al.* 2001). In the Levack *et al.* audit (2001) 37% of patients with MSCC had neurogenic radicular pain, 15% had localised, spinal pain on its own and 47% had localised spinal pain and neurogenic, radicular pain. The median pain intensity was 8 on a scale of 0 to 10 with 0 being ‘no pain’ and 10 ‘the worst imaginable pain’.

Weakness of the limbs is the second most common symptom of cord compression. Eighty five percent of patients in the Levack *et al.* (2001) audit experienced weakness and in the majority pain preceded weakness. Only 18% of patients were able to walk without help at the time of diagnosis of MSCC (Levack *et al.* 2001).

Sensory symptoms are also common and include paraesthesia, decreased sensation and numbness of toes and fingers which may extend to the level of cord compression (Held & Peahota 1993). Fifty two percent of patients had a clinical sensory level but this varied significantly in relation to the true compressive lesion (Levack *et al.* 2001). Autonomic dysfunction is a late consequence of MSCC and rarely occurs without symptoms and signs. This may present as impotence or bladder and bowel dysfunction presenting as urinary retention, incontinence or constipation (Bucholtz 1999). Constipation was the commonest bowel symptom and occurred in 67% of patients (Levack *et al.* 2001).

Over two thirds of cases of MSCC occur in the thoracic spine and between 4 and 7% occur in the cervical cord (Loblaw *et al.* 2003, Levack *et al.* 2002, Cook *et al.* 1998). Seventeen percent of patients have two or more levels of cord compression (Levack *et al.* 2002).

1.5 Survival/mortality

Median survival following a diagnosis of MSCC is reported as being around 2 to 3 months (Loblaw *et al.* 2003, Levack *et al.* 2001) with 17% patients alive at one year and 10% patients at 18 months (Levack *et al.* 2001). The median survival of untreated patients from a diagnosis of MSCC is one month (Loblaw *et al.* 2003) but this may reflect selection bias for treatment. Several studies have reported survival to be significantly associated with the ability to walk at time of diagnosis. The Levack *et al.* audit (2001) found primary tumour site and ability to walk at diagnosis of MSCC as independent predictors of survival.

Loblaw *et al.* (2003) reported large differences in survival following MSCC in different disease groups. Longest survival was reported in patients with haematological malignancies (lymphoma, leukaemia and multiple myeloma) and prostate cancer whereas lung cancer patients had the shortest survival. Similar results were reported by Levack *et al.* (2001) with 66% survival at 3 months for patients with haematological malignancies and 22% survival at 3 months in patients with lung cancer.

Surgically treated patients had significantly better survival at one year (57.4% vs 13.3%) than patients not surgically treated (Levack *et al.* 2001). This is likely to be a result of patient selection rather than a direct relationship.

1.6 Service provision

To inform the development of this guideline a questionnaire survey of incidence, availability of resources and variation in clinical practice in relation to MSCC in England and Wales was carried out. The aim of this survey was to determine differences in service provision, specifically access to:

- MRI
- Spinal surgical services
- Oncological services
- Other services.

A questionnaire was sent to all cancer centres in England and Wales. In addition, questionnaires were also sent to all known orthopaedic and neurosurgical spinal surgery units, palliative care units and rehabilitation units in England and Wales. Copies of these questionnaires will be reproduced in the full needs assesment which will form part of the evidence review. As part of the questionnaire departmental studies or audits were also requested. In total, replies were received from 27/57 (47%) cancer centres, 21/61 (34%) spinal surgery units, 116/353 (33%) palliative care departments and 7/10 (70%) specialist rehabilitation units.

Incidence

The average catchment area for cancer centres is 1.2 million people (median 1 million, range 0.3 to 3 million). On average 80 MSCC cases are seen per year in each centre (median 55, range 10 to 250). Prostate cancer was the commonest primary tumour site in 15 (55%) units.

The mean catchment area for spinal surgery units is 2.4 million people (median 2.2 million range 1.2 to 4.2 million). On average 56 MSCC cases are seen per year in each unit (median 50, range 5 to 150). Breast cancer was the commonest primary tumour site in 13 (62%) units. Prostate cancer was not reported as the commonest primary site in any unit.

The mean catchment area for a palliative care department is 0.42 million people (median 0.35 million, range 0.1 to 2.6 million). On average 16 MSCC cases are seen per year in each department (median 12, range 3 to 150). Prostate cancer was the commonest primary tumour site in 45 (39%) units.

Specialist spinal rehabilitation units have large catchment areas, with an average of 6.4 million people (median 6 million, range 3 to 10 million). The mean number of MSCC patients seen in the 3 units accepting these patients is 4 per year.

MRI

Cancer centres

Of those centres which responded to the questionnaire 23/27 (85%) have a written policy on the investigation of suspected MSCC. Before a confirmed diagnosis 18 (67%) centres routinely keep patients lying flat. Interestingly 8 centres (35%) with a written policy do not recommend patients lie flat before a diagnosis is made.

In all the 27 centres who responded, MRI is available during weekday working hours and 23 (85%) reported that it is 'easy' or 'very easy' to access. A weekday out-of-hours service is available in 16 (59%) centres. All other centres wait until the following morning. An on-site weekend service is available in 16 (59%) centres. Of the remainder, 6 (22%) refer patients to another hospital for scanning over the weekend, and 5 (19%) wait up to 48 hours until Monday morning. In total 19 centres (70%) are able to organise an MRI scan within 24 hours of the medical decision to request one. One centre did however report a delay of up to 72 hours; this centre did not provide an out-of-hours or weekend service. In 23 centres (85%), the whole spine is scanned, in 3 (11%) a limited scan is performed. One centre did not know the extent of scanning.

Spinal surgery units

Of those units which responded to the questionnaire 10/21 (48%) have a written policy on the investigation of suspected MSCC. Before a confirmed diagnosis, 13 units (62%) routinely keep patients lying flat. Eight of the 10 units (80%) with a written policy recommend that patients lie flat before a diagnosis is made, which is higher than in cancer centres. In all 21 units who responded to the questionnaire MRI scanning was available on-site and all patients with suspected MSCC had an MRI scan. In 19 units (90%), MRI is available outside of normal working hours. On a weekday, the remaining 2 units (10%) wait until the following morning, and over the weekend patients are referred to another hospital for scanning. Twelve units (57%) are able to organise an MRI scan within 24 hours of the medical decision to request one. Three units (14%) reported a delay of up to 72 hours despite there being MRI available on site and outside working hours. In 19/21 centres (90%), the whole spine is scanned, in 2 (10%) a limited scan is performed.

Palliative care departments

In 99/116 departments (85%) which responded to the questionnaire more than 75% of patients have an MRI scan to confirm the diagnosis. Only 32 units (28%) routinely lie patients flat 17 (15%) of respondents were unsure); this is much lower than in Cancer Centres or Spinal Surgery Units. Fifty three units (46%) have a written policy on the management of MSCC (8 (7%) of respondents were unsure). On-site MRI is available in 72 units (62%) (24 of 116 departments or (21%) of respondents were unsure). In 110 units (95%) MRI is only available during normal working hours. Access during working hours was deemed as 'very easy' or 'easy' in 96/116 units (83%). The whole spine is scanned in 90 units (78%).

Surgical services

Cancer centres

In total, 19 centres (70%) report it is 'easy' or 'very easy' to contact the surgical team. On site surgical review is available in 10 centres (37%). The average distance to a spinal unit is 10 miles (range 0 to 60 miles). Only a minority of patients are referred for review; in 18 (centres 67%) less than 25% are assessed by the surgical team. Of those patients reviewed, 14 of centres (52%) report that over 50% proceed to surgery.

Spinal surgery units

Sixteen units (76%) do not have a defined policy for selecting patients for surgery. Five units (24%) use the Tokuhashi score. In 11 units (52%) over 75% of the patients referred for surgical review are not operated on. Only 4 units (19%) operated on more than half of the patients seen which is much lower than the surgical rates reported by cancer centres. Surgery is carried out within 72 hours of the decision to operate in all but one centre. In cancer centres and palliative care units prostate cancer seems to be the commonest primary site. However, no spinal unit reported prostate cancer as the commonest malignancy. Breast cancer was the commonest primary tumour site in 13 units (62%). This suggests that either proportionally more breast cancer patients are referred or accepted for surgical review than other primary sites.

Palliative care departments

Surgery is an uncommon treatment for patients, with 104 units (90%) reporting that 25% or less are operated on (9 or 8% of respondents were unsure). Sixty two centres (53%) report it is 'easy' or 'very easy' to contact the surgical team. The average distance to a Spinal Surgery Unit is 14.5 miles (range 0 to 100 miles).

Oncology services

Cancer centres

Most centres (23 or 85%) reported that patients with a diagnosis of MSCC are seen within 24 hours by an oncologist. No centre reported a wait of more than 48 hours. Patients are usually treated with radiotherapy; more than 75% of patients in 25 centres (93%) and 50–75% of patients in 2 centres (7%). Eleven centres (41%) will treat some patients without radiological confirmation of MSCC. The decision to treat without a radiological diagnosis may depend on the availability of MRI; seven centres (26%) treating without MRI wait more than 24 hours for a scan compared to only one (6%) of the remaining centres. It was not asked whether these patients go on to have MRI scans once the radiotherapy has begun. Radiotherapy is started within 24 hours of the diagnostic MRI scan in 25 centres (93%). No centre reported a delay of more than 48 hours in starting radiotherapy. Treatment can start on Saturday in 26 centres (96%) and on Sunday in 22 centres (85%). Various radiotherapy dose regimens are used, but by far the commonest is 20Gy in 5 fractions, which is the schedule of choice in 23 centres (85%). A written policy on steroid usage exists in 20 centres (74%). All centres use dexamethasone and 21 centres (78%) recommend a total daily dose of 16mg.

Spinal surgery units

Thirteen centres (62%) routinely refer more than 75% of patients for post-operative radiotherapy while 8 (38%) refer 25–50%. Access to radiotherapy is reported as 'very easy' or 'easy' in 20 units (95%). A written policy on steroid usage exists in 9 units (43%). Somewhat surprisingly, two units (10%) do not routinely use steroids. All other 19 units use dexamethasone and 15 centres (79%) recommend a total daily dose of 16mg.

Palliative care departments

Access to oncology services is reported as 'very easy' or 'easy' in 84 units (72%). However, 29 departments (25%) report access to oncology services as 'difficult'. Despite this, 90 departments (78%) have oncology review within 48 hours (6 or 5% of respondents were unsure). Radiotherapy

is the commonest treatment for patients with MSCC, with 106 centres (91%) reporting over 50% of patients being treated in this way (4 or 3% of respondents were unsure). Twenty five departments (22%) reported that some patients are treated without prior MRI scanning. Waiting times for radiotherapy are generally good; in 63 units (54%) patients wait less than 24 hours before starting radiotherapy. In only 3 departments (2%) is the wait more than 48 hours (21 or 18% of respondents were unsure). Seventy three departments (63%) reported that radiotherapy can be started on a Saturday (28 or 24% of respondents were unsure). Encouragingly, only 15 departments (13%) reported that radiotherapy cannot start on a Saturday, which is similar to the proportion of cancer centres unable to provide this service. This suggests that patients in palliative care units may get similar access to radiotherapy as those in cancer centres. In total, 56 (48%) have a written policy on steroid usage (30 or 26% of respondents were unsure). All 116 units use dexamethasone and 110 centres (95%) recommend a total daily dose of 16mg.

Other services

Cancer centres

Access to specialist physiotherapy is variable with only 13 centres (48%) providing this service (6 or 22% of respondents were unsure). Daily physiotherapy is available in 17 centres (63%) and 8 centres (30%) have a written policy on mobilisation. Occupational therapy is available in 25 centres (93%) (2 respondents were unsure). Only 8 centres (30%) have a continence adviser (13 or 48% of respondents were unsure). Referral to specialist rehabilitation services is available to patients in 17 centres (63%) (5 or 19% of respondents were unsure). An average of 5 patients per year (range 1 to 10) were referred for specialist rehabilitation in the 9 centres (30%) that provided this information.

Spinal surgery units

Access to specialist physiotherapy is available in 10 units (48%) (2 or 10% of respondents were unsure). Daily physiotherapy is available in 17 units (81%) and 5 units (24%) have a written policy on mobilisation (2 or 40% of respondents were unsure). Occupational therapy is available in 19 units (90%) (1 or 5% of respondents were unsure). Fifteen units (71%) have a continence adviser (3 or 14% of respondents were unsure). Referral to specialist rehabilitation services is available to patients in 16 units (76%) (1 or 5% of respondents were unsure). An average of 5 patients per year (range 2 to 10) were referred for specialist rehabilitation in the 10 centres (48%) that provided this information.

Palliative care departments

Access to specialist physiotherapy is available in 65 departments (56%) (15 or 13% of respondents were unsure). Sixty nine departments (59%) reported that patients are assessed by a physiotherapist within 48 hours of referral. Fourteen departments reported waiting more than 72 hours for physiotherapy review (22 or 19% of respondents were unsure). One department has no inpatient physiotherapy service. It is important to note that following diagnosis it may not be appropriate or necessary for a patient to be reviewed immediately by a physiotherapist; pain relief may need to be optimised and a policy of strict bed rest during radiotherapy is often applied and no mobilisation is attempted. Only 10 departments (9%) have a written mobilisation policy (43/116 or 37% of respondents were unsure).

Specialist spinal rehabilitation units

Only 3 units (43%) accept MSCC patients and these units only see on average four such patients per year. Specialist rehabilitation services are available to patients in at least 17 (63%) cancer centres and 16 (76%) spinal units with an average of five patients per year referred from each cancer centre and spinal unit. This strongly suggests that either our list of rehabilitation units is incomplete or the definition of a rehabilitation unit is not clear. The small number of units accepting MSCC patients makes any meaningful data interpretation very difficult. Surprisingly, two (67%) units reported no access to specialist physiotherapy (One (33%) respondent unsure). Daily physiotherapy is available in all 3 units. Waiting times for transfer are 4 weeks in two (67%) units

and 'variable' in the other. All three units have access to specialist occupational therapy, and 2/3 (67%) units have a continence adviser. All three units have a community rehabilitation team.

1.7 Conclusions

The needs assessment has highlighted several important findings relating to current service provision for patients at risk of or diagnosed with MSCC. Existing epidemiological data in the UK is poor (e.g. incidence, survival, mortality) with no nationally coordinated data collection. In addition there is a recognised lack of an appropriate system for coding a diagnosis of MSCC.

Data derived from the questionnaire survey of cancer centres, spinal surgery units and palliative care departments indicated a range in service provision for this group of patients including availability and access to out of hours MRI, defined policies for patient selection for surgery and access to specialist physiotherapy and rehabilitation services. It is possible that responder bias resulted in proportionally more replies from centres where a high level of care is provided or where there is a special interest in MSCC. The possibility that centres with poor service provision are underrepresented in this audit cannot be excluded. Therefore this data may portray the management of MSCC more favourably than is the reality in some centres. This is reflected in individual patient experiences which are discussed in more detail in Chapter 3 of this guideline.

All these data were presented to the GDG during guideline development to help focus on some of the key priority areas and data from the needs assessment are included as part of the evidence review where appropriate. The full needs assessment (including all the data from the questionnaires) will form part of the final evidence review which will accompany this guideline.

The NCC-C and GDG would like to thank all those health care professionals who completed and returned their questionnaires as part of this needs assessment exercise.

References

Brown PD, Stafford SL, Schild SE (1999). Metastatic spinal cord compression in patients with colorectal cancer. *Journal of Neuro-Oncology*, 44: 175–180.

Bucholtz JD (1999) Metastatic epidural spinal cord compression. *Seminars in Oncology Nursing* 15(3): 150–159

Byrne TN. (1992) Spinal cord compression from epidural metastases. *New England Journal of Medicine* 327: 614–619

Cook AM, Lau TN, Tomlinson MJ (1998). Magnetic Resonance Imaging of the whole spine in suspected spinal cord compression: Impact on management. *Clinical Oncology* 10: 39–43.

Hacking H, Van As H, Lankhorst G (1993). Factors related to the outcome of inpatient rehabilitation in patients with neoplastic epidural spinal cord compression. *Paraplegia* 31: 367–374.

Held JL & Peahota A (1993) Nursing care of the patient with spinal cord compression. *Oncology Nursing Forum*, 20(10): 1507–1516.

Huddart R, Rajan B, law M. (1997) Spinal cord compression in prostate cancer: Treatment outcome and prognostic factors. *Radiotherapy Oncology* 44: 229-236.

Husband DJ (1998) Malignant spinal cord compression: prospective study of delays in referral and treatment; *BMJ* 317:18–21

Kim R, Spencer S, Meredith R. (1990) Extradural spinal cord compression: analysis of factors determining functional prognosis-prospective study. *Radiology* 176: 279–282.

Levack P, Graham J, Collie D (2001) A prospective audit of the diagnosis, management and outcome of malignant spinal cord compression. Clinical Resource and Audit Group Levack *et al.* 2001 97/08.

Levack P, Graham J, Collie D (2002) Don't wait for a sensory level-Listen to the symptoms: a Prospective audit of the delays in diagnosis of malignant cord compression. *Clinical Oncology* 14: 472–480

Loblaw, Laperriere NJ, Mackillop WJ (2003) A population-based study of malignant spinal cord compression in Ontario. *Clinical oncology* 15(4): 211–217.

Patchell RA, Tibbs PA,Regine WF (2005) Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *The Lancet*, 366: 643–648

Portenoy RK (1997). Chronic nociceptive pain syndromes: Cancer pain, in North RB, Levy RM (eds): Neurosurgical Management of Pain. New York, NY, Springer-Verlag, 62–74.

Quinn JA & DeAngelis (2000) neurological emergencies in the cancer patient. *Seminars in Oncology*, 27(3): 311–321.

Royal College of Radiologists (2006) Board of Faculty of Clinical Oncology. Spinal cord compression, Radiotherapy Dose-Fractionation. 4.17, pp. 70

2 Service configuration and urgency of treatment

2.1 Introduction

Those responsible for organising clinical services for patients with metastatic spinal cord compression (MSCC) face particular challenges:

- There is no common pathway of entry into the secondary care system. Patients may present acutely with MSCC under a variety of different specialists unlikely to be members of the oncology multi-disciplinary team (MDT) responsible for the management of the primary disease or its spinal consequences.
- There is limited 24 hour MRI availability.
- The hospital to which the patient is first admitted may be remote from the oncology or spinal surgical centre.

Most patients will be known to have cancer, be under the care of an appropriate primary site specialist and have been discussed at a MDT meeting. For most this will be their first presentation with spinal metastatic disease but there are many patients for whom this will be their first presentation with malignant disease.

The often urgent nature of this condition makes it impractical for all patients to be discussed by a formally convened MDT for MSCC before initial evaluation and treatment. In order to assure appropriate decisions, there must be clear local and network-wide arrangements in place that are widely known, clinically robust and regularly monitored.

Recommendations

- Every cancer network should have a clear care pathway for the diagnosis, treatment, rehabilitation and ongoing care of patients with metastatic spinal cord compression (MSCC).
- Every cancer network should ensure that appropriate services are commissioned and in place for the efficient and effective diagnosis, treatment, rehabilitation and ongoing care of patients with MSCC. These services should be monitored regularly through prospective audit of the care pathway.
- Cancer networks should ensure that there is local access to urgent magnetic resonance imaging (MRI) within 24 hours for all patients with suspected MSCC. This service should be available outside normal working hours and with 24-hour capability in centres treating patients with MSCC.
- Every cancer network should have a network site specific group for MSCC. The group should include representatives from primary, secondary and tertiary care and should have strong links to network site specific groups for primary tumours.

Recommendations (cont.)

- The cancer network should appoint a network lead for MSCC whose responsibilities include:
  - advising the cancer network, commissioners and providers about the provision and organisation of relevant clinical services
  - ensuring that the local care pathway for diagnosis and management are documented, agreed and consistent across the network
  - ensuring that there are appropriate points of telephone contact for the role of an MSCC coordinator and senior clinical advisers
  - maintaining a network-wide audit of the incidence, timeliness of management, and outcomes of patients with MSCC using nationally agreed measures
  - arranging and chairing twice-yearly meetings of the network site specific group for MSCC, at which patient outcomes will be reported and the local care pathway reviewed and amended if necessary.
- Every secondary or tertiary care centre should have an identified lead healthcare professional for MSCC (who is usually, but not necessarily, medical) whose responsibilities include:
  - representing the hospital at network level in the development of care pathways
  - implementing the care pathway and disseminating information about the diagnosis and appropriate management of patients with known or suspected MSCC
  - ensuring timely and effective communication between all relevant healthcare professionals involved in the care of patients with MSCC, including primary care and palliative care
  - raising and maintaining the awareness and understanding of treatments for MSCC among all clinical staff across the locality
  - contributing to regular network audits of the care of patients with MSCC
  - attending and contributing to the twice-yearly network site specific group meeting.
- Commissioners should establish a joint approach with councils responsible for local social services to ensure efficient provision of equipment and support, including nursing and rehabilitation services, to meet the individual needs of patients with MSCC and their families and carers.

Qualifying statement: These recommendations are based on low quality evidence of resource and organisational variation provided by the Needs Assessment (see chapter 1) and GDG consensus.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

2.2 MSCC coordinator and senior clinical adviser – roles and responsibilities

Many healthcare professionals working in the community and acute setting will have limited experience of MSCC, its potential seriousness and how it should be managed. The provision of services varies considerably from region to region and there is often inadequate understanding locally of where and when services are available. As well as having the facilities and processes in place to manage patients with diagnosed MSCC, it is important that a clinical system is in place to ensure the appropriate care of patients with suspected MSCC. The creation of a coordinator role will ensure that someone with enough clinical experience and awareness of the condition and its management and with knowledge of the available local services will be

involved as soon as a patient is suspected of having MSCC. The role of such a coordinator has already been shown to be effective in parts of Scotland.

The coordinators will provide the first point of contact for referring clinicians suspicious that patients may have spinal metastases or MSCC. They will offer advice on the initial management of patients with suspected MSCC including moving and handling, and drug treatment (e.g. dexamethasone and analgesia). They will offer advice on gathering appropriate information and undertaking an appropriate examination of these patients. As well as ensuring that patients requiring emergency admission are admitted in a timely manner, the coordinator will help to avoid inappropriate transfer of frail, symptomatic patients at unsuitable times. They will help to ensure that accurate data are obtained about patients with MSCC. This could include both quantitative data (e.g. relating to time scale) and qualitative data (e.g. presenting symptoms). These roles will also naturally lead to an educational function.

The coordinator role may be delivered by one or more individuals during normal working hours (for example newly appointed whole time equivalent healthcare professionional) but this role could be taken on by healthcare professionals involved in an existing on call rota out of hours (for example oncology/spinal/neurosurgical SpR in rotation). A single telephone contact number will ensure that the system is as simple as possible to access.

The coordinator will not necessarily have any direct clinical contact with the patient or indeed with the acute receiving teams or Senior Clinical Advice (SCA). As detailed below the coordinators roles will be organisational, advisory and supportive. Clinical responsibility for the patient will rest with the health care professionals with direct clinical contact at any given time point (e.g. GP, acute receiving team, spinal surgeon, oncologist).

Recommendations

- Each centre treating patients with MSCC should identify or appoint individuals responsible for performing the role of MSCC coordinator and ensure its availability at all times.
- Each centre treating patients with MSCC should have a single point of contact to access the MSCC coordinator who should provide advice to clinicians and coordinate the care pathway at all times.
- The MSCC coordinator should:
  - provide the first point of contact for clinicians who suspect that a patient may be developing spinal metastases or MSCC
  - perform an initial telephone triage by assessing requirement for, and urgency of, investigations, transfer, and treatment
  - advise on the immediate care of the spinal cord and spine and seek senior clinical advice, as necessary
  - gather baseline information to aid decision-making and collate data for audit purposes
  - identify the appropriate place for timely investigations and admission if required
  - liaise with the acute receiving team and organise admission and mode of transport.

Qualifying statement: These recommendations are based on GDG consensus.

Senior Clinical Advice

Once the diagnosis of MSCC has been made, it is essential that every patient's care is planned and delivered optimally. The decision whether to offer a patient surgery, radiotherapy or supportive care is complex and includes not only the MRI results, but also careful assessment of a range of factors including current performance status and speed of decline,

primary tumour type, extent of disease, co-morbidity, and previous treatments. Decision-making based on MRI results in isolation has a high potential for inappropriate conclusions.

Involving the patient, their family and carers in this process is extremely important but the decision to offer a patient treatment must be made by skilled clinical staff able to judge the prospects and practicalities involved with that patient's care. To ensure that the most appropriate treatment decision is made, the process must be guided by doctors with enough understanding and awareness of the issues involved as well as extensive clinical experience. Although many patients may be transferred to their care for specialist treatment, there may be no need for these doctors to have direct clinical contact with the remainder but they will still have an essential role in the decision-making process and in advising other health professionals. These senior doctors will be responsible for this advisory process, while immediate clinical responsibility will rest with the team currently caring for the patient.

Recommendations

- The optimal care of patients with MSCC should be determined by senior clinical advisers (these include clinical oncologists, spinal surgeons and radiologists with experience and expertise in treating patients with MSCC), taking into account the patient's preferences and all aspects of their condition, with advice from primary tumour site clinicians or other experts, as required.
- Every centre treating patients with MSCC should ensure 24-hour availability of senior clinical advisers to give advice and support to the MSCC coordinator and other clinicians, inform the decision-making process and undertake treatment where necessary.

Qualifying statement: These recommendations are based on GDG consensus that this will improve the speed an quality of decision-making.

Clinical Evidence

No evidence about the effectiveness of MDTs for MSCC patients exists. Other NICE cancer service guidance provides evidence about the effectiveness of MDTs in different settings, including 'Improving outcomes in breast cancer' (2002a), 'Improving outcomes in colorectal cancer' (2002b), 'Improving outcomes for people with sarcoma' (2006a), 'Improving outcomes for people with brain and other CNS tumours' (2006b) and 'Improving outcomes for people with skin tumours including melanoma' (2006c). The NICE guidance on 'Improving supportive and palliative care for adults with cancer' (2004) provides a general overview. Other evidence based guidelines include: 'West of Scotland Guidelines for Malignant Spinal Cord Compression' (2007) and the SIGN Guidelines 'Management of patients with stroke' (2002).

A study by Lee *et al.* (2007) reported improvements in the quality of care for metastatic spinal cord compression over 6 months by ensuring that >90% of patients receive definitive treatment within 24 hours of radiological diagnosis. Interventions evaluated were derived from a process that identified gaps and delays in current practices and clinical pathways used for the acute management of patients presenting with MSCC. The interventions were then fed into a revised clinical pathway for patients to be managed. The study was affected by substantial bias but reported that the mean overall response time to start corticosteroids was statistically significantly reduced from baseline. The mean overall response time to start radiation or surgical therapy was not statistically significantly reduced. The mean overall response time to length of stay was statistically significantly reduced and the mean overall hospitalisation costs were reduced but it was not statistically significant.

References

Lee, K., Tsou, I., Wong, S., Yu, C., Ming, Z., Loh, Y., Shakespeare, T., Mukherjee, R. & Back, M. (2007) Metastatic spinal cord compression as an oncology emergency getting our act together. *International Journal for Quality in Health Care,* 19: 377–381

National Institute for Health and Clinical Excellence (2002a) Improving outcomes in breast cancer. NICE cancer service guidance. London: NICE.

National Institute for Health and Clinical Excellence (2002b) Improving outcomes in colorectal cancer. NICE cancer service guidance. London: NICE.

National Institute for Health and Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. NICE cancer service guidance. London: NICE.

National Institute for Health and Clinical Excellence (2006a) Improving outcomes for people with sarcoma. NICE cancer service guidance. London: NICE.

National Institute for Health and Clinical Excellence (2006b) Improving outcomes for people with brain and other CNS tumours. NICE cancer service guidance. London: NICE.

National Institute for Health and Clinical Excellence (2006c) Improving outcomes for people with skin tumours including melanoma. NICE cancer service guidance. London: NICE.

Scottish Intercollegiate Guidelines Network (2002) Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. Edinburgh: SIGN. Available from www.sign.ac.uk/pdf/sign64.pdf

West of Scotland Malignant Spinal Cord Compression Guidelines (2007). Development Working Group on behalf of the West of Scotland Cancer Network.

3 The patient's experience of MSCC

3.1 Introduction

Early detection and diagnosis of metastatic spinal cord compression (MSCC), before the development of neurological symptoms relies solely on the history taking and diagnostic skills of medical staff eliciting and evaluating information from patients. To explore the patient perspectives of care of MSCC in England and Wales the Guideline Development Group (GDG) decided to write to all relevant patient/carer organisations and charities whose members and contacts included patients with MSCC and their carers and families. Individuals were invited to describe their experience of the condition and their interaction with health services. All correspondence received by the NCC-C was anonymised before consideration by the GDG. Consent to publish extracts was gained from all individuals whose experiences are presented in this chapter. From these narratives, several themes emerged including patients' unawareness of early symptoms, General Practitioner's (GPs) lack of awareness of early symptoms and signs, delays in diagnosis and treatment, lack of supportive and rehabilitative care, and ineffective communication throughout. Each of these themes are displayed in detail.

Patient unawareness of early symptoms and signs

"While on holiday in August 2003 my chronic bad back pain markedly worsened when I lifted 6 heavy water bottles in a supermarket. Subsequently I suffered great discomfort riding on the buses over cobblestones and walking. I went to a pharmacy which suggested pain killers and a cold pack."

"I had received a considerable amount of reading matter about my primary cancer on diagnosis. On completion of treatment and start of follow up I was not given any information about metastatic cancer signs and symptoms to look out for and note or report and how to do this if my next follow up appointment was some time away."

"A few days after doing some manual work erecting a section of garden fence I experienced very bad pain spasms in my upper back and had to take time off work. I contacted my GP surgery for an urgent appointment and spoke to the triage nurse. She encouraged me to take maximum doses of painkillers for a few days to see if this would clear the problem. The fact that I had a prior history of cancer was not mentioned by either of us."

"I started experiencing discomfort when walking, a sort of dull ache down one side of my body. It slowed my walking down and I started walking with a slight limp. I also experienced this pain if I lifted items such as travel bags."

"I experienced severe pain between my shoulder blades if I tried to do any physical activity which involved lifting my arms, walking was painful and driving my car was extremely painful. I nearly mentioned these symptoms in my follow up appointment in October 2003 with the surgical team. However, the doctor I saw was in a rush as the clinic was very busy and I failed to tell her about the pain I had been experiencing."

"It still hadn't occurred to me that all the pain I was experiencing could indicate that I had metastatic breast cancer in my back. I had no awareness of the risk of it developing there and still thought I had an unrelated back problem."

"I was in constant pain, walked with a limp,was unable to stand upright and walked with my head bowed and experienced a sharp pain and sensation of a tight band about my chest if I attempted to cough or take a deep breath. I also noticed a sensation of numbness in my abdomen when lying down. I still did not think to contact either my GP or my Oncologist and had delayed my Oncology follow up appointment by a couple of weeks to the second week of February in order to attend a training course at work."

"One day in July 2006, I started to experience numbness in the top part of my legs and being mindful of a presentation on MSCC symptoms to our User Group by the Network Lead Clinician, I rang the Chemotherapy clinic at my local hospital and they told me to come in immediately. They carried out all the necessary tests including an x ray and it turned out that my cancer had become active again and it was the pressure from the tumour at the bottom of my spine causing the numbness."

Awareness by the GP of early symptoms and signs

In several narratives, GPs failed to recognise the early signs and symptoms of patients with impending MSCC. It is difficult to gauge whether the problem lies with patients not effectively communicating their symptoms or GPs not recognising and reacting to the signals of impending MSCC.

"Back home in England, I presented to the GP who said it was simple back ache as every elderly man experienced (I was 63) and prescribed pain-killers. In desperation I went to a chiropractor who was quite rough with the spine."

"Pain persisted and I became less and less mobile. I went back to the GP and saw one who was not my normal doctor who again prescribed paracetamol and suggested using a back-roll. Some days later I mentioned to my wife that my feet didn't feel right – my gait was changing."

"I developed severe back pain – enough to limit mobility – it became severe and I took to bed. My GP visited and prescribed morphine based pain killers – no tests carried out. A few days later, I developed difficulty in bladder and bowel function. My GP said it was due to the morphine and he would check later. Movement become very painful and limb control was weak and I had to use a bottle for bladder emptying- now very slow. By Saturday, my bladder function was virtually nil and I had no control over my lower body and unable to move and with bladder pain."

"My GP was treating me for backache. I had no toilet functions (prescribed laxatives), loss of walking ability and acute pain. (He just gave me stronger painkillers."

"The main problem we encounter is the difficulty for generalists in recognising early enough."

"At my oncology follow up appointment, I mentioned that I was experiencing pain which I thought was a shoulder muscle problem and asked that I be checked out. I pointed out a puffy area between my shoulder blades that seemed to indicate a soft tissue problem. The appointment was not very long and I was not questioned about the range and severity of the pain symptoms that I was experiencing."

Diagnosis

After referral to a diagnostic centre, several narratives reported delays before imaging was performed and diagnosis of MSCC made.

"On my GP's advice I phoned orthopaedics who insisted that we went the A & E emergency route to be examined immediately which we did. After 4 hours waiting I was examined by a very nice doctor from orthopaedics. My wife asked for an MRI scan and was told that the waiting list was 3 months. An x-ray was done instead. He looked at it with us and decided that although there was something a bit odd about thoracic 7, I had probably had it since birth. We agreed that I had always had a slightly rounded and somewhat stiff back. He asked me to walk

up and down. By then I had considerable drop in the feet. He told us to come back if it got any worse – My wife said it was bad enough already. The next morning the same doctor rang us and asked me to come in for an MRI the next day. He had been thinking overnight and on second thoughts had a feeling there was something wrong on the x-ray after all. He had persuaded his orthopaedics boss that I merited a scan"

"No tests, told of cancer and spinal compression after 3 days in hospital."

"After experiencing considerable pain, inability to walk off a plane properly and having difficulty with breathing. He was subsequently admitted to the local hospital where he spent 2 days nursed flat with oxygen."

"A delay of nearly one week as doctors at local hospital diagnosed only back pain cancelled MRI and admitted to a ward for observation, and pain relief, did not agree with G P's [initial] diagnosis. MRI scan five days after admission to hospital [confirmed SCC]."

"Actual diagnosis took 7 months."

"Experienced early symptoms of impending MSCC for approximately 6 months before a diagnostic MRI was conducted providing a confirmation of MSCC."

"I was told that an area of metastatic cancer in my bone had been found in a single vertebra of my spine. I was to have a single shot of radiotherapy as an outpatient in about twelve days time, to start a different hormone therapy and a bisphosphonate therapy. Again, I was not asked about the sorts of pain symptoms I was experiencing and the risk of MSCC was not mentioned to me. At my brother's insistence, I was given a prescription for morphine and another pain killer, because of the very great deal of pain that I was in."

"I was diagnosed with mets to my spine in 2004 but at no time was I made aware of spinal cord compression, by my surgeon, oncologist or nurse."

Treatment

"In the week preceding my appointment for radiotherapy, I started experiencing the rapid development of neurological symptoms, though I did not realise this was what they were! This included my legs going from under me and falling down, the development of a 'drunken' gait and inability to walk more than a few yards. I had done some research on the internet and the Tuesday before my treatment was due, did speculate to my brother that I was experiencing a spinal cord compression. He suggested my symptoms might be due to the powerful painkillers I was taking. I did not think to contact a doctor about the further symptoms I was experiencing. I was determined to keep going until my outpatients appointment."

"The delays in diagnosis and the speed of onset of my symptoms in the last few days before treatment, meant that there was no window of opportunity to consider whether I would benefit from surgical treatment, which would have entailed a transfer to another hospital some 30 or 40 miles away. This option was only mentioned to me after my radiotherapy treatment, when it was no longer at option."

"It showed that there were several growths on the spine and a fracture at T7 ("compressed, fractured and osteoporotic", the surgeon said, reaching for his scalpel). We were taken to oncology straight away where the consultant met us as he was on duty. He said he was going to start radiotherapy straight away because although he didn't know exactly what I had, he knew I would not walk again unless treated urgently. At 5.30 in the evening the treatment began. Blood tests then showed that I had multiple myeloma."

In general, once MSCC was confirmed, patients received prompt treatment (radiotherapy or surgery). The outcome of the treatment varied according to the patient's clinical status before treatment. Several cases report this as a positive aspect of their care.

Supportive care and rehabilitation

After treatment, the supportive care and rehabilitation delivered to patients was variable with most patients describing sub-optimal post-operative supportive care and rehabilitation.

"My primary care trust lacks in-patient rehabilitation facilities for younger people and it was a concern for my doctors that there was nowhere suitable to send me. Another problem was a lack of Occupational Therapy resource for oncology patients."

"The community rehabilitation physiotherapist did refer me to the physiotherapy department in the local district general hospital. I received a couple of appointments there where I was assessed and given some advice on exercises, but they were unprepared to carry on working with me in the longer term."

"A lack of physiotherapy and other help to get me more independent whilst in hospital. If my wife had not been there every day it would have been extremely difficult for day to day functions."

"On return home I saw a district nurse once a fortnight. My GP has never visited and I have been offered no physiotherapy, in fact no professional support worth mentioning."

Communication

Several respondents reported poor communication at every stage of their journey. It is a complex issue with different factors contributing to the problem. These include: the possibility of developing MSCC; the need for information about symptoms and signs to be aware of (from the patient's perspective and the primary care sector); and the need for more effective communication between different service providers across the healthcare system.

"The biggest barrier to early diagnosis and optimised treatment for my MSCC was my own lack of awareness of this complication, the importance of reporting the signs and symptoms I was experiencing and ensuring that health professionals both listened to me and acted on what I was trying to tell them. Unless patients have enough information to be confident that they deserve to be heard and their symptoms responded to, delays in diagnosing and treating MSCC will continue to be experienced."

"No information was forthcoming about my condition or what the implications were. Naturally my wife and I were very worried! Especially as numerous specialists were examining me but providing little feedback."

"Remove acute fear of the unknown. More physiotherapy time and perhaps more explanation of what to expect during recovery process. Often felt bewildered or frightened due to lack of information or being told "It's normal."

"There was no one available to take any decisions related to his care until Monday when he was reviewed and had three days of radiotherapy. On the 4th day he had surgery to stabilise the spine but sadly this was all done far too late as the damage was done and he was left with no use of his legs, trunk or right arm."

I do think there needs to be better advice to patients, carers and healthcare professionals about spinal cord compression and the urgency of the situation.

"Communication between hospitals poor, transferring X-rays etc."

"When I asked why patients aren't informed of the possibility of having MSCC I was told that it's a very difficult subject to broach without 'freaking' people out. My feeling on this though is that patients who might develop this do have an absolute right to know about this as a possibility because of the disastrous consequences that can happen if action isn't taken quickly. Isn't it better to be informed than the very real scenario of ending up being paralysed for the rest of your life?"

"I do acknowledge that it is a sensitive subject but I also believe that it's a training issue if health professionals are not comfortable in broaching the subject."

Although most respondents were dissatisfied with their care, some described early recognition of symptoms, prompt investigation, diagnosis, treatment, and supportive care and rehabilitation in a very positive manner.

"The specialist Surgical team at [X] was excellent both by the way they provided reassurance and their specialist surgical skills."

"I have the support of my oncology department, doctors surgery are excellent and Macmillan Nurse (x) is my lifeline. I have receive[d] excellent treatment from all area]"

"Professional support from occupational therapist (physio) regular visits by GP and specialist nurse from [X]. Also social worker."

"Onset of symptoms were recognised and subsequent MR scan was conducted on day 3. Patient returned home and receives adequate supportive and rehabilitative care."

Supporting patient decisions

The options for treating spinal metastases and MSCC are numerous, and the decisions about best treatment are complex. Neurological ability at the time of treatment is the prime consideration, but the nature and technical aspects of optimal treatment depend on the behaviour of the primary cancer including its effects on the spinal column, the patient's general health, and their expected longevity. Patients may be poorly informed prior to diagnosis and overwhelmed on diagnosis especially if there is an urgency to treat and a need to transfer for definitive treatment.

Recommendation

- Ensure that communication with patients with known or suspected MSCC is clear and consistent, and that the patients, their families and carers are fully informed and involved in all decisions about treatment.

Qualifying statement: In the absence of research evidence about communication with MSCC patients and their families, this recommendation is based on GDG consensus and extrapolation of evidence from other clinical situations.

Clinical Evidence

Supporting patient decisions

There is no evidence that involves patients with MSCC. However, evidence from other cancer conditions provides a substantial platform for considering the use of decision aids in the healthcare and management of patients with MSCC (Estabrooks *et al.* 2001; Molenaar *et al.* 2000; O'Brien *et al.* 2002; O'Connor *et al.* 2003).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

Research Recommendation

- The role and use of decision aids should be investigated to help patients contribute to the complex decisions required when considering treatment for MSCC.

3.2 Emotional and family support

The diagnosis of MSCC in patients with known cancer can cause significant psychological distress for them and their families and carers. Primary presentation with MSCC combines the distress of new neurological disability with the diagnosis of a life limiting diseases. It is important therefore that all healthcare professionals are alert to the potential psychological support needed.

Recommendations

- Offer patients with MSCC and their families and carers specialist psychological and/or spiritual support appropriate to their needs at diagnosis, at other key points during treatment and on discharge from hospital.
- Provide information to patients with MSCC in an appropriate language and format that explains how to access psychological and/or spiritual support services when needed.
- Offer bereavement support services to patients' families based on the three component model outlined in 'Improving supportive and palliative care for adults with cancer' (NICE cancer service guidance CSGSP).

Qualifying statement: These recommendations are based on GDG consensus, and draw on broader evidence relating to the benefits of psychological and spiritual support in cancer care.

Clinical Evidence

Emotional and family support issues are addressed in the NICE guidance 'Management of depression in primary and secondary care' (2007) and 'Improving supportive and palliative care for adults with cancer' (2004).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

Research Recommendation

- Further research should be undertaken into the reasons why patients with MSCC present late.

References

Estabrooks C, Goel V, Thiel E, Pinfold P, Sawka C, Williams I. (2001) Decision aids: are they worth it? A systematic review. *Journal of Health Services and Research Policy*. 6(3):170–182.

Molenaar S, Sprangers M A, Postma-Schuit F C, Rutgers E J, Noorlander J, Hendriks J, De Haes H C.(2000) Feasibility and effects of decision aids. *Medical Decision Making*. 20(1):112–127.

National Institute for Health and Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. London: NICE.

National Institute for Health and Clinical Excellence (2007) Management of depression in primary and secondary care. *NICE clinical guideline* 23. London: NICE.

O'Brien M A, Villias-Keever M, Robinson P, Skye A, Gafni A, Brouwers M, Charles C, Baldassarre F, Gauld M. Impact of cancer-related decision aids. 2002:386. Rockville, MD, USA: Agency for Healthcare Research and Quality.

O'Connor AM, Stacey D, Entwistle V, Llewellyn-Thomas H, Rovner D, Holmes-Rovner M, Tait V, Tetroe J, Fiset V, Barry M, Jones J. Decision aids for people facing health treatment or screening decisions. Cochrane Database of Systematic Reviews 2003, Issue 1. Art. No.: CD001431. DOI: 10.1002/14651858.CD001431.

4 Early detection

4.1 Introduction

Patients who develop spinal metastases are at risk of irreversible spinal cord damage. Pre-treatment performance is the main determinant of post-treatment outcome and patients able to walk at the time of treatment maintain functional independence better and survive longer. Prompt treatment while the patient is still ambulant or even within 24 hours of the onset of neurological deficit is effective in maintaining the ability to walk and functional independence. Even when the diagnosis is made late, provided some spinal cord function remains, spinal decompression leads to better functional outcome (Loblaw *et al.* 2005). Delay in treatment may lead to complete and irreversible paralysis with loss of functional independence and shortened survival.

4.2 Communicating symptoms and risks

Early recognition and treatment of metastatic spinal cord compression (MSCC) results in improved outcomes. Making patients aware of the risks and early symptoms associated with MSCC may lead to earlier diagnosis. There is some concern that patients may be worried unnecessarily by knowledge of a relatively rare (3–5%) complication of cancer, but there is anecdotal evidence that patients would rather know in advance how their disease might progress rather than find out when it happens.

The difficulty is the level of information to be given to patients and at what stage they should be given the information.

Recommendations

- Inform patients at high risk of developing bone metastases, patients with diagnosed bone metastases, or patients with cancer who present with spinal pain about the symptoms of MSCC. Offer information (for example, in the form of a leaflet; see appendix 2) to patients and their families and carers which explains the symptoms of MSCC, and advises them (and their healthcare professionals) what to do if they develop these symptoms.
- Ensure that patients with MSCC and their families and carers know who to contact if their symptoms progress while they are waiting for urgent investigation of suspected MSCC. See Appendix 2.

Qualifying statement: These recommendations are based on GDG consensus.

Clinical Evidence

No evidence was identifed about how to effectively inform MSCC patients and their carers about the risk of developing bone metastases or the early symptoms of MSCC, or what to do should they develop these symptoms.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

4.3 Early symptoms and signs

A large number of patients are diagnosed annually with cancer but there is a relatively low risk of MSCC. It must also be borne in mind that 23% of patients with MSCC have no prior cancer diagnosis.

Permanent neurological damage including paralysis and incontinence can be prevented or minimised by early diagnosis and treatment of MSCC. It is therefore important to identify symptoms and signs which help to include or exclude the diagnosis of MSCC and to determine which patients should be referred for imaging.

It is not current practice to treat asymptomatic patients with metastatic spinal disease with radiotherapy or surgery. Therefore it is neither practical nor desirable to image patients without spinal symptoms.

Low back pain is a common complaint and frequently caused by other conditions which affects approximately one third of the population each year, 20% of whom visit their GP and are managed conservatively and appropriately without investigation for the most part.

Low back pain alone is non-discriminatory. Patients with cancer suffer non-specific back pain as often if not more frequently than the general population, and less than 0.1% of people who visit their GP with back pain have spinal metastases. However there are some features of pain that are better predictors of spinal cord compression such as localisation in the upper or mid spine (cervical or thoracic spine), progressive discomfort, severe unremitting pain and pain aggravated by activities that increase the pressure within the spinal canal such as coughing, sneezing and defaecating. However, it is extremely difficult to exclude MSCC in any patient with known cancer who complains of localised spinal pain. Even the absence of pain does not exclude MSCC.

Most patients with spinal metastases experience pain for several weeks before developing neurological symptoms and signs of MSCC. It is therefore important to recognise that unremitting spinal pain in a patient with known malignancy requires urgent discussion and preliminary assessment by the patient's multidisciplinary cancer team or MSCC coordinator (and similarly those without a known prior cancer diagnosis but suggestive history and signs need urgent assessment to exclude a malignant cause for their symptoms).

Progression to irreversible neurological impairment can be very variable but patients with slower onset of motor deficit have better outcomes. The presence of radicular pain, difficulty in walking, any numbness or weakness and bladder or bowel dysfunction increase the probability of MSCC and ideally patients should be discussed prior to the onset of these symptoms. Spinal tenderness and any abnormal neurological signs or difficulty in walking found on clinical examination also support the diagnosis.

It is therefore important that healthcare professionals caring for patients with a history of malignancy have a high index of suspicion for metastatic spinal disease.

Recommendations

- Contact the MSCC coordinator urgently (within 24 hours) to discuss the care of patients with cancer and any of the following symptoms suggestive of spinal metastases:
  - pain in the middle (thoracic) or upper (cervical) spine
  - progressive lower (lumbar) spinal pain

Recommendations (cont.)

  - severe unremitting lower spinal pain
  - spinal pain aggravated by straining (for example, at stool, or when coughing or sneezing)
  - localised spinal tenderness
  - nocturnal spinal pain preventing sleep.
- Contact the MSCC coordinator immediately to discuss the care of patients with cancer and symptoms suggestive of spinal metastases, who have any of the following neurological symptoms or signs suggestive of MSCC and view them as an oncological emergency:
  - neurological symptoms including radicular pain, any limb weakness, difficulty in walking, sensory loss or bladder or bowel dysfunction
  - neurological signs of spinal cord or cauda equina compression.
- Perform frequent clinical reviews of patients with cancer who develop lower spinal pain that is clinically thought to be of non-specific origin (that is, it is not progressive, severe or aggravated by straining and has no accompanying neurological symptoms). In particular, look for:
  - development of progressive pain or other symptoms suggestive of spinal metastases (contact the MSCC coordinator within 24 hours), or
  - development of neurological symptoms or signs suggestive of MSCC (contact the MSCC coordinator immediately).
- Perform frequent clinical reviews of patients without a prior diagnosis of cancer who develop suspicious spinal pain with or without neurological symptoms. Treat or refer patients with stable and mild symptoms by normal non-specific spinal pathways, or refer by cancer pathway if concerned. In particular, look for:
  - development of progressive pain or other symptoms suggestive of spinal metastases (contact the MSCC coordinator within 24 hours), or
  - development of neurological symptoms or signs suggestive of MSCC (contact the MSCC coordinator immediately).

Qualifying statement: These recommendations are based on GDG consensus and observational evidence.

Clinical Evidence

Overall the evidence available was of low quality. A systematic review (Loblaw *et al.* 2005) reported that symptoms for MSCC can include sensory changes, autonomic dysfunction, and back pain; however, because of the common incidence of back pain (those with and without MSCC) it was not predictive of MSCC. This review also reported that patients at high risk for MSCC (i.e. patients with known myeloma, breast, prostate, or kidney cancer) should be followed more actively and educated about the symptoms of MSCC, and impending cord compression. One study (Talcott *et al.* 1999) included in this systematic review, reported predictive risk factors for MSCC; these included: inability to walk, increased deep tendon reflexes, compression fractures on radiographs of spine, bone metastases present, bone metastases diagnosed more than 1 year earlier, and age less than 60 years. This study (Talcott *et al.* 1999) concluded that patients with none of the six risk factors had a 4% risk of MSCC compared with an 87% risk of MSCC in patients with five or more risk factors. Back pain failed to differentiate between patients with MSCC and patients without MSCC. Lu *et al.* (2005) determined independent clinical predictors (or potential risk factors) of MSCC, by using data from a cohort of cancer patients with

Clinical Evidence (cont.)

suspected MSCC who underwent spine MRI. Four independent predictors of thecal sac compression (TSC) were identified and included: abnormal neurologic examination, middle or upper back pain, known spinal metastases, and metastatic disease at initial diagnosis. These predictors stratified patients experiencing episodes into subgroups with varying risks of TSC, ranging from 8% (no risk factors) to 81% (three or four risk factors).

The evidence confirms that the evaluation of cancer patients with suspected MSCC should be based upon clinical information that includes cancer-related history, symptom data, and the presence of pertinent neurologic signs.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

Research Recommendation

- The development and patterns of signs and symptoms of MSCC in different patient groups should be researched.

References

Loblaw, D. A., Perry, J., Chambers, A. & Laperriere, N. J. (2005) Systematic review of the diagnosis and management of malignant extradural spinal cord compression: the Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group. *Journal of Clinical Oncology,* 23: 2028–2037.

Lu, C., Gonzalez, R. G., Jolesz, F. A., Wen, P. Y. & Talcott, J. A. (2005) Suspected spinal cord compression in cancer patients: a multidisciplinary risk assessment. *The Journal of Supportive Oncology,* 3: 305–312.

Talcott JA, Stomper PC, Drislane FW, Wen PY, Block CC, Humphrey CC et al. (1999) Assessing suspected spinal cord compression: a multidisciplinary outcomes analysis of 342 episodes. *Support Care Cancer*; 7:31–8.

5 Imaging

5.1 Introduction

Diagnosing the presence or absence of metastatic compression of the spinal cord or cauda equina and predicting the level on the basis of clinical signs alone is difficult and frequently inaccurate. Patients who have a known history of malignancy or symptoms suggestive of spinal metastasis require rapid access to an imaging technique that will predict the most likely pathological cause, accurately identify the extent, and level(s) of spinal column involvement and spinal cord compression, and any associated soft tissue mass.

Although the majority of patients will already be known to have a primary malignancy, for a significant number [23%], metastatic spinal cord compression (MSCC) will be their presenting problem. For patients with symptoms and signs suggestive of spinal cord compression there is therefore an additional need to discriminate between compression from malignancy and from other causes such as spinal degenerative disease or osteoporosis. Patients with known malignancy may also have spinal cord compression from a non-malignant cause.

The ideal imaging technique has to be able to discriminate between these various pathologies and be able to visualise lesions arising within the cord which may have a similar presentation to MSCC.

5.2 Choice of imaging modality

MRI has a high sensitivity for identifying metastatic disease within bone when the correct sequences are used (sagittal T1 and/or STIR (Short T1 Inversion Recovery)). MRI can also show any soft tissue component of the mass and the degree of spinal cord compression (sagittal T2 supplemented with axial T1 or T2 weighted scans) and can usually discriminate between metastatic disease and other pathologies. MRI also allows the whole spine to be imaged, not just the level of suspected spinal cord compression. This ensures that spinal cord compression at other levels is not missed and identifies metastases affecting non-symptomatic vertebrae, which may lead to a change in clinical management. These properties make MRI the investigation of choice in MSCC providing there are no specific contra-indications.

Although modern multi-slice CT scanning is quick and has the ability to image the whole spine, it is less sensitive than MRI for detecting metastases and requires expert interpretation. It is therefore unlikely to replace MRI as the primary investigation but it may be needed to provide additional information on bone integrity and stability and to help plan surgery.

CT myelography may still be required for patients in whom there is a specific contraindication to MRI, for instance those who have a cardiac pacemaker or in whom there is already metal work in the spine which degrades MR image quality by metal artefact.

Radioisotope bone scanning is very sensitive for the detection of metastases but does not show the extent of soft tissue compression of the cord and is not reliable in detecting the level of cord compression.

PET-CT is both sensitive and specific in the diagnosis of MSCC. But it is less widely available than MRI and there is no evidence that PET-CT provides additional clinically relevant information.

Plain radiology is not as sensitive for detecting metastatic bone disease as MRI and does not readily show soft tissue abnormalities.

Recommendations

- MRI of the spine in patients with suspected MSCC should be supervised and reported by a radiologist and should include sagittal T1 and/or short T1 inversion recovery (STIR) sequences of the whole spine, to prove or exclude the presence of spinal metastases. Sagittal T2 weighted sequences should also be performed to show the level and degree of compression of the cord or cauda equina by a soft tissue mass and to detect lesions within the cord itself. Supplementary axial imaging should be performed through any significant abnormality noted on the sagittal scan.
- Contact the MSCC coordinator to determine the most appropriate method of imaging for patients with suspected MSCC in whom MRI is contraindicated and where this should be carried out.
- Consider targeted computerised tomography (CT) scan with three-plane reconstruction to assess spinal stability and plan vertebroplasty, kyphoplasty or spinal surgery in patients with MSCC.
- Consider myelography if other imaging modalities are contraindicated or inadequate. Myelography should only be undertaken at a neuroscience or spinal surgical centre because of the technical expertise required and because patients with MSCC may deteriorate following myelography and require urgent decompression.
- Do not perform plain radiographs of the spine either to make or to exclude the diagnosis of spinal metastases or MSCC.

Qualifying statement: These recommendations are based on observational studies.

Clinical Evidence

From low quality studies, MRI was consistently found to provide superior diagnostic evaluation for MSCC over all other imaging modalities. Studies consistently demonstrate moderate to high sensitivity (44–100%) and specificity (90–93%) of MRI in diagnosing spinal cord compression (Andreasson *et al. 1990*, Colletti *et al.* 1991, Colletti *et al.* 1996, Loblaw *et al.* 2005) and compression fractures (Jung *et al.* 2003).

Health Economic Evaluation

Based on the available evidence, the GDG consenus was that there was a clinical justification for using MRI for the evaluation of MSCC, despite the high unit costs compared to other imaging modalities. Therefore the cost-effectiveness evidence for this topic was not formally investigated.

5.3 Routine MRI and early detection of MSCC

Patients with cancer are at risk of developing bony metastases at some point in their disease but those with certain tumours including breast, lung, prostate, kidney and multiple myeloma are more likely to do so. Even in these patients, regular imaging of the spine to detect early disease has not been recommended in other guidance.

Most patients with spinal metastases experience pain for several weeks before developing MSCC and preliminary assessment by that patient's multidisciplinary cancer team before referral for imaging may reduce the number of unnecessary scans.

Recommendations

- In patients with a previous diagnosis of malignancy, routine imaging of the spine is not recommended if they are asymptomatic.
- Serial imaging of the spine in asymptomatic patients with cancer who are at high risk of developing spinal metastases should only be performed as part of a randomised controlled trial.

Qualifying statement: These recommendations are based on low quality retrospective observational studies and GDG consensus and a lack of economic evidence.

Clinical Evidence

The evidence on imaging modalities is of low quality. There were no randomised controlled comparative imaging studies only several small studies that reported the accuracy of imaging modalities. Most studies investigated metastatic spinal disease (and reported on MSCC if it was detected) (Andraesson *et al.* 1990, Colletti *et al.* 1991, Fuji *et al.* 1995, Kosuda *et al.* 1996, Sarpel *et al.* 1987, Godersky *et al.* 1987). A minority of studies investigated occult MSCC specifically (Venkitaraman *et al.* 2007a, Bayley *et al.* 2001). Only one study examined what the outcome of detecting occult MSCC is with respect to neurological outcomes and survival (Venkitaraman *et al.* 2007b). There was no evidence for the benefit of serial imaging in asymptomatic patients.

For studies that investigated metastatic spinal disease

The sensitivity of MRI of detecting MSCC was 96% (Andraesson *et al.* 1990 and Colletti *et al.* 1991). The detection rate of MSCC ranged from 26% (Fuji *et al.* 1995), 30% (Kosuda *et al.* 1996), 37.5% (Sarpel *et al.* 1987) and 42% (Godersky *et al.* 1987).

From studies investigating occult SCC specifically

The detection rate of MSCC was 27.33% (Venkitaraman *et al.* 2007) and 32% (Bayley *et al.* 2001)

Outcome of early diagnosis

Only one study (Venkitaraman *et al.* 2007b) investigated the outcome of patients with metastatic prostate cancer with clinically occult MSCC identified with MRI and given early radiotherapy. This study reported that there was no statistical difference between subgroups of patients (Group A: patients who had radiological identified MSCC (rMSCC) and received radiotherapy, Group B: patients who did not have rMSCC but received radiotherapy for back pain, Group C: patients who did not have rMSCC or back pain and did not receive radiotherapy) either in neurologic deficit free interval or overall survival.

Health Economic Evaluation

The literature search identified 41 potentially relevant papers. Five of these studies were obtained for appraisal. Three of these studies did not contain an economic evaluation. The remaining two papers both included an economic evaluation but both evaluated the use of MRI scanning to detect cancers in primary care settings, not in people with suspected bone metastases with the aim of preventing MSCC. No de novo modelling was attempted because there was no clinical evidence to support the value of prophylactic treatment of asymptomatic spinal metastases. Thus, scanning people with suspected bone metastases using MRI to prevent MSCC cannot be considered cost-effective given current clinical evidence.

Research Recommendation

- Patient subgroups who might benefit from routine MRI such as those with and without spinal metastases, those with and without pain and different tumour types need to be clearly identified.

5.4 Timing of MRI assessment

Patients with MSCC usually present with progressive back pain or nerve root pain, but otherwise non-specific symptoms and signs. Patients who develop spinal metastases are at risk of irreversible paralysis.

Once MSCC is suspected it is essential that investigation, planning, and treatment take place before any further loss of neurological function. MRI is central to the diagnosis, staging and planning of treatment and must be available in a timeframe to fit the clinical needs of the patient proceeding to urgent or emergency treatment.

Recommendations

- Imaging departments should configure MRI lists to permit time for examination of patients with suspected MSCC at short notice during existing or extended sessions (by moving routine cases into ad hoc overtime or to alternative sessions, if overtime is not possible).
- If MRI is not available at the referring hospital, transfer patients with suspected MSCC to a unit with 24-hour capability for MRI and definitive treatment of MSCC.
- Perform MRI of the whole spine in patients with suspected MSCC, unless there is a specific contraindication. This should be done in time to allow definitive treatment to be planned within 1 week of the suspected diagnosis in the case of spinal pain suggestive of spinal metastases, and within 24 hours in the case of spinal pain suggestive of spinal metastases and neurological symptoms or signs suggestive of MSCC, and occasionally sooner if there is a pressing clinical need for emergency surgery.
- Out of hours MRI should only be performed in clinical circumstances where there is an emergency need and intention to proceed immediately to treatment, if appropriate.

Qualifying statement: These recommendations are based on GDG consensus and evidence of cost effectiveness.

Clinical Evidence

Evidence for this question was drawn from several observational studies (Helweg-Larsen *et al.* 1996, Husband *et al.* 1998, Levack *et al.* 2002, Maranzano *et al.* 1995, Mitera *et al.* 2003, Solberg *et al.* 1999, Turner *et al.* 1993). The findings from this evidence consistently reported that early diagnosis and treatment, while functional status is good, leads to better functional outcome and longer survival.

5.5 Health economic evaluation for timing of MRI in MSCC

It is important that the diagnosis is made quickly enough to permit treatment according to clinical need. Although MRI scans are the diagnostic tool of choice, facilities at most District General Hospitals (DGHs) are not open 24 hours 7 days a week, meaning that patients suspected to have MSCC may have to wait for a diagnosis or be transferred elsewhere. The aim of this economic analysis was therefore to assess the cost-effectiveness of increasing scanning opening times at DGHs.

A systematic review of the literature did not identify existing economic evaluations on this topic, and so a decision model was built. The model was based on a decision tree approach, and assessed the costs and benefits of five different scenarios, each representing different opening hours at a DGH and policies for scanning patients out of hours (Table 5.1). Health benefits were expressed in terms of Quality-Adjusted Life-Years (QALYs). Future costs and benefits were not discounted as the time horizon for the analysis was approximately one year.

Table 5.1 Scenario descriptions

Scenario	Description
1a (baseline scenario)	SWH defined as 9am to 5pm Monday to Friday only. In this scenario it is assumed that all DGH clinic slots are full, and that any person who requires an urgent MRI for suspected MSCC who arrives at the clinic Sunday to Thursday, is therefore required to wait until the next morning to have a MRI at the DGH. People arriving Friday or Saturday are required to wait until the following Monday for a MRI.
1b	All patients arriving at a DGH with suspected MSCC require immediate transfer to a tertiary treatment centre under the assumption that all the DGH MRI slots for that day are full. On arrival at the tertiary centre patients receive an immediate MRI and treatment if necessary.
2a	SWH again defined as 9am to 5pm Monday to Friday but with the added option that if a person urgently requires a MRI for suspected MSCC *during these opening hours*, they are immediately added to the clinic list and receive a MRI that day. The 'expense' of this approach is that the remaining patients on the waiting list for that day are required to wait an extra two hours, meaning that overtime is paid for the MRI-related staff. No MRI facilities are available outside of these times during the week or at the weekend.
2b	The same as 2a) except patients who require a MRI outside of these opening hours are immediately transferred to a tertiary treatment centre for scanning and treatment if required.
3	MRI clinics are assumed to extend their weekday opening hours to 8am to 8pm Monday to Friday and to be open at the weekend 9am to 3pm Saturday and Sunday. Patients requiring a MRI during these times are assumed to receive a scan the same day. People arriving outside of these hours are required to wait until the next morning for a MRI. As weekend cover is included in this scenario, it is implied that no 'urgent' patients are required to wait longer than 24 hours for a MRI.

The main logic underpinning the model was that people arriving at a DGH requiring an urgent MRI for suspected MSCC either received a scan that day, the next day or on the following Monday if they are required to wait over the weekend. Patients required to wait until the next day for a MRI were assumed to have poorer health outcomes compared with people who received an immediate MRI. Moreover, people who were required to wait for a MRI until after the weekend were assumed to experience poorer health outcomes compared with people who had to wait until the next day. Thus, the benefit of longer and more frequent opening hours was faster access to diagnosis and treatment with better health outcomes. Once a MRI had been undertaken, patients with correctly diagnosed MSCC were assumed to undergo appropriate decompression treatment with an associated probability of being either ambulant or not ambulant after this treatment. Although a range of different patients require MRI, the decision was made to attribute all the additional costs of extending opening hours to people with suspected MSCC, as the context for this evaluation was a Clinical Guideline for people with MSCC.

The base case results suggested that paying staff overtime at DGHs to accommodate suspected MSCC patients during standard working hours but transferring patients to specialist tertiary centres outside of these times was the most cost effective option at £9,785 per additional QALY (scenario 2b,Table 5.2). Results from the sensitivity analysis showed that the cost-effectiveness ratios were sensitive to a number of variables, such as the time to paraplegia following successful treatment, but that broadly speaking scenario 2b remained the most cost-effective option.

Table 5.2 Base case results

Scenario	Expected costs	Expected QALYs	ICER*
1	£18,431	0.26	
1a	£18,591	0.28	£7,726
2b	£19,526	0.35	£9,785
1b	£19,310	0.35	Dominated
3	£19,383	0.30	Dominated

*Exact results may vary due to rounding expected costs and QALYs

The analysis showed that paying overtime to MRI-related staff is likely to be the most cost-effective of the evaluated scenarios. It also suggested that under most plausible assumptions, extending opening hours purely for the reason of scanning suspected MSCC patients is unlikely to be cost-effective. The main caveat to these conclusions, however, is that the data used to populate the model were either of poor quality or were based on assumptions.

It also suggested that under most plausible assumptions, extending opening hours at DGHs purely for the reason of scanning suspected MSCC patients is unlikely to be cost-effective. However it is important to note that extending the availability of MRI for reasons other than MSCC permits more patients to be scanned locally in the above scenario.

Outside normal hours (extended by ad-hoc overtime payments where necessary), it is not cost-effective to provide 24-hour availability of MRI for suspected MSCC at DGHs and where urgent scan is clinically necessary out-of-hours these patients need be transferred to a unit capable of urgent MRI and definitive treatment.

References

Andreasson, I., Petren-Mallmin, M., Strang, P., Nilsson, S., Nyman, R. & Hemmingsson, A. (1990) Diagnostic methods in planning palliation of spinal metastases. *Anticancer Research,* 10: 731–733.

Bayley, Milosevic, Blend, Logue, Gospodarowicz, Boxen, Warde, McLean, Catton & Catton. A (2001) prospective study of factors predicting clinically occult spinal cord compression in patients with metastatic prostate carcinoma. *Cancer* 92(2): 303–310. United States.

Colletti PM, S. H. W. M. Y. H. T. MR. (1996) The impact on treatment planning of MRI of the spine in patients suspected of vertebral metastasis: an efficacy study. *Comput Med Imaging Graph,* 20: 159–162.

Colletti, P. M., Dang, H. T., Deseran, M. W., Kerr, R. M., Boswell, W. D. & Ralls, P. W. (1991) Spinal MR imaging in suspected metastases: Correlation with skeletal scintigraphy. *Magnetic Resonance Imaging,* 9: 349–355.

Fujii, Higashi, Owada, Okuno, Mizuno & Mizuno. (1995) Magnetic resonance imaging for the diagnosis of prostate cancer metastatic to bone. *Br J Urol* 75(1): 54–58.

Godersky JC, Smoker WR, Knutzon R (1987) Use of magnetic resonance imaging in the evaluation of metastatic spinal disease. *Neurosurgery* 21, 676–680.

Helweg-Larsen, S. (1996) Clinical outcome in metastatic spinal cord compression. A prospective study of 153 patients. *Acta Neurologica Scandinavica,* 94: 269–275.

Husband, D. J. (1998) Malignant spinal cord compression: prospective study of delays in referral and treatment. *BMJ,* 317: 18–21.

Jung, H. S., Jee, W. H., McCauley, T. R., Ha, K. Y. & Choi, K. H. (2003) Discrimination of metastatic from acute osteoporotic compression spinal fractures with MR imaging. *Radiographics,* 23: 179–187.

Kosuda S, Kaji T, Yokoyama H, Yokokawa T, Katayama M, Iriye T, Uematsu M, Kusano S (1996) Does bone SPECT actually have lower sensitivity for detecting vertebral metastasis than MRI? *Journal of Nuclear Medicine* 37: 975–978.

Levack, P., Graham, J., Collie, D., Grant, R., Kidd, J., Kunkler, I., Gibson, A., Hurman, D., McMillan, N., Rampling, R., Slider, L., Statham, P. & Summers, D. (2002) Don't wait for a sensory level - Listen to the symptoms: A prospective audit of the delays in diagnosis of malignant cord compression. *Clinical Oncology (Royal College of Radiologists),* 14: 472–480.

Loblaw, D. A., Perry, J., Chambers, A. & Laperriere, N. J. (2005) Systematic review of the diagnosis and management of malignant extradural spinal cord compression: the Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group.[see comment]. [Review] [61 refs]. *Journal of Clinical Oncology,* 23: 2028–2037.

Maranzano, E. & Latini, P. (1995) Effectiveness of radiation therapy without surgery in metastatic spinal cord compression: Final results from a prospective trial. *International Journal of Radiation Oncology, Biology, Physics,* 32: 959–967.

Mitera, G., Loblaw, A. (2003) Delays from symptom onset to treatment in malignant spinal cord compression: quantification and effect on pre-treatment neurological status. *Radiother. Oncol* 69: Abstract 141

Sarpel S, Sarpel G, Yu E, Hyder S, Kaufman B, Hindo W, Ezdinli E (1987) Early diagnosis of spinal-epidural metastasis by magnetic resonance imaging. *Cancer* 59: 1112–1116.

Solberg, A. & Bremnes, R. M. (1999) Metastatic spinal cord compression: diagnostic delay, treatment, and outcome. *Anticancer Research,* 19: 677–684.

Turner S, M. B. T. I. B. J. (1993) Malignant spinal cord compression: a prospective evaluation. *Int J Radiat Oncol Biol Phys,* 26: 141–146.

Venkitaraman R *et al.* (2007a) Detection of occult spinal cord compression with magnetic resonance imaging of the spine. *Clinical Oncology* 19: 528–531

Venkitaraman, R *et al.* (2007b) Outcome of early detection and radiotherapy for occult spinal cord compression. *Radiotherapy & Oncology,* 85: 469–472.

6 Treatment of spinal metastases and MSCC

6.1 Introduction

Metastatic spinal cord compression (MSCC) occurs because of pressure on the spinal cord or its vascular supply, and may result from soft tissue tumour occupying the space within the spinal canal (epidural tumour), structural failure including pathological fracture or collapse (deformity or dangerous shift) of the spinal column, or a combination of soft tissue and bony intrusion on the cord.

Patients who develop paraplegia have a significantly impaired quality of life and shortened survival and so it is important to identify possible ways of preventing or improving the outcome of MSCC. Treatments for spinal metastases and MSCC may include control of pain, prevention of spinal collapse and/or paralysis, prolongation of survival, and palliation of residual symptoms.

Surgery is the primary treatment of choice for MSCC from radio-resistant tumours for all patients unless paraplegia is complete, the prognosis too poor, or the patient is too frail to justify the risks. When spinal cord damage is due to soft tumour rather than bony compression radiotherapy and surgery have both been shown to be effective in treating MSCC. But when there are disabling neurological symptoms, surgery is more likely to halt deterioration and allow recovery. Structural failure is usually associated with severe mechanical pain and very unlikely to improve with radiotherapy but may be treated by surgical decompression and stabilisation.

Some tumours such as lymphoproliferative disease, myeloma, breast and prostate carcinoma are more likely than others to respond to radiotherapy or chemotherapy. Post-operative radiotherapy is routinely given even to relatively radio-resistant tumours

The clinical features of metastatic spinal disease and MSCC overlap, as do the treatments for them, but their management may reasonably be considered in two broad groups, both of which may improve symptoms, quality of life and survival:

- *Treatments primarily to relieve pain and/or prevent vertebral collapse and spinal cord compression.*
- *Definitive treatment of bony instability and/or neurological disability.*

Surgery is increasingly the treatment of choice for patients with MSCC, but the two aims of preserving neurological function and also achieving spinal column reconstruction that will remain stable during the patient's remaining life, are not always attainable.

It is important to remember that:

- MSCC is only one manifestation of the underlying malignant disease which itself may need speficic treatment by the primary tumour site specialist ongologist or haemotologist.
- The majority of patients with MSCC have metastases in other bony sites or viscera.
- Even when a solitary metastasis has progressed to the point that MSCC has developed, it is unlikely that extralesional excision will eradicate the cancer.
- Only about 20% of patients with MSCC will survive more than a year

- Treatment of MSCC is primarily to improve the quality of remaining life in most cases.
- Some epidural tumours (including haemotological malignancies) respond to treatments other than surgery or require only limited surgery.

Treatment planning must therefore take account of:

- the degree of neurological disability
- the general health of the patient
- the primary site of tumour
- the presence of other spinal and extraspinal metastases
- the likely response of the tumour to radiotherapy or other adjuvant therapy.

All of these factors as well as the likely time taken to be treated and rehabilitated must be balanced against the likelihood of a good functional outcome and long-term survival.

There are some patients who are too unwell for any intervention and will be given supportive care only. Others, though suitable for treatment are not fit enough for surgery but may be appropriately treated with radiotherapy or other treatments. Finally, there is a group of patients suitable for surgical intervention which itself needs careful planning to ensure that the most appropriate procedure, likely to give the best results, is carried out.

Ideally all patients with MSCC should be fully staged before surgery but if spinal cord function is deteriorating rapidly this may not be possible.

6.2 Treatments for painful spinal metastases and prevention of MSCC

Patients with MSCC usually have some accompanying pain whatever their functional status and ability to walk at the time of diagnosis. This may be due to dural or neural compression, or the effects of tumour on the spinal bone. In some patients this is due to tumour expansion within the vertebral body, and is not affected by posture or movement. This is commonly referred to as non-mechanical pain and is usually treated by non-invasive methods (analgesics, radiotherapy, drugs including bisphosphonates, and occasionally chemotherapy as part of the general treatment of chemosensitive disease) including haemotological malignancies.

In others, vertebral pain may be aggravated by spinal movement, lifting light weights, and even by standing. This pain may be due to weakening of the bone, is commonly referred to as mechanical pain and is often treated by supporting the spine. External devices such as corsets or braces for the trunk, and collars or halo jackets for the neck can be used, with a range of effectiveness. Alternatively the spine can be supported internally. One way of doing this is to inject cement into the vertebra to prevent collapse or reduce pain in a collapsed vertebra (vertebroplasty). Kyphoplasty is a similar technique in which a balloon is inflated in the vertebral body to create a cavity or partially restore height before injecting cement to maintain the shape (balloon kyphoplasty). Open surgery may sometimes be performed with the prime intention to stabilise the painful spine.

Rarely, and for those with intractable pain, invasive treatments may be used including epidural or intrathecal analgesia or neurolysis, open or percutaneous cordotomy, intraventricular or intracisternal opioids, or other interventional neurosurgical procedures.

Analgesia

Conventional analgesia including non-steroidal anti-inflammatory drugs (NSAIDs), non-opiate, and opiate medication have an important role in the care of patients in pain with cancer. Symptom control by more invasive specialist pain techniques are rarely used but offer effective palliation for the pain of advanced cancer.

Recommendations

- Offer conventional analgesia (including NSAIDs, non-opiate and opiate medication) as required to patients with painful spinal metastases in escalating doses as described by the WHO three-step pain relief ladder.
- Consider referral for specialist pain care including invasive procedures (such as epidural or intrathecal analgesia) and neurosurgical interventions for patients with intractable pain from spinal metastases.

Qualifying statement: These recommendations are based on GDG consensus and the WHO three-step pain ladder. [1]

Clinical Evidence

Because of the lack of good evidence for this question the GDG commissioned an expert position paper. This paper addresses the use of pharmacologic/non-pharmacologic interventions, neuro-surgical interventions, pain procedures, epidural, intrathecalanalgesia/ neurolysis, open cordotomy and cisternal administration of opioids (see Appendix B of the Evidence Review which accompanies this guideline).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

Bisphosphonates

Bisphosphonates are a group of drugs which can be given either orally or intravenously and which affect bone metabolism by inhibiting osteoclast activity. They may not prevent skeletal metastases or prevent MSCC, but they are widely used in cancer patients to treat hypercalcaemia and to reduce skeletal-related events (SREs). They are not uniformly effective in all types of cancer, and side effects including nausea, vomiting, anaemia and renal toxicity may limit treatment.

Recommendations

- 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 MSCC, except as part of a randomised controlled trial.

Qualifying statement: These recommendations are based on evidence from a high quality meta-analysis, systematic reviews of RCTs and RCTs with a low risk of bias.

Clinical Evidence

Bisphosphonates have been evaluated in several meta-analyses including patients with different cancer types. (Imrie *et al.* 2005; Saad *et al.* 2004; Tripathy *et al.* 2004; Warr *et al.* 2004; Weinfurt *et al.* 2004; Weinfurt *et al.* 2005; Wong and Wiffen 2002; Yuen *et al.* 2006). Consistently this evidence demonstrates that pain is altered or reduced with bisphosphonates (for breast cancer and multiple myeloma). A meta-analysis by Yuen *et al.* (2006)

[1] http://www.who.int/cancer/palliative/painladder/en/

Clinical Evidence (cont.)

showed a trend favouring bisphosphonates over placebo for the relief of pain from bone metastases in men with prostate cancer, although this was not statistically significant. There was no significant difference between the analgesic consumption of bisphosphonate and placebo groups.

Bisphosphonates have also been reported to manage skeletal complications in patients with metastatic cancer, although some inconsistencies do exist. There is evidence that skeletal related events (SRE) are reduced in patients with multiple myeloma and breast cancer (Imrie *et al.* 2005; Tripathy *et al.* 2004; Warr *et al.* 2004). For prostate cancer the meta-analysis by Yuen *et al.* (2006) showed a modest reduction in skeletal events with bisphosphonate treatment (using trial authors' definitions of skeletal events). The estimated rates for skeletal events were 37.8% and 43.0% for the bisphosphonate and placebo groups respectively: an absolute risk difference of 5.2%. There was inconsistent evidence about the effect of bisphosphonates on the rate of pathological fractures. The rates of spinal cord compression, bone surgery and bone radiotherapy did not differ significantly between bisphosphonate and placebo groups[2]. There were no significant group differences in overall survival or in quality of life. From an included study (Saad *et al.* 2002) in this review and from a follow-up publication (Saad *et al.* 2004), 4mg zoledronic acid was reported to be statistically more effective than placebo with respect to reducing SREs (with SCC a component of the SRE definition). Interestingly, the 8/4mg arm of this study did not show a significant difference for SREs (Saad *et al.* 2002). In Saad *et al.* (2002), SCC occurred less frequently in patients who received either dose of zoledronic acid than in those who received placebo. Yuen *et al.* (2006) conducted statistical analysis on these figures and showed that it was not statically significantly different.

From an RCT that compared zoledronic acid (4 or 8 mg) with a placebo in patients with lung cancer and other solid tumours (Rosen *et al.* 2003) there was no statistically significant difference in SREs (which excluded hypercalcaemia of malignancy – HCM), between 4 mg zoledronic acid versus placebo. However, there was a statistically significant difference between 8/4 mg zoledronic acid versus placebo. In the analysis of all skeletal events (including HCM), 4 mg ZA significantly reduced the proportion of patients with an event as compared with the placebo group. There was minimal difference in the proportion of patients experiencing SCC in any treatment group (4 or 8/4 mg ZA or placebo) – no statistical analysis provided. A multiple event analysis showed a significant 27% risk reduction for multiple skeletal events, in favour of 4 mg zoledronic acid, among patients in both the NSCLC (non small cell lung cancer) and other solid tumour group, versus the placebo group. From an extended treatment time of this RCT (Rosen *et al.* 2004), fewer (though not statistically analysed) patients treated with zoledronic acid developed at least 1 SRE at 21 months compared with patients treated with placebo. There was a statistically significant difference for those treated at the 8/4-mg dose, compared to those treated with placebo. Again as in Rosen *et al.* (2003), there was minimal difference in the proportion of patients experiencing SCC in any treatment group (4 or 8/4 mg zoledronic acid or placebo) – no statistical analysis provided. A 31% reduction in the risk of developing an SRE (including HCM) for a patient treated with 4 mg of zoledronic acid compared with placebo.

Overall, the most common adverse effects reported in this extensive body of evidence are nausea, vomiting, anaemia, bone pain and renal toxicity.

Radiotherapy

External beam radiotherapy is widely used for the treatment of pain resulting from bone metastases at any site, including the spine, and may be effective for up to 12 months. Different radiotherapy regimens ranging from a single dose of 8Gy to fractionated regimens

[2] See Prostate cancer: diagnosis and treatment (2007) NICE clinical guideline 58. Available from www.nice.org.uk/CG058.

Clinical Evidence (cont.)

of 30Gy in 10 doses appear to be equally effective for pain relief. The rate of pathological fracture is lower with multi-fractionation regimens, but single dose radiotherapy may sometimes be repeated.

Although useful for the pain of vertebral involvement by metastatic disease, radiotherapy does not abolish mechanical pain which may progress to bony instability, vertebral collapse and MSCC.

Radiotherapy is occasionally used in patients with spinal metastases without pain with the aim of preventing MSCC but it is unclear whether this is effective.

Recommendations

- Offer patients with spinal metastases causing non-mechanical spinal pain 8 Gy single fraction palliative radiotherapy even if they are completely paralysed.

Qualifying statement: This recommendation is based on evidence from case control and cohort studies of spinal metastases, supplemented by extrapolated evidence from meta-analyses and RCTs of the use of radiotherapy for peripheral skeletal metastases.

- Patients with asymptomatic spinal metastases should not be offered radiotherapy with the intention of preventing MSCC except as part of a randomised controlled trial.

Qualifying statement: This recommendation is based on GDG consensus and lack of evidence of any benefit from prophylactic radiotherapy.

Clinical Evidence

From high quality studies (RCTs and systematic reviews) there was consistent findings that single and multi-fraction radiotherapy were equally effective for pain palliation (Falkmer *et al.* 2003; Hartsell *et al.* 2005; Katagiri *et al.* 1998; Kida *et al.* 2000; Kraiwattanapong *et al.* 2004; Tombolini *et al.* 1994; van der Linden *et al.* 2004, 2006; Roos *et al.* 2003, 2005; Sze *et al.* 2006; Wu *et al.* 2004; Zaidat *et al.* 2002). There was also no apparent dose response relationship from one meta-analysis (Wu *et al.* 2003).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

Research Recommendation

- The use of radiotherapy to prevent the development of MSCC in patients with identified spinal metastases but no pain should be investigated by randomised controlled trial.

Vertebroplasty and kyphoplasty

Both of these minimally invasive techniques have NICE Interventional Procedures Guidance (2003a, 2003b) which permits their use in persistently painful spinal fracture including metastatic disease. The evidence of effectiveness in treating metastatic involvement is small in comparison with that for osteoporotic collapse, but there is considerable interest in their potential to reduce pain and avert vertebral collapse/MSCC. There are risks involved, including cement leakage causing spinal cord compression which may require urgent or emergency surgical intervention.

Recommendations

- Consider vertebroplasty[3] or kyphoplasty[4] for patients who have vertebral metastases and no evidence of MSCC or spinal instability if they have:
  - mechanical pain resistant to conventional analgesia, or
  - vertebral body collapse.
- Vertebroplasty or kyphoplasty for spinal metastases should only be performed after agreement between appropriate specialists (including an oncologist, interventional radiologist, and spinal surgeon), with full involvement of the patient and in facilities where there is good access to spinal surgery.

Qualifying statement: These recommendations are based on evidence from observational studies, qualitative studies, case series, and case reports. There is no health economic evidence regarding vertebroplasty and kyphoplasty for their use in pain control. However, there is evidence of cost effectiveness for vertebroplasty as a definitive treatment for MSCC. GDG consensus was that this is likely to be cost effective for pain in comparison with open surgery.

Clinical Evidence

Systematic reviews (Hulme *et al.* 2006 and Taylor *et al.* 2006, 2007) and international evidence-based guidelines (Blue Cross Blue Shield Association 2005, Adelaide Health Technology Assessment on behalf of MSAC, 2005) provide evidence and commentary about the effectiveness and safety of both vertebroplasty and kyphoplasty for both osteoporotic and neoplastic vertebral collapse. The literature includes no controlled-comparative studies and comprises lower quality evidence from non-randomised comparative studies and several case series studies. The evidence suggests that vertebroplasty is an effective therapy in the management of patients with symptomatic osteoporotic vertebral compression fractures and neoplastic disease. Balloon kyphoplasty is a reasonable alternative to vertebroplasty, although this conclusion is based on evidence from study designs that are susceptable to bias. In general, this low level evidence suggests that vertebroplasty and kyphoplasty provide pain relief and improvement in ambulation. Adverse effects included cement leakage which was more commonly reported for vertebroplasty than for balloon kyphoplasty.

Health Economic Evaluation

The combined literature search for all the sub-sections of this topic identified 1,532 potentially relevant papers. Twenty-five papers were retrieved and reviewed however none specifically examined the cost-effectiveness of treatments to prevent spinal collapse or MSCC in people with known spinal metastases. No de novo modelling was undertaken except for vertebroplasty and kyphoplasty because there was judged to be insufficient clinical evidence establishing a link between treatment and the prevention of spinal collapse and MSCC. See 6.8 health economic evaluation for treatment of MSCC.

Research Recommendation

- The use of vertebroplasty and kyphoplasty in preventing MSCC in patients with spinal metastases should be investigated by randomised controlled trial.

Surgery

Some patients with spinal metastases have mechanical spinal pain suggestive of bony instability but without evidence of structural failure or instability on imaging. Others with evidence

[3] Percutaneous vertebroplasty' (NICE interventional procedure guidance 12). The Medicines and Healthcare Products Regulatory Agency has issued safety notices relating to this procedure (reference MDA/2003/021).

[4] 'Balloon kyphoplasty for vertebral compression fractures' (NICE interventional procedure guidance 166).

of structural failure on MRI or CT imaging are at high risk of progression to MSCC. Complex surgery is increasingly used in the treatment of metastatic spinal disease, including relief of otherwise uncontrollable mechanical pain.

Recommendations

- Urgently consider patients with spinal metastases and imaging evidence of structural spinal failure with spinal instability for surgery to stabilise the spine and prevent MSCC.
- Consider patients with spinal metastases and mechanical pain resistant to conventional analgesia for spinal stabilisation surgery even if completely paralysed.

Qualifying statement: These recommendations are based on evidence from observational studies, qualitative studies, case series, and case reports.

- Consider patients with MSCC who have severe mechanical pain and/or imaging evidence of spinal instability, but who are unsuitable for surgery, for external spinal support (for example, a halo vest or cervico-thoraco-lumbar orthosis).

Qualifying statement: This recommendation is based on GDG consensus.

- Patients with spinal metastases without pain or instability should not be offered surgery with the intention of preventing MSCC except as part of a randomised controlled trial.

Qualifying statement: This recommendation is based on GDG consensus and lack of evidence for benefit from prophylactic spinal surgery.

Clinical Evidence

The best available evidence about the effectiveness of stabilisation surgery was drawn from retrospective case series studies (Hirabayashi *et al.* 2003*;* Holman *et al.* 2005; Jansson *et al.* 2006*;* Sundaresan *et al.* 2002; Vrionis *et al.* 2003*;* Weigel *et al. 1999;* Wise *et al.* 1999). The results of the studies consistently showed an improvement in pain, functional and ambulation status. Increased survival was associated with tumour types (more favourable types included breast, kidney, bone marrow, prostate, myeloma or thyroid) and by younger age (Hirabayshi *et al.* 2003; Sundaresan *et al.* 2002). Decreased survival was reported for patients with extra skeletal metastases. The most commonly reported complication was wound infection.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

Research Recommendation

- The use of surgery to prevent the development of MSCC in patients with identified spinal metastases but no pain should be investigated by randomised controlled trial.

Treatment options

Treatment of metastatic spinal disease is complex usually requiring multi modality treatment. Treatment depends on many factors including tumour type and degree of spread.

Recommendation

- All decisions on the most appropriate combinations of treatment for pain or preventing paralysis caused by MSCC should be made by relevant spinal specialists in consultation with primary tumour site clinicians and with the full involvement of the patient.

Qualifying statement: This recommendation is based on GDG consensus.

6.3 Care of the threatened spinal cord in patients with MSCC

Immediate care of the compressed spinal cord to prevent additional damage when the spinal column is unstable or spinal cord function (neurology) is impaired includes protecting spinal alignment by avoidance of movement, maintenance of cord perfusion by lying flat, and reduction of cord compression by presciption of dexamethasone/high dose steroids.

Mobilisation

Severe mechanical pain suggestive of bony (spinal column) instability, or neurological impairment/paralysis suggestive of neurological (spinal cord) instability due to cord compression, are indicative of a risk that further cord damage might be provoked by inappropriate mobilisation prior to, during and after definitive treatment.

Retrospective audit of clinical practice shows wide variation in the timing of, and methods used to mobilise patients with newly diagnosed MSCC and during treatment. In the past, mobilisation has usually only been started only after radiotherapy or spinal stabilisation, or following an arbitrary period of bed rest. However, there is no research evidence to support any of these approaches.

It is not possible to confirm spinal stability solely through the use of MRI. CT and plain x-ray in conjunction with MRI may indicate that the spine is not at immediate risk from instability. This will allow cautious assessment of graded movement to proceed. Although imaging can help to assess the effectiveness of surgical stabilisation procedures, it is difficult to assess the effect of radiotherapy and at what stage mobilisation is safe by imaging alone.

It is important to recognise that the impaired spinal cord is vulnerable to changes in vascular perfusion pressure. Sitting prematurely may provoke hypotension, loss of cord perfusion, and irretrievably permanent loss of neurological function.

Recommendations

- Patients with severe mechanical pain suggestive of spinal instability, or any neurological symptoms or signs suggestive of MSCC, should be nursed flat with neutral spine alignment (including ‘log rolling’ or turning beds, with use of a slipper pan for toilet) until bony and neurological stability are ensured and cautious remobilisation may begin.
- For patients with MSCC, once any spinal shock has settled and neurology is stable, carry out close monitoring and interval assessment during gradual sitting from supine to 60 degrees over a period of 3–4 hours.
- When patients with MSCC begin gradual sitting, if their blood pressure remains stable and no significant increase in pain or neurological symptoms occurs, continue to unsupported sitting, transfers and mobilisation as symptoms allows.
- If a significant increase in pain or neurological symptoms occurs when patients with MSCC begin gradual sitting and mobilisation, return them to a position where these changes reverse and reassess the stability of their spine.
- After a full discussion of the risks, patients who are not suitable for definitive treatment should be helped to position themselves and mobilise as symptoms permit with the aid of orthoses and/or specialist seating to stabilise the spine, if appropriate.

Qualifying statement: In the absence of definitive research evidence these recommendations have been made with GDG consensus, and are broadly based on the regional guidance formulated by the West of Scotland Cancer Network.

Clinical Evidence

The West of Scotland Guidelines for Malignant Spinal Cord Compression (2007) have provided evidence for these recommendations.

Observational studies reported the effectiveness of a 'care pathway'. These articles were of low quality. Pease *et al.* (2004) provided limited evidence of an evaluation of a rehabilitation intervention with respect to early mobilisation with a small study sample. Implementation of the care pathway resulted in statistically significantly fewer patients being nursed lying flat for the duration of their radiotherapy (≥ 5 days) with the majority of patients starting to sit up within one day. There was no significant difference between the groups with respect to patients experiencing altered mobility scores. Farrell *et al.* (1991), also evaluated a rehabilitation intervention as a case study, (n=1). The study evaluated the effectiveness of physiotherapeutic intervention in facilitating transfers in an elderly patient with spinal cord compression. McLinton and Hutchinson (2006) provided a descriptive audit of clinical practices associated with MSCC patients in one regional centre which included a very brief account of mobilisation practices after treatment.

Health Economic Evaluation

The Guideline Development Group did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

Corticosteroids

Corticosteroids are routinely given to patients with MSCC because they are believed to reduce tumour bulk or spinal cord swelling, relieve spinal cord pressure and improve treatment outcomes. They may result in a rapid improvement of neurological function but long term benefit is limited, and there is no evidence that survival is improved. High-dose, long-duration treatment with corticosteroids causes significant side effects which can be debilitating and occasionally fatal. Antacids or proton pump inhibitors (PPIs) are often given to mitigate the gastrointestinal side effects. Corticosteriods also have a role in the primary treatment of myeloma and lymphoma. However, steroids may impair the histological diagnoses of lymphoma.

Recommendations

- Unless contraindicated (including a significant suspicion of lymphoma) offer all patients with MSCC a loading dose of at least 16 mg of dexamethasone as soon as possible after assessment, followed by a short course of 16 mg dexamethasone daily while treatment is being planned.
- Continue dexamethasone 16 mg daily in patients awaiting surgery or radiotherapy for MSCC. After surgery or the start of radiotherapy the dose should be reduced gradually over 5–7 days and stopped. If neurological function deteriorates at any time the dose should be increased temporarily.
- Reduce gradually and stop dexamethasone 16 mg daily in patients with MSCC who do not proceed to surgery or radiotherapy after planning. If neurological function deteriorates at any time the dose should be reconsidered.
- Monitor blood glucose levels in all patients receiving corticosteroids.

Qualifying statement: These recommendations are based on evidence from RCTs, a systematic review, a case series and GDG consensus.

Clinical Evidence

Evidence for this question comes from a mixture of low-quality randomised controlled trials and observational studies. The comparisons evaluated in the studies included: high dose dexamethasone (96 mg) versus no steroidal treatment (Sorenson *et al.* 1994); high dose

Clinical Evidence (cont.)

dexamethasone (100 mg) versus 10 mg dexamethasone as an adjunct to radiotherapy (Vecht *et al.* 1989); high-dose dexamethasone (96mg) versus 16 mg daily (Heimdal *et al.* 1992); and 96 mg dexamethasone versus 16 mg dexamethasone (Graham *et al.* 2006).

Overall there is a limited body of evidence to conclusively report an advantage of high dose corticosteroid dose over a lower dose. There is insufficient evidence of effect of high versus low dose of dexamethsasone, as well as high versus no steroids and the evidence is lacking for low versus no steroids. Ambulation was an outcome reported across the studies, with some improvement indicated (though not statistically significantly different) for patients on higher doses of dexamethasone (96 or 100mg). With higher doses of dexamethasone, a higher rate of adverse events were consistently reported.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

6.4 Case selection for definitive treatment of MSCC

The functional outcome of patients with MSCC after treatment depends primarily on their functional status at the time of treatment.

Long-term survival is largely determined by the behaviour of the primary tumour and the general health of the patient including the effects of the tumour. Other important factors are the presence, extent and treatability of multiple spinal metastases and their spinal levels, extraspinal osseous and visceral metastases, any previous treatments, and the time from cancer diagnosis to MSCC. Younger patients and those with a longer time interval between the initial cancer diagnosis and developing MSCC are more likely to live longer.

Treatment while patients are still ambulant is effective in maintaining their ability to walk and functional independence. Delay in treatment is associated with loss of motor and bladder function that may be irreversible. Even when the diagnosis is late (non-ambulatory patients or patients with bladder dysfunction, and even patients with paraplegia) urgent spinal decompression may lead to a better functional outcome (mobility post op) than delayed or no surgery. The main causes of delay are failure to recognise spinal cord compression, or failure to refer, investigate, or treat urgently.

Recommendation

- Start definitive treatment, if appropriate, before any further neurological deterioration and ideally within 24 hours of the confirmed diagnosis of MSCC.

Qualifying statement: This recommendation is based on consistent evidence from well conducted observational studies and GDG consensus.

Clinical Evidence

Evidence for this question was drawn from several observational studies (Helweg-Larsen *et al.* 1996, Husband *et al.* 1998, Levack *et al.* 2002, Maranzano *et al.* 1995, Mitera *et al.* 2003, Solberg *et al.* 1999, Turner *et al.* 1993). The findings from this evidence consistently reported that early diagnosis and treatment, while functional status is good, leads to better functional outcome and longer survival.

Nature of metastases

The histology of the primary tumour is probably the best predictor of survival. Patients with MSCC can be divided into three groups:

- those with myeloma (especially solitary plasmacytoma), lymphoma, breast or thyroid cancer: survival 18 months or more.
- those with renal or prostate cancer, or metastatic sarcoma: survival 12 to 18 months.
- those with melanoma, lung or gastro-intestinal cancer, or unknown primary tumours: survival less than 12 months.

Recommendations

- Attempt to establish the primary histology of spinal metastases (including by tumour biopsy, if necessary) when planning definitive treatment.

Qualifying statement: This recommendation is based on GDG consensus.

- Stage the tumours of patients with MSCC to determine the number, anatomical sites and extent of spinal and visceral metastases when planning definitive treatment.

Qualifying statement: This recommendation is based upon case series evidence.

Functional ability, general fitness, previous treatments and fitness for anaesthesia

Surgery cannot reliably rescue lost neurological function and rarely achieves more than one or two grades of motor improvement. Many patients with MSCC are frail with poor or failing health, or may have persistent or recurrent tumour despite previous treatments and may not be fit enough for the complex surgery required for optimal treatment or even suitable for a general anaesthetic.

Recommendations

- Take into account the preferences of patients with MSCC as well as their neurological ability, functional status, general health and fitness, previous treatments, magnitude of surgery, likelihood of complications, fitness for general anaesthesia and overall prognosis when planning treatment.
- Patients with suspected MSCC, a poor performance status and widespread metastatic disease should wherever possible be discussed with their primary tumour site clinician and spinal senior clinical adviser before any urgent imaging or hospital transfer.
- Patients with suspected MSCC who have been completely paraplegic or tetraplegic for more than 24 hours should wherever possible be discussed urgently with their primary tumour site clinician and spinal senior clinical adviser before any imaging or hospital transfer.
- Patients who are too frail or unfit for specialist treatment for MSCC should not be transferred unnecessarily.

Qualifying statement: These recommendations are based upon GDG consensus.

Age

There may be a tendency to use age as a criterion for selecting treatment. There is no strong evidence that age is an independent predictor of outcome.

Recommendation

- Patients with MSCC should not be denied either surgery (if fit enough) or radiotherapy on the basis of age alone.

Qualifying statement: This recommendation is based on evidence from high quality and well-conducted case-control and cohort studies.

Summary of prognostic indicators:

Good prognosis	Poor prognosis
Breast cancer as the primary site	Lung or melanoma primary
Solitary or few spinal metastases	Multiple spinal metastases
Absence of visceral metastases	Visceral metastases
Ability to walk aided or unaided	Unable to walk
Minimal neurological impairment	Severe weakness (esp.Frankel A/B).
No previous radiotherapy.	Recurrence after radiotherapy.

Clinical Evidence

Case selection for surgery

Evidence of predictive factors for positive outcomes after a surgical intervention was drawn from observational studies, case reports and case series studies. (Cooper *et al.* 1993; Enkaoua *et al.* 1997; Finkelstein *et al.* 2003; Gabriel *et al.* 2004; Gokaslan *et al.* 1998; Harris *et al.* 1996; Hosone *et al.* 2005; Livingston *et al.* 1978; Nanassis *et al.* 1997; North *et al.* 2005; Oda *et al.* 2006; Portenoy *et al.* 1987; Ryken *et al.* 2003; Schoeggl *et al.* 2002; Sinardet *et al.* 2000; Sioutos *et al.* 1995; Sundaresan *et al.* 1995; Tabbara *et al.* 1990; Tokuhashi *et al.* 2005; Tomita *et al.* 2001; Tomita *et al.* 1994; Wang *et al.* 2004; Wise *et al.* 1999; Witham *et al.* 2006).

Several studies stated that a life expectancy of more than three months was an inclusion criterion for the study. Several studies defined the study population by the received treatment, not the diagnosis. In most publications the primary site of the cancer analysed as a distinguishing feature for survival of patients, however, the rank order of cancer types varied, the most consistently reported was the poor prognosis of spinal metastases secondary to lung cancer. The affected vertebral bodies have been identified as a predictor of surgery outcome in a number of studies; however, there was little consistency regarding which area is associated with a poor outcome. There is conflicting evidence regarding the factors age and previous treatment such as radiation therapy. Several authors acknowledged that patients with a poor pre-operative performance status often have the worst prognosis but concluded that a substantial number of those may have an improvement in symptoms and quality of life.

The total Tokuhashi score (Tokuhashi *et al.* 2005) which included different risk factors was significantly correlated with survival in a palliative surgery and an excisional surgery group. These factors included performance status, number of extraspinal bone metastases foci, number of metastases in the vertebral body, metastases to the major internal organs, primary site of the cancer and palsy.

Several case series studies reported that even in patients with poor survival prognosis, symptom relief could be achieved after surgery. (Schoeggl *et al.* 2002; Sioutos *et al.* 1995; Livingston & Perrin 1978; Tabbara & Sibley 1990; Harris *et al.* 1996; Cooper *et al.* 1993; Sinardet *et al.* 2000; Tomita *et al.* 1994; Wang *et al.* 2004; Gokaslan *et al.* 1998; North *et al.* 2005; Oda *et al.* 2006). A systematic review of case series (Ryken *et al.* 2003) concluded that "surgical intervention for patients presenting with neurological deficits may

Clinical Evidence (cont.)

experience marked improvement after surgical decompression and fusion, assuming that the individual does not present with complete paraplegia".

Case selection for radiotherapy

The evidence identified is variable in quality (Graham *et al.* 2006; Helweg-Larsen *et al.* 2000; Kim *et al.* 1990; Kovner *et al.* 1999; Huddart *et al.* 1997; Loblaw *et al.* 2005; Maranzano *et al.* 1991, 1992, 1997, 2005; Rades *et al.* 2007a, 2007b, 2008). Most studies reported on the most common factors to influence post-treatment radiotherapy for patients with MSCC. There was general agreement between them for ambulatory status before radiotherapy, absence of visceral metastases and a favourable histology to improve survival. Fewer factors were reported for the effects on motor function however a favourable histology and ambulatory status before treatment were the most common.

Case selection for both surgery and radiotherapy

This evidence summary is a subset of studies from the evidence body used for case selection for surgery and radiotherapy. These studies examine factors for successful outcomes from surgery and radiotherapy interventions. The evidence included three systematic reviews, one prospective randomised study and several observational studies (Bach *et al.* 1990; Barcena *et al.* 1984; Hill *et al.* 1993, Katagiri *et al.* 2005; Klimo *et al.* 2005; Loblaw *et al.* 2003; Loblaw *et al.* 2005; Martenson *et al.* 1985; Patchell *et al.* 2005). Treatment with surgery and radiotherapy, favourable primary tumour, and a favourable ambulatory status after treatment consistently predicted for better survival. In predicting motor function the main factors included surgery and radiotherapy as well as a favourable ambulatory status before treatment.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

The role of scoring systems

Scoring systems using a combination of prognostic factors have been devised and have been correlated with the clinical outcome to predict survival.

Some patients are unlikely to benefit from surgery because of their poor prognosis or the long time required for recovery. Recognition of this group may prevent inappropriate referral and transfer and minimise unnecessary distress for both patients and relatives.

Recommendations

- When deciding whether surgery is appropriate, and if so its type and extent, use recognised prognostic factors including the revised Tokuhashi scoring system[5] and American Society of Anaesthetists (ASA) grading. Systematically record and take into account relevant comorbidities.

Qualifying statement: This recommendation is based on a systematic review of prognostic factors derived from case series, GDG consensus and a comparison of the predictive value of the available scoring systems derived from case series.

- Only consider major surgical treatments for patients expected to survive longer than 3 months.

Qualifying statement: This recommendation is based on evidence from case-control and cohort studies and GDG consensus.

[5] See appendix 3

Clinical Evidence

Overall the quality of the evidence for this topic was poor, accumulated from case series or expert opinion studies.

The validity of Tomita and Tokuhashi scoring systems

The scoring system of Tokuhashi (1990) may be useful for the selection of patients for treatment. Three studies all used different cut-offs but demonstrated a correlation of the total score with survival (Enkaoua *et al*. 1997; Huch *et al.* 2005; Ulmar *et al.* (2007a). Several publications (Bünger *et al*. 1999; Enkaoua *et al*. 1997; Ulmar *et al*. 2007a, Tokuhashi *et al*. 1990) reported favourable results for the Tokuhashi (1990) system, although this has since been revised by the authors (Tokuhashi *et al.* 2005). Tokuhashi and colleagues have repeatedly reported data to support their 2005 revision of the scoring system (Tokuhashi *et al*. 2002; Tokuhashi *et al*. 2005). Huch *et al*. (2005) and Ulmar *et al.* (2007a) applied the Tomita system and did not replicate its proposed usefulness.

Identification of gaps in these systems

Several publications (Bünger *et al.* 1999; Clar, 2004; Enkaoua *et al*. 1997; Tokuhashi *et al*. 2002, 2005; Tomita *et al*. 2001) suggested a revision of the scoring system developed by Tokuhashi *et al.* (1990). This evidence suggests it may be useful to differentiate the primary site of the cancer further which is now incorporated in the revised Tokuhashi system (Tokuhashi *et al*. 2005). Furthermore, the studies suggested it may be useful to further differentiate the treatment options for patients with a life expectancy of more than six months (Enkaoua *et al*. 1997 and Tokuhashi *et al*. 2005).

Assessment of systems currently described in the literature that address the gaps in the established systems.

The revised scoring system of Tokuhashi *et al.* (2002, 2005) may be useful for the selection of patients for treatment. Other evidence about scoring systems comes from several studies suggesting a combination of established scoring systems with other modifications. (Bartanusz & Porchet, 2003; Bartels *et al.* 2007; Bilsky *et al.* 2007; Chow *et al.* 2006; Clar 2004; Day *et al*. 1998 Katagiri *et al*. 2005 ; Kluger *et al*. 1997; Ulmar *et al*. 2007b).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectivness literature on this topic has not been reviewed.

6.5 Surgery for the definitive treatment of MSCC

General principles

The prime purpose of spinal surgery is to preserve or recover neurological function in the hope of maintaining functional independence and highest possible quality of remaining life. This may include either separately or in combination: spinal cord decompression to avert or treat MSCC, spinal column stabilisation to treat mechanical pain or bony instability, and resection/ reconstruction of the spinal column in the hope of a durable surgical result providing good quality long-term survival. Simple decompression of the spinal cord is the least demanding of the patient and may be sufficient to optimise neurological outcome, but stabilisation of the involved levels is usually required to maximise spinal stability and duration of effect.

The spinal cord may be decompressed and the spinal column stabilised by rods connected to pedicle screws in the healthy vertebra above and below the diseased level with or without postero-lateral inter-transverse grafts. Alternatively, or additionally, the diseased vertebral body can be resected and replaced with bone graft and/or metal cages or cement. Decompression and stabilisation may be performed in isolation or in combination by a variety of methods: either conventionally or by minimal access; from behind, in front, or both (360^0).

Surgery cannot be expected to reverse paraplegia, but may occasionally have a role in the treatment of mechanical pain even in the presence of complete paralysis (see section 6.2).

The exact surgical technique varies with the individual patient, type of spinal involvement, neurological impairment and overall prognosis. The higher risks of complex surgery must be balanced against the potential benefits in patients already frail or ill with advanced life-limiting primary disease (see section 6.2)

Recommendation

- If surgery is appropriate in patients with MSCC, attempt to achieve both spinal cord decompression and durable spinal column stability.

Qualifying statement: This recommendation is based on case series and GDG consensus.

Neurological ability

Neurological outcome depends primarily on the degree of neurological impairment before treatment (as does the duration of survival to a lesser extent). Patients who are able to walk, even with help, at the time of treatment can usually be kept walking and survive the longest. Between 25% and 50% of patients who cannot walk, but have some preservation of lower limb sensation and movement, may walk again after surgery. Patients with complete paraplegia are less likely to gain useful lower limb function after surgery and are at increased risk of developing post-operative complications, especially infection. They often have a very poor prognosis.

Recommendations

- Patients with MSCC who are suitable for surgery should have surgery before they lose the ability to walk.
- Patients with MSCC who have residual distal sensory or motor function and a good prognosis should be offered surgery in an attempt to recover useful function, regardless of their ability to walk.
- Patients with MSCC who have been completely paraplegic or tetraplegic for more than 24 hours should only be offered surgery if spinal stabilisation is required for pain relief.

Qualifying statement: These recommendations are based on evidence from high-quality and well-conducted case-control and cohort studies.

Timing

Patients with MSCC experience neurological deterioration that may be gradual, rapid or instant in onset. The timing of surgery is an important factor contributing to the likely neurological outcome. If it is gradual, careful monitoring is required and unless further deterioration occurs surgery can be planned for the next scheduled list after staging to permit optimal decision-making. If rapid deterioration is obvious, surgical intervention is an emergency and needs to be done as soon as possible. When instant or presenting as an anterior spinal artery syndrome it may represent vascular spinal cord infarction (“cord stroke”) which is unlikely to respond to decompression.

Recommendation

- Consider the speed of onset, duration, degree and site of origin of neurological symptoms and signs (cord or cauda equina) when assessing the urgency of surgery.

Qualifying statement: This recommendation is based upon GDG consensus and case series evidence.

Technical factors

Over the last twenty years there have been changes in the surgical approach to the compressed spinal cord. Initially laminectomy alone was performed, decompressing the spinal cord but adding to the problems of instability and failing to address anterior spinal pathology, which is a much commoner cause of MSCC than posterior bony or epidural tumour compression. Pedicle screw attachment of posterior instrumentation was the first major surgical development providing more effective stabilisation than sub-laminar wiring. Subsequent development of anterior (or combined anterior and posterior) surgery produced better results but involved a larger operation with a higher risk of complications. More recently posterior decompression combined with stabilisation (usually with posterior pedicle screws) and when the prognosis justifies, postero-lateral inter-transverse grafting, or postero-lateral vertebral body grafting has permitted more to be achieved by a limited posterior procedure at less risk to the patient. For those with the best prognosis, formal anterior vertebral body resection via anterior, posterior or combined approaches are all options. For patients with limited long-term survival, bone cement may be used satisfactorily in place of vertebral body bone grafting.

The anatomical site of cord compression influences the surgical approach, particularly at junctional areas where surgical access and stabilisation may be more difficult i.e. cervico-thoracic junction (complex anterior approach) or thoraco-lumbar junction (necessitating thoraco-abdominal exposure with splitting of the diaphragm) with a potential increase in complications.

For most patients posterior decompression with internal fixation using pedicle screw and rod constructs is an adequate solution. Anterior reconstruction of the vertebral column may be done simultaneously or subsequently if staging confirms a high probablility of longer survival. This is usually carried out through an anterior approach, but can be achieved from a postero-lateral approach. Both procedures are more complex, and demand more of both patient and surgeon.

Choosing the optimal treatment for the tumour requires careful assessment of the site and characteristics of the vertebral metastasis, the extent of disease and whether MSCC is due to tumour alone or structural spinal failure.

The technical considerations and surgical goals include:

- decompression of the spinal cord and spinal nerves.
- restoration of structural integrity and stability of the vertebral column.
- the feasibility of tumour eradication.

Operative planning requires not only consideration of the technical aspects and goals of surgery but also the general fitness of the patient, the presence of co-morbidity and the risk of serious and even life-threatening complications. The patient's motivation and wishes to participate in joint decision-making are also important.

It is recognised that optimal surgical treatment may on occasion require transfer to other centres for particularly complex reconstruction.

Recommendations

- Carefully plan surgery to maximise the probability of preserving spinal cord function without undue risk to the patient, taking into account their overall fitness, prognosis and preferences.
- Posterior decompression alone should not be performed in patients with MSCC except in the rare circumstances of isolated epidural tumour or neural arch metastases without bony instability.
- If spinal metastases involve the vertebral body or threaten spinal stability, posterior decompression should always be accompanied by internal fixation with or without bone grafting.
- Consider vertebral body reinforcement with cement for patients with MSCC and vertebral body involvement who are suitable for instrumented decompression but are expected to survive for less than 1 year.
- Consider vertebral body reconstruction with anterior bone graft for patients with MSCC and vertebral body involvement who are suitable for instrumented decompression, are expected to survive for 1 year or longer and who are fit to undergo a more prolonged procedure.

Qualifying statement: These recommendations are based on consistent results from case series.

- 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).

Qualifying statement: This recommendation is based on case series evidence and GDG consensus.

Clinical Evidence

Surgery

The evidence included for this question ranges from moderate to low quality. Very few reports exist on comparative interventions. Most report on retrospective analysis of a case series (Chen *et al.* 2007; Harris *et al.* 1996; Jansson *et al.* 2006; Klimo *et al.* 2003, 2004; Kwok *et al.* 2006; Lewandrowsky *et al.* 2004; Loblaw *et al.* 2005; Prasad & Schiff 2005; Senel *et al.* 2007; Shehadi *et al.* 2007, Witham *et al.* 2006) but there is one prospective non-comparative study (Mannion *et al.* 2007) and one RCT (Patchell *et al.* 2005). Klimo *et al.* (2005) conducted an indirect comparative, meta-analysis (which included uncontrolled studies with diverse study populations) of surgery versus conventional radiotherapy for the treatment of metastatic spinal epidural disease.

There is consistent evidence that laminectomy alone in case of ventral compression is associated with poor outcomes. Anterior, posterior or combined decompression with immediate stabilisation have been shown to provide improved patient outcomes, when compared with historical reports of radiotherapy, decompressive laminectomy without stabilisation or combined radiotherapy and laminectomy. The evidence indicates that in appropriately selected patients surgery should be the initial treatment of choice, as it is usually able to maintain ambulation, provides pain relief, provides a significant chance of recovery of neurologic function, acceptable peri-operative morbidity and mortality and prevention of late neurologic deterioration. Overall complications are higher for vertebral body resection compared to laminectomy. The rate of complications is significantly increased in patients who have received radiotherapy before surgery than in patients who received surgery first. Surgical complications included wound infection and failure of fixation that required additional surgery.

Clinical Evidence (cont.)

A meta-analysis by Klimo *et al.* (2005) compared the effect of surgery versus conventional radiotherapy on the ambulatory status of people with metastatic spinal epidural disease. Surgery involved decompression of the spinal cord circumferentially, followed by reconstruction and stabilisation, with radiation given either pre-operatively, post-operatively, or not at all. This review reported that, compared with conventional radiotherapy, surgery improved ability to walk for people with metastatic cancer in the spine. The study conducted an indirect comparison between observational studies of radiotherapy and surgery. Although providing insight into the effects of radiotherapy compared to surgery, the extent of bias associated with this kind of comparison, requires that conclusions be considered with caution. Mannion *et al.* (2007) conducted a prospective non-comparative study that evaluated the long term outcomes of patients with MSCC who received decompression surgery with fixation followed by radiotherapy. Median survival was 13 months, significant improvements were reported for ambulation, continence and in SF36 quality of life scores as well as pain. Patchell *et al.* (2005) reported a randomised trial that evaluated the efficacy of direct decompressive surgery plus postoperative radiotherapy compared to radiotherapy alone in patients with MSCC. Significantly more patients in the surgery group than in the radiotherapy group were ambulant after treatment. Patients treated with surgery plus radiotherapy retained the ambulation significantly longer than did those with radiotherapy alone. Significantly more patients in the surgery group regained ambulation than patients in the radiotherapy group. The use of opioid analgesics was significantly reduced in the surgical group. Patient selection for this study has some influence on results reported (as suggested by Loblaw A. 2004 and Maranzano and Trippa 2007) and therefore, the results of this trial cannot be used to justify surgery in all patients with MSCC and apply only to patients comparable to those included in the Patchell *et al.* (2005) study.

Health Economic Evaluation

See section 6.7 health economic evaluation for treatment of MSCC.

6.6 Radiotherapy for the definitive treatment of MSCC

Surgery is the initial treatment of choice for patients with spinal cord compression and mechanical pain suggestive of bony instability or proven bony instability who meet the other criteria for being suitable for surgery. Radiotherapy will not treat structural failure and so decompression and/or stabilisation (with or without bone graft, instrumentation, and vertebral reconstruction) is needed to prevent further neurological damage. Pre-operative radiotherapy may be associated with an increased risk of post-operative problems, especially wound healing, but after successful surgery, post-operative radiotherapy has an important role to play.

Radiotherapy is also an option for all other patients. For some with epidural tumour alone it may be the primary teatment of choice. For those without mechanical pain or bony instability where surgery is not required it may produce significant improvements in pain control and neurological function. For patients not suitable for surgery, radiotherapy is often used even for relatively radio-resistant tumours. For others, even when paraplegia is complete, radiotherapy is sometimes given as a palliative measure to improve pain control (see section 6.2). However not all patients will benefit and for some patients transfer to the cancer centre may be inappropriate and unhelpful. For example, it is unlikely that patients who have been paraplegic for more than 24 hours will recover neurological function after radiotherapy. Careful case selection is therefore very important.

Radiotherapy may be delivered as a single treatment or a number of consecutive smaller treatments (fractionation). For patients with MSCC current clinical practice is to give fractionated radiotherapy, generally in five or ten fractions, especially for patients after surgery and for those with good prognostic factors, for whom the duration of tumour response may be important. The use of short fractionation regimens is the subject of continuing research. The radiobiological equivalence of the commonly used regimens is shown in Table 6.1.

Table 6.1 Radiobiological equivalent doses for commonly used RT regimens.

RT Regimen	BED (10): Tumour	BED (1.7): Spinal cord
40Gy/20F/4W	48Gy	87Gy
30Gy/10F/2W	39Gy	83Gy
20Gy/5F/1W	28Gy	67Gy
16Gy/2F/8d	29Gy	91Gy
10Gy/1F/1d	20Gy	69Gy
8Gy/1F/1d	14Gy	46Gy

BED (y) = biologically effective dose in Gray (Gy), calculated by the formula BED(y) = n x d (1 + d / /), where n= number of fractions, d = size of each fraction (Gy) and / is constant, of value y for a given tissue.

Recommendations

- Ensure urgent (within 24 hours) access to and availability of radiotherapy and simulator facilities in daytime sessions, 7 days a week for patients with MSCC requiring definitive treatment or who are unsuitable for surgery.
- Offer fractionated radiotherapy as the definitive treatment of choice to patients with epidural tumour without neurological impairment, mechanical pain or spinal instability.
- Offer a fractionated rather than a single fraction regimen to patients with a good prognosis who are having radiotherapy as their first-line treatment.
- Preoperative radiotherapy should not be carried out on patients with MSCC if surgery is planned.
- Postoperative fractionated radiotherapy should be offered routinely to all patients with a satisfactory surgical outcome once the wound has healed.

Qualifying statement: These recommendations are based on well conducted case series studies and evidence of cost effectiveness.

- Offer urgent radiotherapy (within 24 hours) to all patients with MSCC who are not suitable for spinal surgery unless:
  - they have had complete tetraplegia or paraplegia for more than 24 hours and their pain is well controlled; or
  - their overall prognosis is judged to be too poor.

Qualifying statement: This recommendation is based on GDG consensus.

Clinical Evidence

Radiotherapy

Evidence from RCTs enabled some conclusions about radiotherapy (30 Gy given in 10 fractions of 3Gy) vs radiotherapy plus surgery (stabilisation) (Patchell *et al.* 2005) and split-course radiotherapy (5 Gy X 3, 4-day-rest, and then 3 Gy X 5, to a total dose of 30 Gy in 2 weeks) vs short-course radiotherapy (8 Gy, 6-day rest, and then 8 Gy, to a total dose of 16 Gy in 1 week) (Marazano *et al.* 2005). Observational studies have compared the effectiveness of different radiotherapy regimens (Loblaw 2004; Rades 2004a, 2004b, 2005, 2006, 2007b) which can then be considered alongside Marazano *et al.* (2005). However, giventhe low quality of case series studies conclusions are limited about the effectiveness of different radiotherapy regimens. No evidence was identified that addressed the effectiveness of radio-surgery or intensity-modulated radiotherapy in patients with MSCC.

Clinical Evidence (cont.)

Patchell *et al.* (2005) reported a randomised trial evaluating the effectiveness of direct decompressive surgery plus post-operative radiotherapy compared to radiotherapy alone in patients with MSCC. Significantly more patients in the surgery group than in the radiotherapy group were ambulant after treatment. Patients treated with surgery also retained the ambulation significantly longer than did those with radiotherapy alone. The use of opioid analgesics was significantly reduced in the surgical group. Patient selection for this study may have some influence on results reported (as suggested by Loblaw A. 2004 and Maranzano and Trippa 2007) and therefore, the results of this trial cannot be used to justify surgery in all patients with MSCC and apply only to patients comparable to those included in the Patchell *et al.* (2005) study. The meta-analysis by Klimo *et al.* (2005) reported that, compared with conventional radiotherapy, surgery improved ability to walk for people with metastatic cancer in the spine. Given the extent of bias associated with this comparison, conclusions made by the author need to considered with caution. Mannion *et al.* (2007) conducted a prospective non-comparative study that evaluated the long term outcomes of patients with MSCC who received decompression surgery with fixation followed by radiotherapy. Median survival was 13 months, significant improvements were reported for ambulation, continence and in SF36 quality of life scores as well as pain.

The evidence from the RCT by Maranzano *et al.* (2005) and from observational studies (Loblaw *et al.* 2005; Rades *et al.* 2004a, 2004b, 2005, 2006, 2007b) showed no statistical difference in outcomes such as motor function, ambulation or survival for the different radiotherapy regimens listed in above. From a multivariate analysis, which included various different patient characteristics as well as long and short radiotherapy treatment regimens; long course radiotherapy was associated with improved survival compared to short dose radiotherapy, (Rades *et al.* 2007c). The RCT by Maranzano *et al.* (2005) showed that although in-field recurrences occurred only in patients treated with the short-course radiotherapy regimen, no significant difference was found in the median duration of the improvement in walking ability. From case series studies, local control or recurrence was shown to be significantly different with longer courses of radiotherapy compared to shorter courses (Rades *et al.* 2005, 2006 and 2007a).

An abstract of an RCT by Maranzano *et al.* 2006 indicated that short course radiotherapy (8 Gy X 2) schedule indicated better response rates than single fraction radiotherapy (8Gy) in back pain control and in ability to walk maintenance. The accrual for this study is incomplete and will continue until the established sample size of 300.

Health Economic Evaluation

See section 6.7 health economic evaluation for treatment of MSCC

Research recommendation

- Further research should investigate what are the most clinically and cost effective regimens of radiotherapy to treat patients with established MSCC and investigate the use of new techniques, such as Intensity Modulated Radiotherapy (IMRT).

6.7 Health economic evaluation for treatment of MSCC

Without treatment virtually all the patients with MSCC will become paraplegic and will have limited survival (Kwok *et al.* 2006). There is the general belief among the clinical community that surgery for MSCC patients may prevent paraplegia. Preventing paraplegia may be worth doing (despite high overall costs of the surgical procedures) if the health benefits derived from that are large enough. Major surgery for MSCC has been reported to be beneficial, especially for patients who are still ambulant before surgery (Patchell *et al.* 2005; Sucher *et al.* 1994). However, even if most patients ambulant before surgery will maintain their ability to walk after surgery, some of them will become paraplegic at some point (Patchell *et al.* 2005). In addition,

there is a group of MSCC patients that are neurologically compromised and have tumours that are not very radiosensitive, for whom it is not clear what is the most appropriate treatment choice.

A systematic review of the literature identified one full economic evaluation (Thomas *et al.* 2006) and two published abstracts which appeared to refer to the same original study (Furlan *et al.* 2007; Klinger *et al.* 2007), which assessed the use of surgery in combination with radiotherapy (SRT) versus radiotherapy alone. None of these studies was conducted in a UK setting and, moreover, limited information was reported for the published abstracts, which made it difficult to assess the reliability of the results and their applicability to the UK context.

Given the limited economic evidence available and the lack of studies conducted in the UK, two economic analyses were conducted. The first analysis aimed to identify under what conditions (in terms of success rates for surgery, time of ambulation, survival and quality of life) vertebroplasty, major surgery or radiotherapy would become cost-effective compared to no treatment. This analysis took into account that not all the treatments are alternative options for all MSCC patients and the decision about what treatment is adequate for an MSCC patient will depend on the patient's clinical characteristics (whether there is neurological compromise, pain, or whether tumours are radiosensitive or not).

A second analysis was undertaken to assess the cost-effectiveness of SRT compared to radiotherapy alone for the treatment of neurologically compromised MSCC patients with poorly radiosensitive tumours in terms of the incremental cost per additional day ambulant, per additional life year gained and per QALY gained. This analysis consisted of adapting to a UK setting the only full economic evaluation available comparing these two interventions for the treatment of MSCC patients (Thomas *et al.* 2006).

The perspective of the National Health Service and the Personal Social Services was adopted for both economic analyses. The cost categories included were: treatment costs (surgery and/or radiotherapy, depending on the type of option evaluated), and post-treatment costs of caring for patients until they died. The resources consumed depending on the type of treatment were mainly taken from an audit conducted at the Royal Orthopaedic Hospital in Birmingham, and the corresponding follow-up care costs were primarily estimated based on expert opinion. Unit costs were mostly derived from the NHS Reference Costs and from the Personal and Social Services Research Unit (PSSRU). The price year was 2006–2007.

The results of the first analysis showed that, under an ideal scenario (under which the mortality associated with the different procedures would be null, all patients would remain ambulant after surgery and would maintain their ability to walk during survival, see Table 6.1), any of the considered treatments (major surgery, vertebroplasty or radiotherapy) would be more effective and less costly than the option of no treatment. Under scenario 2 (see Table 6.2) which was thought to be more realistic (since it included procedure-related mortality and the surgical and radiotherapy success rates for patients remaining ambulant after treatment), radiotherapy lost its condition of dominant strategy and presented an incremental cost per additional QALY gained equal to £3,309 when compared to no treatment; this is identified as being cost-effective following NICE's thresholds, while major surgery and vertebroplasty maintained their position of dominant strategies (i.e. more effective and less costly) when compared to no treatment. For all the comparisons between treatments and no treatment, it was observed that any of these treatments would be more cost-effective in the following situations: the higher the success rate after treatment (in terms of the proportion of patients remaining ambulant after treatment), the longer the overall survival for patients, the longer the patients remained ambulant after treatment, and the longer the specific survival for patients non-ambulant after treatment and for those patients non-treated (the results of the thresholds obtained are presented in Appendix 4.

Table 6.2 Results of the cost-effectiveness analysis comparing treatment for MSCC versus no treatment: ideal scenario

Ideal scenario	Average cost per patient (£)	Average survival per patient (months)	Average time ambulant per patient (months)	Average QALYs per patient	ICER: Δ Cost per QALY (£)
RT alone	9,390	11.57	11.57	0.67	Dominant
No treatment	48,673	11.57	0	0.1	–
Vertebroplasty	18,622	11.57	11.57	0.67	Dominant
No treatment	48,673	11.57	0	0.1	–
Major surgery	22,299	11.57	11.57	0.67	Dominant
No treatment	48,673	11.57	0	0.1	–

Table 6.3 Results of the cost-effectiveness analysis comparing treatment for MSCC versus no treatment: scenario 2

Scenario 2	Average cost per patient (£)	Average survival per patient (months)	Average time ambulant per patient (months)	Average QALYs per patient	ICER: Δ Cost per QALY (£)
RT alone	30,523	7.13	1.90	0.15	3,309
No treatment	30,208	7.13	0.00	0.06	–
Vertebroplasty	37,749	10.99	6.49	0.42	Dominant
No treatment	48,673	11.57	0.00	0.10	–
Major surgery	40,516	10.99	6.49	0.42	Dominant
No treatment	48,673	11.57	0.00	0.10	–

The results of the second analysis (see Table 6.4) showed that, when the same utility scores as those used for the first analysis were taken into account, the incremental cost per additional QALY gained with SRT compared to radiotherapy was £17,117, which falls well under the threshold value identified by NICE for cost-effective interventions (i.e. £20,000 per QALY).

Table 6.4 Average cost, mean ambulation, survival and ICERs for comparisons between SRT and RT alone for patients neurologically compromised and with poor radiosensitive tumours

Intervention	Average cost per patient (£)	Days ambulant	Survival (days)	QALYs	ICER – Days ambulant	ICER – Life-years gained	ICER – QALYs
SRT	27,536	312.47	377.06	0.62	31.5	16,207	17,117
RT	20,611	92.36	221.11	0.21	–	–	–

Selection of treatment following previous radiotherapy

Occasionally patients who have been successfully treated with radiotherapy for MSCC or have had previous radiotherapy for spinal metastases may develop signs of recurrent or new MSCC within the previously irradiated spine. There is understandable anxiety about re-irradiating the spinal cord because of the known limits of tolerance. But it is generally believed that a certain amount of recovery in the spinal cord takes place and that for patients with limited life expectancy in whom a few months have elapsed since previous radiotherapy, re-irradiation may be safe.

If maximum radiotherapy has already been given surgery may be the only appropriate method to achieve maintenenace of neurologcial function.

Recommendations

- Consider further radiotherapy or surgery for patients who have responded well to previous radiotherapy and develop recurrent symptoms after at least 3 months.
- If patients have further radiotherapy, the total dose should be below a biologically equivalent dose of 100 Gy_2 where possible. Discuss the possible benefits and risks with the patient before agreeing a treatment plan.

Qualifying statement: These recommendations are based on GDG consensus.

Clinical Evidence

From case series studies that observed re-treatment of patients (Rades *et al.* 2005, 2006, 2007b), re-irradiation was reported to improve motor function in 31–39% of retreated patients. From Loblaw *et al.* (2005) the following was reported about the treatment options for recurrent MSCC in an area previously irradiated in two retrospective studies (Schiff *et al.* 1995, Wong *et al.* 1994). Schiff *et al.* (1995) retrospectively reviewed 54 patients with MSCC who had at least two radiotherapy treatments (cumulative dose: range, 36.5 to 81 Gy; median, 54 Gy) overlapping the spinal cord (range, 5 to 25 cm; median, 10 cm). There were equivalent neurological outcomes to radiotherapy-naive patients with MSCC (ambulatory rate of 90% in ambulatory patients, 43% in non-ambulatory patients) and only one episode of radiation myelopathy over an 18-year retrospective chart review. The retrospective review of Wong *et al.* (1994) reported no myelopathy when spinal cord received less than BED 100 Gy (corrected for biologically equivalent dose, α/β = 2Gy).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

Research recommendation

- Further research is required into the tolerance of the spinal cord to radiation damage and its ability to recover and tolerate repeated courses.

References

Adelaide-Health-Technology-Assessment-on-behalf-of-MSAC. (2005) Vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture.

Bach, F., Larsen, B. H., Rohde, K., Borgesen, S. E., Gjerris, F., Boge-Rasmussen, T., Agerlin, N., Rasmusson, B., Stjernholm, P., and Sorensen, P. S. (1990) Metastatic spinal cord compression. Occurrence, symptoms, clinical presentations and prognosis in 398 patients with spinal cord compression. *Acta Neurochir.*(Wien.) 107(1–2): 37–43.

Barcena A, Lobato RD, Rivas JJ, Cordobes F, de CS, Cabrera A, Lamas E (1984) Spinal metastatic disease: analysis of factors determining functional prognosis and the choice of treatment. *Neurosurgery* 15: 820–827

Bartanusz, V. & Porchet, F. (2003). Current strategies in the management of spinal metastatic disease. *Swiss Surgery*, 9: 55–62.

Bartels, R. H. M. A., Feuth, T., van der Maazen, R., Verbeek, A. L. M., Kappelle, A. C., Grotenhuis, J. A. & Leer, J. W. (2007) Development of a model with which to predict the life expectancy of patients with spinal epidural metastasis. *Cancer,* 110: 2042–2049.

Bilsky, M. H. & Azeem, S. (2007) The NOMS framework for decision making in metastatic cervical spine tumors. *Current Opinion in Orthopedics,* 18: 263–269.

Blue Cross and Blue Shield Association. (2005) Percutaneous Kyphoplasty for Vertebral Fractures Caused by Osteoporosis or Malignancy. Assessment Program Volume 20, No. 7.

Bünger, C. Laursen, M., Hansen, E.S., Neumann, P., Bjarke, F., Høy, K. & Helmig, P. (1999). A new algorithm for the surgical treatment of spinal metastases. *Current Opinion in Orthopedics*, 10: 101–105.

Chen, Y. J., Chang, G. C., Chen, H. T., Yang, T. Y., Kuo, B. I., Hsu, H. C., Yang, H. W. & Lee, T. S. (2007) Surgical results of metastatic spinal cord compression secondary to non-small cell lung cancer. *Spine,* 32: E413–E418.

Chow, E., Harris, K. & Fung, K. (2006). Successful validation of a survival prediction model in patients with metastases in the spinal column. *Int. J. Radiation Oncology Biol. Phys.,* 65 (5): 1522–1527.

Clar, H. E. (2004). Operatives oder konservatives Behandlungskonzept bei spinalen Metastasen. *Klinikarzt*, 33(5): 149–152.

Cooper, P.,R., Errico, T.J., Martin, R., Crawford, B. & DiBartolo, T. (1993). A systematic approach to spinal reconstruction after anterior decompression for neoplastic disease of the thoracic and lumbar spine. *Neurosurgery*, 32 (1) : 1–8.

Day, G.A., McPhee, I.B., Swanson, C., Tomlinson, F.H., McCombe, P. & Coyne, T. (1998). Outcomes following treatment of metastatic spine tumors. Bulletin – *Hospital for Joint Diseases*, 57: 11–15.

Enkaoua, E. A., Doursounian, L., Chatellier, G., Mabesoone, F., Aimard, T. & Saillant, G. (1997). Vertebral metastases: A critical appreciation of the preoperative prognostic Tokuhashi Score in a series of 71 cases. *Spine*, 22(19): 2293–2298.

Falkmer, U., Jarhult, J., Wersall, P., & Cavallin-Stahl, E. (2003), A systematic overview of radiation therapy effects in skeletal metastases. *Acta Oncologica*, 42(5–6): 620–633.

Farrell, J. C. (1991) Transfer ability in a patient with spinal cord compression: A multiple baseline design. *Physiotherapy Theory & Practice.* 7(1): 3943.

Finkelstein, J.A. (2003). A population-based study of surgery for spinal metastases. *Journal of Bone and Joint Surgery – British Volue*, 85B.7: 1045–50.

Furlan J, Kelvin C, Sandoral G *et al.* (2007) A cost utility analysis of surgery and radiotherapy versus radiotherapy alone in the management of patients with metastatic spinal cord compression. Abstract. Neurosurgery 61 (1):217.

Gabriel, K. & Schiff, D. (2004). Metastatic spinal cord compression by solid tumors. *Seminars in Neurology*, 24 (4): 375–383.

Gokaslan, Z.L., York, J.E., Walsh, G.L., McCutcheon, I.E., Lang, F.F., Putnam, J.B., Wildrick, D.M., Swisher, S.G., Abi-Said, D. & Sawaya, R. (1998). Transthoracic vertebrectomy for metastatic spinal tumors. *J. Neurosurg.*, 89: 599–609.

Graham PH, Capp A, Delaney G, Goozee G, Hickey B, Turner S, Browne L, Milross C, Wirth A (2006) A pilot randomised comparison of dexamethasone 96 mg vs 16 mg per day for malignant spinal-cord compression treated by radiotherapy: TROG 01.05 Superdex study. *Clinical oncology* 18: 70–76.

Harris, J.K., Sutcliffe, J.C. & Robinson, E. (1996). The role of emergency surgery in malignant spinal extradural compression: assessment of functional outcome. *British Journal of Neurosurgery*, 10(1): 27–33

Hartsell, W. F., Scott, C. B., Bruner, D. W., Scarantino, C. W., Ivker, R. A., Roach, M., III, Suh, J. H., Demas, W. F., Movsas, B., Petersen, I. A., Konski, A. A., Cleeland, C. S., Janjan, N. A., & DeSilvio, M. (2005), Randomized trial of short- versus long-course radiotherapy for palliation of painful bone metastases.[*Journal of the National Cancer Institute*, 97(11): 798–804.

Heimdal, K., Hirschberg, H., Slettebo, H., Watne, K. & Nome, O. (1992) High incidence of serious side effects of high-dose dexamethasone treatment in patients with epidural spinal cord compression. *Journal of Neuro-Oncology*, 12: 141–144.

Helweg-Larsen, S. (1996) Clinical outcome in metastatic spinal cord compression. A prospective study of 153 patients. Acta Neurologica Scandinavica, 94: 269–275.

Helweg-Larsen, S., Sorensen, P.S., Kreiner, S., (2000) Prognostic Factors In Metastatic Spinal Cord Compression: A Prospective Study Using Multivariate Analysis Of Variables Influencing Survival And Gait Function In 153 Patients, Int. J. Oncology Biol. Phys, 46: 1163–1169

Hill, M. E., Richards, M. A., Gregory, W. M., Smith, P., and Rubens, R. D.(1993) Spinal cord compression in breast cancer: A review of 70 cases. *Br.J.Cancer* 68(5): 969–973.

Hirabayashi H, Ebara S, Kinoshita T, Yuzawa Y, Nakamura I, Takahashi J, Kamimura M, Ohtsuka K, Takaoka K (2003) Clinical outcome and survival after palliative surgery for spinal metastases – Palliative surgery in spinal metastases. *Cancer* 97: 476–484.

Holman PJ, Suki D, McCutcheon I, Wolinsky JP, Rhines LD, Gokaslan ZL (2005) Surgical management of metastatic disease of the lumbar spine: experience with 139 patients. *Journal of Neurosurgery-Spine* 2: 550–563.

Hosone, N., Ueda, T., Tamura, D., Aoki, Y., & Yoshikawa, H. (2005). Prognostic relevance of clinical symptoms in patients with spinal metastases. *Clinical Orthopaedics and Related Research*, 436: 196–201.

Huch, K., Cakir, B., Ulmar, B., Schmidt, R., Puhl, W. & Richter, M. (2005). Prognose, operative Therapie und Verlauf bei zervikalen und hochthorakalen Tumorosteolysen. *Z.Orthop.Ihre Grenzgeb.* 143(2): 213–218.

Huddart RA, Rajan B, Law M, Meyer L, Dearnaley DP (1997) Spinal cord compression in prostate cancer: treatment outcome and prognostic factors. *Radiotherapy and Oncology* 44: 229–236.

Hulme, Krebs, Ferguson & Berlemann (2006). Vertebroplasty and kyphoplasty: a systematic review of 69 clinical studies. *Spine* 31(17).

Husband, D. J. (1998) Malignant spinal cord compression: prospective study of delays in referral and treatment. *BMJ,* 317: 18–21.

Imrie, K., Stevens, A., Makarski, J., Esmail, R., Meharchand, J. & Meyer, R. M. (2005) Role of bisphosphonates in the management of skeletal complications in patients with multiple myeloma. *Current Oncology,* 12: 3–17.

Jansson KA, Bauer HCF (2006) Survival, complications and outcome in 282 patients operated for neurological deficit due to thoracic or lumbar spinal metastases. *European Spine Journal* 15: 196–202.

Katagiri, H., Takahashi, M., Inagaki, J., Kobayashi, H., Sugiura, H., Yamamura, S., & Iwata, H. (1998), Clinical results of nonsurgical treatment for spinal metastases, *International Journal of Radiation Oncology, Biology, Physics*, 42(5): 1127–1132.

Katagiri, H., Takahashi, M., Wakai, K., Sugiura, H., Kataoka, T., and Nakanishi, K.(2005) Prognostic factors and a scoring system for patients with skeletal metastasis. *Journal of Bone and Joint Surgery-British.* 87B[5], 698–703.

Kida, A., Taniguchi, S., Fukuda, H., & Sakai, K. (2000), Radiation therapy for metastatic spinal tumors. *Radiation Medicine* 18(1): 15–20.

Kim RY, Spencer SA, Meredith RF, Weppelmann B, Lee JY, Smith JW, Salter MM (1990) Extradural spinal cord compression: analysis of factors determining functional prognosis–prospective study. *Radiology* 176: 279–282

Klimo, P., Dailey, A.T., Fessler, R.G. (2004) Posterior surgical approaches and outcomes in metastatic spine disease. *Neurosurgery Clinics of North America* 15: 425–435

Klimo, P., Jr., Kestle, J. R. & Schmidt, M. H. (2003) Treatment of metastatic spinal epidural disease: a review of the literature. *Neurosurgical Focus*, 15: E1.

Klimo P, Thompson C J, Kestle J R, Schmidt M H. (2005) A meta-analysis of surgery versus conventional radiotherapy for the treatment of metastatic spinal epidural disease. *Neuro-Oncology* 7(1): 64–76

Klinger C, Chan K, Fehlngs M, Furlan J, Lam K, Laporte A, Sandoral G (2007) Direct surgical decompression with portoperative radiotherapy versus radiotherapy alone in the palliative care of patients with metastatic epidural spinal cord compression (MESCC): an economic evaluation. J. Palliative Care 23 (3):236.

Kluger, P., Korge, A. & Scharf, H.-P. (1997). Strategy for the treatment of patients with spinal neoplasms. *Spinal Cord*, 35: 429–436.

Kovner F, Spigel S, Rider I, Otremsky I, Ron I, Shohat E, Rabey JM, Avram J, Merimsky O, Wigler N, Chaitchik S, Inbar M (1999) Radiation therapy of metastatic spinal cord compression. Multidisciplinary team diagnosis and treatment. *Journal of Neuro-Oncology* 42: 85–92.

Kraiwattanapong, C., Buranapanitkit, B., & Kiriratnikom, T. (2004), Results of radiotherapy in non round cell spinal metastasis *Journal of the Medical Association of Thailand*, 87(3): 239–245.

Kwok, Y., Tibbs, P.A., Patchell, R.A. (2006) Clinical Approach to metastatic epidural spinal cord compression. *Hematology – Oncology Clinics of North America*, 20: 1297–1305

Levack, P., Graham, J., Collie, D., Grant, R., Kidd, J., Kunkler, I., Gibson, A., Hurman, D., McMillan, N., Rampling, R., Slider, L., Statham, P. & Summers, D. (2002) Don't wait for a sensory level – Listen to the symptoms: A prospective audit of the delays in diagnosis of malignant cord compression. *Clinical Oncology (Royal College of Radiologists),* 14: 472–480.

Lewansrowsky, K.U., Hecht, A.C., DeLaney, T.F., Chapman, P.A., Horniceck, F.J., Pedlow, F.X. (2004) Anterior spinal arthrodesis with structural l cortical allografts and instrumentation for spine tumour surgery. *Spine*. 29(10):1150–59

Livingston, K.E. & Perrin, R.G. (1978). The neurosurgical management of spinal metastases causing cord and cauda equine compression. *J of Neurosurg*, 49: 839–843.

Loblaw, A (2004) Does surgery provide better outcomes in malignant spinal cord compression. The journal of Supportive Oncology 2(5) 391–393

Loblaw DA, Laperriere NJ, Mackillop WJ (2003) A population-based study of malignant spinal cord compression in Ontario. *Clinical Oncology (Royal College of Radiologists).* 15(4): 211–7, 2003

Loblaw DA, Perry J, Chambers A, Laperriere NJ (2005) Systematic review of the diagnosis and management of malignant extradural spinal cord compression: the Cancer Care Ontario Practice Guidelines Initiative's Neuro-Oncology Disease Site Group. *Journal of Clinical Oncology* 23: 2028–2037.

Mannion, R. J., Wilby, M., Godward, S., Lyratzopoulos, G. & Laing, R. J. C. (2007) The surgical management of metastatic spinal disease: prospective assessment and long-term follow-up. *British Journal of Neurosurgery*, 21: 593–598.

Maranzano E, Bellavita R, Rossi R, De A, V, Frattegiani A, Bagnoli R, Mignogna M, Beneventi S, Lupattelli M, Ponticelli P, Biti GP, Latini P (2005) Short-course versus split-course radiotherapy in metastatic spinal cord compression: results of a phase III, randomized, multicenter trial. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 23: 3358–3365

Maranzano, E. & Latini, P. (1995) Effectiveness of radiation therapy without surgery in metastatic spinal cord compression: Final results from a prospective trial. *International Journal of Radiation Oncology, Biology, Physics,* 32: 959–967.

Maranzano E, Latini P, Checcaglini F, Perrucci E, Aristei C, Panizza BM, Ricci S (1992) Radiation therapy of spinal cord compression caused by breast cancer: report of a prospective trial. *International Journal of Radiation Oncology, Biology, Physics* 24: 301–306

Maranzano E, Latini P, Checcaglini F, Ricci S, Panizza BM, Aristei C, Perrucci E, Beneventi S, Corgna E, Tonato M (1991) Radiation therapy in metastatic spinal cord compression. A prospective analysis of 105 consecutive patients. *Cancer* 67: 1311–1317

Maranzano E, Latini P, Perrucci E, Beneventi S, Lupattelli M, Corgna E (1997) Short-course radiotherapy (8 Gy x 2) in metastatic spinal cord compression: an effective and feasible treatment. *International Journal of Radiation Oncology, Biology, Physics* 38: 1037–1044

Maranzano E and Trippa F. (2007) Be careful in getting cost-effectiveness conclusions from a debatable trial! I. *J. Radiation Oncology.* 68(1): 314–315

Maranzano E, Trippa F, Rossi R, Bellavita R, Lupattelli M, Marafioti L, Pergolizzi S, Mignogna M, Cossa S, Fusco V (2006) Two hypofractionated radiotherapy (RT) schedules (8 Gy x 2 vs. 8 Gy) in metastatic spinal cord compression (MSCC). Updating of an ongoing phase III randomized multicentretrial. *Radiotherapy and Oncology* 81: 740 (ABSTRACT ONLY)

Martenson, J. A., Jr., Evans, R. G., Lie, M. R., Ilstrup, D. M., Dinapoli, R. P., Ebersold, M. J. & Earle, J. D. (1985) Treatment outcome and complications in patients treated for malignant epidural spinal cord compression (SCC). *Journal of Neuro-Oncology,* 3: 77–84.

McLinton A, Hutchison C (2006) Malignant spinal cord compression: a retrospective audit of clinical practice at a UK regional cancer centre. *Br.J.Cancer* 94 486–491.

Mitera, G., Loblaw, A. (2003) Delays from symptom onset to treatment in malignant spinal cord compression: quantification and effect on pre-treatment neurological status. *Radiother. Oncol* 69: Abstract 141

Nanassis, K., Alexiadou-Rudolf, A., Rudolf, J. & Frowein, R.-A. (1997). Surgical indications and prognosis in spinal metastases. *Neurosurg. Rev.*, 20: 99–103.

National Institute for Health and Clinical Excellence (2003a). Balloon kyphoplasty for vertebral compression fractures. IPG20.

National Institute for Health and Clinical Excellence. (2003b) Percutaneous vertebroplasty. IPG12.

North, R.B., LaRocca, V.R., Schwartz, J., North, C.A., Zahurak, M., Davis, M., McAfee, P.C. (2005) Surgical management of spinal metastases: analysis of prognostic factors during a 10 year experience. *J. Neurosurg. Spine* 2: 564–73

Oda, I., Abuni, K., Ito, M., Kotani, Y., Oya, T., Hasegawa, K., Minami, A. (2006). Palliative spinal reconstruction using cervical pedicle screws for metastatic lesions of the spine: a retrospective analysis of 32 cases. *Spine*, 13: 1439–1444.

Patchell, R.A., Tibbs, P.A., Regine, W.F., Payne, R. (2005) Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial, *Lancet,* 366:643–48

Pease NJ, Harris RJ, Finlay IG (2004) Development and audit of a care pathway for the management of patients with suspected malignant spinal cord compression. *Physiotherapy*. 90, 27–34.

Portenoy, R. K., Lipton, R. B. & Foley, K. M. (1987). Back pain in the cancer patient: An algorithm for evaluation and management. *Neurology*, 37 (1), 134–138.

Prasad, D., Schiff, D. (2005) Malignant Spinal Cord Compression. *Lancet Oncol.* 6:15–24

Rades, D., Dunst, J. & Schild, S. E. (2008) The first score predicting overall survival in patients with metastatic spinal cord compression. *Cancer,* 112: 157–161

Rades D, Fehlauer F, Hartmann A, Wildfang I, Karstens JH, Alberti W (2004b) Reducing the overall treatment time for radiotherapy of metastatic spinal cord compression (MSCC): 3-year results of a prospective observational multi-center study. *Journal of Neuro-Oncology* 70, 77–82

Rades D, Fehlauer F, Schulte R, Veninga T, Stalpers LJ, Basic H, Bajrovic A, Hoskin PJ, Tribius S, Wildfang I, Rudat V, Engenhart-Cabilic R, Karstens JH, Alberti W, Dunst J, Schild SE (2006) Prognostic factors for local control and survival after radiotherapy of metastatic spinal cord compression. *Journal of Clinical Oncology* 24: 3388–3393

Rades D, Fehlauer F, Stalpers LJ, Wildfang I, Zschenker O, Schild SE, Schmoll HJ, Karstens JH, Alberti W (2004a) A prospective evaluation of two radiotherapy schedules with 10 versus 20 fractions for the treatment of metastatic spinal cord compression: final results of a multicenter study. *Cancer* 101, 2687–2692.

Rades D, Hoskin PJ, Karstens JH, Rudat V, Veninga T, Stalpers LJ, Schild SE, Dunst J (2007a) Radiotherapy of metastatic spinal cord compression in very elderly patients. *International Journal of Radiation Oncology, Biology, Physics* 67: 256–263

Rades D, Karstens JH, Hoskin PJ, Rudat V, Veninga T, Schild SE, Dunst J (2007b) Escalation of radiation dose beyond 30 Gy in 10 fractions for metastatic spinal cord compression. *International Journal of Radiation Oncology, Biology, Physics* 67, 525–531

Rades D, Stalpers LJ, Veninga T, Schulte R, Hoskin PJ, Obralic N, Bajrovic A, Rudat V, Schwarz R, Hulshof MC, Poortmans P, Schild SE (2005) Evaluation of five radiation schedules and prognostic factors for metastatic spinal cord compression. *Journal of Clinical Oncology* 23, 3366–3375.

Rades, D., Veninga, T., Stalpers, L. J., Basic, H., Hoskin, P. J., Karstens, J. H., Schild, S. E. & Dunst, J. (2007c) Improved posttreatment functional outcome is associated with better survival in patients irradiated for metastatic spinal cord compression. *International Journal of Radiation Oncology, Biology, Physics,* 67: 1506–1509

Roos, D. E., Turner, S. L., O'Brien, P. C., Smith, J. G., Spry, N. A., Burmeister, B. H., Hoskin, P. J., Ball, D. L., & Trans-Tasman Radiation Oncology Group (2005) Randomized trial of 8 Gy in 1 versus 20 Gy in 5 fractions of radiotherapy for neuropathic pain due to bone metastases (Trans-Tasman Radiation Oncology Group, TROG 96.05), *Radiotherapy & Oncology*, 75(1): 54–63.

Roos, D. E. & Fisher, R. J. (2003) Radiotherapy for painful bone metastases: an overview of the overviews.[comment][erratum appears in Clin Oncol (R Coll Radiol). 2003 Dec;15(8):509, *Clinical Oncology (Royal College of Radiologists),* 15(6): 342–344.

Rosen *et al.* (2003) Zoledronic acid versus placebo in the treatment of skeletal metastases in patients with lung cancer and other solid tumours. JCO 21(16): 3150–3157

Ryken, T.C., Eichholz, K.M., Gerszten, P.C., Welch, W.C., Gokaslan, Z.L. & Resnick, D.K. (2003). Evidence-based review of the surgical management of vertebral column metastatic disease. *Neurosurg Focus,* 15 (5), 1–10.

Saad, F., Gleason, D. M., Murray, R., Tchekmedyian, S., Venner, P., Lacombe, L., Chin, J. L., Vinholes, J. J., Goas, J. A. & Zheng, M. (2004) Long-term efficacy of zoledronic acid for the prevention of skeletal complications in patients with metastatic hormone-refractory prostate cancer. *J Natl Cancer Inst,* 96: 879–882.

Schiff D, Shaw EG, Cascino TL (1995): Outcome after spinal re-irradiation for malignant epidural spinal cord compression. *Ann Neurol* 37:583–589.

Schoeggl, A., Reddy, M. & Matula, C. (2002). Neurological outcome following laminectomy in spinal metastases. *Spinal Cord,* 40, 363–366.

Senel, A., Kaya, A.H., Kuroglu, E., Celik, F., (2007) Circumferential stabilisation with ghost screwing after posterior resection of spinal metastases via transpedicular route. *Neurosurgical Review*, 30:131–137

Shehadi, J. A., Sciubba, D. M., Suk, I., Suki, D., Maldaun, M. V. C., McCutcheon, I. E., Nader, R., Theriault, R., Rhines, L. D. & Gokaslan, Z. L. (2007) Surgical treatment strategies and outcome in patients with breast cancer metastatic to the spine: a review of 87 patients. *European Spine Journal,* 16: 1179–1192.

Sinardet, D., Chabane, A., Khalil, T., Seigneuret, E., Sankari, F., Lemaire, J.J., Chazal, J. & Irthum, B. (2000). Evolution neurologique de 152 patients operes de metastases rachidiennes. *Neurochirugie,* 46 (1), 4–10.

Sioutos, P.J., Arbit, E., Meshulam, C. F., Galicich, J.H. (1995). Spinal metastases from solid tumors: Analysis of factors affecting survival. *Cancer*, 76, 1453–1459.

Solberg, A. & Bremnes, R. M. (1999) Metastatic spinal cord compression: diagnostic delay, treatment, and outcome. *Anticancer Research,* 19: 677–684.

Sørensen, S., Helweg-Larsen, S., Mouridsen, H. & Hansen, H. H. (1994) Effect of high-dose dexamethasone in carcinomatous metastatic spinal cord compression treated with radiotherapy: a randomised trial. *European journal of cancer* 30A: 22–27.

Sucher E, Margulies JY, Floman Y, Robin GC (1994) Prognostic factors in anterior decompression for metastatic cord compression. An analysis of results. Eur Spine 3: 70–75.

Sundaresan N, Rothman A, Manhart K, Kelliher K (2002) Surgery for solitary metastases of the spine – Rationale and results of treatment. *Spine* 27, 1802–1806.

Sundaresan, N., Sachdev, V.P., Holland, J.F., Moore, F., Sung, M. Paciucci, P.A., Wu, L. Kelligher, K. & Hough, L. (1995). Surgical treatment of spinal cord compression from epidural metastasis. *Journal of Clinical Oncology*, 13 (9), 2330–2335.

Sze WM, Shelley M, Held I, Mason M. Palliation of metastatic bone pain: single fraction versus multifraction radiotherapy. Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD004721. DOI: 10.1002/14651858.CD004721.

Tabbara, I.A., Sibley, D.S. & Quesenberry, P.J. (1990). Spinal cord compression due to metastatic neoplasm. *South.Med.J,* 83.5, 519–523.

Taylor, Taylor & Fritzell (2006) Balloon kyphoplasty and vertebroplasty for vertebral compression fractures – A comparative systematic review of efficacy and safety. *Spine* 31 (23).

Taylor, R. S., Fritzell, P. & Taylor, R. J. (2007) Balloon kyphoplasty in the management of vertebral compression fractures: an updated systematic review and meta-analysis. *European Spine Journal,* 16: 1085–1100.

Thomas K, Nosyk B, Fisher CG *et al.* (2006) cost-effectiveness of surgey plus radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression. Int J. Rad.Onc.Biol.Phys. 66 (4):1212–1218.

Tokuhashi, Y. (2002). Surgery for metastatic spine tumor. *Jpn J Neurosurg* (Tokyo), 11, 446–452.

Tokuhashi, Y., Matsuzaki, H., Oda, H., Oshima, M. & Junnosuke, R. (2005). A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. *Spine,* 30 (19), 2186–2191.

Tokuhashi, Y., Matsuzaki, H., Toriyama, S., Kawano, H. & Ohsaka, S. (1990). Scoring system for the preoperative evaluation of metastatic spine tumor prognosis. *Spine*, 15 (11), 1110–1112.

Tombolini, V., Zurlo, A., Montagna, A., Notarianni, E., Osti, M. F., Enrici, R. M., & Pirolli, C. (1994), Radiation therapy of spinal metastases: results with different fractionations *Tumori*, 80(5): 353–356.

Tomita, K., Kawahara, N., Kobayashi, T., Yoshida, A., Murakami, H. & Akamaru, T. (2001). Surgical strategy for spinal metastases. *Spine*, 26 (3), 298–306.

Tomita, K., Toribatake, Y., Kawahara, N., Ohnari, H. & Kose, H. (1994). Total en bloc spondylectomy and circumspinal decompression for solidary spinal metastasis. *Paraplegia*, 3, 36–46.

Tripathy, D., Lichinitzer, M., Lazarev, A., MacLachlan, S. A., Apffelstaedt, J., Budde, M. & Bergstrom, B. (2004) Oral ibandronate for the treatment of metastatic bone disease in breast cancer: efficacy and safety results from a randomized, double-blind, placebo-controlled trial. *Ann Oncol,* 15: 743–750.

Turner S, M. B. T. I. B. J. (1993) Malignant spinal cord compression: a prospective evaluation. *Int J Radiat Oncol Biol Phys,* 26: 141–146.

Ulmar, B., Huch, K., Naumann, U., Catalkaya, S., Cakir, B., Gerstner, S. & Reichel, H. (2007b) Evaluation of the Tokuhashi prognosis score and its modifications in 217 patients with vertebral metastases. *EJSO,* 33: 914–919.

Ulmar, B., Naumann, U., Catalkaya, S., Muche, R., Cakir, B., Schmidt, R., Reichel, H. & Huch, K. (2007a) Prognosis scores of Tokuhashi and Tomita for patients with spinal metastases of renal cancer. *Annals of Surgical Oncology*, 14(2), 998–1004.

van der Linden, Y. M., Lok, J. J., Steenland, E., Martijn, H., van, H. H., Marijnen, C. A., Leer, J. W., & Dutch Bone Metastasis Study Group. (2004), Single fraction radiotherapy is efficacious: a further analysis of the Dutch Bone Metastasis Study controlling for the influence of retreatment *International Journal of Radiation Oncology, Biology, Physics*, 59(2): 528–537.

van der Linden, Y. M., Steenland, E., van Houwelingen, H. C., Post, W. J., Oei, B., Marijnen, C. A., Leer, J. W., & The Dutch Bone Metastasis Study Group. (2006), Patients with a favourable prognosis are equally palliated with single and multiple fraction radiotherapy: results on survival in the Dutch Bone Metastasis Study. *Radiotherapy & Oncology*, 78(3): 245–253.

Vecht, C. J., Haaxma-Reiche, H., van Putten, W. L., de, V. M., Vries, E. P. & Twijnstra, A. (1989) Initial bolus of conventional versus high-dose dexamethasone in metastatic spinal cord compression. *Neurology.* 39: 1255–1257.

Vrionis FD, Small J (2003) Surgical management of metastatic spinal neoplasms. *Neurosurgical Focus* 15, E12.

Wang, J.C., Boland, Pl, Mitra, N., Yamada, Y., Lis, E., Stubblefield, M. & Bilsky, M.H. (2004). Single-stage posterolateral transpedicular approach for resection of epidural metastatic spine tumors involving the vertebral body with circumferential reconstruction: results in 140 patients. *J Neurosurg* (Spine 1), 3, 287–298.

Warr, D., Johnston, M. & Breast Cancer Disease Site Group . Use of bisphosphonates in women with breast cancer: practice guideline report #1-11 (Version 2.2002). #1-11 (Version 2.2002). 2004. Ontario, Cancer Care Ontario Program. Program in Evidence-based Care (A Cancer Care Ontario Program).

Weigel B, Maghsudi M, Neumann C, Kretschmer R, Muller FJ, Nerlich M (*1999)* Surgical management of symptomatic spinal metastases – Postoperative outcome and quality of life. *Spine* 24, 2240–2246.

Weinfurt, K. P., Castel, L. D., Li, Y., Timbie, J. W., Glendenning, G. A. & Schulman, K. A. (2004) Health-Related Quality of Life Among Patients With Breast Cancer Receiving Zoledronic Acid or Pamidronate Disodium for Metastatic Bone Lesions. (References). *Med Care,* 42: 164–175.

Weinfurt, K. P., Li, Y., Castel, L. D., Saad, F., Timbie, J. W., Glendenning, G. A. & Schulman, K. A. (2005) The significance of skeletal-related events for the health-related quality of life of patients with metastatic prostate cancer. *Ann Oncol,* 16: 579–584.

West of Scotland Malignant Spinal Cord Compression Guidelines (2007) Development Working Group on behalf of the West of Scotland Cancer Network.

Wise JJ, Fischgrund JS, Herkowitz HN, Montgomery D, Kurz LT (1999) Complication, survival rates, and risk factors of surgery for metastatic disease of the spine. *Spine* 24, 1943–1951

Witham, T.F., Khavkin, Y.A., Gallia, G.L. Wolinsky, J.P., Gokaslan, Z.L. (2006) Surgery insight: current management of epidural spinal cord compression from metastatic spine disease. *Nature Clinical Practice Neurology*, 2006, 2 (2) 87–94

Wong CS, van Dyk J, Milosevic M, *et al.* (1994): Radiation myelopathy following single courses of radiotherapy and re-treatment. *Int J Radiat Oncol Biol Phys* 30:575–581.

Wong R, Wiffen PJ . Bisphosphonates for the relief of pain secondary to bone metastases. 2002 *Cochrane Database of Systematic Reviews*, Issue 2. Art. No.: CD002068. DOI: 10.1002/14651858.CD002068.

Wu, J. S., Wong, R., Johnston, M., Bezjak, A., Whelan, T., & Cancer Care Ontario Practice Guidelines Initiative Supportive Care Group. (2003), Meta-analysis of dose-fractionation radiotherapy trials for the palliation of painful bone metastases. *International Journal of Radiation Oncology, Biology, Physics*, 55(3): 594–605.

Wu, J. S., Wong, R. K., Lloyd, N. S., Johnston, M., Bezjak, A., Whelan, T., & Supportive Care Guidelines Group of Cancer Care Ontario. (2004), Radiotherapy fractionation for the palliation of uncomplicated painful bone metastases – an evidence-based practice guideline *BMC Cancer*, vol. 4, p. 71.

Yuen KK, Shelley M, Sze WM, Wilt T, Mason MD. 2006 Bisphosphonates for advanced prostate cancer. *Cochrane Database of Systematic Reviews*, Issue 4. Art. No.: CD006250. DOI:10.1002/14651858.CD006250

Zaidat, O. O. & Ruff, R. L. (2002), Treatment of spinal epidural metastasis improves patient survival and functional state. *Neurology*, 58(9): 1360–1366.

7 Supportive care and rehabilitation

7.1 Introduction

Rehabilitation and supportive care are integral to the promotion of independence and quality of life in people with cancer. Some of these patients will, for oncological and general medical reasons, be unsuitable for active treatment of MSCC. NHS guidance for these patients has been issued[1]. The NICE guidance on 'Improving supportive and palliative care for adults with cancer' recommends the provision of holistic, client centred rehabilitation and care through well organised, multi-professional team working.

People with MSCC often experience significant functional losses coupled with the emotional distress associated with advancing disease. However, published evidence specifically examining the effectiveness of rehabilitation and supportive care for people with MSCC is limited. The following is an amalgamation of best available evidence from MSCC and other conditions.

7.2 Interventions for thromboprophylaxis

Risk factors for venous thromboembolism (VTE) include malignancy, reduced mobility, hospital stay for greater than four days, and major surgery including spinal surgery. All patients with MSCC and especially those undergoing surgery for MSCC are at high risk of VTE.

There is a balance in spinal surgery between the risk of thrombo-embolic complications and the risk of post-operative haemorrhage causing recurrent cord compression. Where heparin is recommended, low molecular weight heparin (LMWH) is preferred because it leads to fewer thrombotic events and fewer bleeding complications compared with unfractionated heparin.

Recommendations

- Offer all patients who are on bed rest with suspected MSCC thigh-length graduated compression/anti-embolism stockings unless contra-indicated, and/or intermittent pneumatic compression or foot impulse devices.
- Offer patients with MSCC who are at high risk of venous thromboembolism (including those treated surgically and judged safe for anti-coagulation) subcutaneous thromboprophylactic low molecular weight heparin in addition to mechanical thromboprophylaxis[2].

[1] www.endoflifecareforadults.nhs.uk/eolc/pathway.htm.

[2] See 'Venous thromboembolism' (NICE clinical guideline 46) for information on reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing spinal surgery.

Recommendations (cont.)

- For patients with MSCC, individually assess the duration of thromboprophylactic treatment, based on the presence of ongoing risk factors, overall clinical condition and return to mobility.

Qualifying statement: These recommendations are based on existing NICE guidance and extrapolation of evidence from research in surgical patients, patients with malignancy and patients with traumatic spinal cord injury. The optimal duration of therapy is unknown.

Clinical Evidence

Thromboprophylaxis is addressed in the NICE clinical guideline 'Venous thromboembolism: reducing the risk of venous thromboembolism in inpatients undergoing surgery' (2007a). It is also addressed in the SIGN guidance on 'Prophylaxis of venous thromboembolism' (2002) and 'Antithrombotic therapy' (1999), and evidence-based guidance from the Department of Health 'Report of the independent expert working group on the prevention of venous thromboembolism in hospitalised patients' (2007).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

7.3 Management of pressure ulcers

Pressure ulcers may affect quality of life and rehabilitation outcomes. They are difficult to treat and potentially life threatening. People with MSCC are at very high risk of developing pressure ulcers because of impaired mobility and sensation, as well as compromised bowel and bladder function. Pressure relieving mattresses or other pressure relieving devices are often not enough to prevent pressure ulcers.

Recommendations

- Undertake and document a risk assessment for pressure ulcers (using a recognised assessment tool) at the beginning of an episode of care for patients with MSCC. Repeat this assessment every time the patient is turned while on bed rest and at least daily thereafter.
- While patients with MSCC are on bed rest, turn them using a log rolling technique at least every 2–3 hours. Encourage patients who are not on bed rest to mobilise regularly (every few hours). Encourage and assist those who are unable to stand or walk to perform pressure relieving activities such as forward/sideways leaning at least hourly when they are sitting out.
- Promptly provide pressure relieving devices to patients with MSCC appropriate to their pressure risk assessment score. Offer patients with restricted mobility or reduced sensation cushions and/or mattresses with very high-grade pressure-relieving properties.
- When caring for patients with MSCC, adhere to the pressure sore assessment, prevention and healing protocols recommended in 'The use of pressure-relieving devices for prevention of pressure ulcers' (NICE clinical guideline 7) and 'The management of pressure ulcers in primary and secondary care' (NICE clinical guideline 29).

Qualifying statement: These recommendations are based on existing NICE guidance relating to the prevention and management of pressure ulcers and GDG consensus.

Clinical Evidence

Pressure ulcer management is addressed in the NICE clinical guidelines 'Pressure ulcer prevention: pressure ulcer risk assessment and prevention, including the use of pressure relieving devices for the prevention of pressure ulcers in primary and secondary care' (2003) and 'The management of pressure ulcers in primary and secondary care' (2005).

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

7.4 Bladder and bowel continence management

Impairment of bladder and bowel sensation and function have major impact on the care and well-being of patients with MSCC, including incontinence, retention, constipation, obstruction, infection, discomfort and occasionally severe ill-health or death.

The management of bladder and bowel disturbance and paraplegia may differ depending on the level of neurological disability (upper motor neuron versus lower motor neuron).

Recommendations

- Assess bowel and bladder function in all patients with MSCC on initial presentation and start a plan of care.
- Monitor patients with MSCC who are continent and without urinary retention or disturbed bowel function at least daily for changes in bladder and bowel function.
- Manage bladder dysfunction in patients with MSCC initially by a urinary catheter on free drainage. If long-term catheterisation is required, consider intermittent catheterisation or suprapubic catheters.
- Offer a neurological bowel management programme to patients with MSCC and disturbed bowel habit as recommended in 'Faecal incontinence' (NICE clinical guideline 49). Take account of patient preferences when offering diet modification, faecal softeners, oral or rectal laxatives and/or constipating agents as required. Digital stimulation, manual evacuation, rectal irrigation and surgical treatment may be offered, as required.

Qualifying statement: These recommendations are based on NICE guidance and GDG consensus.

Clinical Evidence

Bowel management is addressed in the NICE clinical guideline 'Faecal incontinence: the management of faecal incontinence in adults' (2007b).

No studies were retrieved that included patients with MSCC specifically. However, several Cochrane systematic reviews provided relevant evidence about bladder management that can be extrapolated to MSCC patients. Jahn *et al.* (2007) evaluated which type of in-dwelling urinary catheter is best to use for long-term bladder drainage in adults. Overall, the included trials provided insufficient evidence to indicate which types of catheters are best to use in which patients. One trial did suggest, that the use of a hydrogel coated latex catheter rather than a silicone catheter may be better tolerated. Jamison *et al.* (2004) assessed the effects of using different types of urinary catheters and external (sheath) catheters in managing the neurogenic bladder, compared to alternative management strategies or interventions. Out of 400 studies considered no studies were found that met the inclusion criteria. Niël-Weise *et al.* (2005a) reviewed catheter policies in order to determine if any were better than others in terms of effectiveness, complications, quality of life and cost-effectiveness in long-term catheterised adults and children. Limited evidence indicated that when antibiotic

Clinical Evidence (cont.)

prophylaxis was compared with antibiotics when clinically indicated, for patients using intermittent catheterisation, there were inconsistent findings about the effect of antibiotic prophylaxis on symptomatic urinary tract infection (UTI). For patients using indwelling urethral catheterisation, one study reported fewer events of symptomatic UTI in the prophylaxis group. When antibiotic prophylaxis was compared with giving antibiotics when microbiologically indicated, for patients using intermittent catheterisation, there was limited evidence that receiving antibiotics reduced the rate of bacteriuria (asymptomatic and symptomatic). There was also limited evidence that prophylactic antibiotics reduced symptomatic bacteriuria. Niël-Weise *et al.* (2005b) investigated the outcomes of alternative approaches to catheterisation for short-term bladder drainage in adults. Patients managed with an indwelling catheter had more cases of bacteriuria, more frequent recatheterisation and more suffered discomfort than patients managed with suprapubic catheterisation. There was no evidence of complications during insertion, although not all trials reported this outcome explicitly. Findings from three studies suggested that when indwelling urethral catheterisation was compared to intermittent catheterisation there were fewer cases of bacteriuria in patients with the intermittent catheterisation. Only a proportion of the participants in the studies included in these reviews had spinal cord injury.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

7.5 Maintaining circulatory and respiratory functioning

Alterations of sympathetic vascular tone, relative parasympathetic overactivity, and respiratory muscle paralysis may cause complex and sometimes life-threatening vascular and cardio-respiratory changes in people with MSCC. These include hypoventilation, hypotension, bradycardia, and autonomic dysreflexia especially in the acute phase of paralysis or with high spinal cord lesions.

Recommendations

- Include heart rate and blood pressure measurement, respiratory rate and pulse oximetry in the initial assessment and routine monitoring of all patients with MSCC.
- Symptomatic postural hypotension in patients with MSCC should be managed initially by patient positioning and devices to improve venous return (such as foot pumps and graduated compression/anti-embolism stockings). Avoid overhydration which can provoke pulmonary oedema.
- Include clearing of lung secretions by breathing exercises, assisted coughing and suctioning as needed in the prophylactic respiratory management of patients with MSCC. Treat retained secretions and the consequences by deep breathing and positioning supplemented by bi-phasic positive airway pressure and intermittent positive pressure ventilation if necessary.

Qualifying statement: In the absence of definitive research evidence these recommendations have been made with GDG consensus, supported by a moderate quality clinical guideline and poor quality observational studies.

Clinical Evidence

Respiratory management

The evidence-based guideline from the Consortium for Spinal Cord Medicine (2005) provided some of the evidence for respiratory management for MSCC patients. This guideline was appraised using the AGREE Instrument (2003), it was rated as being of moderate quality.

Clinical Evidence (cont.)

Maintaining circulatory functioning

Two expert reviews reported outcomes from using fludrocortisone (Bloomfield *et al.* 2002, Claydon *et al.* 2006), although widely used, there was no high level evidence of effect on hypotension. Clinical consensus as described in these studies recommended that fludrocortisone be used as treatment of vasovagal syncope and orthostatic hypotension. For compression bandages, two studies (one small non-randomised, comparative study (Rimaud *et al.* 2007) and one expert review (Claydon *et al.* 2006)) reported outcomes. This very limited evidence suggested the use of compression bandages or support stockings to restrict venous pooling in the visceral area and dependent limbs to manage hypotension. For electrically induced and voluntary activation of physiologic muscle pump, one comparative, non-randomised study evaluated this intervention (Faghri *et al.* 2002). Limited evidence indicated effectiveness of functional electrical stimulation (FES) during standing and tilting in spinal cord-injured individuals and may prevent orthostatic hypotension and circulatory hypokinesis and improve tolerance to tilting and standing.

The evidence from two very small non-randomised comparative studies (Svensson *et al.* 1995, Ter *et al.* 2006) evaluating passive leg movements suggest that passive leg movements do not prevent thrombosis in acute spinal cord injury (SCI) patients or alter the arterial peripheral circulation in patients with SCI or control participants.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

7.6 Access to specialist rehabilitation and transition to care at home

The potential benefits of specialist in-patient neurological and functional rehabilitation have to be weighed against the time required to achieve these (often small) gains for patients with MSCC. Additionally the general health and ability and wish to return home of patients with a life-limiting diagnosis and decreasing functional ability needs to be considered.

Survival rates at one year for people with MSCC have been reported as being less than 20%. Because of this, MSCC should be regarded as a life-limiting disease, and considerable attention needs to be paid to ensuring high quality, individualised support for people when they return home. Emphasis is on a coordinated, person-centred discharge planning process which takes into account the individual circumstances of each patient and their carers. The timing of these discussions needs to be sensitive to the emotional adjustments that the patient and carer may be experiencing. Communication between secondary, primary and tertiary care needs to be geared towards smooth transfer and continuity of care for patients.

Recommendations

- Ensure that all patients admitted to hospital with MSCC have access to a full range of healthcare professional support services for assessment, advice and rehabilitation.
- Focus the rehabilitation of patients with MSCC on their goals and desired outcomes, which could include promoting functional independence, participation in normal activities of daily life and aspects related to their quality of life.
- Offer admission to a specialist rehabilitation unit to those patients with MSCC who are most likely to benefit, for example, those with a good prognosis, a high activity tolerance and strong rehabilitation potential.

Qualifying statement: These recommendations are based on GDG consensus.

Recommendations (cont.)

- Discharge planning and ongoing care, including rehabilitation for patients with MSCC, should start on admission and be led by a named individual from within the responsible clinical team. It should involve the patient and their families and carers, their primary oncology site team, rehabilitation team and community support, including primary care and specialist palliative care, as required.

Qualifying statement: This recommendation is based on GDG consensus as well as the NICE guidance 'Improving supportive and palliative care for adults with cancer' (2004) and 'West of Scotland Cancer Network Guidelines for Malignant Spinal Cord Compression' (2007).

- Ensure that community-based rehabilitation and supportive care services are available to people with MSCC following their return home, in order to maximise their quality of life and continued involvement in activities that they value.
- Ensure that people with MSCC are provided with the equipment and care they require in a timely fashion to maximise their quality of life at home.

Qualifying statement: These recommendations are based on GDG consensus.

- Offer the families and carers of patients with MSCC relevant support and training before discharge home.

Qualifying statement: This recommendation is based on GDG consensus as well as the NICE guidance 'Improving supportive and palliative care for adults with cancer' (2004) and 'West of Scotland Cancer Network Guidelines for Malignant Spinal Cord Compression' (2007).

- Clear pathways should be established between hospitals and community-based healthcare and social services teams to ensure that equipment and support for people with MSCC returning home and their carers and families are arranged in an efficient and coordinated manner.

Qualifying statement: This recommendation is based on GDG consensus.

Clinical Evidence

There is limited evidence of effectiveness of specialised rehabilitation for patients with MSCC. There were no randomised, controlled comparisons available between specialised rehabilitation and no rehabilitation or any other form of rehabilitation. The available evidence comes from case series studies and includes populations of which a very small proportion were MSCC patients. (Eriks 2003; Hacking 1993; McKinley *et al.* 1999, McKinley *et al.* 2000 and McKinley *et al.* 2001 ; New 2005). In general patients with traumatic spinal cord injury had greater improvement in their functional independence than non-traumatic spinal cord injury patients (this group contained a subset of MSCC patients). Spinal epidural metastasis (SEM) treatment plus intensive rehabilitation programme was compared to receiving only SEM treatment in a biased observational study (Ruff *et al.* 2007). Patients who received intensive rehabilitation survived longer. Median survival for the rehabilitation group was significantly longer compared to the no rehabilitation group. Patients in the rehabilitation group were statistically more likely to be discharged home than the no rehabilitation group. Patients in the no rehabilitation group were statistically more likely to be diagnosed with clinical depression compared to rehabilitation patients. After completing rehabilitation, the rehabilitation group had significantly higher satisfaction with life score than that of the no rehabilitation group patients. After completion of rehabilitation intervention, the rehabilitation group had lower pain levels than the group of patients with no rehabilitation.

Health Economic Evaluation

The GDG did not rate this topic as a health economic priority; therefore the cost-effectiveness literature on this topic has not been reviewed.

References

Bloomfield DM (2002) Strategy for the management of vasovagal syncope. *Drugs & Aging* 19, 179–202.

Claydon VE (2006) Orthostatic hypotension following spinal cord injury: Understanding clinical pathophysiology. *Spinal Cord* 341–351.

Consortium for Spinal Cord Medicine (2005) Respiratory management following spinal cord injury: a clinical practice guideline for health-care providers. Available from www.pva.org/site/DocServer/resmgmt.pdf?docID=703

Department of Health/Chief Medical Officer (2007) Report of the independent expert working group on the prevention of venous thromboembolism in hospitalised patients.

Eriks, Angenot & Lankhorst. (2004) Epidural metastatic spinal cord compression: functional outcome and survival after inpatient rehabilitation. *Spinal Cord.* 42(4), 235–239.

Faghri PD (2002) Electrically induced and voluntary activation of physiologic muscle pump: A comparison between spinal cord-injured and able-bodied individuals. *Clinical Rehabilitation* 878–885.

Hacking, Van As & Lankhorst. (1993) Factors related to the outcome of inpatient rehabilitation in patients with neoplastic epidural spinal cord compression. *Paraplegia* 31:6, 367–374.

Jahn P, Preuss M, Kernig A, Seifert-Hühmer A, Langer G. Types of indwelling urinary catheters for long-term bladder drainage in adults. Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD004997. DOI: 10.1002/14651858.CD004997.pub2.

Jamison J, Maguire S, McCann J (2004) Catheter policies for management of long term voiding problems in adults with neurogenic bladder disorders. Cochrane Database of Systematic Reviews CD004375.

McKinley, Huang & Brunsvold (1999) Neoplastic versus traumatic spinal cord injury: an outcome comparison after inpatient rehabilitation. *Archives.of Physical.Medicine & Rehabilitation* 80(10), 1253–1257.

McKinley, Huang & Tewksbury (2000) Neoplastic vs. traumatic spinal cord injury: an inpatient rehabilitation comparison. *American. Journal of Physical.Medicine & Rehabilitation* 79(2), 138–144.

McKinley WO, Seel RT, Gadi RK, Tewksbury MA (2001) Nontraumatic vs. traumatic spinal cord injury: a rehabilitation outcome comparison. *Am J Phys Med Rehabilitattion;* 80: 693–699.

New. PW. (2005) Functional Outcomes and Disability After Nontraumatic Spinal Cord Injury Rehabilitation: Results From a Retrospective Study*Arch Phys Med Rehabilitation* 86 (2) 250–261

National Institute for Health and Clinical Excellence (2003) Pressure relieving devices: the use of pressure relieving devices for the prevention of pressure ulcers in primary and secondary care. NICE clinical guideline 7. London: NICE.

National Institute for Health and Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. NICE cancer service guidance. London: NICE.

National Institute for Health and Clinical Excellence (2005) Pressure ulcers: The management of pressure ulcers in primary and secondary care. NICE clinical guideline 29. London: NICE.

National Institute for Health and Clinical Excellence (2007a) Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery. NICE clinical guideline 46. London: NICE.

National Institute for Health and Clinical Excellence (2007b) Faecal incontinence: the management of faecal incontinence in adults. NICE clinical guideline 49. London: NICE.

Niël-Weise BS, van den Broek PJ. Urinary catheter policies for short-term bladder drainage in adults. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD004203. DOI: 10.1002/14651858.CD004203.pub2.

Niël-Weise BS, van den Broek PJ. Urinary catheter policies for long-term bladder drainage. Cochrane Database of Systematic Reviews 2005, Issue 1. Art. No.: CD004201. DOI: 10.1002/14651858.CD004201.pub2.

Rimaud D, Calmels P, Roche F, Mongold JJ, Trudeau F, Devillard X (2007) Effects of graduated compression stockings on cardiovascular and metabolic responses to exercise and exercise recovery in persons with spinal cord injury. *Archives of Physical Medicine & Rehabilitation* 88, 703–709.

Ruff, R. L., Adamson, V. W., Ruff, S. S. & Wang, X. (2007) Directed rehabilitation reduces pain and depression while increasing independence and satisfaction with life for patients with paraplegia due to epidural metastatic spinal cord compression. *Journal of Rehabilitation Research & Development,* 44: 1–10.

Scottish Intercollegiate Guidelines Network (1999). Antithrombotic therapy. SIGN publication no. 36. Edinburgh: SIGN. Available from www.sign.ac.uk/pdf/sign36.pdf

Scottish Intercollegiate Guidelines Network (2002). Prophylaxis of venous thromboembolism. SIGN publication no. 62. Edinburgh: SIGN. Available from www.sign.ac.uk/pdf/sign62.pdf

Svensson M, Siosteen A, Wetterqvist H, Sullivan L (1995) Influence of physiotherapy on leg blood flow in patients with complete spinal cord injury lesions. *Physiotherapy Theory and Practice* 11, 97–107.

Ter WW, De Groot PC, van Kuppevelt DH, Hopman MT (2006) Passive leg movements and passive cycling do not alter arterial leg blood flow in participants with spinal cord injury. *Physical Therapy* 86, 636–645.

West of Scotland Malignant Spinal Cord Compression Guidelines (2007) Development Working Group on behalf of the West of Scotland Cancer Network.

Appendix I

An economic evaluation of extending MRI scanning hours at a district general hospital for people with suspected metastatic spinal cord compression

Introduction

People with metastatic spinal cord compression (MSCC) and early signs of neuralgia are at high risk of developing irreversible spinal cord damage and paralysis if not diagnosed and treated urgently. Indeed, there is evidence to suggest that better patient outcomes (survival and quality of life) are achieved when the time between the early signs and symptoms of MSCC and appropriate treatment is minimised (Prasad & Schiff 2005, Husband 1998, Conway *et al*. 2007, Back *et al*. 1990).

There are a number of reasons why appropriate diagnosis and treatment might be delayed. These include a failure by health care professionals to refer potential MSCC patients for appropriate specialist diagnosis and a lack of awareness by patients in terms of identifying the early signs and symptoms of the condition. However, another is that NHS diagnostic facilities at District General Hospitals (DGHs) are often only open during 'standard working hours'. Thus, patients with suspected MSCC referred outside of these times, have to wait until at least the next morning to undergo the appropriate diagnostic test, usually a MRI, or are referred to tertiary treatment centres. While MRI clinic opening hours at DGHs could be extended, it is not clear whether it's cost-effective to do so in the context of identifying people with MSCC.

Aim

The aim of this study is to assess the cost-effectiveness of expanding the opening hours of existing NHS MRI scanning services at DGHs to identify people with suspected MSCC.

Method

Existing economic evidence

A systematic review of the literature did not identify any existing economic evaluations on this topic. Thus *de novo* modelling was undertaken using results from the systematic review of the clinical literature and a number of other supplementary non-systematic literature searches.

The economic evaluation was performed using a decision tree approach. Decision trees consist of relevant events (given the subject matter for the model), probabilities of these events occurring, and the costs and health consequences of each of these events. It is a basic but frequently used form of decision modelling and was chosen because the time frame over which salient events can happen is relatively short and they do not frequently recur. Thus more complex forms of modelling such as Markov models were not considered to be necessary.

The evaluation was performed from a NHS and Personal Social Services cost perspective and health outcomes were expressed in terms of Quality-Adjusted Life-Years (QALYs); both approaches are recommended in NICEs Clinical Guidelines Manual. QALYs are calculated by adjusting evidence on patient survival by evidence on health-related quality-of-life. The index

used to represent health-related quality-of-life is known as a 'utility'. A utility value of 1 is taken to be equivalent to perfect health whereas a value of 0 is equivalent to death. Remaining health states have values somewhere between these levels, although values below 0 for particularly poor health states are plausible.

Future costs and benefits were not discounted because in all but a small number of scenarios, these events occured within a year of initial diagnosis and treatment.

The decision problem

An economic evaluation is essentially a comparison of the cost and benefits of two or more courses of action. In this instance, the courses of action are 'MRI during standard working hours (SWH)' compared with 'extended opening hours (EOH)'. However, as both SWH and EOH are continuous/variable concepts rather than absolutes (meaning that many different combinations of SWH and EOH are possible), and after consultation with various members of the GDG, only five strategies have been formally evaluated (Table A1.1). It should also be noted that the model relates specifically to patients arriving at DGHs, as the GDG have already made the recommendation that 24/7 MRI scanning should be made available at tertiary/specialist units.

People with suspected MSCC can present with a number of different signs and symptoms ranging from non-specific back pain to established paraplegia. However, for the purposes of this modelling exercise the patient group has been restricted to people with 'early onset paralysis' on the assumption (as discussed with the Guideline Chair) that people who are still mobile can feasibly 'wait' for a MRI without adversely affecting the outcome of treatment (if required) and people who have been paralysed for longer periods of time are less likely require 'urgent' diagnosis and treatment. Thus the only patients considered in the model are those considered to require an 'urgent' MRI.

Table A1.1 Scenario descriptions for the base case analysis.

Scenario	Description
1a	SWH defined as 9am to 5pm Monday to Friday only. In this scenario it is assumed that all DGH clinic slots are full, and that any person who requires an urgent MRI for suspected MSCC who arrives at the clinic Sunday to Thursday, is therefore required to wait until the next morning to have a MRI at the DGH. People arriving Friday or Saturday are required to wait until the following Monday for a MRI.
1b	All patients arriving at a DGH with suspected MSCC require immediate transfer to a tertiary treatment centre under the assumption that all the DGH MRI slots for that day are full. On arrival at the tertiary centre patients receive an immediate MRI and treatment if necessary.
2a	SWH again defined as 9am to 5pm Monday to Friday but with the added option that if a person urgently requires a MRI for suspected MSCC *during these opening hours*, they are immediately added to the clinic list and receive a MRI that day. The 'expense' of this approach is that the remaining patients on the waiting list for that day are required to wait an extra two hours, meaning that overtime is paid for the MRI-related staff. No MRI facilities are available outside of these times during the week or at the weekend.
2b	The same as 2a) except patients who require a MRI outside of these opening hours are immediately transferred to a tertiary treatment centre for scanning and treatment if required.
3	MRI clinics are assumed to extend their weekday opening hours to 8am to 8pm Monday to Friday and to be open at the weekend 9am to 3pm Saturday and Sunday. Patients requiring a MRI during these times are assumed to receive a scan the same day. People arriving outside of these hours are required to wait until the next morning for a MRI. As weekend cover is included in this scenario, it is implied that no 'urgent' patients are required to wait longer than 24 hours for a MRI.

(Note that although only these five scenarios have been evaluated, the model is sufficiently flexible to consider most other plausible options).

The 'exclusivity' assumption

An important issue when assessing the cost-effectiveness of extending MRI opening hours for people with suspected MSCC is that MRI facilities are (routinely) used for a number of other patient groups eg. spinal trauma and transient ischaemic attack. This means that extending MRI opening hours benefits more than just MSCC patients and that the costs of this potential extension are therefore not solely attributable to this patient group. Two approaches to accommodating this cost issue were possible: attribute *all* of the additional costs to patients with suspected MSCC and conduct appropriate sensitivity analysis or, attribute *an appropriate proportion* of the extra costs to patients with suspected MSCC and conduct appropriate sensitivity analysis. The problem with the second approach is that it is not clear that it would be cost-effective to extend opening hours for these unknown patient groups, which is implicit in this approach. Moreover, the proportion of MRIs that is given to patients with suspected MSCC is likely to be very small given all demands for MRIs. Thus, the additional costs of extending hours for patients with suspected MSCC would be negligible, and in all likelihood it would appear cost-effective in all scenarios. For these reasons, it has been assumed that all the costs and benefits of extending opening hours are 'exclusive' to patients with MSCC. However, appropriate sensitivity analysis was undertaken to examine the robustness of the results to alternative costing assumptions.

Time horizon

The model considers a range of possible events over an 'average' week for an 'average' DGH, in terms of estimating the costs and benefits of providing EOH services compared with SWH. However, the actual time horizon for the analysis is the time from referral for a MRI to the death of the patient from metastatic disease, which was approximately one year in most scenarios for ambulant patients. Thus the model estimates the expected costs and benefits of diagnosis and treatment for patients referred over an average week until death.

That activity within a DGH over a week period has been chosen is important in terms of explaining the models construction but has no significance in terms of the actual model results. For example, if a period of two- or four-weeks had instead been chosen, *all* the costs and benefits of diagnosis and treatment would be multiplied by two and four respectively, making no difference to the overall incremental cost-effectiveness ratio (ICER).

The model structure

The model structure is shown in Figure A1.1. Broadly speaking it is the same for all three scenarios, but the probabilities associated with the events differ as a result of different MRI opening hours. People who arrive at the clinic with suspected MSCC requiring an urgent MRI either receive a scan that day, the next day or on the following Monday if they are required to wait over the weekend. Patients who are required to wait until the next day for a MRI are assumed to have poorer health outcomes compared with people who receive an immediate MRI. Moreover, people who are required to wait for a MRI until after the weekend are assumed to experience poorer health outcomes compared with people who had to wait until the next day. Thus, the benefit of longer and more frequent opening hours is faster access to diagnosis/treatment with subsequently improved health outcomes. Once a MRI has been undertaken, patients with correctly diagnosed MSCC are assumed to undergo appropriate decompression treatment with an associated probability of being ambulant/not ambulant post this treatment.

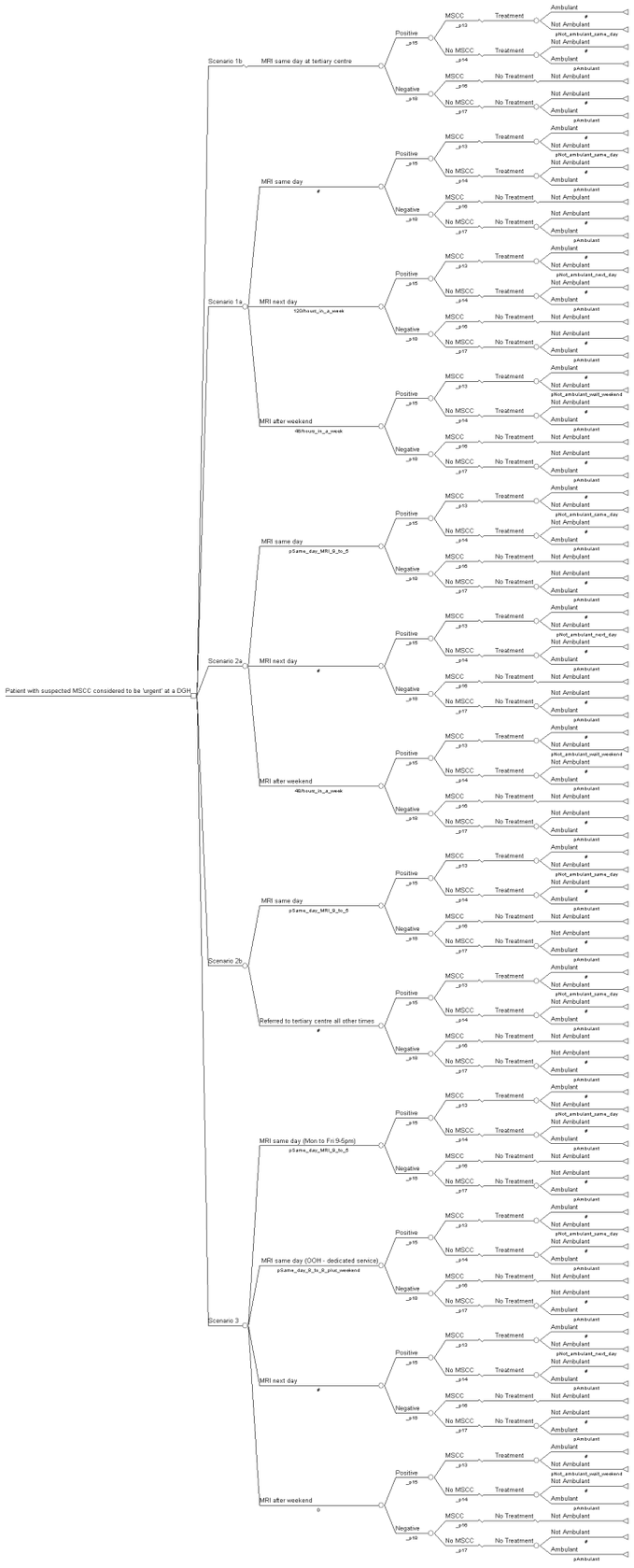


Figure A1.1 Outline of model decision tree

Four possible MRI scan results were assumed to be possible:

True positives (people who tested positive who had MSCC)

People who are true positives were assumed to undergo emergency spinal cord decompression with a subsequent chance of being ambulant or non-ambulant post surgery.

False positives (people who tested positive who did not have MSCC)

All false positive patients were assume to incur the cost of spinal cord decompression but were not assumed to actually undergo it, 50% were assumed to return to an ambulant health state until death.

True negatives (people who tested negative who did not have MSCC)

All true negative patients did not undergo decompression treatment and 50% were assumed to return to an ambulant health state until death.

False negatives (people who tested negative but did have MSCC)

All false negative patients were assumed not to undergo decompression (despite needing it) and to become non-ambulant until death.

Event probabilities

The probability of a person with suspected MSCC requiring an urgent MRI during SWH was calculated to be 27% in the base case analysis, on the basis that patients uniformally[1] arrive at clinics and that there are 168 hours (7 x 24 hours) in a week and therefore a 27% (45/168) chance of arriving at a clinic during SWH. For scenario 3), the equivalent probability was calculated to be 43% (72/168) given that the clinic is open 72 hours per week (note that a 0% probability is equivalent to a clinic being permanently closed whereas 100% is equivalent to it being open 24 hours 7 days a week).

The probability of testing true/false/negative/positive is a function of three factors: the sensitivity of the test (here MRI), its specificity and the prevalence (also known as a 'prior' or 'pre-test probability') of the condition (here MSCC) in people attending the clinic. More formally, the likelihood of each of these test results can be calculated using the following formula (Huinink & Glasziou 2001):

$$P(H|E) = ((PE|H) * P(H)) / P(E)$$

Where H is the hypothesis being tested (that is, whether or not a person has MSCC), E is the test result (positive or negative) and P(H) is the 'prior' associated with the condition (or the proportion of people attending a clinic with early paralysis that is directly attributable to the presence of MSCC).

Evidence suggests that both the sensitivity and specificity of MRI in detecting MSCC are extremely high; therefore both values were set to 0.99 in the baseline analysis. However, there is little evidence on which to estimate the proportion of people with early paralysis specifically associated with MSCC in people attending UK clinics. The most appropriate study was considered to be by Lu *et al.* in 2005. The study was undertaken between 1998 and 1999 in two US teaching hospitals and consisted of patients attending clinics with suspected MSCC, a previous diagnosis of cancer, confirmation from the treating physician that the aim of the MRI was to rule out the possibility of metastatic epidural cancer and no prior diagnosis of metastatic epidural cancer. Clinical records for a total of 136 cases were reviewed, with MRI revealing that 37% of patients had thecal sac compression. This value was used in the baseline analysis to estimate the prior, however it was increased to 81% in the sensitivity analysis as the study showed that this value could be achieved if the patient group was restricted to including only

[1] This uniformity assumption means that patients are equally likely to arrive at a clinic on any day at any time throughout the given week.

people with at least 3 predictive factors (either an abnormal neurological examination, stage IV cancer at initial diagnosis, known spinal metastases and middle/upper back pain).

The probabilities associated with post-treatment outcomes were taken from randomised and non-randomised sources; the RCT by Patchell *et al.* (2005) did not provide sufficient information to be used as the sole source of information. The RCT only included non-ambulant patients if they had been paraplegic for less than 48 hours. Of the non-ambulant patients in the surgery plus radiotherapy treatment arm, 62.5% were ambulant post-treatment (n= 10/16). This percentage was used in the model to estimate the probability of being ambulant post surgery for patients who were diagnosed with MSCC and treated immediately (that is, those with early onset paraplegia, see Table A1.2). The non-randomised study by *Bach et al.* (1990) was used to estimate the probability of being ambulant post treatment for people with more established paralysis as it contained the largest number of patients. Its results showed that only 6% of people with paraplegia were ambulant post-surgery, although it should be noted that this study was performed in 1990 and few details are provided as to the duration of pre-treatment paraplegia. All patients required to wait longer than 24 hours for a MRI were assumed to be paraplegic post treatment.

Table A1.2 Base case input variables by health state for patients with MSCC

	Health state post treatment		Source
Health state pre treatment	**Ambulant**	**Not ambulant**	
Immediate MRI and treatment if needed (percentage)	62.5%	37.5%	Assumption based on Patchell *et al.* (2005)
Wait <24 hours for MRI and treatment if needed (percentage)	6%	94%	Assumption based on Bach *et al.* (1990)
Wait > 24 hours for MRI (percentage)	0%	100%	Complete assumption
Time to paraplegia after being ambulant post treatment (years)	0.61	–	Patchell *et al.* (2005)
Survival – ambulant patients (years)	0.96	–	Thomas *et al.* (2006)
Survival – paraplegic patients (years)	–	0.24	Maranzano *et al.* (1998)
Utilities	0.7	0.4	Assumption based on Falicov *et al.*
Costs – mean home care post treatment (per diem)	£12.65	£192.80	Calculated as part of Topic 8
Costs – mean rehabilitation cost (one-off cost)	£844		Calculated as part of Topic 8

While the aim of decompression surgery is to prevent paraplegia, the results from the Patchell *et al.* (2005) RCT showed that of the 60% of people who were paraplegic pre treatment, the average post-treatment time to paraplegia was approximately 0.61 years. Thus in the baseline analysis it was assumed that people for whom treatment was successful remained ambulant for 0.61 years, after which time they became paraplegic until death (Table A1.2**)**. However, this value was altered in the sensitivity analysis to allow for the assumption that successful treatment was permanent.

Post-treatment patient survival for ambulant patients was assumed to be 0.96 years on the basis of the Patchell *et al.* (2005) RCT for people who underwent decompression surgery and radiotherapy. However, two limitations with this data should be noted. First, this value includes an unspecified proportion of patients who were paraplegic post-treatment, although it is likely to be small. Second, older, but recently published UK data, suggest that this median time was nearer to 6 months (Conway *et al.* 2007). A corresponding survival time for people who were paraplegic post surgery was not available from the RCT (Patchell *et al.* 2005), but was estimated to be 0.24 years based on an adjusted analysis of the results reported in the uncontrolled study by Maranzano *et al.*(1998). While other studies were available with which to

estimate this parameter, the reported mean/median survival times were broadly similar. The analysis does not formally consider patient outcome by underlying histology. However, post-treatment survival times can be varied in the sensitivity analysis, which is entirely equivalent.

Utility values

A number of studies have reported utility values that have relevance to this analysis. However, they all have significant limitations in terms of their direct use for this modelling exercise. For example, the results do not relate specifically to ambulant/non-ambulant health states, which are the outcomes used in this model. Moreover, the study by Hollingworth *et al.* (2003) is based on the Quality of Well Being Scale, which is not a utility-based instrument.

In order to be consistent with Topic 8, utility values of 0.7 and 0.4 were chosen as representing the health states 'ambulant' and 'not ambulant' respectively in the base case analysis. Briefly, Falicov *et al.* (2006) reported these values in people with MSCC, but they were reported as bi-modal values, rather than scores that related specifically to the two health states. Thus they represent poor quality evidence.

Costs

Decompression treatment

The hospital cost of 'major surgery' was calculated to be £13,410 per procedure in Topic 8. An additional average rehabilitation cost of £844 per patient was also calculated for patients who were ambulant post-surgery. The cost of 'major surgery' was chosen to represent the cost of decompression treatment from amongst the various options costed in Topic 8, as it encompasses a number of different types of surgery. However, it should be noted that as the sensitivity/specificity of the MRI test are high and all patients in the model bar a small minority receive treatment, the precise value of the treatment cost has negligible effect on the results. That is, the cost of decompression treatment has virtually no influence on the cost-effectiveness of expanding MRI opening hours[2]. All decompression treatment was assumed to be undertaken at tertiary treatment centres. Thus an additional cost was incurred of transferring patients (if they received their MRI at a DGH, see later in the methods section).

Health state specific costs (ambulant/non-ambulant)

The analysis from Topic 8 also suggests that the average post-treatment home care costs associated with being 'ambulant and 'non-ambulant' are £12.65 and £192.80 per diem respectively. However, broadly speaking they include the costs of community nursing and caring from social services.

The costs of expanding MRI opening hours

Estimating the additional costs of expanding MRI opening hours is complex not least because 1) there is no (published) information on the topic and 2) because it depends on the configuration of existing services, which varies across existing scanning units. Therefore, the following steps were followed and assumptions made with the aim of estimating the additional cost of a MRI:

- The cost of each MRI during SWH was assumed to be £244 on the basis of national NHS unit cost information. The cost of a MRI at tertiary treatment centres was also assumed to be £244 per scan.
- Two MRI costs were applied in scenario 2a. Patients requiring a scan that had to wait until at least the next day for a scan were again assumed to cost £244 per scan. However, those who arrived during SWH (Monday to Friday 9am to 5pm) who were slotted into the day's list were assumed to cost: the standard cost of a MRI plus 2 hours radiographer overtime with an additional 20% overtime allowance (£42), and a quarter programmed activity per consultant

[2] The exception to this, which is not included in this model, would be if MRI was sufficiently delayed to completely remove any clinical rationale for intervention.

radiologist (£57). Thus the cost of a MRI in scenario during SWH for scenario 2) was (£244 + £42 + £57) = £343 per scan.

- Similarly for scenario 3, two different MRI tariffs were assumed to apply, depending on the time the MRI was undertaken. As per scenario 1) patients requiring a MRI between Monday to Friday 9am to 5pm, and patients who were required to wait until the next day for a scan, were assumed to cost £244 per scan. However, people requiring a scan during the extended opening hours (ie. between 8–9am Mondays to Fridays, 5–8pm Mondays to Fridays and between 9am-3pm Saturdays and Sundays) were assumed to cost *£3,878 per scan*[3]. Based on the following assumptions:
  a. It was estimated (assumed) that moving from scenario 1) to 3) would require 2 extra full-time radiographers, each costing £33500 per annum, or £644 per week. This is equivalent to an extra 32-hours per week of clinic opening time.
  b. Each MRI during these extended hours is also assumed to require an additional quarter programmed activity per consultant radiologist (£57).
  c. Audit data from James Paget University Hospital showed that 19[4] people with suspected MSCC required a MRI over a 10-week period, equivalent to 1.9 scans a week.
  d. If it is assumed that there are 168 hours in a week, and patients uniformally require MRIs, then 19% (32 hours/168 hours) of 1.9 patients will attend during the extended daily working hours, equivalent to 0.36 patients per week.
  e. Thus the *cost per scan during the extended opening hours* is equal to [((£644*2) / 0.36) + £244 + £57] = £3,878. Note that this is calculated on the basis that all costs of extending the opening hours are attributable to diagnosing suspected MSCC patients, as described earlier in the methods section under the 'exclusivity assumption'.

Tertiary treatment centre costs

The costs of emergency transfers to tertiary treatment centres were assumed to be £247 per transfer, on the basis of HRG PSTEU – Paramedic emergency transfers in an urban setting. The call out costs for a radiographer was assumed to be £42 per scan as per scenario 2a. The additional costs of calling out a neuroradiologist were not included as they were already assumed to be on call.

Results and sensitivity analysis

Results are presented as expected costs, QALYs and ICERs for each treatment strategy. An ICER is defined as the difference in health benefits between the strategies divided by the difference in the clinical benefits. This is the traditional method of presenting the results of economic evaluations.

A number of sensitivity analyses (where input variables are changed, the model re-run and a revised ICER calculated) were undertaken to highlight the variables that were the most important in terms of determining the cost-effectiveness of treatment.

Results

Results from the baseline analysis are shown in Table A1.3. The results show that the marginal benefits of moving across the strategies are relatively modest, but that the ratio of marginal benefits to costs of moving to scenario 2a from scenario 1a, and to 2b from 2a, are beneath NICE's considered willingness to pay for an extra QALY range of £20,000–£30,000 per QALY level. The base case results also show that scenarios 1b and 3 are 'dominated' by other scenarios meaning that in the baseline analyses, they cannot be considered to be cost-effective options.

[3] Attributing the additional costs only to the periods of additional / extended hours, rather than averaging across all opening hours, is consistent with the marginal cost principle and thus is correct.

[4] Note that 19 patients is a maximum number of patients, as data for 7 of the patients had yet to be fully analysed.

Table A1.3 Base case results

Scenario	Expected Costs	Expected QALYs	ICER*
1a	£18,431	0.26	–
2a	£18,591	0.28	£7,726
2b	£19,256	0.35	£9,785
1b	£19,269	0.35	Dominated**
3	£19,383	0.30	Dominated**

*Exact results may vary due to rounding expected costs and QALYs

**'Dominated' in this instance means that other scenarios are associated with more or the same number of QALYs but at less cost

The results from the sensitivity analyses are shown in Tables A1.4–10. Although they show that the expected costs and QALYs, and to a lesser extent the associated ICERs, are relatively labile, the ordering of the scenarios is relatively constant and consistent with the base case results. That is, scenario 2b appears to be the most cost-effective option in most of the analyses. Indeed, 2b remains the most cost-effective option (at a £30,000 per additional QALY threshold) even if the prior/prevalence of MSCC in suspected patients is as low as 6%. Moreover, in most of the results, scenarios 1b and 3 are shown not to be cost-effective. Changing the utility associated with the health state not-ambulant from 0.4 to 0.1 had negligible affect on the base case ICER. The same is true for the survival time associated with this health state. This is because patients in all scenarios who enter the health state not-ambulant, only remain in it for relatively short periods of time. Indeed, both variables only become a significant predictor of the cost-effectiveness ratio if it was firstly assumed that patients ambulant post surgery remained so until death.

Table A1.4 Sensitivity analysis – halving the costs of a MRI scan (£1,939 instead of £3,878) for scenario 3

Scenario	Expected Costs	Expected QALYs	ICER	ICER*
1a	£18,431	0.26	–	–
2a	£18,591	0.28	£7,726	£7,726
3	£19,044	0.30	£23,607	ED
2b	£19,256	0.35	£4,444	£9,785
1b	£19,269	0.35	Dominated	Dominated

*A second set of ICERs are calculated in this scenario because at least one of the scenarios is 'extendedly dominated' (ED) by a blend of other scenarios. In this example, scenario 3 is extendedly dominated by a blend of scenarios 2a and 2b. ED means that a preferable ratio of benefits to costs can be achieved by 'skipping over' an existing option.

Table A1.5 Sensitivity analysis – doubling the costs of radiographer over time (£82 instead of £42) for scenario 2a and 2b

Scenario	Expected Costs	Expected QALYs	ICER
1a	£18,431	0.26	–
2a	£18,601	0.28	£8,200
2b	£19,306	0.35	£10,241
3	£19,383	0.30	Dominated
1b	£19,269	0.35	Dominated

Table A1.6 Sensitivity analysis – halving the prior prevalence of MSCC in patients attending a DGH (0.185 instead of 0.37)

Scenario	Expected Costs	Expected QALYs	ICER
1a	£14,616	0.30	–
2a	£14,708	0.31	£8,856
2b	£15,155	0.35	£12,974
1b	£15,159	0.35	Dominated
3	£15,437	0.32	Dominated

Table A1.7 Sensitivity analysis – increasing the utility of being ambulant post treatment (0.8 instead of 0.7)

Scenario	Expected Costs	Expected QALYs	ICER
1a	£18,431	0.29	–
2a	£18,591	0.31	£6,670
2b	£19,256	0.39	£8,562
1b	£19,269	0.39	Dominated
3	£19,383	0.33	Dominated

Table A1.8 Sensitivity analysis – increasing the probability of not being ambulant post treatment if treated immediately (50% instead of 37.5%)

Scenario	Expected Costs	Expected QALYs	ICER
1a	£18,431	0.26	–
2a	£18,560	0.27	£8,047
2b	£19,138	0.33	£10,467
1b	£19,142	0.33	Dominated
3	£19,329	0.29	Dominated

Table A1.9 Sensitivity analysis – doubling the time to paraplegia following successful treatment (1.22 years instead of 0.61 years)

Scenario	Expected Costs	Expected QALYs	ICER	ICER
1a	£19,347	0.40	–	–
2a	£19,643	0.44	£7,161	£7,161
3	£20,562	0.48	£23,934	ED
2b	£20,771	0.58	£2,107	£8,191
1b	£20,775	0.58	Dominated	Dominated

Table A1.10 Sensitivity analysis – assuming it costs £432 (NHS HRG HC21A) per inpatient day for people who have to wait for a MRI.

Scenario	Expected Costs	Expected QALYs	ICER	
1a	£19,100	0.26	–	
2a	£19,167	0.28	£2,756	ED
2b	£19,265	0.35	£1,421	£1,729
1b	£19,269	0.35	Dominated	Dominated
3	£19,630	0.30	Dominated	Dominated

Discussion

The aim of this analysis was to assess the cost-effectiveness of extending/altering MRI scanning hours for people with suspected MSCC who arrive at DGHs. The results from the analysis suggests that there could be economic merit in scanning suspected patients sooner rather than later if the resources required to do this are only employed when required (ie. paying over time to staff), rather than being permanently on station. Moreover, that this option should be explored prior to transferring patients to tertiary centres for diagnosis and treatment, but in its absence, transferring patients is the next economically viable option. The analysis also showed that in virtually no circumstance was extending MRI scanning hours purely for the benefit of suspected MSCC patients cost-effective. This is perhaps an artefact of the assumptions used to cost this service, but reflects the fact that MSCC is a relatively rare condition meaning that the additional costs incurred opening for longer hours is shared by a relatively small number of patients.

Having said this, the results from the sensitivity analysis show that the cost-effectiveness ratios are dependent on a number of assumptions and variables for which the evidence is relatively poor. For example, the model is underpinned by the notion that faster access to diagnosis and treatment ultimately leads to improved health outcomes. While there is reasonable clinical evidence to show that better health outcomes are achieved if patients are ambulant rather than immobile prior to decompression treatment, there is almost no evidence that has specifically quantified the impact of faster access to diagnosis and treatment. Thus, these results must be treated with a certain degree of caution.

One of the particular difficulties of undertaking this analysis was estimating the costs of extending scanning hours – the results from the sensitivity analysis clearly show that cost-effectiveness of scenario 3 is highly dependent on this variable. This is because there is no (published) information on MRI cost functions (that is, the relationship between inputs and outputs) and the additional costs are clearly dependent on existing service configurations. Thus one units extended hours might already represent another unit's standard working hours and even defining what is meant by extended hours is in itself problematic. It should be noted therefore, that the additional costs of extending standard working hours have been based exclusively on expert opinion rather than on data per se and the analysis has been restricted to the consideration of five scenarios, which were discussed with relevant GDG members. A more robust analysis of the costs and effects of extending MRI opening hours could benefit from a specially commissioned primary analysis of MRI cost data.

As described in the methods section, the assumption was made that all of the additional costs of extending scanning hours (for scenario 3) were attributable to patients with suspected MSCC. While in the context of performing an analysis for a MSCC specific clinical guideline, this approach was considered to be the most appropriate approach[5], it is clearly unrealistic as the costs are likely to be shared across the many patient groups who utilise the service. While it is not precisely clear which other patient groups are likely to be involved, it is likely that suspected MSCC patients will be a small minority. Thus, while the base case analysis suggests that dedicated extended opening scanning hours for suspected MSCC patients is probably not cost-effective, this does not mean to say that patients with suspected MSCC should not be scanned urgently if extended opening hours *are already* in place as the additional costs of doing so are likely to be much smaller than estimated in this analysis.

The analysis includes the costs of staffing the MRI clinic, the MRI scan itself, the costs of undertaking any subsequent treatment and the costs associated with the resulting health states (that's, whether a person is ambulant or not ambulant post treatment). However, it does not include the potential costs of calling in surgical staff out of hours as it is understood that in most tertiary centres they are already on call, thus the expense has already been incurred. Similarly the inpatient costs of having to wait until the next day or until after the weekend have not been included in the analysis. However, including them would only increase the cost-effectiveness of

[5] Because the guideline can only include recommendations with respect to MSCC patients and consideration of other patients would require recommendations for these additional patient groups to be made

some of the scenarios, including 2b. Thus while it is feasible that the ordering (in terms of cost-effectiveness) may alter, scenario 2b will remain the option of choice.

A number of other assumptions that are implicit in the analysis require highlighting. The analyses involving scenario 2a assume that people with suspected MSCC are slotted onto the day's scanning list whenever feasible. Moreover, that this is achieved at the expense of delaying scanning for other non-MSCC patients *at no health consequence to them*. Whether this is an accurate assumption or not clearly depends on the type of patient(s) who are required to wait. But as the incremental health benefits associated with scenario 2a are relatively small (0.02 QALYs), any dis-benefit experienced by other patients as a consequence of having to wait longer for a scan could easily cause the this over-time scenario to become a non-cost-effective option. Similarly, it has been assumed that patients transferred to tertiary centres do not experience any dis-utility associated with travelling, and that travelling does not affect treatment outcome.

In summary, the results from this model and base case analysis suggest that scanning patients with suspected MSCC outside of standard working hours is cost-effective in some circumstances. However, it should be noted that the clinical evidence on which the cost-effectiveness estimates have been based is poor.

References

Bach F *et al.* (1990) Metastatic spinal cord compression *Acta Neurochirurgica* 107: 37–43.

Conway R *et al.* (2007) What happens to people after malignant cord compression? Survival, function, quality of life, emotional well-being and place of care 1 month after diagnosis *Clinical Oncology* 19(1): 56–62.

Falicov A *et al.* (2006) Impact of surgical intervention on quality of life in patients with spinal metastases *Spine* 31(24): 2849–2856.

Hollingworth W *et al.* (2003) Rapid magnetic resonance imaging for diagnosing cancer-related low back pain: a cost-effectiveness analysis *Journal of General Internal Medicine* 18: 303–312.

Huinink M and Glasziou P (2001) Decision making in health and medicine Cambridge: Cambridge University Press.

Husband DJ (1998) Malignant spinal cord compression: prospective study of delays in referral and treatment *BMJ* 317(7150): 18–21.

Lu C *et al.* (2005) Suspected spinal cord compression in cancer patients: A multidisciplinary risk assessment. *Journal of Supportive Oncology* 3(4): 305–312.

Maranzano E *et al.* (1998) Comparison of two different radiotherapy schedules for spinal cord compression in prostate cancer *Tumori* 84(4): 472–477.

Patchell RA *et al.* (2005) Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial *Lancet* 366(9486): 643–648.

Prasad, D and Schiff D (2005) Malignant spinal-cord compression. *Lancet Oncology* 6(1): 15–24.

Thomas K, Nosyk B, and Fisher CG (2006) Cost-effectiveness of surgery plus radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression *International Journal of Radiation Oncology Biology Physics* 66: 1212–1218.

Appendix 2

An example of a patient information leaflet

Name:

Consultant:

Sometimes when people have cancer it can spread to the spinal column and cause the spinal nerves to be squeezed. This leaflet is not intended to scare you but to help you recognise the important symptoms to report early so that tests and treatment may be done as soon as possible. When the spinal nerves are squeezed it can cause damage to the spinal cord to the point of complete paralysis from the neck, chest or waist down. This is quite rare, and unlikely to affect you, but it is very important to pick it up quickly as the earlier treatments are started the better the result usually is.

Symptoms to watch out for:

- Back pain in one bit of your spine that is severe, distressing or different from your usual pain (especially if it affects the upper spine or neck).
- Severe increasing pain in the spine that changes with lying down or standing up, when lifting or straining, wakes you at night or prevents sleep.
- Pain which starts in the spine and goes around the chest or abdomen.
- Pain down the leg or arm.
- A new feeling of clumsiness or weakness of the arms or legs or difficulty walking.
- Numbness in the arms or legs.
- Difficulty in control of your water or bowels.

If you have any of the above symptoms:

- Speak with a doctor, nurse or paramedic as soon as is practical (certainly within 24 hours).
- Tell them that you have cancer, are worried about your spine and would like to see a doctor.
- Show the doctor this card.
- Try to bend your back as little as possible.

For the doctor or healthcare professional

- This patient has cancer and is therefore at risk of metastatic spinal cord compression (MSCC).
- If they have any of the symptoms on the front of this card then please consider MSCC as a possible diagnosis and discuss further management with the local MSCC Coordinator (telephone XXXXXXX).

Appendix 3

Tokuhashi scoring system: A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis Spine 2005, 30 (19), 2186–2191

Table 2 Evaluation System for the Prognosis of Metastatic Spine Tumors

Characteristic	Score
General condition (performance status)	
Poor (PS 10–40%)	0
Moderate (PS 50–70%)	1
Good (PS 80–100%)	2
Number of extraspinal bone metastases foci	
≧3	0
1-2	1
0	2
Number of metastases in the vertebral body	
≧3	0
2	1
1	2
Metastases to the major internal organs	
Unremovable	0
Removable	1
No metastases	2
Primary site of the cancer	
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	0
Liver, gall bladder, unidentified	1
Others	2
Kidney, uterus	3
Rectum	4
Thyroid, breast, prostate, carcinoid tumor	5
Palsy	
Complete (Frankel A, B)	0
Incomplete (Frankel C, D)	1
None (Frankel E)	2

Characteristic	Score
Criteria of predicted prognosis:	
Total Score (TS) 0–8 < 6 months,	
TS 9–11 ≥ 6 months,	
TS 12–15 ≥ 1 year	

This table has been reproduced from: Tokuhashi, Y., Matsuzaki, H., Oda, H., Oshima, M. & Junnosuke, R. A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis. Spine 2005, 30 (19), 2186–2191 with permission from Lippincott Williams and Wilkins Publishers. Corrections have been made with permission from Yasuaki Tokuhashi MD.

Appendix 4

An economic evaluation of treatments for people with suspected metastatic spinal cord compression

Introduction

Without treatment virtually all the patients with metastatic spinal cord compression (MSCC) will become paraplegic and will have limited survival (Kwok *et al* 2006). There is the general belief among the clinical community that surgery for MSCC patients may prevent paraplegia. Preventing paraplegia may be worth doing (despite high overall costs of the surgical procedures) if the health benefits derived from it are large enough. The decision about what treatment modality is adequate for an MSCC patient depends on the patient's clinical characteristics, such as whether there is neurological compromise, pain, or whether tumours are radiosensitive or not. In the treatment of patients threatened with paraplegia radiotherapy (RT) is relatively cheap and may be given in a single palliative dose for pain control, although more commonly it requires two or more weeks of daily treatments in an attempt to prevent disease progression to paraplegia. Around 70% of patients are able to walk after RT, and the median duration of the functional improvement is 3.5 months approximately, although there are some side effects related to treatment with RT, such as toxicity (Maranzano *et al* 2005). RT alone is not suitable for patients with instability pain, where the addition of vertebroplasty/kyphoplasty may provide vertebral column support by minimalist techniques. Alvarez *et al*. (2003) showed that the proportion of fully ambulant patients after vertebroplasty improved from 38% to 76% (although a study by Fourney *et al.* (2003) showed no statistically significant improvement in ambulant status). Vertebroplasty/kyphoplasty are not suitable for patients where cord compression or paraparesis already exists, and larger operations are required in order to attempt the rescue of people from deteriorating neurological states. Radical surgery for MSCC has been reported to be beneficial, especially for patients who are still ambulant before surgery (Patchell *et al* 2005; Sucher *et al* 1994).

Even if patients who are ambulant before treatment are likely to maintain their ability to walk afterwards, especially after radical surgery, some of them will become paraplegic at some point (Patchell *et al* 2005); therefore, it is important to assess whether the health benefits obtained from these interventions are worth the costs. In addition, there is a group of MSCC patients that are neurologically compromised and have tumours that are not very radiosensitive, for whom it is not clear what the best treatment choice is between the options of RT versus surgery followed by RT. These issues highlight the need of economic analyses to assess the cost-effectiveness of treatments for MSCC patients.

Existing economic evidence

A systematic review of the literature was conducted to identify published economic evaluations that could shed light on the cost-effectiveness of treatments for MSCC patients. In total, three studies were identified: one full economic evaluation (Thomas *et al* 2006) and two published abstracts (Furlan *et al* 2007; Klinger *et al* 2007). All three studies assessed the use of SRT versus RT alone in MSCC patients. None of these studies was conducted in a UK setting and, moreover, limited information was reported for the published abstracts. The clinical evidence used in all these studies was obtained from the randomised controlled trial –RCT- by Patchell and collaborators (Patchell *et al* 2005), which excluded MSCC patients with radiosensitive tumours.

The study by Thomas *et al* (2006) used decision modelling based on Monte-Carlo simulation to estimate the incremental costs per life year gained with SRT compared to RT alone. This study adopted a societal perspective that included medical and non-medical costs (e.g. out-of-pocket expenses related to home care), although indirect costs related to productivity losses were not included. QALYs were not estimated due to the lack of utility data for this group of patients; the absence of a QALY estimation limited the direct usefulness of the study for this guideline since QALY is the measure of health benefit preferred by NICE to make decisions based on cost-effectiveness. The study concluded that SRT "is cost-effective both in terms of cost per additional day of ambulation, and cost per life-year gained" (Thomas *et al* 2006). As the authors mentioned, the cost-effectiveness of SRT compared to RT alone depends greatly on the value that society and patients place on ambulatory function.

The abstract by Furlan *et al* (2007) presented a cost-utility analysis in which the health gains, in terms of QALYs, and the associated costs of SRT, compared to RT alone, were estimated. The study was conducted from the perspective of the public health care insurer and used a decision analytic model to estimate the QALY gains and the costs incurred with SRT versus RT alone. A probabilistic sensitivity analysis based on Monte-Carlo simulation was conducted to assess uncertainty. The authors concluded that adjunctive surgery is cost-effective when compared to RT alone. The other abstract (Klinger *et al* 2007) seemed to be a cost-effectiveness analysis using the same RCT data, and it concluded that SRT is more costly and more effective than the combination of RT and corticosteroids. However, limited information was reported for both abstracts; therefore, it is difficult to assess the reliability of these results and their applicability to the UK context.

Aims

Given the limited cost-effectiveness evidence available on treatments for MSCC patients, two economic assessments were conducted. Based on the hypothesis that surgery for the treatment of MSCC may prevent a number of patients from developing paraplegia, the objective of the first analysis was to identify under what conditions the different types of treatments (including surgery) for MSCC patients would become cost-effective. This was conducted by comparing the costs of potential treatments (i.e. radical or major surgery, vertebroplasty or RT) and the follow-up care associated with them, to the costs of caring for untreated MSCC patients who develop paraplegia. Once these costs were estimated, the specific conditions (in terms of ambulatory rates after surgery, time remaining ambulant after surgery, survival, etc.) were identified that would make these treatments cost-effective compared to no treatment.

In addition, a second analysis was conducted which assessed the cost-effectiveness of radical surgical procedures in combination with RT compared to RT alone for the treatment of MSCC patients that are neurologically compromised and have tumours that are not very radiosensitive. This analysis consisted of adapting to a UK setting the only full economic evaluation available comparing the use of surgery in combination with RT (SRT) versus RT alone for the treatment of MSCC patients (Thomas *et al* 2006). The economic evaluation had been conducted within a Canadian setting and was based on the only available RCT comparing surgery plus RT versus RT alone (Patchell *et al* 2005). A deterministic analytic decision model was used, and the incremental cost per additional day ambulant and per additional life year gained were estimated. An attempt was also made to estimate QALYs and the incremental cost per QALY gained with SRT compared to RT.

The perspective adopted in both analyses was that of the National Health Service (NHS) and Personal Social Services, which meant that all the costs and health consequences to be included were those relevant to the NHS. Costs were estimated based on 2006–2007 prices. A lifetime horizon was considered for the estimation of costs and health benefits in both assessments.

Costing paraplegia and treatment options for MSCC patients

Methods

Introduction

For the first economic analysis, the costs of treatment and follow-up care of the potential treatments for MSCC patients were compared to those of caring for untreated MSCC patients who develop paraplegia in order to identify under what conditions (mainly in terms of ambulatory rates after surgery, time remaining ambulant after surgery and survival) the potential treatments for MSCC would become cost-effective. For this, the types of patients included in the analysis and their corresponding potential appropriate treatments were identified, and the costs associated with each of the identified treatments were estimated. Additionally, it was necessary to identify baseline values for the ambulation rates, the time remaining ambulant and the mean survival after the different types of treatments so that an accurate costing of the post-hospitalisation health care cost could be conducted. Threshold analyses were then undertaken to identify the values of these parameters (i.e. ambulation rates, time remaining ambulant and average survival) that would make the potential treatments cost-effective when compared to no treatment.

Patient population and interventions

Only patients that were ambulant at the time of treatment were considered in this analysis. Three independent assessments were conducted within this study, based on the potential treatments available for the different types of patients (i.e. RT, vertebroplasty or major/complex surgery), which were chosen according to patients' characteristics and surgeon's judgement:

1. RT versus no treatment: for patients ambulant at presentation, who have multiple metastasis without immediate potential for mechanical or neurological compromise but who are at risk of developing paraplegia, or for those patients with radiosensitive tumours (such as lymphoma, myeloma and germ cell tumours) in whom surgery is not necessary.
2. Vertebroplasty in combination with RT versus no treatment: for patients ambulant at presentation, with spinal pain and/or vertebral collapse from metastasis but with no evidence of MSCC or spinal instability. The interest in vertebroplasty was based on the belief that this is a less costly option to perform than major surgery and it can prevent paraplegia if performed at an early stage.
3. Major/complex surgery in combination with RT versus no treatment for patients presenting ambulant to the hospital with a general health condition good enough as to undergo surgery and who had a good prognosis, i.e. at least 12 weeks of life expectancy.

Cost estimation

The relevant cost categories included were identified by personal communication with the collaborating GDG members and from the published literature on MSCC treatment interventions and prognosis. Some of the systematic reviews of the clinical evidence conducted within the MSCC Guideline were consulted as well, mainly those related to MSCC preventative treatments (i.e. vertebroplasty/kyphoplasty), surgical treatments and RT. The cost categories included in the analysis were: cost related to the administration of RT (including the cost of treating RT-related complications); surgery costs (including the cost of transferring the patient for surgery, the cost of pre-surgical computed tomography-guided biopsy, pre- and post-operative visits required, the use of the surgical theatre and the time of the staff involved in the surgical procedure, the cost related to the length of stay –LOS- and other consumable costs, such as implants, anaesthetics and blood transfusions); post-treatment costs, i.e. home care and care at the nursing home; and costs related to the care of the patient during the last weeks of life (either at home or at the nursing care home). Table A4.1 presents a detailed description of the resources used, the unit costs and the average costs per patient associated with each type of treatment and subsequent follow-up care.

The costs of RT were estimated based on the cost per fraction of complex RT as provided by the University Hospital in Birmingham. The average cost per patient related to RT administration was estimated to be £1,250 (assuming that 5 RT fractions per patient were administered). The cost of RT-related complications was based on the information provided in the economic model by Thomas *et al* (2006), according to which, the probability of major complications was 2.1%, while the probability of minor complications was 27.3%. Major complications included a combination of myelopathy, vertebral fracture and neurodeficit while minor complications included a combination of nausea, bone pain, diarrhoea or esophagitis. The total cost of RT per patient, including both administration of RT and treatment of major and minor complications, was £1,276.50.

The categories of costs considered in the costing of surgeries (i.e. major surgery and vertebroplasty) were as follows: transfer costs, cost of CT-guided biopsy, pre- and post-operative visits by the surgeon and the anaesthetist, theatre use and staff time during the procedure, consumables (i.e. implant costs, blood transfusions and anaesthetics) and LOS. The measurement of the resources consumed for surgical procedures was based, whenever possible, on the data from an audit conducted at the Royal Orthopaedic Hospital (ROH) in Birmingham, which included 56 MSCC patients who underwent these surgical procedures at ROH between June 2006 and October 2007. The audit provided resource consumption related to surgical costs and consumables mainly (i.e. transfer costs, cost of CT-guided biopsy, theatre time, implant costs and LOS). The number and specialisation of the surgical staff involved in the surgical procedures was identified by personal communication with the GDG members, and included: a surgeon, an assistant registrar, an anaesthetist, an anaesthetist SpR, an anaesthetist's assistant, a scrub nurse, an off-table nurse and an auxiliary. The average surgical cost per patient undergoing vertebroplasty was £9,350 while that for a patient undergoing major surgery was £13,094.

In relation to the post-treatment, follow-up care, there is not clear pattern of care for MSCC patients after treatment. It was common belief among the GDG members that patients ambulant after treatment are most likely to be discharged home, and this was confirmed by the ROH audit (with around 85% of patients ambulant post-treatment being discharged home after surgical treatment). On the other hand, patients non-ambulant after treatment are likely to be cared at home if the family can fill in the gaps in between the community care visits, otherwise it is likely that, if the patients are bed-bounded, they will be institutionalised in a nursing care home (if beds are available), otherwise they may remain in hospital (often in an acute bed if non-acute facilities are scarce in the area) until they die. Based on this, it was assumed that all patients ambulant after treatment were discharged home, and the type of care received included community nurse visits, access to the GP and out-of-hours services, and rehabilitation. On the other hand, patients non-ambulant after treatment were assumed to be discharged either home or to a nursing care home (50/50 respectively, taken as an arbitrary value since no information was available to inform this proportion). The type of care received by post-treatment non-ambulant patients discharged home included community nurse visits, care from the social services, and access to the GP and out-of-hours services. The total daily cost per patient cared at home was £13 if the patient was ambulant and £193 if the patient was non-ambulant. The daily cost for being cared at a nursing home was £81.

The cost of eventual care during the last weeks of life was assumed to depend on whether the patient was cared at home, or at a nursing care home. Following previous assumptions, patients that were ambulant after treatment were assumed to be cared at home until the end of their lives, while it was assumed that half of the non-ambulant patients were cared at home, and the other half at a nursing care home during the last weeks of their life until they died. The amount of time corresponding to end of life care was assumed to be the last two weeks of life. The average daily cost per patient for the end of life care was £274 if cared at home, and £81 if cared at the nursing care home.

Table A4.1 Cost estimation of MSCC treatments and subsequent follow-up care.

	Resource use	Unit costs (£2006/07)	Estimated cost per patient (£2006/07)	Source
	Mean (95% CI)	Mean	Mean (range)	
RT:				
Fractions	250	5	1250	University Hospital Birmingham 2007
Major complications	0.021	605.47	13	Thomas *et al* 2006; OECD PPP
Minor complications	0.273	50.48	14	Thomas *et al* 2006; OECD PPP
Vertebroplasty:				
Transfer rates	0.5	257	129	ROH audit, PSSRU 2007
Pre- and post-operative visits: surgeon	2	77.5	155	Expert opinion, PSSRU 2008
Pre- and post-operative visits: anaesthetist	2	58.125	116	Expert opinion, PSSRU 2009
CT-guided biopsy	0	864	0	ROH audit
Theatre time per patient (hours)	2.72	79.27	215	ROH audit, Rivero-Arias *et al* 2005
	(1.93, 3.50)			
Theatre personnel*	–	–	2547	Expert opinion, ROH audit, PSSRU 2007
Anaesthetics*	–	–	25	ROH audit, Rivero-Arias *et al* 2005
Implants	–	–	2696	ROH audit
Blood transfusions (units of red cell)	3	127.61	383	Expert opinion; Blood & Components price list 2004/5, PSSRU 2007 to update to 2006/2007
LOS in HDU†	1	900	900	Expert opinion, PSSRU 2008
LOS in acute bed†	8.27	264	2184	Expert opinion, ROH audit, PSSRU 2007
Total cost of surgery			9350	
Major surgery:				
Transfer rate	0.5294	257	136	ROH audit, PSSRU 2007
Pre- and post-operative visits: surgeon	2	77.5	155	Expert opinion, PSSRU 2008
Pre- and post-operative visits: anaesthetist	2	58.125	116	Expert opinion, PSSRU 2009
CT-guided biopsy	0.3	864	259	ROH audit
Theatre time per patient (hours)	4.11	79.27	326	ROH audit, Rivero-Arias *et al* 2005
	(3.61, 4.60)			
Theatre personnel*	–	–	3852	Expert opinion, ROH audit, PSSRU 2007
Anaesthetics*	–	–	38	ROH audit, Rivero-Arias *et al* 2005
Implants	–	–	3311	ROH audit

	Resource use	Unit costs (£2006/07)	Estimated cost per patient (£2006/07)	Source
	Mean (95% CI)	Mean	Mean (range)	
Blood transfusions (units of red cell)	3	127.61	383	Expert opinion; Blood & Components price list 2004/5, PSSRU 2007 to update to 2006/2007
LOS in HDU†	1	900	900	Expert opinion, PSSRU 2008
LOS in acute bed†	13.71	264	3619	Expert opinion, ROH audit, PSSRU 2007
Total cost of surgery			13094	
Home care:				
Daily home care costs per ambulant patient	–	–	13	Expert opinion for quantities used; PSSRU 2007 costs for unit costs per hour
Daily home care costs per non-ambulant patient	–	–	193	Expert opinion for quantities used; PSSRU 2007 costs for unit costs per hour
Nursing care home:				
Daily care per patient	–	–	81	www.jrf.org.uk/knowledge/findings/socialcare/612.asp
Care during the last weeks of life				
Daily cost per patient cared at home			274	Expert opinion for quantities used; PSSRU 2007 costs for unit costs per hour
Daily cost per patient cared at nursing care home			81	www.jrf.org.uk/knowledge/findings/socialcare/612.asp

* Based on average time spent at the surgical theatre

† From the total LOS, it was assumed that one day was spent at the HDU and the rest in acute bed

Clinical evidence and assumptions related to the effectiveness of the alternative treatments and the resulting quality of life

In order to be able to estimate the average cost per patient incurred with each of the alternative treatments mentioned above (RT, vertebroplasty, major surgery, or no treatment) it was necessary to identify some initial clinical data in terms of the successful rates of the different options to keep patients ambulant after treatment, and in terms of the survival of patients depending on whether they were ambulant or non-ambulant after treatment. This allowed a more accurate allocation of the different health care costs according to the survival of patients and the different intensities of care required because of their functional status. An initial analysis was undertaken, which was based on what has been called here the 'ideal scenario'. This 'ideal scenario' aimed to reflect a situation where the different treatments would lead to the most favourable outcomes after treatment (in terms of ambulation rates after treatment and time retaining ability to walk). From there, the values for the clinical parameters could be changed to identify how effective the different types of treatments should be in improving ambulation, survival and quality of life by preventing paraplegia in MSCC patients in order to make those treatments cost-effective.

Based on expert opinion, it was assumed that all the patients were ambulant at presentation. In the 'ideal scenario' the success rate of treatment (RT, vertebroplasty and of major surgery), in terms of the number of patients ambulant after treatment, was assumed to be 100%. All patients

ambulant after treatment were assumed to remain ambulant during their entire survival, independently of the treatment received. Patients not receiving any treatment were assumed to become paraplegic within 24 hours. This was because treatment is usually conducted on the brink of paraplegia, although the clinical belief is that if treatment could be conducted before paraplegia occurs, there would be costs avoided by preventing some patients becoming paraplegic. In this situation, the health benefits for the patients would improve because the life expectancy and the quality of life are better for ambulant patients versus those non-ambulant. In terms of the procedure-related mortality rates, under the initial, ideal scenario it was assumed that there would be no deaths due to the different treatments undergone. This is actually not a realistic assumption and was therefore tested in further analysis by substituting the assumption with published clinical evidence. The information on mean survivals reported in the study by Thomas *et al* (2006) was used to identify survival for patients ambulant and non-ambulant after treatment. In this study, which was based on the RCT by Patchell *et al* (2005), the mean survival per patient was 351.96 days (i.e. 11.57 months) for patients undergoing surgery plus RT and 216.86 days (7.13 months) for patients undergoing RT alone. According to expert opinion, all groups can be regarded for this initial analysis as surviving for a similar time, regardless of the treatment received (since survival is determined by histology rather than intervention) and whether they were ambulant or not after treatment, and it was assumed to be equal to 11.57 months (Thomas *et al* 2006). No studies were found that reported specific average survival for patients non-ambulant after major surgery. However, following recommendations of the GDG members, the survival of patients non-ambulant after treatment or after doing nothing can be considered as similar to that of the ambulant patients since it was highlighted that, in general terms, treatment improves ambulation rates while survival may remain the same. Mean time to paraplegia and mean survivals rather than medians were used in the analysis since "the decision about whether an intervention is cost-effective is made on the basis of the expected costs and effects at the population level" (Griffin *et al* 2006). The values of the clinical parameters and assumptions made for the initial, ideal scenario have been presented in Table A4.2.

Table A4.2 Values of the clinical parameters used in the analysis.

Parameter	Ideal scenario	Scenario 2: Sensitivity analysis	Sources
Procedure-related mortality rate			
After vertebroplasty	0	0.05	Assumption/Assumption
After major surgeries	0	0.05	Assumption/Witham 2005
After RT	0	0	Assumption/Assumption
Post-treatment ambulant status			
Proportion of ambulant patients after vertebroplasty	1	0.94	Assumption/Assumption
Proportion of ambulant patients after major surgeries	1	0.94	Assumption/Patchell 2005
Proportion of ambulant patients after RT	1	0.74	Assumption/Patchell 2005
Time to paraplegia for post-treatment ambulant patients (in months)			
After vertebroplasty	11.57	7.26	Assumption/Assumption
After major surgeries	11.57	7.26	Assumption/Patchell 2005
After RT	11.57	2.56	Assumption/Patchell 2005
After doing nothing	0.00	0.00	Assumption/Assumption
Survival for post-treatment ambulant patients (in months)			
After vertebroplasty	11.57	11.57	Assumption/Assumption
After major surgeries	11.57	11.57	Thomas 2006/Thomas 2006
After RT	11.57	7.13	Assumption/Thomas 2006

Parameter	Ideal scenario	Scenario 2: Sensitivity analysis	Sources
Survival for non-ambulant patients (in months)			
After vertebroplasty	11.57	11.57	Assumption/Assumption
After major surgeries	11.57	11.57	Thomas 2006/Thomas 2006
After RT	11.57	7.13	Assumption/Thomas 2006
After doing nothing – compared to vertebroplasty	11.57	11.57	Assumption/Assumption
After doing nothing – compared to major surgery	11.57	11.57	Assumption/Assumption
After doing nothing – compared to RT	11.57	7.13	Assumption/Assumption

Regarding the utility weights to use in the analysis in order to estimate QALYs, one study was found that assessed the health-related quality of life of patients with MSCC that underwent surgery (Falicov *et al* 2006). The results of this study showed that at 1 year after MSCC surgical intervention, the two most common utility values reported by patients were 0.1 and 0.7. Although there was no evidence in the paper to make any reliable interpretation about the type of patients that would be reporting such values, the following assumptions were made for the purpose of this modelling exercise:

1. The utility value for people who were not ambulant was assumed to be 0.1.
2. The utility value for people who were ambulant was assumed to be 0.7.

Based on this interpretation, the previous values were used for the analysis in the following terms: a utility of 0.7 was assigned to those patients ambulant after treatment while a utility of 0.1 was assigned to the non-ambulant patients and to patients at the end of life (i.e. 2 last weeks of life). From the Cost-Effectiveness Analysis (CEA) Registry (https://research.tufts-nemc.org/cear/default.aspx), which provides public electronic access to a comprehensive database of cost-effectiveness ratios in the published medical literature, some other utility weights were found in relation to MSCC patients (Hollingworth *et al* 2003; Hillner *et al* 2000; Blackmore *et al* 1999). The limitation with these utility weights is that they have not been reported according to the functional status of the patients and were not specific for the type of MSCC treatments considered in this analysis.

Structure of the model

A model was developed in Excel to combine the effectiveness and cost data previously described and to conduct all the required calculations and threshold analyses. According to the model structure followed (see Figure A4.1), ambulant patients presenting to the health care centre may be potential candidates for RT, vertebroplasty or major surgery. The alternatives compared are treatment versus no treatment. If patients received appropriate MSCC treatment (i.e. vertebroplasty with RT, major surgery with RT or RT alone), there is a procedure-mortality risk associated. Patients surviving vertebroplasty, major surgery or RT may end up being either ambulant or non-ambulant after treatment and the success of the different treatments will determine how many patients avoid becoming paraplegic. Different successful rates were considered for each treatment (in terms of patients ambulant versus non-ambulant afterwards and in terms of the proportions of patients retaining their ability to walk), and different average survivals as well, depending on whether patients were ambulant or not after treatment. Each of these potential treatments was compared to the no treatment alternative, which comprised only one branch since, as it was assumed in the analysis, all patients ambulant at presentation who were not treated became paraplegic immediately. The model considered a lifetime horizon.

Cost-effectiveness comparisons

The treatments assessed in this study were not options for all types of MSCC patients since the decision about what treatment modality is adequate will depend on the patient's clinical characteristics (e.g. whether MSCC has already developed, whether there is neurological compromise,

pain, or whether tumours are radiosensitive or not). Based on this, three independent cost-effectiveness assessments were conducted, each of them referring to a particular intervention appropriate for a specific sub-group of MSCC patients:

1. RT versus no treatment
2. Vertebroplasty in combination with RT versus no treatment
3. Major/complex surgery in combination with RT versus no treatment

ICERs were calculated for these three sets of comparisons for those cases in which the treatment considered was more effective and, at the same time, more costly than no treatment. Once the ICERs were calculated, threshold analyses were conducted on each of the relevant parameters or set of parameters to identify the values at which each of the treatments (i.e. RT, vertebroplasty or major surgery) would result in an incremental cost per QALY equal or lower than £20,000 versus £30,000 or higher since, following NICE's thresholds for cost-effectiveness interventions, an ICER lower than £20,000 would ensure MSCC treatments to be accepted as cost-effective while ICERs between £20,000 and £30,000 would require strong reasons to consider the interventions cost-effective (Social Value Judgements 2007; document currently under consultation). Estimated health benefits and costs were not discounted since average survival for MSCC patients is short, i.e. around 1 year, and therefore, discounting was considered to be irrelevant for this analysis.

Sensitivity analysis

Some of the assumptions made in the initial, ideal scenario may not reflect accurately the clinical reality of the treatment and prognosis for MSCC patients since such an ideal situation has not been achieved yet in clinical practice. Therefore, alternative scenarios were further considered by modifying some of the relevant assumptions in an attempt to create a more realistic scenario from which to develop further threshold analyses to identify again values of the parameters, under these new, more realistic circumstances, which would lead to the different treatments being cost-effective when compared to no treatment.

Scenario 2:

In this scenario, it was considered that procedure-related mortality could occur. A 5% mortality rate was considered for major surgery (as reported by the study by Witham *et al* 2006). The same mortality rate was assumed for vertebroplasty, and patients undergoing RT were considered not to die from RT treatment. Survival for patients dying because of the surgery was assumed to be null (i.e. in the case of surgical treatment patients would die intra-operatively due to procedure-related complications). The success rate of major surgery to retain the ability to walk of initially ambulant patients was 94.12%, and the same rate was assumed for vertebroplasty; for RT, the rate of patients ambulant after treatment was assumed to be 74.3% (Patchell *et al* 2005). Patients ambulant after treatment were assumed to become paraplegic sometime before dying. As it was reported in the RCT by Patchell *et al* (2005), patients initially ambulant that underwent surgery retained their ability to walk, on median, 153 days (or 220.73 days, on average, following the adjustments proposed by Griffin *et al* 2006 to convert medians to means). On the other hand, patients initially ambulant that underwent RT retained their ability to walk, on median, 54 days (or 77.91 days on average). Given these circumstances, the daily cost of home care for post-treatment ambulant patients was £13 during the period they retained their ability to walk, although this cost increased to £192 once patients became paraplegic.

Survival for patients undergoing surgery remained the same as for the initial, ideal scenario (i.e. 11.57 months) although in this second, more realistic scenario, patients ambulant after RT alone were considered to survive shorter than under the ideal scenario and, on average, 7.13 months (Thomas *et al* 2006). Survival for non-treated patients was assumed to be 11.57 months for comparisons with patients undergoing major surgery or vertebroplasty, and 7.13 months for comparisons with patients undergoing RT. For the threshold analyses on survival times, it was necessary to modify jointly survival and time to paraplegia; to do this, the time to paraplegia was assumed to be a proportion of the total survival for ambulant patients. For example, in the case of major surgery, time to paraplegia was 7.26 months, which represented the 63% of the total survival; then, when survival for ambulant patients after major surgery was modified, the time

to paraplegia was always considered to be 63% of the average survival. The rest of the parameter values remained the same as for the ideal scenario (see Table A4.2).

Results

RT versus no treatment

The results of the analysis based on the 'ideal scenario' showed that no treatment at all would result in higher average costs per patient (£48,673), similar survival (11.57 months) and lower number of QALYs gained (0.10 QALYs) when compared to RT alone (which would cost £9,390 per patient, and would obtain 11.57 months of survival and 0.67 QALYs per patient Table A4.3). Due to the assumptions made in this ideal scenario (i.e. the patient retained her ability to remain ambulant during her entire survival), on average, patients treated with RT remained ambulant 11.57 months, while those not receiving treatment became immediately paraplegic. Therefore, no treatment was a strategy dominated by RT alone under the conditions presented in the ideal scenario.

Table A4.3 Cost-effectiveness results for the ideal scenario and for scenario 2 when RT was compared to no treatment.

	Average cost per patient	Average survival per patient	Average time ambulant per patient	Average QALYs per patient	ICER: Δ Cost per QALY
Ideal scenario					
RT alone	9390	11.57	11.57	0.67	Dominant
No treatment	48673	11.57	0.00	0.10	–
Scenario 2					
RT alone	30523	7.13	1.90	0.15	3309
No treatment	30208	7.13	0.00	0.06	–

Table A4.4 below reports the results of the threshold analyses conducted to identify the extreme values of some of the relevant parameters at which the ICERs would be either lower than £20,000, between £20,000 and £30,000 or higher than £30,000. Under the circumstances presented in the ideal scenario (and assuming that the rest of parameters remained unchanged), RT would result in an ICER lower than £20,000 in the following situations: when the percentage of patients ambulant after treatment was higher than 2.45%; when the average survival for all patients was at least 0.92 months (by considering that survival and time to paraplegia were varied together and the same value was allocated to both of them); and when the time to paraplegia for patients ambulant after RT (when modified independently) was, at least, 3.33 months. On the other hand, uncertainty would exist when: the percentage of patients ambulant after RT ranged between 2.20% and 2.45%; when the average survival per patient (when modified jointly with time to paraplegia for those patients ambulant after RT) was between 0.83 and 0.92 months; and when time to paraplegia for patients ambulant after RT alone (assuming the initial value for survival did not vary, i.e. it was 11.57 months) was between 3.1 months and 3.33 months. Under these circumstances, the ICER related to RT compared to no treatment would range between £20,000 and £30,000, which would mean that strong reasons should exist to recommend RT as a cost-effective option. For lower values of these parameters, the ICER would be higher than £30,000 per QALY gained, which is generally considered as not to be cost-effective.

Table A4.4 Threshold analysis to identify extreme values of parameters that make the ICER for RT cost-effective (i.e. < £20,000), with questionable cost-effectiveness (i.e. £20,000–£30.000), or no cost-effective (i.e. > £30,000) when compared to no treatment under the ideal scenario and under scenario 2

	ICER ≤ £20,000	ICER: £20,000–£30,000	ICER ≥ £30,000
Ideal scenario			
Proportion of ambulatory patients	≥ 0.0245	0.0220–0.0245	≤ 0.0220
Survival for post-treatment patients (in months, modifying jointly time to paraplegia)	≥ 0.92	0.83–0.92	≤ 0.83
Time to paraplegia for post-treatment ambulant patients (in months)	≥ 3.33	3.09–3.33	≤ 3.09
Survival for non-ambulant patients (in months) as a proportion of the ambulant (Scenario 3)	SNF	SNF	SNF
Scenario 2			
Proportion of ambulatory patients	≥ 0.3311	0.2485–0.3311	≤ 0.2485
Survival for post-treatment patients (in months, modifying jointly time to paraplegia)	≥ 3.69	2.86–3.69	≤ 2.86
Time to paraplegia for post-treatment ambulant patients (in months)	≥ 2.23	2.07–2.23	≤ 2.07
Survival for non-ambulant patients (in months) as a proportion of the ambulant (Scenario 3)	≥ 6.59	6.25–6.59	≤ 6.25
Daily costs of home care for non-ambulant patients (£)	≤ 284	284–338	≥ 338
Costs of treatment (£)	≤ 2864	2864–3816	≥ 3816

SNF = Solution not found

When scenario 2 was assessed (which was considered to be more realistic than the ideal scenario), RT was no longer the dominant strategy since it became more expensive than no treatment (£30,523 per patient for RT versus £30,208 per patient for no treatment), although it would still be more effective in terms of time to paraplegia and number of QALYs gained (not in terms of survival since one of the basic assumptions was that survival would be the same, independently of whether treatment was administered or not). Under scenario 2, patients would survive, on average, 7.13 months and they would maintain their ability to walk during only 1.9 months, on average, while the number of QALYs achieved would be 0.15 with RT compared to 0.06 with no treatment (see Table A4.3). Under this scenario, the incremental cost per additional QALY gained with RT, when compared to no treatment, under this scenario, was £3,309. The results of the threshold analysis showed that small variations in the modified variables had a considerable impact on the cost-effectiveness of RT (see Table A4.4). For example, if average patient survival was higher than 3.69 months, then the ICER for RT compared to no treatment would be lower than £20,000, making RT cost-effective according to NICE thresholds. A survival time of less than 2.86 months would make the ICER increase over £30,000. When the time to paraplegia for patients ambulant after RT was longer than 2.23 months, the ICER of RT compared to no treatment was lower than £20,000; for values of the time to paraplegia between 2.07 and 2.23 months, the ICER ranged between £20,000 and £30,000; if the time to paraplegia was shorter than 2.07 months, the ICER would exceed £30,000. Therefore, very small variations in the time to paraplegia have a huge impact on the resulting ICER. This may be due to the fact that caring for patients that are ambulant after RT but that become paraplegic at some point after treatment is expensive and would negatively affect the resulting ICER. Therefore, the longer the patients remain ambulant after RT, the more cost-effective RT will

be when compared to no treatment. If the survival for non ambulant patients was varied independently of that for ambulant patients (the later keeping the initial value for this analysis, i.e. 7.13 months), then non-ambulant patients would need to survive at least 6.59 months for RT to have an ICER lower than £20,000 per QALY gained when compared to no treatment; for values between 6.25 and 6.59 months, the ICER will range between £20,000 and £30,000, while if non-ambulant patients survived for less than 6.25 months, the ICER would be higher than £30,000. Therefore, the longer the survival for non-treated patients, the more cost-effective RT will be due to the fact that caring for a non-ambulant patient is expensive and the differential cost between RT and no treatment will be reduced, reducing therefore the total value of the ICER.

Some further sensitivity analyses were conducted. Under the ideal scenario, if all the parameters remained constant but only the utility weights considered for ambulant patients, non-ambulant patients or patients at the end of their life were changed, no value of these utility weights individually would change the condition of dominance of RT over no treatment: individual changes in these parameters would always lead to an ICER below £20,000 when considering the ideal scenario. However, under scenario 2, if the utility value for patients ambulant after RT was 0.20 or lower, then the ICER would increase over £20,000, while if the utility values for non-ambulant patients and those for patients in the end of life were 0.60 or higher, then the ICER would again be £20,000 or higher, which does not seem to reflect a situation that could be realistically found in clinical practice.

Vertebroplasty versus no treatment

When comparisons between vertebroplasty and no treatment were conducted under the base case scenario, vertebroplasty was not only more effective (in terms of patients retaining longer their ability to walk and in terms of more QALYs gained) but it resulted to be a cheaper option when compared to no treatment (£18,622 versus £48,673, respectively). Therefore, vertebroplasty was the dominant strategy (see Table A4.5 below).

Table A4.5 Cost-effectiveness results for the ideal scenario and for scenario 2 when vertebroplasty was compared to no treatment.

	Average cost per patient	Average survival per patient	Average time ambulant per patient	Average QALYs per patient	ICER: Δ Cost per QALY
Ideal scenario					
Vertebroplasty	18622	11.57	11.57	0.67	Dominant
No treatment	48673	11.57	0.00	0.10	–
Scenario 2					
Vertebroplasty	37749	10.99	6.49	0.42	Dominant
No treatment	48673	11.57	0.00	0.10	–

The results of the threshold analyses when the ideal scenario was considered (see Table A4.6) showed that the ICER for vertebroplasty when compared to no treatment would be under £20,000 for: ambulation rates after vertebroplasty higher than 18.36% (the higher this proportion, the lower the ICER will be and therefore the more cost-effective vertebroplasty will be when compared to no treatment); for average survivals longer than 2.85 months; for times to paraplegia among patients ambulant after vertebroplasty longer than 4.5 months; and for survivals for non ambulant patients of, at least, 1.14 months. If the proportion of patients that are ambulant after vertebroplasty falls under 16.49%, or the overall survival per patient becomes shorter than 2.58 months, or the time to paraplegia for patients ambulant after vertebroplasty decreases to less than 4.18 months, the ICER will exceed £30,000 per QALY gained. Values for this ICER between £20,000 and £30,000 will be obtained when the proportion of ambulant patients ranges between 16.49% and 18.36%, when the overall survival per patient is between 2.58

and 2.85 months, and when the time retaining the ability to walk for patients ambulant after vertebroplasty ranges between 4.18 months and 4.50 months.

Table A4.6 Threshold analysis to identify extreme values of parameters that make the ICER for vertebroplasty cost-effective (i.e. < £20,000), with questionable cost-effectiveness (i.e. £20,000-£30.000), or no cost-effective (i.e. > £30,000), compared to no treatment, under the ideal scenario and under scenario 2.

	ICER ≤ £20,000	ICER: £20,000–£30,000	ICER ≥ £30,000
Ideal scenario			
Proportion of ambulatory patients	≥ 0.1836	0.1649–0.1836	≤ 0.1649
Survival for post-treatment patients (in months, modifying jointly time to paraplegia)	≥ 2.85	2.58–2.85	≤ 2.58
Time to paraplegia for post-treatment ambulant patients (in months)	≥ 4.50	4.18–4.50	≤ 4.18
Survival for non-ambulant patients (in months) as a proportion of the ambulant	≥ 1.14	≤ 1.14	SNF
Scenario 2			
Proportion of ambulatory patients	≥ 0.2715	0.2413–0.2715	≤ 0.2413
Survival for post-treatment patients (in months, modifying jointly time to paraplegia)	≥ 4.06	3.63–4.06	≤ 3.63
Time to paraplegia for post-treatment ambulant patients (in months)	≥ 4.27	3.97–4.27	≤ 3.97
Survival for non-ambulant patients (in months) as a proportion of the ambulant (Scenario 3)	≥ 6.98	6.01–6.98	≤ 6.01
Daily costs of home care for non-ambulant patients (£)	SNF	SNF	SNF
Costs of treatment (£)	≤ 26666	26666–29862	≥ 29862

SNF = Solution not found

When scenario 2 was considered, vertebroplasty still retained its condition of dominant strategy, since it was still less costly than no treatment (£37,749 per patient treated with vertebroplasty when compared to £48,673 per patient not treated), and more effective in terms of time to paraplegia and number of QALYs gained, although not in terms of survival (the average survival resulted to be longer for non-treated patients due to the mortality rate associated to the vertebroplasty procedure). Under scenario 2, patients would survive, on average, 10.99 months if treated with vertebroplasty, and 11.57 months if not treated. This result is an artefact of the assumption considered in the model about equal survival for patients treated and non-treated, while the procedure-mortality rate would reduce slightly the survival for patients treated. Patients treated with vertebroplasty would retain their ability to walk during 6.49 months, on average, and the additional number of QALYs gained with vertebroplasty when compared to no treatment would be 0.32. The results of the threshold analyses for this scenario 2 showed that vertebroplasty will be cost-effective (with ICERs under £20,000) when: the percentage of patients ambulant after treatment would exceed 27.15%; for overall survival longer than 4.06 months; when the average time that patients ambulant after vertebroplasty retained their ability to walk was longer than 4.27 months; and when the average survival for non-ambulant patients was longer than 6.98 months. For success rates between 24.13% and 27.15%, for overall survivals between 3.63 and 4.06 months, for times to paraplegia for patients ambulant after vertebroplasty ranging between 3.97 and 4.27 months, and for survivals for non-ambulant patients between 6.01 and 6.98 months, the ICER will range between £20,000 and £30,000. Therefore, the higher the success rate for vertebroplasty, the overall survival for patients, the time to

paraplegia for patients ambulant after treatment and the specific survival for patients non-ambulant after treatment, the more cost-effective vertebroplasty is. When the success rates for vertebroplasty are under 24.13%, or the overall survival becomes shorter than 3.63 months, or the time to paraplegia becomes shorter than 3.97 months, or the survival for non-ambulant patients decreases to less than 6.01 months, the ICER will be higher than £30,000. Considering variations in the costs of the vertebroplasty procedure only (i.e. cost of the intervention, which was £9,350 under the ideal scenario), any cost of the procedure under £26,666 would make vertebroplasty cost-effective (if all the rest of parameters remained the same), while any cost of the procedure higher than £29,862 would lead to ICER values over £30,000.

In both scenarios, the ideal scenario and scenario 2, the utility weights considered for ambulant patients, non-ambulant patients or patients at the end of their life were changed individually and all the other parameters were left constant (i.e. according to the values chosen for each of the scenarios) to see whether different thresholds for the ICER could be achieved. Overall, no sensible value of these individual utility weights would change the condition of dominance of vertebroplasty over no treatment: individual changes in these parameters would always lead to an ICER below £20,000 per QALY gained.

Major surgery versus no treatment

When comparisons of major surgery versus no treatment were undertaken under the ideal scenario, the overall cost per patient treated with major surgery was £22,299 when compared to £48,673 per non-treated patient. Major surgery resulted in 11.57 months retaining the ability to walk per patient and higher number of QALYs when compared to no treatment (0.67 QALYs versus 0.10 QALYs, respectively; see Table A4.7 below). Therefore, major surgery was a dominant strategy when compared to no treatment.

Table A4.7 Cost-effectiveness results for the ideal scenario and for scenario 2 when major surgery was compared to no treatment.

	Average cost per patient	Average survival per patient	Average time ambulant per patient	Average QALYs per patient	ICER: Δ Cost per QALY
Ideal scenario					
Major surgery	22299	11.57	11.57	0.67	Dominant
No treatment	48673	11.57	0.00	0.10	–
Scenario 2					
Major surgery	40516	10.99	6.49	0.42	Dominant
No treatment	48673	11.57	0.00	0.10	–

The results of the threshold analyses (see Table A4.8) showed that, as long as the percentage of patients that will be ambulant after major surgery is higher than 24.57%, the ICER for the ideal scenario will remain under the threshold of £20,000. If this proportion of patients ranged between 22.04% and 24.57%, then the ICER will be within the range of £20,000 and £30,000, and for any value under 22.04%, the ICER will exceed £30,000. As it would be expected, these results show that the higher the successful rate of major surgery in terms of maintaining ambulance status for patients after treatment, the more cost-effective the intervention will be when compared to no treatment. The ICER of major surgery compared to no treatment would be under £20,000 if the overall survival is, at least, 3.62 months; for survivals between 3.28 and 3.62 months, the ICER would be within £20,000 and £30,000, and for survivals shorter than 3.28 months, the ICER would go beyond the threshold of £30,000. Similarly, the longer the time to paraplegia for patients ambulant after major surgery, the more cost-effective this intervention will be when compared to no treatment. When the time to paraplegia for patients ambulant after major surgery is longer than 4.92 months, the ICER will be lower than £20,000; for values of the time to paraplegia between 4.56 and 4.92 months, the ICER will vary between £20,000 and £30,000; and values of time to paraplegia for patients ambulant after treatment

shorter than 4.56 months will result in ICERs higher than £30,000. On the other hand, the ICER will remain under £20,000 when the survival for non-ambulant patients (i.e. patients non-ambulant after major surgery and patients no treated) is longer than 2.06 months, while for survivals between 0.38 and 2.06 months for these groups of patients, the ICER will range between £20,000 and £30,000, and for survivals lower than 0.38 months, the ICER will overpass the threshold of £30,000 per QALY gained.

Table A4.8 Threshold analysis to identify extreme values of parameters that make the ICER for major surgery cost-effective (i.e. < £20,000), with questionable cost-effectiveness (i.e. £20,000–£30.000), or no cost-effective (i.e. > £30,000) under the ideal scenario and under scenario 2.

	ICER ≤ £20,000	ICER: £20,000–£30,000	ICER ≥ £30,000
Ideal scenario			
Proportion of ambulatory patients	≥ 0.2457	0.2204–0.2457	≤ 0.2204
Survival for post-treatment patients (in months, modifying jointly time to paraplegia)	≥ 3.62	3.28–3.62	≤ 3.28
Time to paraplegia for post-treatment ambulant patients (in months)	≥ 4.92	4.56–4.92	≤ 4.56
Survival for non-ambulant patients (in months) as a proportion of the ambulant (Scenario 3)	≥ 2.06	0.38–2.06	≤ 0.38
Scenario 2			
Proportion of ambulatory patients	≥ 0.3848	0.3416–0.3848	≤ 0.3416
Survival for post-treatment patients (in months, modifying jointly time to paraplegia)	≥ 5.26	4.70–5.26	≤ 4.70
Time to paraplegia for post-treatment ambulant patients (in months)	≥ 4.75	4.41–4.75	≤ 4.41
Survival for non-ambulant patients (in months) as a proportion of the ambulant	≥ 7.71	6.76–7.71	≤ 6.76
Daily costs of home care for non-ambulant patients (£)	SNF	SNF	SNF
Costs of treatment (£)	≤ 27644	27644–30840	30840

SNF = Solution not found

When scenario 2 was considered, the average cost per patient treated with major surgery was still lower than that incurred by a patient not treated (£40,516 versus £48,673, respectively), while major surgery would still be more effective in terms of time to paraplegia and number of QALYs gained (not in terms of survival due to the assumption of similar survivals for all patients and the procedure-related mortality associated with major surgery). Under scenario 2, patients treated with major surgery would retain their ability to walk during 6.49 months, on average, and the additional number of QALYs gained with major surgery when compared to no treatment would be 0.32. Therefore, major surgery will still maintain its condition of dominance in terms of time ambulant and number of QALYs gained (see Table A4.7).

The results of the threshold analyses for scenario 2 showed that major surgery would result in an ICER lower than £20,000 if the success rate for major surgery was over 38.48, if the overall patient survival was longer than 5.26 months; if the time to paraplegia for patients ambulant after major surgery was longer than 4.75 months, or if the survival for non-ambulant and non-treated patients was over 7.71 months. On the other hand, an ICER between £20,000 and £30,000 per QALY would be obtained if the success rates for major surgery were between 34.16% and 38.48%; if the overall patient survival was between 4.70 and 5.26 months; if the time to paraplegia for patients ambulant after major surgery was between 4.41 and 4.75 months;

or if the specific survival for non-ambulant and non-treated patients was between 6.76 and 7.71 months. When the success rate of major surgery was lower than 34.16%, or the overall patient survival was shorter than 4.70 months, or the time to paraplegia for patients ambulant after major surgery was shorter than 4.41, or the survival for non-ambulant and non-treated patients was shorter than 6.76, then the ICERs for major surgery compared to no treatment surpassed the threshold of £30,000. In addition, the cost of the procedure (i.e. major surgery alone) could be as high as £27,644 to make major surgery cost-effective (i.e. with an ICER under £20,000 per QALY), while if this cost was over £30,840, the ICER per QALY would exceed £30,000. When only the utility weights considered for ambulant patients, non-ambulant patients or patients at the end of their life were changed individually (and all the other parameters remained constant), no value of these utility weights individually was found that would change the ICER across the different thresholds set by NICE (i.e. lower than £20,000; between £20,000 and £30,000; and higher than £30,000).

Cost-effectiveness analysis of surgery in combination with radiotherapy (SRT) versus radiotherapy alone (RT): update to the Canadian model to the UK setting

Methods

Introduction

There is a group of MSCC patients that are neurologically compromised and have tumours that are not very radiosensitive, for whom it is not clear what the best treatment choice is between the options of RT versus surgery followed by RT. A second analysis was undertaken to assess the cost-effectiveness of radical surgical procedures in combination with RT (SRT) compared to RT alone (RT) for the treatment of this specific group of MSCC patients. This analysis consisted of adapting to a UK setting the only economic evaluation available comparing these two interventions for the treatment of MSCC patients (Thomas *et al* 2006). This economic evaluation had been conducted within a Canadian setting and was based on the only available RCT comparing SRT versus RT (Patchell *et al* 2005). The aim of our study was to update this Canadian model to reflect the costs that would be incurred if the interventions were conducted in the UK context. For this, the perspective of the National Health Service and the Personal Social Services was adopted.

Patient population and interventions

The patient population considered for this economic evaluation comprises a highly selective group of MSCC patients that are neurologically compromised and have moderately or poorly radiosensitive tumours. Patients with very radiosensitive tumours such as lymphoma, myeloma and germ cell tumours have been excluded from the analysis as surgery in these instances is usually not necessary. The interventions compared in the economic evaluation were: radical surgical decompression in combination with RT (SRT) versus RT alone. As reported in the Canadian paper, 'surgery was performed within 24 h of study entry with the intent to remove as much [tumour] as possible, provide immediate decompression, and stabilise the spine'. A total dose of 30 Gy was administered at 3 Gy per fraction per day. Patients undergoing SRT received RT 2 weeks after surgery (Thomas *et al* 2006).

Clinical evidence

The clinical evidence in terms of effectiveness of SRT versus RT alone used in the economic evaluation by Thomas *et al* (2006) was obtained from the RCT published by Patchell *et al* (2005). The same clinical evidence was considered in the update of the model for the UK setting. The primary endpoint for this RCT was the number of days patients retained their ability to walk after treatment, although survival was assessed as well as a secondary endpoint. For the purpose of our economic evaluation, both time retaining ability to walk and survival were considered as the endpoints for the cost-effectiveness assessment.

In the study by Thomas *et al* (2006), Weibull curves were estimated from the results of the RCT (Patchell *et al* 2005) for both endpoints of the analysis: time retaining the ability to walk and survival, and for each of the treatments assessed (SRT versus RT), the resulting expected days of ambulation and survival have been presented in Table A4.9 below. These values were used as input parameters and endpoints for the model estimating the cost-effectiveness of SRT versus RT in the UK context. Additionally, an attempt was made to estimate the number of QALYs gained with each intervention by using the same utility scores as those used in the previous model (i.e. 0.7 for ambulant patients, and 0.1 for non-ambulant patients).

Table A4.9 Estimated clinical outcomes from Weibull curves.

Clinical outcomes	RT alone	SRT
Expected days of survival (mean)	221.11	377.06
Expected days of ambulation (mean)	92.36	312.47

Source: Thomas *et al* (2006)

Cost analysis

The perspective adopted for the analysis was that of the NHS and Personal Social Services. The price year was 2006–2007. The aggregated categories of costs included in the analysis were: the costs of treatment with SRT, the cost of treatment with RT and the post-treatment costs of caring for patients until they die. These costs were directly derived from the cost analysis conducted in the previous economic analysis. Based on that cost analysis, the average cost per patient undergoing surgery was £13,094 and the average total cost per treatment with RT was £1,276.50. Although the model by Thomas *et al* (2006) included the costs of diagnosing MSCC patients, this cost was excluded from the UK update since it was considered to be the same across both groups of patients (SRT versus RT alone). For the purposes of this analysis, the LOS was obtained from the ROH data rather than from the RCT by Patchell *et al* (2005) to reflect clinical practice in the UK context (see Table A4.1). Similar assumptions to those formulated in the previous economic analysis were considered for this economic evaluation. For example, it was assumed that patients ambulant would be cared at home, at a cost of £13 per day, while patients non-ambulant would be either cared at home or at a nursing care home (50/50 arbitrarily assumed), depending on whether the family could care for the patient in between community visits. The daily cost for being cared at home when non-ambulant was £193 (ROH audit; NHS Reference Costs 2006/07) and £81 if cared at the nursing home (Joseph Rowntree Foundation). Additionally, the period of end of life corresponded to the last 2 weeks lived by the patient. For the last weeks of life it was arbitrary assumed (as it had been done in the previous analysis) that 50% of patients could be cared at home, at a daily cost of £274, otherwise they had to be cared at the nursing care home (again at a cost of £81 per day).

Cost-effectiveness comparisons

The results of the economic evaluation are presented as average costs, average time retaining the ability to walk and average survival per patient, following what had been done in the Canadian model (Thomas *et al* 2006). When applicable (i.e. when one of the treatment strategies was more effective and at the same time more costly than the other), ICERs were estimated. In addition, based on the estimation of the number of QALYs gained following what had been done in the previous model, the incremental cost per QALY gained was also estimated when applicable. It is important to highlight that this was just an attempt to capture QALY gains with SRT and RT, given the limitations presented by the utility scores used. Discounting of health benefits and costs was not necessary given the short survival of these MSCC patients.

Sensitivity analysis

Deterministic one-way and two-way sensitivity analyses were conducted to assess the robustness of the results, which means the values of one or two variables were modified at a time to see if the conclusions of the cost-effectiveness assessment would change when different values of the relevant parameters were considered at analysis. An approximate 95% confidence interval for the average cost of surgery (95% CI: 12,143, 14,048) was obtained from the ROH audit

data and this interval was used as the range of plausible values to consider in the sensitivity analysis. In addition, the cost of MSCC surgery obtained from the Payment by Results (PbR) National Tariffs was also taken into account to see how the results obtained for the base-case analysis changed. Two-way sensitivity analyses were conducted on the average survival and the average time ambulant by considering the 25th and 75th percentiles of the means (Thomas *et al* 2006). The percentage of patients discharged to a rehabilitation care unit after SRT was considered to be 12.5% in a one-way sensitivity analysis. The 95% CI for the LOS was used to assess the impact that modifications on the values of this variable had on the results. In addition, the daily cost of caring at home for a patient non-ambulant after treatment with RT or with SRT was modified upwards and downwards by 25% to see the impact of this change on the final results. Finally, the daily post-hospitalisation care cost for patients treated with either SRT or RT were varied by 25%. Additionally, a threshold analysis was conducted to identify the values of the utility scores that would make SRT either cost-effective (i.e. with an ICER of £20,000 or lower per QALY gained), with questionable cost-effectiveness (with an ICER between £20,000 and £30,000 per QALY gained) or very unlikely to be considered cost-effective at all (i.e. when the ICER was over £30,000 per QALY gained) when compared to RT alone.

Results

The results of the base-case analysis showed that patients treated with SRT would retain their ability to walk for 220 days more when compared to those treated only with RT, while the difference in survival in favour of the SRT group would be of 156 days. The average cost per patient treated with SRT was £27,536, compared to £20,611 in the case of patients treated with RT alone (the costs per category have been presented in Table A4.10). This small difference in costs is believed to be due to the fact that, although the administration of RT by itself is less expensive than the specific cost of surgery, patients treated with RT will become paraplegic earlier and the costs of caring for a non-ambulant patient are more than twice higher than those of caring for an ambulant patient, which is finally reflected in the total cost for the RT alone strategy. Each additional day of ambulation obtained by SRT would cost an extra £31.46 when compared to RT alone, while each additional life year gained with SRT would cost £16,207 extra.

Table A4.10 Baseline results.

Baseline results*	SRT	RT
Surgery costs/hospitalisation costs	13,096	0
RT costs	1,276	1,276
Post-hospitalisation costs	13,164	19,335
Total cost	27,536	20,611
Days ambulant	312.47	92.36
Survival	377.06	221.11
QALYs	0.62	0.21
Δ Cost	6,925	–
Δ Effectiveness – Days ambulant	220.11	–
Δ Effectiveness – Survival	155.95	–
Δ Effectiveness – QALYs	0.41	–
ICER – Days ambulant	31.46	–
ICER – Survival (per day)	44.40	–
ICER – Survival (per year)	16,207	–
ICER – QALYs	17,117	

*Comparisons between SRT and RT
Costs in UK£ 2006/07

A summary table with the resulting ICERs obtained from the one-way and two-way sensitivity analyses undertaken has been presented (see Table A4.11). The results for the incremental cost per life year gained with SRT compared to RT were under £10,000 when: the cost of surgery

was that of the PbRs National Tariffs; non-ambulant patients that could not be cared at home were assumed to remain in the hospital rather than to be cared at a nursing care home; the daily cost of care for a patient after being treated with RT alone increased by 25%; and when the daily cost of care for a patient after being treated with SRT decreased by 25%. On the other hand, ICERs per life year gained over £20,000 were observed for the following scenarios: when the daily cost of care for a patient after being treated with SRT increased by 25%, when the survival and the ambulation time for patients treated with SRT was considered to be equal to the 25th lower percentile; and when the daily cost of care for a patient after being treated with RT alone decreased by 25% (this latter case presented the highest ICER observed in the analysis: £27,520 per additional life year gained with SRT when compared to RT alone.

Table A4.11 Incremental cost per life year gained: results from the baseline and the sensitivity analyses.

Parameters modified	ICER
Baseline Results	16207
One-way sensitivity analysis: surgery – 95% CI upper	18437
One-way sensitivity analysis: surgery – 95% CI lower	13977
One-way sensitivity analysis: surgery – PbR National Tariff for non-elective intervention	1903
One-way sensitivity analysis: patients cared at hospital rather than at nursing care unit	2434
One-way sensitivity analysis: 12.5% of patients cared at rehab care unit included for surgery	18054
One-way sensitivity analysis: LOS – upper 95% CI	17819
One-way sensitivity analysis: LOS – lower 95% CI	14595
One-way sensitivity analysis: daily cost for non-ambulant at home + 25%	12588
One-way sensitivity analysis: daily cost for non-ambulant at home – 25%	19826
Two-way sensitivity analysis: RT:surv/amb lower/p25	13570
Two-way sensitivity analysis: RT: surv/amb upper/p75	18645
Two-way sensitivity analysis: SRT:surv/amb lower/p25	25354
Two-way sensitivity analysis: SRT: surv/amb upper/p75	12925
PH Daily costs for SRT: +25%	23910
PH Daily costs for SRT: –25%	8505
PH Daily costs for RT: +25%	4894
PH Daily costs for RT: –25%	27520

However, the cost per life year gained is difficult to interpret since there is not a threshold identified as cost-effective, as it is the case with the incremental cost per life year gained. Therefore, an attempt was made to estimate the number of QALYs gained with SRT compared to RT alone. When the number of QALYs were estimated based on the utility scores used for the previous model (i.e. 0.7 for ambulant patients and 0.1 for non-ambulant patients) the number of QALYs obtained per patient undergoing SRT were 0.62 compared to 0.21 QALYs obtained by patients with RT alone; therefore, the incremental QALY gained with SRT, compared to RT alone, was 0.41 and the incremental cost per each additional QALY gained with SRT compared to RT alone was £17,117, which was under the threshold identified by NICE for cost-effective interventions (i.e. £20,000 per QALY gained).

Threshold analysis were carried out to identify the values of the utility scores that would make SRT either cost-effective (i.e. with an ICER of £20,000 or lower per QALY gained), with questionable cost-effectiveness (with an ICER between £20,000 and £30,000 per QALY gained) or very unlikely to be cost-effective at all (i.e. when the ICER was over £30,000 per QALY gained) when compared to RT alone (see Table A4.12). When the utility score for ambulant patients was left fixed to a value equal to 0.7, the utility for non-ambulant patients had to be 0.43 or lower so that SRT remained cost-effective, i.e. the ICER obtained per QALY gained remained lower than £20,000. There was not value found for the utility score of non-ambulant patients that would lead to an ICER higher than £30,000 if the utility score for ambulant patients was 0.7.

On the other hand, when the utility score for non-ambulant patients was left fixed to a value equal to 0.1, the utility score for ambulant patients had to be at least 0.60 or higher so that SRT remained cost-effective, i.e. the ICER obtained per QALY gained remained lower than £20,000 when the utility score for ambulant patients was 0.60 or more, or lower than £30,000 if this utility was 0.41 or higher.

Table A4.12 Threshold analysis to identify the extreme values of the utility scores that would make the ICER for SRT cost-effective (i.e. < £20,000), with questionable cost-effectiveness (i.e. £20,000–£30.000), or no cost-effective (i.e. > £30,000) when compared to RT alone.

Utility values		ICER: Δ cost / Δ QALYs
Ambulant	Non-ambulant	
Base-case:		
0.7	0.1	17,117
Threshold analyses:		
0.7	≥ 0.4317	≥ 20000
≤ 0.6033	0.1	≥ 20000
0.7	SNF	≥ 30000
≤ 0.4119	0.1	≥ 30000

SNF = Solution not found

Discussion

Two economic analyses were undertaken in an attempt to shed light about what type of treatments are cost-effective for MSCC patients when compared to either no treatment (which was the aim of the first analysis and focused on comparing RT versus no treatment, vertebroplasty versus no treatment and major surgery versus no treatment), or when two alternative treatments were compared (which was the purpose of the second analysis and compared SRT with RT).

The first analysis identified under what conditions (in terms of rates of success of surgery, time of ambulation, survival and quality of life) vertebroplasty, major surgery or RT would become cost-effective when compared to no treatment. The aim of the analysis was to assess at what point these different interventions would be cost-effective at keeping patients ambulant when compared to no treatment at all: if MSCC patients are left without treatment, they will become paraplegic; then the purpose of the analysis was to identify how long patients would have to survive and to remain ambulant in order to make the treatments worthwhile. Treatment selection was taken out of the economic evaluation by considering that the surgeons would follow the Tokuhashi scores (Tokuhashi *et al* 2005) for the selection of the appropriate treatment according to the patient's clinical status. This meant that, for this first analysis, not all the treatments were alternative options for all the MSCC patients and the decision about what treatment modality was adequate for an MSCC patient was assumed to depend on the patient's clinical characteristics (e.g. whether there is neurological compromise, pain, or whether tumours are radiosensitive or not). Therefore, each assessed treatment was a stand alone intervention in the sense that a specific type of patient could get either a specific type of treatment (lets say RT alone) or no treatment at all, but there was not the option to compare different types of treatments for the same patient. The costs of each treatment and the corresponding follow-up care were compared to the costs of caring for untreated MSCC patients who develop paraplegia, and threshold analysis were conducted to identify extreme values for the ICERs.

It was observed that under the base-case scenario, all three treatments (each for a particular type of MSCC patient) resulted to be dominant interventions (they resulted in higher number of QALYs at a lower cost) when compared to no treatment. Under scenario 2, which was thought to be more realistic (since it included procedure-related mortality and the surgical and RT success rates for patients remaining ambulant after treatment), RT lost its condition of dominant strategy

and presented an incremental cost per additional QALY gained equal to £3,309 when compared to no treatment; this is identified as being cost-effective following NICE's thresholds. For all the comparisons between treatments and no treatment, it was observed that any of these treatments would be more cost-effective in the following situations: the higher the success rate in terms of the percentage of ambulant patients after treatment, the longer the overall survival for patients, the longer the patients remained ambulant after treatment, and the longer the specific survival was for patients non-ambulant after treatment and for those patients non-treated. In some cases very small variations in the values considered for some of the variables modified in the threshold analysis made a considerable impact on the cost-effectiveness of the treatments, passing from thresholds of £20,000 to thresholds of £30,000 per QALY gained without too much variation in the value of the parameter, for example, for small changes in the overall survival post-treatment, and for small changes in the time to paraplegia for patients ambulant after treatment. Based on the assumptions presented under scenario 2 (the scenario considered to be more realistic), patients undergoing major surgery had to survive at least 5.26 months for the ICER to be under the £20,000 per QALY. This seems to be achievable in a UK context. A recently published prospective study conducted in UK (Mannion *et al* 2008) assessed patients with actual or imminent MSCC that were carefully selected to undergo surgical decompression with fixation, when required, followed by RT, according to the severity of paraparesis, pain, primary tumour and the extent of the disease. According to the results observed, the median survival was 13 months and the percentage of patients ambulant after surgery was 80% (compared to 68% before surgery). Additionally, 50% of the patients initially non-ambulant recovered the ability to walk after surgery (i.e. 10 patients out of 20). The authors of this study concluded that careful patient selection can result in successful outcomes after surgery among this patient population.

An additional finding from the threshold analyses was that the higher the survival for non-ambulant patients (including those patients that did not receive treatment), the more cost-effective MSCC treatments will be, since non-ambulant patients surviving longer would incur in high care costs during their survival, increasing the cost of caring for patients not treated. Therefore, it is important to clearly identify what the most likely value for the survival of non-ambulant patients is in reality to get a more accurate idea of the cost-effectiveness of the MSCC treatments when compared to no treatment.

According to the published evidence, the survival of patients is proportional to diagnosis, general health, and neurological ability (e.g., lung cancer has a worse prognosis compared to that of breast or prostate cancer). The analysis here presented did not consider what happens with the cost-effectiveness of the individual treatments assessed when different types of patients, according to their type of tumour, are the basis for the analysis. Moreover, the analyses are based on a series of assumptions; some of them may reflect the reality better than others. The threshold analyses undertaken were conducted to shed light about the uncertainty surrounding assumptions and data.

Some relevant costs were excluded from the analysis, mainly due to the difficulties to obtain some minimally reliable data to incorporate them:

- Intra-operative and post-operative complications, such as wound breakdown, stabilisation failure, wound infections and excessive haemorrhage, which may occur with major MSCC surgery, while leak seems to be a common complication of vertebroplasty.
- Additional costs associated with procedure-related mortality: it is likely that mortality due to MSCC surgery will incur in high costs before the patient dies. However, the analysis did not consider any additional cost in this kind of situation, but only the normal cost of the procedure.
- Rehabilitation costs for non-ambulant patients have not been included since only very few of them would receive any kind of rehabilitation at home (only those showing clear prospects of regaining control in their lower limbs while in hospital).
- Home adaptation: MSCC patients who become paraplegic are likely to require some home adaptation. For that, community occupational therapists (OTs) may arrange equipment or modifications to the patient's home in order to increase their independence, safety and quality of life. Between 2 and 3 visits from the OTs will be required, apart from the costs incurred in the equipment and/or modifications (which will differ across patients).

- Reoperation rates: some patients may require secondary surgery after undergoing a major procedure (Schoeggl *et al* 2002; Sucher *et al* 1994), and this has not been considered in the cost estimation.

It is important to highlight that the threshold analyses were conducted by modifying one or several variables at a time so that the modifications undertaken were as realistic as possible. For example, for the base-case analysis, which assumed that ambulant patients would remain ambulant their entire survival, modifications of survival for ambulant patients were accompanied for similar modifications in the time to paraplegia in order to keep the assumption stable. In addition, scenario 2 considered that time to paraplegia could vary as a proportion of the overall survival, and the survival for non-ambulant patients could vary as a proportion of that for ambulant patients. Therefore, these variables were modified jointly to identify the values leading to the alternative ICER thresholds (i.e. £20,000 versus £30,000 per QALY gained). The ROH audit provided relevant data on resource quantities used during surgery (both major surgery and vertebroplasty), and it was the basis for the cost estimation. Data from 54 patients were available. It is not clear what role selection bias and information bias may have played in the cost results obtained. However, it is the belief of the GDG members that the costs obtained are not too different from those observed during clinical practice.

Data on RT-related complications were obtained from the study by Thomas *et al* (2006), which used a questionnaire sent to the surgeons at different places in Canada to ask for the most common types of complications experienced by MSCC patients undergoing RT. Therefore, the estimation of these costs reflected the Canadian clinical experience and was not evidence-based. As a consequence, the applicability of this information to the UK context may be limited if the type of complications experienced by patients and the patterns of treatment for those complications differ across contexts. For the purposes of these analyses, the average cost per patient for RT-related complications was rather small (£27), therefore it is very unlikely that this may have influenced the results.

The second economic analysis undertaken assessed the cost-effectiveness of radical surgical procedures in combination with RT compared to RT alone for the treatment of MSCC patients that are neurologically compromised and have tumours that are not very radiosensitive. For these patients it is not clear what the best treatment choice is. This analysis consisted of adapting the only economic evaluation available comparing the use of surgery in combination with radiotherapy (RT) versus RT alone for the treatment of MSCC patients (Thomas *et al* 2006) to reflect the costs incurred if the interventions were conducted in a UK setting. The ICERs in terms of the incremental cost per life year gained obtained in the UK setting appear to be higher than those obtained in the study by Thomas *et al* (2006) for the Canadian setting: the incremental cost per additional life year gained with SRT when compared to RT alone in UK was £16,207, while that for the Canadian setting (once adjusted to £2006–2007 prices; OECD Purchase Power Parities, PSSRU 2006/07) was around £7,840. Additionally, an economic evaluation on the same topic (SRT versus RT alone) has been recently published in the form of an abstract (Furlan *et al* 2007). For this economic evaluation, a cost-utility assessment was conducted (i.e. it estimated QALYs as the measure of health benefit of the analysis) based on the same clinical data (i.e. the RCT published by Patchell *et al* 2005), and deriving utilities from the Harvard University Catalogue and the Health Outcomes Data Repository Data Health Utility list. Using an analytic decision model to combine clinical effectiveness and costs, the results of this study showed that the ICER for SRT, when compared to RT alone, was Can$43,796 (or £22,017 in 2006 prices); therefore, SRT seemed to be a strategy with borderline cost-effectiveness compared to RT alone. However, given the limited data reported in the abstract, the methodological quality of the study could not be assessed and therefore there is uncertainty regarding the reliability and applicability of these results to the UK setting. What it seems clear from the abstract is that hospice palliative care was a relevant component of the care received by MSCC patients, which is not applicable to the UK context, where hospice care is not a common way of managing MSCC patients.

One of the limitations of this second analysis was in the estimation of the number of QALYs gained. The information on quality of life for patients with MSCC is very limited, which seems to be the reason why in the Canadian economic evaluation the incremental cost per QALY was not estimated. NICE has established that its preferred measure of health benefit is the QALY

because it takes into account not only the increased life expectancy from an intervention, but also the quality of the increased life. According to NICE, interventions presenting an ICER lower than £20,000 per QALY gained are presumed to be cost-effective, while there should be strong reasons for recommending health care interventions with ICERs higher than £20,000, and even stronger reasons if the ICER exceeds £30,000 (Social Value Judgements 2007). Therefore, an attempt was made to estimate the number of QALYs gained with SRT when compared to RT alone by using the utility scores considered for the first analysis. Besides, some further threshold analyses were undertaken and, according to the obtained results, SRT seemed to be a cost-effective strategy in most of the cases.

Conclusion

Based on the results obtained, it seems that each of the independently assessed MSCC treatments (i.e. RT, vertebroplasty and major surgery) seemed cost-effective when compared to no treatment. The conditions that have resulted from the threshold analyses and that need to be met in order to consider RT, vertebroplasty and major surgery cost-effective interventions when compared to no treatment seem to be attainable. Additionally, SRT seemed to be cost-effective as well, when compared to RT alone, for patients neurologically compromised and that have moderately or poorly radiosensitive tumours.

References

Alvarez L, Perez-Higueras A, Quiñones D, Calvo E, Rossi RE. Vertebroplasty in the treatment of vertebral tumours: postprocedural outcome and quality of life. *Eur Spine* J 2003; 12:356–360.

Blackmore CC, Ramsey SD, Mann FA, Deyo RA. Cervical spine screening with CT in trauma patients: a cost-effectiveness analysis. *Radiology* 1999; 212:117–125.

Falicov A, Fisher CG, Sparkes J *et al.* Impact of surgical intervention on quality of life in patients with spinal metastasis. *Spine* 2006; 31(24):2849–2856.

Furlan J, Kelvin C, Sandoval G *et al.* A cost-utility analysis of surgery and radiotherapy versus radiotherapy alone in the management of patients with metastatic spinal cord compression [Abstract]. *Neurosurgery* 2007; 61(1):217.

Griffin S, Bojke L, Main C and Palmer S. Incorporating direct and indirect evidence using Bayesian methods: an applied case study in ovarian cancer. *Value in Health* 2006;9(2):123–131.

Hillner BE, *et al.* Pamidronate in prevention of bone complications in metastatic breast cancer: a cost-effectiveness analysis. *Journal of Clinical Oncology*, 2000. 18(1):72–79.

Hollingworth WD, Gray T, *et al.* Rapid magnetic resonance imaging for diagnosing cancer-related low back pain: a cost-effectiveness analysis. *Journal of General Internal Medicine* 2003; 18(4): 303–312.

Klinger C, Chan K, Fehlings M, Furlan J, Lam K, Laporte A, Sandoval G. Direct surgical decompression with postoperative radiotherapy versus radiotherapy alone in the palliative care of patients with metastatic epidural spinal cord compression (MESCC): an economic evaluation. *Journal of Palliative Care* 2007; 23(3):236.

Kwok Y, Tibbs PA, Patchell RA. Clinical approach to metastatic epidural spinal cord compression. *Hematol Oncol Clin North Am* 2006; 20(6):1297–305 [Abstract]

Mannion RJ, Wilby M, Godward S, Lyratzopoulos G, Laing RJC. The surgical management of metastatic spinal disease: prospective assessment and long-term follow-up. *British Journal of Neurosurgery* 2008; 21(6):593–598.

Maranzano E, Bellavita R, Rossi R, *et al.* Short-course versus split-course radiotherapy in metastatic spinal cord compression: results of a phase III, randomised, multicentre trial. *Journal of Clinical Oncology* 2005; 23:3358–3365.

Nagata M, Ueda T, Komiya A *et al.* Treatment and prognosis of patients with paraplegia or quadriplegia because of metastatic spinal cord compression in prostate cancer. *Prostate Cancer and Prostatic Diseases* 2003; 6:169–173.

Organisation for Economic Co-operation and Development. Purchasing Power Parities (PPPs) for OECD Countries 1980–2007 (http://www.oecd.org/LongAbstract/ 0,3425,en_2649_34357_1876126_119656_1_1_1,00.html)

Patchell RA, Tibbs PA *et al.* Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet* 2005; 366(9486): 643–648.

Rivero-Arias O, Campbell H, Gray A *et al.* Surgical stabilisation of the spine compared with a programme of intensive rehabilitation for the management of patients with chronic low back pain: cost utility analysis based on a randomised controlled trial. *BMJ* 2005;330:1239–1244.

Schoeggel A, Reddy M and Matula C. Neurological outcome following laminectomy in spinal metastases. Spinal Cord 2002; 40:363–366.

Sucher E, Margulies JY, Floman Y and Robin GC. Prognostic factors in anterior decompression for metastatic cord compression. Ana analysis of results. *Eur Spine* 1994; 3:70–75.

Thomas K Nosyk B, Fisher CG *et al.* Cost-effectiveness of surgery plus radiotherapy versus radiotherapy alone for metastatic epidural spinal cord compression. *Int J Radiation Oncology Biol Phys* 2006; 66(4):1212–1218.

Tokuhashi Y, Matzuzaki H, Oda H *et al.* A revised scoring system for preoperative evaluation of metastatic spine tumour prognosis. *Spine* 2005; 30:2186–2191.

Witham TF, Khavkin YA, Gallia GL *et al.* Surgery insight: current management of epidrual spinal cord compression from metastatic spine disease. *Nature Clinical Practice* 2006; 2(2): 87–94

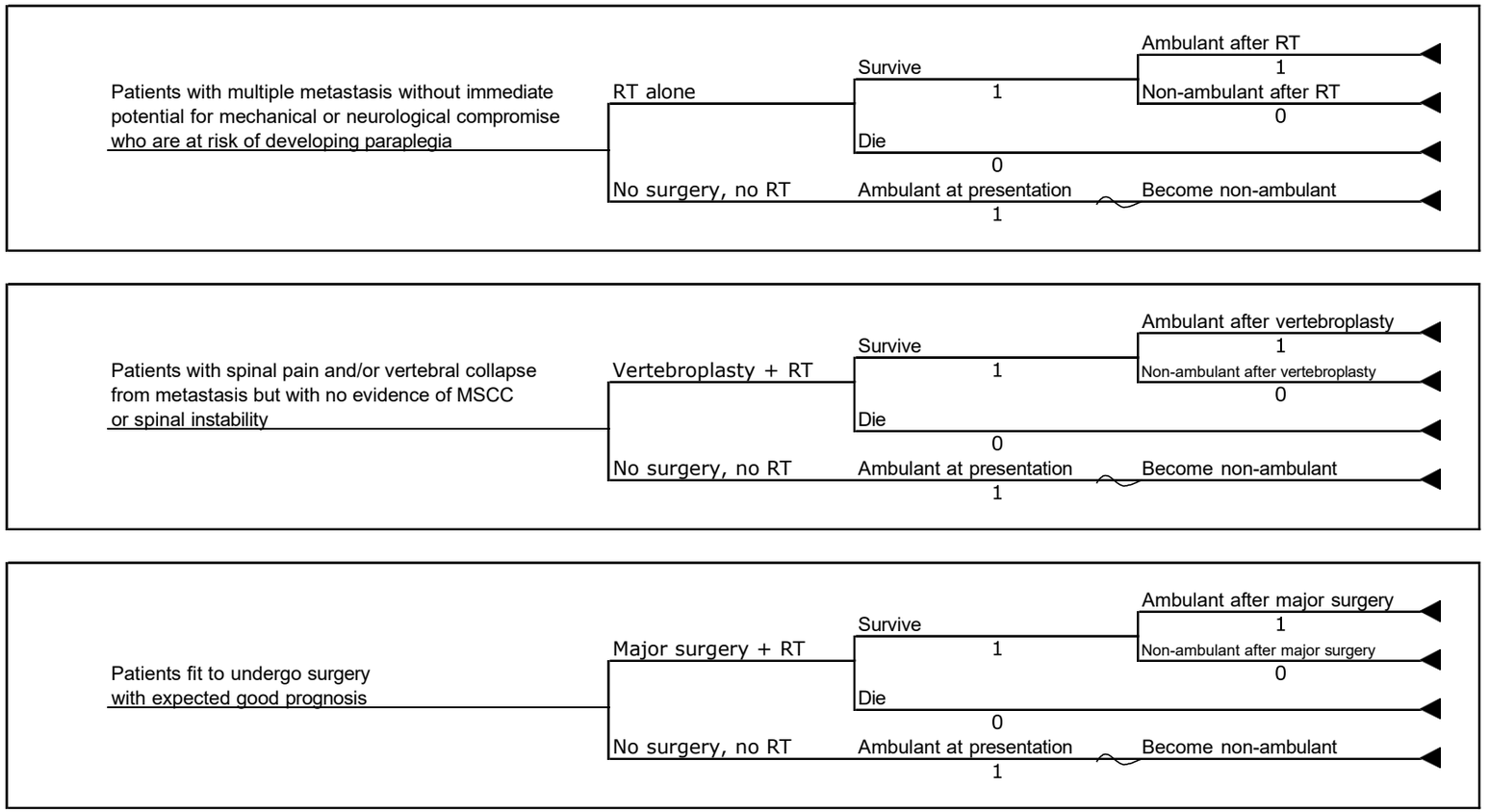


Figure A4.1 Model structure used for the threshold analyses which independently compared potential treatments for MSCC patients with no treatment (parameters shown correspond to the ideal scenario).

Appendix 5

Abbreviations

BED	biological equivalent dose
CNS	clinical nurse specialist
CT	computed tomography
DH	Department of Health
EBRT	external beam radiotherapy
GDG	guideline development group
HRQoL	health related quality of life
ICER	incremental cost effectiveness ratio
MDT	multi-disciplinary team
MRI	magnetic resonance imaging
MSCC	metastatic spinal cord compression
NCC-C	National Collaborating Centre for Cancer
NICE	National Institute for Health and Clinical Excellence
OR	odds ratio
PET	positron emission tomography
PPI	proton pump inhibitors
QALY	quality adjusted life years
RBE	radio biological equivalent
RCT	randomised controlled trial
RR	relative risk
RT	radiotherapy
SRE	skeletal related event

Appendix 6

Glossary

Analgesia

A condition where there is an insensitivity to pain, usually following an interruption of the nerve supply or under the influence of a drug that blocks the pain sensation. The individual is fully conscious.

Biological equivalent dose

A means of comparing different types of radiation or radiation delivered over different time frames, so that the effect on tissue can be assessed.

Cauda equine

A bundle of spinal nerve roots that arise from the bottom end of the spinal cord. The cauda equina comprises the roots of all the spinal nerve roots below the level of the first lumbar (L1) vertebra, namely the sacral and coccygeal nerves.

Chemotherapy

The use of drugs that kill cancer cells, or prevent or slow their growth.

Clinical oncologist

A doctor who specialises in the treatment of cancer patients, particularly through the use of radiotherapy, but may also use chemotherapy.

Cohort studies

Research studies in which groups of patients with a particular condition or specific characteristic are compared with matched groups who do not have it.

Computed tomography (CT)

An x-ray imaging technique, which allows detailed investigation of the internal organ of the body.

Cordotomy

Any operation on the spinal cord.

Deep venous thrombosis

A blood clot that forms in a vein resulting in obstruction of venous flow, most common clinically in the lower extremities.

Epidemiology

The study of populations in order to determine the frequency and distribution of disease and measure risks.

Epidural

Situated within the spinal canal, on or outside the dura mater

Histological

Relating to the study of cells and tissue on the microscopic level.

Hypercalcaemia

A medical condition in which abnormally high concentrations of calcium compounds are found in the bloodstream.

Intensity modulated radiotherapy (IMRT)

In intensity modulated radiation therapy (IMRT), very small beams, or beamlets, are aimed at a tumor from many angles. During treatment, the radiation intensity of each beamlet is controlled, and the beam shape changes hundreds of times during each treatment. As a result, the radiation dose bends around important healthy tissues in a way that is impossible with other techniques. Because of the complexity of these motions, physicians use special high-speed computers, treatment-planning software, diagnostic imaging and patient-positioning devices to plan treatments and control the radiation dose during therapy. (Mayo Clinic definition)

Intra cisternal

Within one of the subarachnoid cisternae

Intra ventricular

Injection into a ventricle.

Key worker

Person who, with the patient's consent and agreement, takes a key role in coordinating the patient's care and promoting continuity, ensuring the patient knows who to access for information and advice.

Kyphoplasty

A minimally invasive spinal surgery procedure used to treat painful, progressive vertebral compression fractures (VCFs). Kyphoplasty involves the use of a device called a balloon tamp to restore the height and shape of the vertebral body. This is followed by application of bone cement to strengthen the vertebra

Laminectomy

A surgical procedure that is performed to alleviate pain caused by neural impingement. The laminectomy surgery is designed to remove a small portion of the bone over the nerve root and/or disc material from under the nerve root to give the nerve root more space and a better healing environment.

Log rolling

A technique to maintain neutral spinal alignment when turning a patient.

Magnetic resonance imaging (MRI)

A special imaging technique used to image internal structures of the body, particularly the soft tissues. An MRI image is often superior to a normal plain x-ray image. It uses the influence of a large magnet to polarize hydrogen atoms in the tissues and then monitors the summation of the spinning energies within living cells. Images are very clear and are particularly good for soft tissue, brain and spinal cord, joints and abdomen. These scans may be used for detecting some cancers or for following their progress.

Mechanical pain

Type of back pain, which is caused by putting abnormal stress and strain on the muscles which support the vertebral column.

Metastases/metastatic disease

spread of cancer away from the primary site to somewhere else via the bloodstream or the lymphatic system.

Multi disciplinary team (MDT)

A team with members from different health care professions (e.g. urology, oncology, pathology, radiology, nursing).

Myelography

Myelography is an imaging examination that shows the passage of contrast material in the space around the spinal cord (the subarachnoid space) using a real-time form of plain x-ray (radiography) called fluoroscopy, in which organs can be seen over many seconds (rather than in the static image called a plain x-ray or radiograph).

Neurolysis

Destruction of nerve tissue

Occupational therapist

A healthcare professional who works with people of all ages helping them to carry out activities that they need or want to do in order to live healthy and fulfilling lives

Oncology

The study of cancers

Opioids

A chemical substance that has a morphine-like action in the body. The main use is for pain relief

Orthopaedic surgeon

A doctor who specialises in the surgery of bones.

Osteoporosis

A reduction in the amount of bone mass, leading to fractures after minimal trauma.

Palliative

Anything which serves to alleviate symptoms due to the underlying cancer but is not expected to cure it.

Palliative care

The active holistic care of patients with advanced, progressive illness. Management of pain and other symptoms and the provision psychological, social and spiritual support is paramount. The goal of palliative care is achievement of the best quality of life for patients and families. Many aspects of palliative care are also applicable earlier in the course of the illness in conjunction with other treatments.

Paraplegia

Paralysis of the legs and lower part of the body.

Percutaneous

Performed through the skin, as injection of radiopacque material in radiological examination or the removal of tissue for biopsy accomplished by a needle

Physiotherapist

A healthcare professional concerned with human function, movement and maximising potential.

Plain x-ray

A radiograph made without use of a contrast medium.

Positron emission tomography (PET)

A specialised imaging technique using a radioactive tracer to produce a computerised image of metabolic activity in body tissues and find abnormalities. PET scans may be used to help diagnose cancer, to see how far it has spread and to investigate response to treatment. Since PET looks at function, it is often combined with CT [PETCT] which reveals the underlying structure.

Prognosis

A prediction of the likely outcome or course of a disease; the chance of recovery or recurrence.

Psychological support

Professional support which can help people with a wide range of psychological problems such as anxiety and depression, and can provide emotional assistance during times of distress.

Radicular pain

Pain in a nerve root distribution, typically extending down the arm, round the trunk of the leg.

Radiculopathy

Where root compression is more pronounced there may be alteration of sensory function (feeling) or motor function (weakness) in the distribution of that nerve.

Radiograph

An image produced on a radiosensitive surface, such as a photographic film, by radiation other than visible light, especially by plain x-rays passed through an object or by photographing a fluoroscopic image.

Radiographer

A healthcare professional who is qualified to undertake and interpret radiographic images. In oncology, radiographers are highly trained in the use of high energy radiation and the management of patients with cancer.

Radioisotope

A version of a chemical element that has an unstable nucleus and emits radiation during its decay to a stable form. Radioisotopes have important uses in medical diagnosis, treatment, and research. A radioisotope is so-named because it is a radioactive isotope, an isotope being an alternate version of a chemical element that has a different atomic mass.

Radiologist

A doctor who specialises in acquiring and interpreting pictures of areas inside the body using Plain x-rays and other specialised imaging techniques. An interventional radiologist specialises in the use of imaging techniques for treatment, for example catheter insertion for abscess drainage.

Radiotherapy

The use of radiation, usually plain x-rays or gamma rays, to kill cancer cells and treat tumours.

Randomised controlled trial (RCT)

A type of experiment which is used to compare the effectiveness of different treatments. The crucial feature of this form of trial is that patients are assigned at random to groups which receive the interventions being assessed or control treatments. RCTs offer the most reliable (i.e. least biased) form of evidence of effectiveness.

Spinal cord pain

Neurogenic pain-radicular pain: Pain arising from neural irritation, compression or damage, usually in the case of MSCC by direct pressure or indirect vascular effects to disturb neurological function and cause pain of a typical nature and recognisable distribution (band-like deep-seated aching discomfort in the case of nerve root, burning cold indescribable in the case of the cord with or without sensory disturbance or weakness in a distinct clinical pattern reflecting the level nature and extent of neurological compression).

Spinal instability

Clinical stability definition: The ability of the spine under physiologic loads to limit patterns of displacement so as not to damage or irritate the spinal cord or nerve roots and, in addition, to prevent incapacitating deformity or pain due to structural changes.

Description and Examples: Any disruption of the spinal components (ligaments, discs, facets) holding the spine together will decrease the clinical stability of the spine. When the spine loses enough of these components to prevent it from adequately providing the mechanical function of protection, surgical or other measures are taken to reestablish stability.

Spinal pain

Pain in or arising from the bones, joints, or soft tissues of the spinal column. It may be mechanical (increased by movement and relieved by rest), postural (worse with prolonged standing and eased by movement), recumbent (worse when lying and improved by standing – sometimes associated with cord compression), or non-specific (without change due to posture or movement). All are thought to result from disturbance of the dynamic structural integrity of the spinal column (or filling of the spinal canal in the case of recumbancy pain) without symptoms or signs of associated neurological injury.

Spinal shock

"a state of transient physiological (rather than anatomical) reflex depression of cord function below the level of injury with associated flaccid areflexia loss of all sensory and motor function"

Supine

Lying on the back.

Supportive care

'… helps the patient, partners, carers and their family to cope with cancer and treatment of it – from pre-diagnosis, through the process of diagnosis and treatment, to cure, continuing illness or death and into bereavement. It helps the patient to maximise the benefits of treatment and to live as well as possible with the effects of the disease. It is given equal priority alongside diagnosis and treatment.'

Tetraplegia

Paralysis of all four limbs, both arms and both legs, as from a high spinal cord accident or stroke. Severe or complete loss of motor function in all four limbs which may result from brain diseases; spinal cord diseases; peripheral nervous system diseases; neuromuscular diseases; or rarely muscular diseases. The locked-in syndrome is characterized by quadriplegia in combination with cranial muscle paralysis. Consciousness is spared and the only retained voluntary motor activity may be limited eye movements. This condition is usually caused by a lesion in the upper brain stem which injures the descending cortico-spinal and cortico-bulbar tracts.

Thoracotomy

An incision into the chest.

Valsalva manoeuvre

Any forced expiratory effort (strain) against a closed airway, whether at the nose and mouth or at the glottis, the reverse of muller's manoeuvre; because high intrathoracic pressure impedes venous return to the right atrium, this manoeuvre is used to study cardiovascular effects of raised peripheral venous pressure and decreased cardiac filling and cardiac output, as well as post-strain responses.

Venous thromboembolism

A condition in which a blood clot (thrombus) forms in a vein. Blood flow through the affected vein can be limited by the clot, causing swelling and pain. Venous thrombosis most commonly occurs in the 'deep veins' in the legs, thighs, or pelvis. This is known as a deep vein thrombosis.

Vertebroplasty

Vertebroplasty is an image-guided, minimally invasive, nonsurgical therapy used to strengthen a broken vertebra (spinal bone) that has been weakened by osteoporosis or, less commonly, cancer. Percutaneous vertebroplasty involves the injection of acrylic bone cement into the vertebral body in order to relieve pain and/or stabilise the fractured vertebrae and in some cases, restore vertebral height.

Appendix 7

Guideline scope

Guideline title

Metastatic spinal cord compression: diagnosis and management of adults at risk of and with metastatic spinal cord compression

Short title

Metastatic spinal cord compression

Background

The National Institute for Health Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Cancer to develop a clinical guideline on the diagnosis and management of patients with metastatic spinal cord compression for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations on clinical practice and service provision that are based on the best available evidence of clinical and cost effectiveness.

The Institute's service guidance will support the implementation of the National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued will have the effect of updating the Framework.

This guideline will support current national initiatives outlined in the 'NHS cancer plan', the 'Calman Hine report', the 'Cameron report', the 'Manual of cancer service standards for England' and the 'Wales cancer standards'. The guideline will also refer to other NICE guidance including 'Referral guidelines for suspected cancer', 'Improving supportive and palliative care for adults with cancer', and 'Improving outcomes for people with brain and other CNS tumours'. Cross reference will be made to these and other documents as appropriate.

NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and their carers and families, where appropriate) can make informed decisions about their care and treatment.

Clinical need for the guideline

It is difficult to know what the true incidence of metastatic spinal cord compression (MSCC) is in England and Wales because the cases are not systematically recorded. However, evidence from an audit carried out in Scotland between 1997 and 1999[1] and from a published study

[1] Levack, P, Collie D, Gibson A et al. (2001) A prospective audit of the diagnosis, management and outcome of malignant cord compression (CRAG 97/08). Edinburgh: CRAG.

from Ontario, Canada[2], suggests that the incidence may be up to 80 cases per million population per year. This would mean around 4000 cases per year in England and Wales or more than 100 cases per cancer network per year.

The Clinical Resource and Audit Group (CRAG) audit clearly showed that there were significant delays from the time when patients first developed symptoms until hospital doctors and general practitioners recognised the possibility of spinal cord compression and made the appropriate referral. The median times from the onset of back pain and nerve root pain to referral were 3 months and 9 weeks respectively. As a result, 48% of patients were unable to walk at the time of diagnosis and of these the majority (67%) had recovered no function at 1 month. Of those walking unaided at the time of diagnosis (34%), 81% were able to walk (either alone or with aid) at 1 month. The ability to walk at diagnosis was also significantly related to overall survival.

At present, relatively few patients with malignant spinal cord compression in the UK receive surgery for the condition. But research evidence suggests that early surgery may be more effective than radiotherapy in a selected subset of patients.

The guideline

The guideline development process is described in detail in two publications which are available from the NICE website (see 'Further information'). 'The guideline development process: an overview for stakeholders, the public and the NHS' describes how organisations can become involved in the development of a guideline. 'The guidelines manual' provides advice on the technical aspects of guideline development.

This document is the scope. It defines exactly what this guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health (see appendix).

The scope forms the basis on which the work of a guideline development group is planned and should be very clear about which patient groups are included and which areas of clinical care will be considered (sections 4.1–4.3).

The areas that will be addressed by the guideline are described in the following sections.

Population

Groups that will be covered

- 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.
- Adults with primary malignant tumours (for example, lung cancer, mesothelioma or plasmacytoma) and direct infiltration that threatens spinal cord function.

Groups that will not be covered

- Adults with spinal cord compression due to primary tumours of the spinal cord and meninges.
- Adults with spinal cord compression due to non-malignant causes.
- Adults with nerve root tumours compressing the spinal cord.
- Children.

Healthcare setting

- Primary care, including referral, rehabilitation, continuing care and follow up.
- Secondary care, including diagnosis, treatment and rehabilitation.
- Tertiary care in cancer centres, neurosurgical units and spinal surgery units.

[2] Loblaw DA, Laperriere NJ, Mackillop WJ (2003) A population-based study of malignant spinal cord compression in Ontario. *Clinical Oncology* 15 (4) 211–7.

- Specialist rehabilitation centres.
- Palliative care services.

Clinical management (including service delivery where appropriate)

- Identification of patients at risk.
- Diagnosis – clinical and radiological.
- Treatment:
  - radiotherapy
  - surgery
  - interventional radiology
  - medical therapy.
- Rehabilitation and supportive care.
- Specific elements of palliative care that meet the particular needs of patients with metastatic spinal cord compression and of their families and carers.
- Communication and information resources for patients, carers, family members and health-care professionals.
- Follow up.

Status

Scope

This is the final version of the scope.

The development of the guideline recommendations will begin in September 2006.

Further information

Related NICE guidance

- Improving outcomes for people with brain and other CNS tumours. NICE cancer service guidance (2006). Available from www.nice.org.uk/csgbraincns
- Improving outcomes for people with sarcoma. NICE cancer service guidance (2006). Available from www.nice.org.uk/csgsarcoma
- Referral guidelines for suspected cancer. NICE clinical guideline 27 (2005). Available from www.nice.org.uk/CG027
- Improving supportive and palliative care for adults with cancer. NICE cancer service guidance (2004). Available from www.nice.org.uk/csgsp

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

Appendix – Referral from the Department of Health

The Department of Health asked the Institute to develop a guideline on:

'Diagnosis and management of patients with metastatic spinal cord compression, including service delivery where appropriate.'

Appendix 8

List of topics covered by each chapter

Chapter 2 – Service configuration and urgency of treatment

- What is the most effective way of delivering care and coordinating services for patients with MSCC or suspected MSCC?

Chapter 3 – The patient's experience of MSCC

- How effective are decision aids for patients with MSCC facing treatment decisions?
- What is the most effective emotional and family support interventions for patients with MSCC?
- In patients with MSCC, what effect does delay from presentation to definitive treatment have on clinical outcomes (mobility, urinary continence, lack of pain, survival independent living)?
- In patients with MSCC, what effect does performance status at the time of treatment have on clinical outcomes (mobility, urinary continence, lack of pain, survival independent living)?
- In patients with a clinical diagnosis of malignant spinal cord compression, how soon should definitive treatment be undertaken to prevent permanent neurological deficit?

Chapter 4 – Early detection

- What is the most effective way to communicate the risks of MSCC to patients with primary carcinoma [to your patient]?
- What is the most effective way to communicate the symptoms of MSCC to patients with primary carcinoma [to your patient]?
- In patients with cancer at risk of developing spinal cord compression, what symptoms and signs give early indications that malignant SCC is developing?
- In patients with suspected bone metastases in the spine, does MRI (or CT?) scanning (compared to not scanning) identify patients at risk of developing MSCC and improve clinical outcomes (prevention of established MSCC, mobility, cost)
- In patients with known bone metastases in the spine, does serial imaging identify patients at risk of developing MSCC improve clinical outcomes (prevention of established MSCC, improve mobility, cost)

Chapter 5 – Imaging

- What is the best imaging modality for diagnosis of spinal cord compression?

Chapter 6 – Treatment of spinal metastases and MSCC

- Is epidural/spinal/intrathecal anaesthesia a safe and effective intervention in suspected/confirmed MSCC?
- What is the effectiveness of Bisphosphonates at treating spinal pain and/or preventing spinal collapse and/or spinal cord compression?

- What is the effectiveness of RT at treating spinal pain and/or preventing spinal collapse and/or spinal cord compression?
- What is the effectiveness of Vertebroplasty/Kyphoplasty at treating spinal pain and/or preventing spinal collapse and/or spinal cord compression?
- What is the effectiveness of Stabilisation surgery to prevent vertebral collapse, (where Stabilisation surgery is +/– Intra-lesional debulking to prevent cord compromise)?
- For patients with known MSCC who have had surgery/RT/no treatment does 'early' mobilisation give better outcomes (mobility, pain) than 'delayed' (needs definition).
- For patients with suspected/confirmed MSCC, what is the most effective steroid regimen wrt preserving or improving mobility; neurology; duration of effect and toxicity?
- Case selection for treatment – What is the validity of Tomita and Tokuhashi scoring systems?
- Case selection for surgery – For patients with an established diagnosis of MSCC, what factors predict for successful outcomes (mobility, continence, lack of pain, survival) following surgery?
- Case selection for radiotherapy – For patients with an established diagnosis of MSCC, what factors predict for successful outcomes (mobility, continence, lack of pain, survival) following RT?
- What surgical technique is the most effective in treating patients with known MSCC in terms of outcomes outlined below?
- In patients with known MSCC referred for radiotherapy, what is the most effective and cost effective dose fractionation regimen?

Chapter 7 – Supportive care and rehabilitation

- What is the most effective bladder and bowel management for patients with spinal cord injury (MSCC)
- What is the most effective thrombo-prophylactic management for patients with spinal cord injury (MSCC)
- What is the most effective pressure ulcer management for patients with spinal cord injury (MSCC)
- What is the most effective respiratory and circulatory management for patients with spinal cord injury (MSCC)
- Given that specialised centres for patients with spinal injuries (or specialised wards for neuro-patients) exist and provide services that benefit patients; can MSCC patients also benefit from these kinds of services (wards/centres)?
- Which MSCC patient factors will predict for beneficial outcomes from specialised services?

Appendix 9

People and organisations involved in production of the guideline

Appendix 9.1

Members of the Guideline Development Group (GDG)

GDG Chair

Mr Barrie White	Neurosurgeon, Queen's Medical Centre, Nottingham

GDG Lead Clinician

Mr Alistair Stirling	Consultant Orthopaedic Spinal Surgeon, The Royal Orthopaedic Hospital, Birmingham

Group Members

Margaret Berg	Patient/Carer Representative
Dr Bernard Brett	Divisional Director Emergency Division & Consultant Physician & Gastroenterologist, James Paget Healthcare NHS Trust
Dr Juliet Britton	Consultant Neuroradiologist, St George's Hospital, London
Nicola Cornelius	Consultant Radiographer, Lincoln County Hospital, Lincoln
Dr Angela Gall	Consultant Rehabilitation Spinal Cord Injury Centre, Royal National Orthopaedic Hospital, Urologist, Middlesex
Dr Linda Garvican	Public Health Director & Quality Assurance Director, Sussex Cancer Network
Dr David Levy	Medical Director, North Trent Cancer Network, Sheffield
Dr Victoria Lidstone	Consultant in Palliative Medicine, North Glamorgan NHS Trust
Daniel Lowrie	Senior Occupational Therapist, Royal Marsden NHS Trust
Mr Robert Marshall	Consultant Orthopaedic Surgeon, Royal Berkshire Hospital, Reading
Dr Euan Paterson	General Practitioner & Macmillan GP Facilitator, Glasgow
Michael Scanes	Patient/Carer Representative, User Involvement Facilitator, Essex Cancer Network
Dr David Spooner	Consultant Clinical Oncologist, Queen Elizabeth Hospital, Birmingham
Helen Tyler	Clinical Lead Physiotherapist, Velindre Cancer Centre, Velindre NHS Trust
Christine Ward	Nurse Consultant for Adult Palliative Care, North Yorkshire & York Primary Care Trust

Declarations of Interests

The Guideline Development Group were asked to declare and possible conflicts of interest which could interfere with their work on the guideline.

GDG Member	Interest Declared	Type of Interest	Decisions Taken
Barrie White (Chair)	Investigator in multi-centre trial to determine the safety and performance of the PEARSAU's artificial viscooelastic cervical NEODISC for degenerative cervical disc disease.	Non-personal pecuniary, non-specific	Declare and can participate in discussions on all topics as the interventions included in the trial are not being investigated by the guideline.

Appendix 9.2

Organisations invited to comment on guideline development

The following stakeholders registered with NICE and were invited to comment on the scope and the draft version of this guideline.

3 Counties Cancer Network Palliative Care Lead Clinicians Group

Anglia Cancer Network

Arden Cancer Network

Association of Chartered Physiotherapists in Oncology and Palliative Care

Association for Continence Advice

Association for Palliative Medicine of Great Britain and Ireland

Barnsley Acute Trust

Bedfordshire & Hertfordshire NHS Strategic Health Authority

Birmingham Cancer Network

Bournemouth and Poole PCT

Brain and Spine Foundation

Breakthrough Breast Cancer

Breast Cancer Care

Brighton & Sussex University Hospitals Trust

British Association of Day Surgery

British Association of Neuroscience Nurses

British Association of Spine Surgeons

British Lymphology Society

British National Formulary (BNF)

British Nuclear Medicine Society

British Paramedic Association

British Society of Neuroradiologists

Calderdale PCT

Cancer Research UK

Cardiothoracic Centre – Liverpool NHS Trust

CASPE Research

Chartered Society of Physiotherapy

College of Occupational Therapists

Commission for Social Care Inspection

Connecting for Health

Cancerbackup

Cancer Research UK

Department of Health

Derby-Burton Cancer Network

Essex Cancer Network

Health and Safety Executive

Healthcare Commission

Health Commission Wales

Hove Polyclinic

Humber and Yorkshire Coast Cancer Netwok

Huntleigh Healthcare

Institute of Biomedical Science

James Cook University Hospital

King's College Hospital NHS Trust

Kirklees PCT

Leicestershire Northamptonshire and Rutland Cancer Network

Leeds PCT

Leukaemia Research Fund

Liverpool PCT

Marie Curie Cancer Care

Medicines and Healthcare Products Regulatory Agency

Medtronic Ltd

Mental Health Act Commission

Midlands Centre for Spinal Injuries

National Council for Palliative Care

National Patient Safety Agency

National Public Health Service – Wales

National Treatment Agency for Substance Misuse

NCCHTA

NHS Health and Social Care Information Centre

NHS Lothian

NHS Quality Improvement Scotland

North Bristol NHS Trust

North East London Cancer Network

North Trent Cancer Network

North Yorkshire and York PCT

Northwest London Hospitals NHS Trust

Novartis Pharmaceuticals UK Ltd

PERIGON (formerly The NHS Modernisation Agency)

Regional Public Health Group – London

Royal College of General Practitioners

Royal College of Midwives

Royal College of Nursing

Royal College of Paediatrics and Child Health

Royal College of Physicians of London

Royal College of Radiologists

Royal United Hospital Bath NHS Trust

Sandwell PCT

Sheffield South West PCT

Sheffield Teaching Hospitals NHS Foundation Trust

Society and College of Radiographers

South Birmingham PCT

South East Wales Cancer Network

Stockport PCT

Sussex Cancer Network

Thames Valley Cancer Network

University Hospital Aintree

University of Hertfordshire

Welsh Assembly Government

Welsh Scientific Advisory Committee (WSAC)

Western Cheshire PCT

York NHS Trust

Appendix 9.3

Individuals carrying out literature reviews and complementary work

Overall Coordinators	
Dr Fergus Macbeth	Director, National Collaborating Centre for Cancer, Cardiff
Dr Andrew Champion	Centre Manager, National Collaborating Centre for Cancer, Cardiff
Angela Bennett	Assistant Centre Manager, National Collaborating Centre for Cancer, Cardiff
Project Manager	
Katrina Asquith-Coe	National Collaborating Centre for Cancer, Cardiff
Senior Researcher	
Angela Melder	National Collaborating Centre for Cancer, Cardiff
Researchers	
Dr Rossela Stoicescu	External Researcher
Dr Susanne Hempel	External Researcher
Information Specialists	
Sabine Berendse	National Collaborating Centre for Cancer, Cardiff
Health Economists	
Dr Alec Miners	Lecturer in Health Economics, London School of Health and Tropical Medicine
Professor John Cairns	London School of Health and Tropical Medicine
Raquel Aquiar-Ibanez	London School of Health and Tropical Medicine
Dr Neill Calvert[1]	London School of Health and Tropical Medicine
Needs Assessment	
Dr Emma Hudson	Velindre NHS Trust
Dr Seema Arif	Velindre NHS Trust

[1] From Dec 2006 to May 2007

Appendix 9.4

Expert advisers to the guideline development group

Dr Manohar Lal Sharma	Consultant in Pain Medicine and Anaesthesia, The Walton Centre for Neurology and Neurosurgery, Liverpool
Trudy McLeay	Project Manager, North of Scotland Cancer Network (NOSCAN)

Appendix 9.5

Members of the Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The members of the Guideline review Panel were as follows

John Hyslop (Chair)

Consultant Radiologist, Royal Cornwall Hospital NHS Trust

Peter Gosling

Lay Member

Jonathan Hopper

Medical Director (Northern Europe), ConvaTec Ltd

Ash Paul

Deputy Medical Director, Health Commission Wales

Liam Smeeth

Professor of Clinical Epidemiology, London School of Hygiene and Tropical Medicine