National Institute for Health and Care Excellence

Draft for consultation

Metastatic spinal cord compression

[B] Evidence review for service configuration and delivery (management and rehabilitation)

NICE guideline number tbc

Evidence reviews underpinning recommendations 1.1.1 to 1.1.4, 1.1.11, 1.1.12, 1.1.22 to 1.1.28 and 1.12.1 to 1.12.5 in the NICE guideline

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These evidence reviews were developed by NICE

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ISBN:

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Service configuration and delivery (management and rehabilitation)

Review question

What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Introduction

The management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression requires coordination between various specialties including primary care, haematology, oncology, palliative care, physiotherapy, radiology, and spinal surgery. This review aims to summarise the effectiveness of different service delivery models for the care and early rehabilitation of people with malignant spinal cord compression or spinal metastases.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Adults with confirmed • metastatic spinal disease • direct malignant infiltration of the spine Adults with confirmed spinal cord or nerve root compression because of • metastatic spinal disease • direct malignant infiltration of the spine

Intervention	Any practice and service delivery models (approaches, configurations of resources and services) for the management and early rehabilitation of malignant spinal cord compression or spinal metastases. For example:
	• Delivery arrangements:
	  ○ Who provides care and how the healthcare workforce is managed
	  ○ Where care is provided, for example -
	  - Specialist centres
	  - Local hospitals
	  - Neurorehabilitation units
	  - Rehab while on oncology ward
	  ○ How and when care is delivered, for example -
	  - Early rehabilitation
	• Coordination of care and management of care processes:
	  ○ Care pathways
	  ○ Service user management (models responsive to individual needs)
	  ○ Communication / referral between providers, for example -
	  - Specialist centres and general physiotherapy (for rehabilitation)
	  - Physiotherapy/orthotics training by specialist centres for local hospitals
	  ○ Multidisciplinary teams

Comparison	Interventions compared with: • Each other

	• Combinations of interventions

Outcome	**Critical**
	• Overall survival
	• Quality of life
	• Pain
	• Neurological and functional status including:
	  ○ Bowel and bladder function
	  ○ Mobility or ambulatory status
	Important
	• Emergency admission to hospital and length of hospital stay
	• Access to services:
	  ○ Local availability (for example, time/distance travelled to access services)
	  ○ Waiting times for services

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

The NICE methods and process manual emphasises the value of real-world data, setting out best practices in the NICE Real world evidence framework. As part of this approach an audit dataset from the MSCC service at the UK Clatterbridge Cancer Centre was analysed specifically for this review question and the associated health economic model (Appendix I). This is an audit of all people referred to an MSCC service between January 2018 until end of May 2022 covering a population of 2.4 million people across Cheshire, Merseyside, and the surrounding areas. The impact of changes to the MSCC service configuration on overall survival (adjusted for age and sex) was calculated for the group as a whole as well as for different primary cancers and according to deprivation quintile.

This was a minor deviation from the protocol which stated that service evaluations and audits would only be included in the in the absence of comparative randomised or non-randomised studies. The Clatterbridge Cancer Centre data, however, provided up-to-date data from a UK setting, something that was lacking the included published studies.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

Effectiveness evidence

Included studies

Four published studies were included in this review (Cui 2021, Fitzpatrick 2012, Guddati 2017, Malik 2020) plus one analysis specifically conducted for this guideline using an audit of all people referred to an MSCC service between January 2018 until end of May 2022 in the UK Clatterbridge Cancer Centre regional MSCC service (covering a population of 2.4 million people across Cheshire, Merseyside, and the surrounding areas) – referred to from hereon in as Clatterbridge 2022. See also the de novo economic model based on this audit in appendix I.

Three were retrospective (Cui 2021, Guddati 2017 and Malik 2020) and 2 were prospective (Clatterbridge 2022, Fitzpatrick 2012).

One study was conducted in the UK (Clatterbridge 2022), 2 in the United States (Guddati 2017 and Malik 2020), 1 in Canada (Fitzpatrick 2012), and 1 study in China (Cui 2021).

The included studies are summarised in Table 2.

One study (Clatterbridge 2022) compared outcomes before and after an MSCC service configuration change. One study compared surgery being done within 3 days, between 4 and 7 days or after 7 days after the onset of symptoms (Cui 2021), another study compared virtual consultation between oncologists and spinal surgeons to no virtual consultation (Fitzpatrick 2012). One study compared early to late intervention (before or after 48 hours of hospitalization) with radiotherapy or surgery (Guddati 2017) and 1 study compared spinal metastasis surgery by orthopaedic surgeons or neurosurgeons on patient outcomes (Malik 2020).

See also the related evidence review of service configuration related to investigations and referral (evidence review A).

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix K.

Summary of studies included in the evidence review

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies.

Study	Population	Intervention	Comparison	Outcomes
Clatterbridge 2022 Prospective cohort study UK	N=3173 People referred to an MSCC service via an MSCC referral pathway Age, mean, years (SD): 69 (not reported). Sex - male/female: 1884/1289	<u>Before service change</u> MSCC service organised in accordance with the NICE 2008 guideline	<u>After service change</u> This was a refinement of the 'before' service configuration where members of the MSCC team were upskilled in MSCC coordination (to make initial clinical decisions on referrals into the service)	• Overall survival
Cui 2021 Retrospective cohort study China	N=75 People with incomplete with incomplete spinal cord injury Age, mean, years (SD): Overall age not reported but provided in groups according to timing of surgery: • within 4 days: 60 (4)	<u>Timing of surgery</u> Whether surgery was performed within 4 days, between 4 and 7 days or after 7 days after the onset of symptoms	<u>Timing of surgery</u> Whether surgery was performed within 4 days, between 4 and 7 days or after 7 days after the onset of symptoms	• Neurological and functional status ○ improvement in AIS scale grade post-operatively ○ ambulatory status • Length of hospital stay

Study	Population	Intervention	Comparison	Outcomes
	• between 4 and 7 days: 63 (3) • after 7 days: 61 (2) Sex – male/female: 19/56			
Fitzpatrick 2012 Prospective cohort study Canada	N=151 People with metastatic spinal cord compression. Age, median, years (range): 60 (30 to 90) Sex – male/female: 94/57	Virtual consultation Virtual consultation process using telemedicine (real time sharing of patient information over internet and telephone) to facilitate the provision of multidisciplinary care between radiation oncology and spinal surgery.	No virtual consultation	• Overall survival • Access to services ○ number of candidates for surgery missed
Guddati 2017 Retrospective cohort study USA	N=13457 People with metastatic spinal cord compression. Overall age not reported but number of people in age ranges given: • 18–34 N=530 • 35–49 N=1962 • 50–64 N=4703 • 65–79 N=4789 • 80 and above N=1468 Sex – male/ female: 7895/5562	Early intervention Intervention was classified as 'early' when provided within the first 48 hours and 'late' when provided after 48 hours of hospitalisation.	Late intervention Intervention was classified as 'early' when provided within the first 48 hours and 'late' when provided after 48 hours of hospitalization.	• Overall survival ○ In-hospital mortality • Length of hospital stay
Malik 2020 Retrospective cohort study USA	N=887 People with spinal metastasis. Overall age not reported but number of people in age ranges given: • <45 N=16 • 45-64 N=204 • 65-79 N=582 • ≥80 N=86	Orthopaedic surgeon Surgical intervention for spinal metastasis (laminectomy, osteotomy/ corpectomy and/ or fusion) performed by an orthopaedic surgeon.	Neurosurgeon Surgical intervention for spinal metastasis (laminectomy, osteotomy/ corpectomy and/ or fusion) performed by a neurosurgeon.	• Overall survival ○ 90-day mortality • Emergency department visits • 90-day readmissions

Study	Population	Intervention	Comparison	Outcomes
	Sex – male/ female: 539/348			

AIS: American Spinal Injury Association Impairment Scale; mg: milligram; MRI: Magnetic Resonance Imaging.

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Summary of the evidence

There was very low quality evidence of an important benefit in terms of overall survival for people with lung, unknown primary or other (non-prostate or breast) cancers following up-skilling of the staff in an MSCC service to act as MSCC co-ordinators and make initial clinical decisions on referrals into the service. There was no important difference for patients with prostate or breast cancer, however.

One study provided low to moderate quality evidence of an important benefit with earlier intervention in terms of in hospital mortality and length of hospital stay. Very low quality evidence from another study indicated important benefit in terms of hospital stay with earlier intervention, but no evidence of difference for neurological and functional status outcomes.

There was no evidence of important difference when comparing virtual consultation between spinal surgeons and oncologists with no virtual consultation as a way to identify people with MSCC candidates for surgery. This evidence was of low quality.

There was very low quality evidence of no important difference in outcomes of surgery for spinal metastases carried out by neurosurgeons and by orthopaedic surgeons.

See the evidence profiles in appendix F.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

A single economic search was undertaken for all topics included in the scope of this guideline. See supplement 2 for details.

Excluded studies

Economic studies not included in this review are listed, and reasons for their exclusion are provided in supplement 2.

Summary of included economic evidence

Table 3: Economic evidence profile of an economic evaluation of the addition of radiotherapy for people undergoing surgery for metastatic spinal cord compression

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effect	Cost effectiveness	

NICE 2023 Up-skilling of team members to undertake the MSCC co-ordinator role to enable them to make initial clinical decisions	Potentially serious limitations[1]	Directly applicable[2]	Sub-grouped by deprivation quintile in secondary analysis	-£132	0.0470 QALYs	Up-skilling team members dominant[3]	Conclusions robust to probabilistic sensitivity analysis

[1] Weaknesses in controlling for all confounders in underlying outcome evidence
[2] UK NHS perspective with QALYs valued using EQ-5D utility values
[3] Upskilling of team members to undertake the MSCC co-ordinator role to enable them to make initial clinical decisions was both cost saving and health improving

Economic model

An economic model was developed for this topic looking at the cost effectiveness of up-skilling team members to undertake the MSCC co-ordinator role which would enable them to make initial clinical decisions around referrals to 1 regional MSCC centre. The full economic model is reported in appendix I.

The economic model was based on audit data, covering the period from January 2018 to May 2022 from 1 regional MSCC service. The MSCC service was set-up in January 2017 with the full launch of the pathway in January 2018 reflecting recommendations made in the previous guideline around co-ordinated pathways for MSCC and having one point of contact for confirmed metastatic spinal emergencies.

A before and after study design was used to look retrospectively at differences in survival, QALYs and costs following upskilling of team members to be able to undertake the MSCC co-ordinator role. The model was also designed to look at trends in survival and costs since the launch of the service to make inferences about improvements over time. The model also used English Indices of Multiple Deprivation to investigate whether these outcomes differed by socio-economic status.

The economic analysis found that there was benefit in terms of improving outcomes and reducing costs from upskilling staff although these benefits were not evenly distributed across all deprivation groups with the largest benefits coming in the second and third least deprived quintiles. The analysis also highlighted an increase in survival over time since the creation of the regional MSCC service.

There were a number of weaknesses with the economic model. It was not possible to control for all confounding factors in the before and after group that could have resulted in differences between outcomes, so it was difficult to assign all changes in the difference between groups to the upskilling intervention. There were also difficulties in estimating all potential costs and QALYs for the two groups.

Evidence Statement

NICE 2023 was a cost utility analysis, developed to inform this evidence review, reporting outcomes in terms of cost per QALY gained from upskilling team members to undertake the MSCC co-ordinator role.

The study found the upskilling of team members to be cost saving and health improving. These results were robust to sensitivity analysis although subgroup analysis found that the most and least deprived groups did not benefit as much from the intervention with the majority of the benefit being in the second and third least deprived quintiles. The study was deemed to be directly applicable to the review question with potentially serious methodological limitations.

The committee's discussion and interpretation of the evidence

The outcomes that matter most

Overall survival, quality of life, patient satisfaction and neurological and functional status were chosen as critical outcomes. This is because efficient referral and care pathways should lead to quicker diagnosis and treatment of metastatic spinal disease leading to better patient outcomes. Emergency admission to hospital and length of stay were important outcomes because an inefficient or delayed referral pathway could increase emergency hospital admissions and result in longer hospital stays. Access to services was chosen as an important outcome to capture service availability in terms of geographic location and waiting times for services. Different configurations (for example centralised versus local) mean that patients may have to travel or wait longer for services.

The quality of the evidence

The quality of the evidence was assessed using GRADE and all outcomes were rated as low to very low quality. This was predominately due to a very serious overall risk of bias in the evidence contributing to the outcomes, and serious levels of imprecision in the effect estimates. Due to the design of the included studies, it was difficult to avoid confounding between the different intervention groups (for example patients receiving early interventions might be different from those receiving delayed intervention in these studies because a delay in receiving interventions is not an option for some patients in need of urgent care). As a result, the committee also used their expertise and experience when making recommendations.

No evidence was identified for the outcomes quality of life, pain and waiting times.

Benefits and harms

The committee discussed that the previous guideline set service configuration standards for care with some detailed recommendations about how they should function. The guideline also led to a NICE quality standard for MSCC which featured service configuration as an important driver for improvements in MSCC care with 1 of the standards relating to supportive care and rehabilitation (statements 7 - Metastatic spinal cord compression in adults – QS56). The committee agreed that the previous guideline's standards ought to be maintained and improved upon where variation still exists. They therefore used the previous guideline's recommendations as a starting point for their discussion.

They also discussed the Clatterbridge Cancer Centre regional MSCC service. Whilst the outcomes were uncertain due to the nature of such audits which cannot account for all potential confounders and therefore assessed as low quality, the committee agreed that the audit was directly applicable to the UK context and provided a complete dataset. They therefore gave this (which also informed the economic model) more weight than other evidence in their dis-

cussion because it reflected current best practice based on the previous guideline's recommendations and their service has evolved since first implementation to show steady improvement in survival.

Cancer alliances

The evidence on clinical care pathways was inconclusive; however, the committee agreed, based on their own experience, to draft a recommendation emphasising the value of these as a means of improving access to services for people with spinal metastases, direct malignant infiltration of the spine and metastatic spinal cord compression. They discussed the analysis of the Clatterbridge Cancer Centre regional MSCC service audit (which adopted the NICE 2008 guideline including recommendations on how cancer alliances should function) and noted that it showed steady improvement in length of survival over time. This was consistent with the committee's experience of the positive impact that the previous guideline had, particularly in the area of service configuration. Based on the evidence and their experience the committee decided to recommend that cancer alliances should work to ensure that appropriate services covering all parts of the pathway, for example, diagnosis, early rehabilitation, etc, are commissioned to enable any implemented pathway to function effectively and efficiently. A pathway would be a means by which people with the condition and healthcare professionals from all settings can navigate the care they receive and people know what to expect. This is particularly important for MSCC services because of the many different specialties that are involved in care. The committee noted the importance of service review and agreed to recommend that cancer alliances regularly monitor their services to ensure that they are suitable and meet any targets or quality standards (such as the timing around MRI assessments). Monitoring this by the means of prospective audit allows conclusions to be drawn about what works well and what could be improved to make services work better and improve outcomes.

Based on their experience of current practice and services, the committee agreed that cancer alliances work most effectively when there is good organisational and clinical leadership, with clearly defined responsibilities. They therefore agreed to recommend that each cancer alliance appoints a lead who provides oversight and chairs the steering committee. This would include advising the cancer alliance about the organisation of services on behalf of the steering group because any changes could have an impact on the whole cancer alliance. The committee also agreed that reviewing the implementation of care pathways is an important responsibility so that any gaps in implementation can be identified and escalated if necessary. Monitoring services would also be an important part of the role so that any improvements are recognised and concerns can be raised where necessary. There is also the organisational aspect of chairing and arranging the meetings of the steering group which would be a part of their responsibilities so that meetings run smoothly and all necessary issues are raised and discussed.

The committee also emphasised the importance of joint working and coordination within the cancer alliance itself and agreed to recommend that each service forming part of the alliance should identify a lead healthcare professional for metastatic spinal cord compression who provides oversight of the clinical care pathway at a local level and is a member of the steering committee. They listed some of the role's responsibilities. The committee agreed that they should represent the setting that they are based in to ensure that the steering group knows what works best or where there are concerns taking into account all perspectives. Each service lead should also disseminate the decisions made about the care pathway so that they are implemented locally. They would also liaise with other healthcare professionals involved in the pathway so effective and timely communication is needed to ensure people work collaboratively and constructively together to meet people's needs. Another important responsibility is that they make sure that the healthcare professionals within their service are aware of the treatments that are being used and that they understand them as this would make it easier for everyone to know which treatment the person may require and why. The committee discussed the importance of data collection to learn lessons about what worked

well and where there may be concerns which would help improve services. They decided to recommend that lead healthcare professionals should contribute to regular audits so that outcomes could be measured so that positive or negative changes can be identified. Attending steering group meetings would also be within the role's remit so that they can raise any issues that may have arisen in their locality and contribute to the overall aims of the steering group.

Based on their experience and knowledge of what works well in current services, including in the Clatterbridge Cancer Centre regional MSCC service which is based on the previous NICE guideline's service configuration standards and showed steady improvement in survival times, the committee also agreed to recommend that each cancer alliance should have a steering group for metastatic spinal cord compression to oversee service to ensure that care pathways and commissioned services meet people's needs. The committee agreed that input from people with lived experience of metastatic spinal cord compression would be especially important in this regard. They discussed that user input could also be an important way to highlight concerns that people may have and identify potential inequalities in service provision and access to services. It is also important that there is representation from healthcare professionals from all care settings and relevant specialties (for instance alliance groups for primary tumours) as well as representation from the MSCC service in these steering groups. This would mean that all perspectives are taken into account to help implement care pathways effectively and ensure they meet people's needs. It would also mean that there is full accountability from the MSCC service to the steering group and up to alliance level.

Providing a coordinated MSCC service

The committee noted, based on experience, that communication and coordination between specialist and community-based services can often be difficult, particularly in relation to discharge from hospital and care continuity. This can have a detrimental impact on patient outcomes. To address these difficulties the committee agreed to recommend that each metastatic spinal cord compression service should work to establish effective links with relevant services in the community such as primary care, social services, and palliative care. This would mean that information is shared between services which prevents the frustration of people being discharged having to provide the details themselves to every different service that they may have contact with post discharge. It may also prevent important information being missed. The committee discussed that this is consistent with the last NICE guideline's recommendation and has been an important part of the service of the Clatterbridge Cancer Centre regional MSCC service which coordinates care based on the principle of that guideline and has shown steady improvement in length of survival.

The committee discussed the importance of data collection and audit processes (such as the Clatterbridge Cancer Centre regional MSCC service audit), noting that some services were more proactive in this regard than others. They agreed that comprehensive and well-run audits are an essential step in ensuring that services are appropriate and effective and meet people's needs. They agreed to recommend that metastatic spinal cord compression services put systems and processes in place to record data and investigate and report incidents so barriers and facilitators to effective services and improved outcomes can be identified.

Providing support and rehabilitation services

No evidence was identified in relation to services around early rehabilitation. The committee agreed that whilst the recommendations from the previous guideline were still relevant, they should be updated to better reflect current practice.

The committee discussed that there is variation in discharge planning and that this results in people staying longer in hospital than needed and that is not only detrimental to the person's quality of life but also costly. They emphasised that community-based nursing and rehabilitation services and access to equipment and support from social services are an essential

component of care for people with suspected or confirmed spinal metastases, direct malignant infiltration of the spine, or metastatic spinal cord compression to make discharge to home possible without delay. They therefore agreed to recommend that commissioners and local authorities should work together to arrange these services so that people can safely return home.

The previous guideline had recommended that care in a specialist rehabilitation unit should be offered to people with spinal metastases, direct malignant of the spine, or metastatic spinal cord compression. Whilst the committee agreed that specialist rehabilitation may sometimes be needed, they agreed that this did not routinely need to take place on an inpatient basis. They noted that services have evolved to make some of rehabilitation previously only provided in a specialist unit possible in the community. They therefore agreed that it would not lower standards set by the previous guideline to not make the recommendation that rehabilitation should routinely be provided in units. The committee also agreed that decisions about who should be offered specialist rehabilitation are dependent on a range of factors such as level of function, treatment, and the benefit the person is likely to get from such care. The committee recognised that they could not be prescriptive in regard to this recommendation on who might be defined as specifically benefitting from specialist rehabilitation and agreed that it was appropriate to leave this to clinical judgement.

The committee also discussed the importance of discharge planning and agreed upon the importance of coordination. As a result, the committee agreed to recommend that a named individual from the responsible clinical team leads the process. They noted that this was one of the principles promoted in the previous NICE guideline and implemented in the Clatterbridge Cancer Centre regional MSCC service. To enable safe discharge the named individual (which may or may not be the MSCC co-ordinator) would have to liaise with all relevant people that would enable people to return home, such as the person and their family or carers. This means that their wishes and concerns can be taken into account. They discussed that the named individual would also need to liaise with the primary oncology team in order to arrange follow-up treatment or review where necessary, the rehabilitation team to help mobilise the person or provide support to reach other rehabilitation goals as well as working collaboratively with other community healthcare support services for instance primary care service, to ensure that relevant information is shared and if necessary make arrangements with palliative care to provide medical and other support to the person who may be approaching the end of life.

They acknowledged that there are other NICE guidelines that are relevant to support safe discharge from hospital and decided to raise awareness that these are also appropriate for this guideline's context, in relation to support and training that is needed, hospital discharge planning and other rehabilitation principles and so they signposted to them (see the 'other factors the committee took into account' section below for links to these guidelines).

Rehabilitation and supportive care

The committee discussed that rehabilitation needs are not only addressed by service configuration so they agreed that some high-level clinical rehabilitation principles should be highlighted despite there not being a clinical review of rehabilitation as a topic in the scope for this guideline. Whilst it is not strictly service organisation, they decided that services need to adopt those principles so that safe discharge is timely and safe. They also noted that there is a lot of other NICE guidance available that is relevant to this topic and wanted to raise awareness that these also apply to the condition addressed by this guideline (see the 'other factors the committee took into account' section for details of the related guidelines).

One of these principles 'is that rehabilitation does not only start at the end of a person's hospital stay but should be taken into account from diagnosis onwards so that the relevant specialties can be involved throughout the person's pathway to support them with the management plan and help them to achieve their goals. They highlighted that the NICE guideline on

rehabilitation after traumatic injury contains a whole section on setting goals with the person so that rehabilitation can be tailored to the person's wishes and preferences. They provided 3 examples of what these goals may be which related to the person's autonomy (in way of function and activities of daily living) and improving quality of life.

They also agreed, based on their own experience, that currently there is variation in practice in when in the care pathway discharge planning is considered which can result in delay if planning is started late. To address this, they agreed that discharge planning works best when it is initiated at the point of admission to hospital so that rehabilitation needs are reviewed throughout and all services and support are in place to make discharge possible in a timely manner.

With MSCC being associated with serious neurological sequalae it is essential that people receive specialist rehabilitation where needed, so that they can maintain or regain function. Whilst this can be costly and resource intensive the committee discussed that it will save money because where possible people can return home and live independently which improves quality of life and reduces resource use such as longer hospital stays. They therefore decided that this should be routinely offered.

They noted that there are many clinical issues that may be relevant during rehabilitation and supportive care ranging from risk of venous thromboembolisms when being immobilised, developing pressure ulcers during hospital admission, fecal and urinary incontinence as a result of the neurological impact of MSCC and other clinical matters. They therefore signposted to the relevant NICE guidance so that this can be followed to address these clinical matters (see the 'other factors the committee took into account' section below).

Cost effectiveness and resource use

The committee considered the before and after study and economic evaluation developed for this evidence report. The model looked at the cost effectiveness of upskilling staff to make decisions around decisions around less complex cases in line with the role of the MSCC co-ordinator. This was a refinement to the implementation of the MSCC service model as recommended by the previous NICE guideline which was the 'before' state in the 'before and after' audit analysis and economic model. The economic model found that doing so improved overall survival, increased QALYs and reduced cost. The committee acknowledged the weaknesses in the economic model but were confident that cost savings and health improvements were likely from the intervention and ongoing improvements within the service, for example basing it in the oncology team which made collaboration with other specialties more efficient (see also evidence review A). They also highlighted that health outcomes had improved year on year since the creation of the regional MSCC service.

Whilst the committee did not explicitly make recommendations around upskilling staff, they believed it highlighted the need to have clear pathways. Clear pathways allow for the appropriate staff to quickly make a diagnosis and plan treatment for patients and lead to optimal intervention. The committee believed it was unlikely that the increased benefits and reduced costs per person, estimated by the economic model, would be achieved without such pathways in place. The committee also highlighted that the audit data used in the model had a first observation after the launch of the MSCC regional service and that survival improved and cost savings got larger over the course of the time horizon of the model. The committee used this evidence to infer that improvements had in part been achieved from the launch of this service and used the operating model of the Clatterbridge Cancer Centre regional MSCC service to inform recommendations around setting up services. These included recommendations around pathways, having a lead healthcare professional and an alliance lead, clear auditing and commissioning a steering group including people with lived experience.

For areas where such a regional centre is not already formed there will be large costs from setting this up through recruiting members of panels, setting up computer systems for recording patient information, auditing outcomes and for forming and disseminating pathways. As

cost savings increased since the introduction over the time horizon of the economic model the committee thought these one-off costs would be fully recouped over the first few years of the service operating.

Discharge planning at the point of admission to hospital should lead to less delays in discharge, reducing the number of bed days in hospital for people and freeing up health care professionals. Whilst there may need to be some reconfiguration so this task is undertaken earlier, as it needs to be performed anyway, there should be no initial increase in resource use.

There will be an initial resource impact with recommendations around specialist rehabilitation with this not always being received by people needing it. Despite not identifying any economic evidence around this the committee highlighted it was consistent with previous NICE guidelines. Given the potential for catastrophic events such as paraplegia and that specialist rehabilitation will be the most likely pathway for these people to return home and live independently, there will be cost savings through reduced need for community care at later times and through avoidance of the costs associated with adverse events.

Other factors the committee took into account

The committee noted that there are a range of NICE guidelines relevant to the topic of support and rehabilitation after discharge and agreed to reference these in the recommendations. These included rehabilitation after traumatic injury, venous thromboembolism in over 16s, prevention and management of pressure ulcers, urinary incontinence due to neurological conditions and fecal incontinence in adults.

Recommendations supported by this evidence review

This evidence review supports recommendations 1.1.1 to 1.1.4, 1.1.11, 1.1.12, 1.1.22 to 1.1.28 and 1.12.1 to 1.12.5 in the NICE guideline.

References – included studies

Effectiveness

Clatterbridge 2022

Clatterbridge Cancer Centre. Upskilling staff in MSCC coordination to make initial decisions around referrals to a metastatic spinal cord compression service without senior clinician support. A ‘before and after’ study from one UK centre. [*Unpublished audit*]; 2022 see appendix I.

Cui 2021

Cui Y, Shi X, Li C, et al. Effect of the Timing of Surgery on Neurological Recovery for Patients with Incomplete Paraplegia Caused by Metastatic Spinal Cord Compression. Therapeutics and Clinical Risk Management 17, 831-40, 2021

Fitzpatrick 2012

Fitzpatrick D, Grabarz D, Wang L, et al. How effective is a virtual consultation process in facilitating multidisciplinary decision-making for malignant epidural spinal cord compression? International Journal of Radiation Oncology, Biology, Physics 84, e167-72, 2012

Guddati 2017

Guddati A, Kumar K, Shapira I. Early intervention results in lower mortality in patients with cancer hospitalized for metastatic spinal cord compression. Journal of Investigative Medicine, 65, 787-793, 2017

Malik 2020

Malik A, Baek J, Alexander J, et al. Orthopaedic vs. Neurosurgery – Does a surgeon's specialty have an influence on 90-day complications following surgical intervention of spinal metastases? Clinical Neurology and Neurosurgery 192, 105735, 2020

Appendices

Appendix A Review protocols

Review protocol for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Table 4: Review protocol

ID	Field	Content
0.	PROSPERO registration number	CRD42022303725
1.	Review title	Effective service configuration and delivery arrangements in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression
2.	Review question	What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?
3.	Objective	To establish effective service configuration and delivery arrangements in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression
4.	Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Cumulative Index to Nursing and Allied Health Literature (CINAHL) • Embase • Emcare • Epistemonikos

ID	Field	Content
		• International Health Technology Assessment (IHTA) database • MEDLINE & MEDLINE In-Process Searches will be restricted by: • Systematic review/meta-analysis study design filter • RCT/non-randomised controlled trials study design filter • Date: 1990 onwards (see rationale under Section 10) • English language studies • Human studies Other searches: • Reference searching • Citation searching • Inclusion lists of systematic reviews • Websites The searches will be re-run 6-8 weeks before final submission of the review and further studies retrieved for inclusion. The full search strategies for MEDLINE database will be published in the final review.
5.	Condition or domain being studied	Service configuration and delivery arrangements in the management and early rehabilitation of adults with confirmed metastatic spinal cord compression

6.	Population	**Inclusion**:
		• Adults with confirmed
		  ○ metastatic spinal disease
		  ○ direct malignant infiltration of the spine
		• Adults with confirmed spinal cord or nerve root compression because of
		  ○ metastatic spinal disease
		  ○ direct malignant infiltration of the spine

ID	Field	Content
		Exclusion: • Adults with spinal cord compression because of primary tumours of the spinal cord, meninges or nerve roots. • Adults with spinal cord compression because of non-malignant causes. • Adults with primary bone tumours of the spinal column. • Children and young people under the age of 18.

7.	Intervention/Exposure/Test	Any practice and service delivery models (approaches, configurations of resources and services) for the management and early rehabilitation of malignant spinal cord compression or spinal metastases. For example:
		
		• Delivery arrangements:
		  ○ Who provides care and how the healthcare workforce is managed
		  ○ Where care is provided, for example,
		  ▪ Specialist centres
		  ▪ Local hospitals
		  ▪ Neurorehabilitation units
		  ▪ Rehabilitation while on oncology ward
		  ○ How and when care is delivered, for example,
		  ▪ Early rehabilitation
		• Coordination of care and management of care processes:
		  ○ Care pathways
		  ○ Service user management (models responsive to individual needs)
		  ○ Communication / referral between providers, for example,
		  ▪ Specialist centres and general physiotherapy (for rehabilitation)
		  ▪ Physiotherapy/orthotics training by specialist centres for local hospitals
		  ○ Multidisciplinary teams

8.	Comparator/Reference standard/Confounding factors	Interventions compared with: • Each other • Combinations of interventions

ID	Field	Content
9.	Types of study to be included	• Randomised controlled trials • Non-randomised comparative studies (including before and after designs) • Systematic reviews/meta-analyses. • Service evaluations and audits will be included in the absence of comparative randomised or non-randomised studies.
10.	Other exclusion criteria	**Inclusion**: • Full text papers **Exclusion**: • Conference abstracts • Articles published before 1990 (MRI became available in the early 1990s and is a key test for investigation and management of metastatic spinal cord compression). • Papers that do not include methodological details will not be included as they do not provide sufficient information to evaluate risk of bias/ study quality. • Non-English language articles
11.	Context	Metastatic spinal cord compression in adults: risk assessment, diagnosis and management (2008) NICE guideline will be updated by this review question

12.	Primary outcomes (critical outcomes)	• Overall survival
		• Quality of life
		• Pain
		• Neurological and functional status including:
		  ○ Bowel and bladder function
		  ○ Mobility or ambulatory status

13.	Secondary outcomes (important outcomes)	• Emergency admission to hospital and length of hospital stay
		• Access to services:
		  ○ Local availability (for example, time/distance travelled to access services)
		  ○ Waiting times for services

14.	Data extraction (selection	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated.

ID	Field	Content
	and coding)	Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required. The full set of records will not be dual screened because the population, interventions and relevant study designs are relatively clear and should be readily identified from titles and abstracts. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
15.	Risk of bias (quality) assessment	Risk of bias of individual studies will be assessed using the preferred checklist as described in Appendix H of Developing NICE guidelines: the manual • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs and quasi-RCTs • The non-randomised study design appropriate checklist. For example Cochrane ROBINS-I tool for non-randomised controlled trials and cohort studies; the EPOC RoB tool for controlled before and after studies. The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
16.	Strategy for data synthesis	Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. <u>Data Synthesis</u> Where possible, pairwise meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios for dichotomous outcomes. Peto odds ratio will be used for outcomes with zero events Mean differences or standardised mean differences will be calculated for

ID	Field	Content

		continuous outcomes.
		If sufficient RCTs are available forming a network of relevant interventions, network meta-analysis will be done using MetaInsight V3 (Owen, RK, Bradbury, N, Xin, Y, Cooper, N, Sutton, A. MetaInsight: An interactive web-based tool for analyzing, interrogating, and visualizing network meta-analyses using R-shiny and netmeta. Res Syn Meth. 2019; 10: 569-581)
		
		<u>Heterogeneity</u>
		Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. I2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively.
		In the case of serious or very serious unexplained heterogeneity (remaining after pre-specified subgroup and stratified analyses) meta-analysis will be done using a random effects model.
		
		<u>Minimal important differences (MIDs)</u>
		Default MIDs will be used for risk ratios and continuous outcomes only, unless the committee pre-specifies published or other MIDs for specific outcomes
		• For risk ratios: 0.8 and 1.25.
		• For continuous outcomes:
		  ○ MID is calculated by ranking the studies in order of SD in the control arms. The MID is calculated as +/- 0.5 times median SD.
		  ○ For studies that have been pooled using SMD (meta-analysed): +0.5 and -0.5 in the SMD scale are used as MID boundaries.
		
		<u>Validity</u>
		The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/

17.	Analysis of sub-groups	Evidence will be stratified by: • None Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes: • Subgroups listed in the equality impact assessment form: age, race, sex & socioeconomic status

ID	Field	Content		
		Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.		
18.	Type and method of review	☒	Intervention	
		☐	Diagnostic	
		☐	Prognostic	
		☐	Qualitative	
		☐	Epidemiologic	
		☒	Service Delivery	
		☐	Other (please specify)	
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	24/01/2022		
22.	Anticipated completion date	23/08/2023		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	☑	☑
		Piloting of the study selection process	☑	☑
		Formal screening of search results against eligibility criteria	☑	☑
		Data extraction	☑	☑
		Risk of bias (quality) assessment	☑	☑

ID	Field	Content
		Data analysis ☑ ☑
24.	Named contact	**5a. Named contact** National Guideline Alliance **5b Named contact e-mail** metastaticspinal@nice.org.uk **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and National Guideline Alliance
25.	Review team members	NGA Technical Team
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Alliance which receives funding from NICE.
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage].
29.	Other registration details	
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=303725
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social

ID	Field	Content	
		media channels, and publicising the guideline within NICE.	
32.	Keywords	Metastatic spinal cord compression, service, delivery, early rehabilitation and management.	
33.	Details of existing review of same topic by same authors	None	
34.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35.	Additional information	None	
36.	Details of final publication	www.nice.org.uk	

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B Search strategy (clinical/economic)

Literature search strategies for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Database: Medline – OVID interface

#	Searches
1	Spinal Cord Compression/
2	((spine or spinal or vertebr*) and (metast* or oligometastasis)).tw.
3	(mescc or mscc).tw.
4	(((cauda equina or cervical* or cervicothoracic or cord* or coccyx or duralsac* or dural sac* or intervertebr* or lumbar or lumbosac* or lumbo sac* or medulla* or orthothoracic or sacral or sacrum or spinal or spine* or thecal sac* or thoracic or vertebr* or epidural or extradural or extra dural or ((axon* or neuron* or nerve*) adj2 root)) adj3 (collaps* or compress* or pinch* or press*)) and (adeno* or cancer* or carcinoma* or chordoma* or intraepithelial* or intra epithelial* or malignan* or metast* or neoplas* or oligometast* or tumo?r*)).ti,ab.
5	or/1-4
6	Case Management/ or "Continuity of Patient Care"/ or Critical Pathways/ or "Delivery of Health Care"/ or "Delivery of Health Care,Integrated"/ or Models, Organizational/ or Patient Care Management/ or Patient Care Planning/ or Patient Care Team/ed, og or Patient-Centered Care/
7	Community-Institutional Relations/ or Hospital-Patient Relations/ or Hospital-Physician Relations/ or Interdepartmental Relations/ or Interinstitutional Relations/ or exp Interprofessional Relations/ or Intersectoral Collaboration/ or Public Relations/
8	(collaboration or team work* or teamwork*).tw.
9	((collaborat* or coordinat* or co ordinat* or integrat* or shared or stepped or systematic) adj2 (care or effort* or health* or interven* or liais* or manag* or model* or pathway* or service* or work*)).ti,ab.
10	((configur* or model*) adj5 (care or healthcare or organi?ation* or practice* or service*)).ti,ab.
11	((case or disease or user*) adj (manag* or plan*)).ti,ab. or (patient* adj5 (mana* or plan*)).ti. or (patient? adj3 manag*).ab. /freq=2
12	(((enhanced or managed) adj care) or multi component or multicomponent).tw.
13	(algorithm* or care manag* or chronic care* or complex intervention* or consultation liais* or cooperative behav* or co operative behav* or multifacet* or multi facet* or multiintervention* or multiple intervention* or organi?ation* intervention* or transdisciplin* or trans disciplin*).tw.
14	(interdisciplin* or inter disciplin* or interinstitutional or inter institutional or interpersonal relation* or inter personal relation* or interprofession* or inter profession* or intraprofession* or intra profession* or (joint adj (disciplin* or profession* or working)) or multidisciplin* or multi disciplin* or multiprofession* or multi profession*).tw.
15	((joint or inter or intra or multi*) adj3 (disciplin* or profession*) adj5 (collaborat* or communicat* or conversation* or educat* or learn* or taught or teach* or train*)).ti,ab.
16	(patient? adj3 care adj3 team?).tw.
17	((communicat* or refer*) adj5 (professional* or disciplin* or interdisciplin* or provider*)).tw.
18	(continuity adj3 (care or healthcare)).tw.
19	((care or healthcare or service*) adj5 delivery).tw.
20	(interprofessional relation* or inter professional relation* or managed care program* or (measur* adj2 care) or ((patient care adj (management or planning or team*)) or professional patient relation*)).ti,ab.
21	((leader* adj2 style*) or ((team or unit) adj2 (culture or lead* or manager*)) or ((human resources or nurs* or rn or personnel or staff*) adj2 leader* adj2 manag*) or (nurs* adj team*)).ti,ab.
22	(((nurs* or staff* or workforce or work force or worker*) adj2 (delivery or high intensity or model* or staffing or system*)) or (model* adj3 integrat*) or ((allocation or modular or team*) adj2 model*) or planning model*).ti,ab.
23	((associate director* or deputy head or doctor? or health professional? or lead? or leader? or manager? or member? or nurs* or registrar? or staff or team?) adj3 communicat*).ti,ab.
24	(efficien* adj2 practice*).ti,ab.
25	((effectiv* or facilitat* or improv*) adj3 (communicat* or team*)).ti,ab.
26	((team* or role* or workforce* or work force*) adj2 (flex* or reflex*)).ti,ab.
27	((rapid* adj3 communicat*) or (enhanc* adj3 (communicat* or team*))).ti,ab.
28	or/6-27
29	exp Health Personnel/ or Health Workforce/
30	(allied health professional* or AHP*1 or clinician* or consultant* or coordinator* or co ordinator* or general practitioner* or GP*1 or h?ematologist* or medic* or neurologist* or neurosurgeon* or nurse* or occupational therapist* or oncologist* or OT*1 or physician* or physiotherapist* or physical therapist* or radiologist* or registrar* or surgeon* or worker* or workforce or work force).ti. or ((allied health professional* or AHP*1 or clinician* or consultant* or coordinator* or co ordinator* or general practitioner* or GP*1 or h?ematologist* or medic* or neurologist* or neurosurgeon* or nurse* or occupational therapist* or oncologist* or OT*1 or physician* or physiotherapist* or physical therapist* or radiologist* or registrar* or surgeon* or worker* or workforce or work force).ab. adj7 ((manag* or rehab* or ablat* or log?roll* or corticosteroid* or dexamethasone or gastric protection or immobili* or kyphoplast* or occupational therap* or physical therap* or physiotherap* or physio therap* or radiotherap* or surgery or surgical or vertebroplast*).ti,ab. or rh.fs.))
31	or/29-30
32	exp Hospitals/ or exp Hospital Units/ or Rehabilitation Centers/
33	((centre* or center* or hospital* or unit? or ward?) adj7 (manag* or neurorehab* or rehab* or ablat* or logroll* or log roll* or corticosteroid* or dexamethasone or gastric protection or immobili* or kyphoplast* or physical therap* or physiother-

#	Searches
	ap* or physio therap* or occupational therap* or radiotherap* or surgery or surgical or vertebroplast*)).ti,ab.
34	(general* adj3 (physiotherap* or physio therap* or physical therap*)).tw.
35	MDT*1.tw.
36	((physio* or orthotic*) adj5 train*).tw.
37	((specialist or tertiary) adj3 (centre* or center* or hospital* or unit*)).tw.
38	(rehab* adj3 (centre* or center*)).tw.
39	or/32-38
40	or/28,31,39
41	exp Emergency Service, Hospital/
42	((community adj2 diagnos* adj (centre* or center* or hub*)) or cdh or one stop shop*).ti,ab.
43	(faster diagnostic standard* or fds).ti,ab.
44	(((express or same day or one stop) adj2 clinic*) or rapid diagnostic centre* or rapid diagnostic center* or rdc).ti,ab.
45	(a&e or (emergency adj (department* or room* or unit*)) or immediate management or ((emergency or urgen*) adj2 (manag* or refer* or treatment* or ward*))).ti,ab.
46	(accident adj2 emergenc*).ti,ab
47	(((("2" or two) adj week*) or "14 day*") and pathway*) or ((two or "2") adj week wait)).ti,ab.
48	(("7 day" adj7 scan*) or (one week adj3 present*)).ti,ab.
49	(mscc adj (coordinat* or co ordinat*)).ti,ab.
50	(early adj2 (involv* or rehab*)).ti,ab.
51	or/41-50
52	"Personnel Staffing and Scheduling"/ or Shift Work Schedule/ or Work-Life Balance/ or Work Schedule Tolerance/ or Workload/ or og.fs.
53	(handover* or hand over* or handoff* or hand off* or ((nurs* or staff*) adj2 (delivery or mix* or model*)) or roster* or rota? or shift? or skill?mix* or (skill* adj2 mix) or staffing or team brief* or teambuild* or (team* adj2 build*)).ti,ab.
54	(patient* adj2 ratio*).ti,ab.
55	((advance? practice adj2 nurs*).ti,ab.
56	(nurs* adj (advisor* or clinician* or consultant* or practitioner* or specialist*)).ti,ab.
57	((alter* or chang* or expand* or expansion* or shift* or staff*) adj2 (activit* or duty or duties or responsibilit* or role* or task*)).ti,ab.
58	or/52-57
59	or/51,58
60	or/40,59
61	5 and 60
62	exp ANIMALS, LABORATORY/ or exp ANIMAL EXPERIMENTATION/ or exp MODELS, ANIMAL/ or exp RODENTIA/ or (rat or rats or mouse or mice).ti.
63	LETTER/ or EDITORIAL/ or NEWS/ or exp HISTORICAL ARTICLE/ or ANECDOTES AS TOPIC/ or COMMENT/ or CASE REPORT/ or (letter or comment*).ti.
64	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
65	63 not 64
66	62 or 65
67	61 not 66
68	limit 67 to (english language and yr="1990 -Current")

Health economics search

Database: Medline – OVID interface

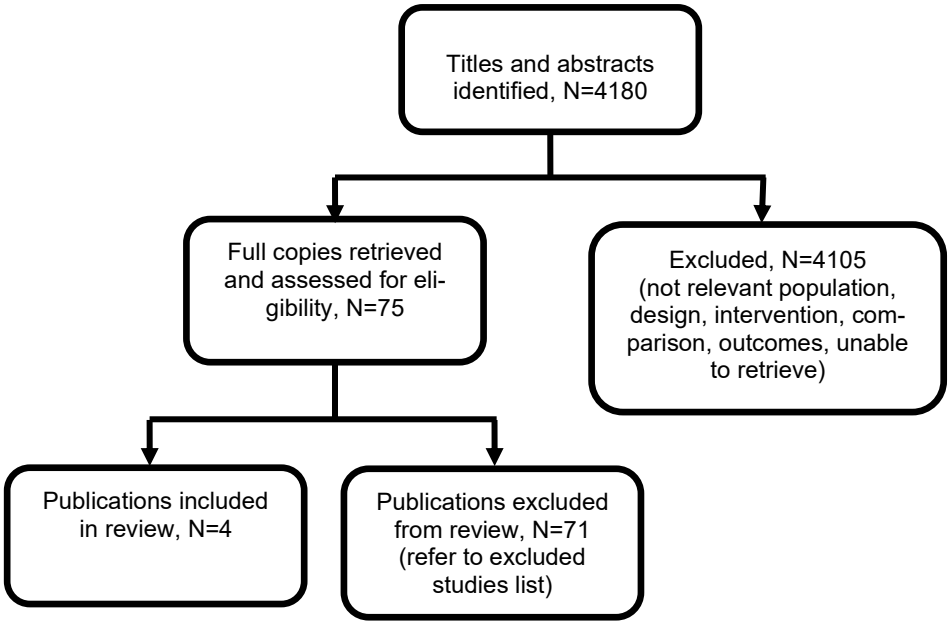
#	Searches
1	exp Spinal Cord Neoplasms/ or Spinal Neoplasms/
2	((spine or spinal or vertebr*) adj2 (adeno* or cancer* or carcinoma* or intraepithelial* or intra epithelial* or malignan* or neoplas* or tumo?r*)).tw.
3	((spine or spinal or vertebr*) and (metast* or oligometast*)).tw.
4	or/1-3
5	Spinal Cord Compression/
6	((cauda equina or cervical* or cervicothoracic or cord* or coccyx or duralsac* or dural sac* or intervertebr* or lumbar or lumbosac* or lumbo sac* or medulla* or orthothoracic or sacral or sacrum or spinal or spine* or thecal sac* or thoracic or vertebr* or epidural or extradural or extra dural or ((axon* or neuron* or nerve*) adj2 root)) and (collaps* or compress* or pinch* or press*) and (adeno* or cancer* or carcinoma* or chordoma* or intraepithelial* or intra epithelial* or malignan* or metast* or neoplas* or oligometast* or tumo?r*)).tw.
7	(myelopath* or myeloradiculopath* or radiculopath*).tw,hw. or (radicular adj2 (disorder* or syndrome*)).tw.
8	(mescc or mscc).tw.
9	or/5-8
10	((adeno* or cancer* or carcinoma* or intraepithelial* or intra epithelial* or malignan* or metast* or neoplas* or tumo?r*) adj3 (escap* or infiltrat* or invasiv* or metast* or spread*) adj5 (cauda equina or cervical* or cervicothoracic or cord* or coccyx or duralsac* or dural sac* or intervertebr* or lumbar or lumbosac* or lumbo sac* or medulla* or orthothoracic or sacral or sacrum or spinal or spine* or thecal sac* or thoracic or vertebr* or epidural or extradural or extra dural or ((axon* or neuron* or nerve*) adj2 root))).tw.
11	or/4,9-10

#	Searches
12	Economics/ or Value of life/ or exp "Costs and Cost Analysis"/ or exp Economics, Hospital/ or exp Economics, Medical/ or Economics, Nursing/ or Economics, Pharmaceutical/ or exp "Fees and Charges"/ or exp Budgets/
13	(cost* or economic* or pharmacoeconomic*).ti.
14	(budget* or financ* or fee or fees or price* or pricing* or (value adj2 (money or monetary))).ti,ab.
15	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
16	or/12-15
17	11 and 16
18	limit 17 to english language
19	limit 18 to yr="2005 -Current"

Appendix C Effectiveness evidence study selection

Study selection for: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Table 5: Evidence tables

Clatterbridge Cancer, 2022
Clatterbridge Cancer Centre. Upskilling staff to make decisions around referrals to a metastatic spinal cord compression service without senior clinician support. A 'before and after study from one UK centre [Unpublished audit]. 2022

Study details

Country/ies where study was carried out	UK
Study type	Before-and-after study
Study dates	January 2018 to May 2022
Inclusion criteria	All patients referred to the Clatterbridge Cancer Centre MSCC service through the MSCC pathway.
Exclusion criteria	Patients were excluded from the survival analysis by cancer type if they had been inappropriately referred to the MSCC service for a non-malignant spinal cord compression or inappropriately referred with no compression of the spinal cord.
Patient characteris-tics	N=3173 Age, mean years: 69 Female=1289, male=1884 **Before service change:** • N=1342 • Age (mean) years: 68.5 • Male: 59.3% • Deprivation quintile (mean): 2.4 • Primary cancer: breast 13%, lung 19%, prostate 22%, unknown primary 14%, other 33 **After service change:** • N=1831 • Age (mean) years: 69.5 • Male: 59.4%

	• Deprivation quintile (mean): 2.6 • Primary cancer: breast 12%, lung 15%, prostate 21%, unknown primary 18%, other 33%
Intervention(s)/control	Before service change: the MSCC service was organised in accordance with the NICE 2008 guideline. This included for example the role of the MSCC co-ordinator, the organisation of services to enable prompt MRI and radiotherapy. After service change: this was a refinement of the previous model where members of the MSCC team were upskilled to coordinate MSCC cases by making more advanced clinical decisions on less complex referrals. The background for this was a move of the main functions of the hospital to a new site in Liverpool city centre. The MSCC service is a virtual facilitative service, and the MSCC team remained at the Wirral site while the clinical decisions unit and medical on call team moved to the Liverpool site. The medical model also changed to being a different Consultant on call each day and COVID restrictions meant that multiple services, including Consultant clinical opinions could be remote from home. This made accessing the Consultants quickly for opinion more challenging and many did not feel comfortable making decisions on patients they were not going to treat or treating patients they did not make clinical decisions on. This led to an increase in the number of referrals being re-discussed multiple times. It became difficult for the service to absorb this extra activity, so this led to the MSCC team being upskilled to make decisions on less complex referrals.
Duration of follow-up	Follow-up of 1 year for survival analysis
Sources of funding	No specific funding received
Sample size	3173

Outcomes

Overall survival – patients with lung cancer

Outcome	**After service change vs before service change, 1 year, N2=282, N1=248**
Overall survival (adjusted for age and sex) HR < 1 favours After Service Change group Hazard ratio (95% CI)	0.72 (0.6 to 0.87)

Overall survival - patients with prostate cancer

Outcome (adjusted for age)	**After service change vs before service change, 1 year, N2=390, N1=291**
Overall survival (adjusted for age) HR < 1 favours After Service Change group Hazard ratio (95% CI)	1.08 (0.9 to 1.3)

Overall survival - patients with breast cancer

Outcome (adjusted for age)	**After service change vs before service change, 1 year, N2=225, N1=178**
Overall survival	0.86 (0.65 to 1.14)

Outcome (adjusted for age)	**After service change vs before service change, 1 year, N2=225, N1=178**
HR < 1 favours After Service Change group Hazard ratio/95% CI	

Overall survival - patients with unknown primary cancer

Outcome (adjusted for age and sex)	**After service change vs Before service change, 1 year, N2=328, N1=184**
Overall survival HR < 1 favours After Service Change group Hazard ratio (95% CI)	0.67 (0.53 to 0.84)

Overall survival patients with other cancers

Outcome (adjusted for age and sex)	**After service change vs Before service change, 1 year, N2=606, N1=440**
Overall survival HR < 1 favours After Service Change group Hazard ratio (95% CI)	0.84 (0.73 to 0.97)

Critical appraisal – ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Serious. *Limited adjustment for confounders (primary cancer, age & sex).*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Serious *(2 different time periods were compared – likely to be systematic differences in the care provided e.g. impact of change of hospital site & COVID-19)*
5. Bias due to missing data	Risk of bias judgement for missing data	Low
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Low
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Low
Overall bias	Risk of bias judgement	Very serious. *The study has some important problems (limited adjustment for confounders and likely deviation*

Section	Question	Answer
		from intended intervention).
Overall bias	Directness	Directly applicable

Cui 2021
Cui Y, Shi X, Li C, et al. Effect of the Timing of Surgery on Neurological Recovery for Patients with Incomplete Paraplegia Caused by Metastatic Spinal Cord Compression. Therapeutics and Clinical Risk Management 17, 831-40, 2021

Study details	
Country/ies where study was carried out	China
Study type	Retrospective cohort study
Study dates	November 2010 to September 2017
Inclusion criteria	Patients with incomplete spinal cord injury
Exclusion criteria	Excluded patients with incomplete data, lumbar spine metastases, normal spinal cord function and ambulatory status, complete paraplegia, and spinal cord function deteriorated within 2 weeks after surgery due to tumor progression.
Patient characteristics	Group A: n=8 Group B: n=14 Group C: n=53 Age: A: 60±4; B: 63±3; C: 61±2 Sex: female A: 5 B: 11 C: 40 Tokuhashi score A: 6 (3–10) B: 7 (2–11) C: 7 (2–10)
Intervention(s)/control	Whether surgery was performed within 4 days, between 4 and 7 days or after 7 days
Duration of follow-up	2 weeks
Sources of funding	This study was supported by the Opening Foundation of State key laboratory of molecular developmental biology

Sample size	n=75 Group A n=8 Group B n=14 Group C n=53

Outcomes (post-operative)

Outcome	Within 3 days (group A), 2 weeks, n=8	Between 4 and 7 days (group B), 2 weeks, n=14	After 7 days (group C), 2 weeks, n=53
Neurological and functional status - Improvement at least 1 grade of AIS scale (injury, 6 point scale)	n=6/8	n=10/14	n=25/53
Neurological and functional status - Ambulatory status improvement	n=2/8	n=5/14	n=29/53
Emergency admission to hospital: length of post-operative hospital stay, days, median (range). IQR not reported.	13.5 (6 – 44)	11.5 (5 – 66)	16 (7 – 61)
Emergency admission to hospital: total length of hospital stay, days, median (range). IQR not reported.	15 (8 – 47)	14 (10 – 68)	22 (8 – 64)

Critical appraisal – ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Serious. *No adjusting for confounders. There are likely to be differences between those whose surgery is/is not delayed.*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low
5. Bias due to missing data	Risk of bias judgement for missing data	Low
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Low
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Low
Overall bias	Risk of bias judgement	Serious. *The study has some important problems (no adjusting for confound-*

Section	Question	Answer
		ers.
Overall bias	Directness	Directly applicable

Fitzpatrick, 2012
Fitzpatrick D, Grabarz D, Wang L, et al. How effective is a virtual consultation process in facilitating multidisciplinary decision-making for malignant epidural spinal cord compression? Inter-national Journal of Radiation Oncology, Biology, Physics 84, e167-72, 2012

Study details

Country/ies where study was carried out	Canada
Study type	Prospective cohort study
Study dates	2004 - 2008
Inclusion criteria	All patients at a single University Health Network with a radiological diagnosis of malignant epidural spinal cord compression (MESCC) were eligible. Patients were identified by attending radiation oncologist or spinal surgeon through prospective screening of new case referrals.
Exclusion criteria	Patients whose diagnostic images could not be retrieved were excluded from the analysis (n=6). Patients referred directly to the spinal surgeon by the community referring physician were not eligible for virtual consultation (n=20).
Patient characteris-tics	N=151 Age: median 60 years (range 30 to 90) Sex: male 94; female 57. Primary site • Lung 35 (24%) • Breast 19 (13%) • Gastrointestinal 17 (12%) • Multiple myeloma 19 (13%) • Prostate 15 (11%) • Renal cell 12 (8%) • Unknown primary 11 (8%) • Others 17 (12%) Level of spinal cord compression • Cervical 24 (16.5%)

	• Thoracic 112 (77%) • Lumbar 4 (2.5%) • Junction of a vertebral segments 5 (3%)
Intervention(s)/control	Virtual consultation process (VCP) using telemedicine (real time sharing of patient information over internet & telephone) to facilitate the provision of multidisciplinary care between radiation oncology and spinal surgery for the management of patients diagnosed with MSCC. A set of clinical and radiological parameters relevant to decision making were agreed beforehand. When VCP was initiated (typically by the radiation oncologists), details on these parameters and the diagnostic images on PACS system (e-film) were conveyed, typically through e-mail or direct phone discussion between radiation and spinal oncologists. A shared network PACS system (e-film) permitted the spinal surgeons to directly review patients' images. A joint opinion as to whether the patient should be managed with combined modality was typically made within few minutes or on the same day, depending on the degree of urgency of the attending physicians. Patients considered suitable for surgery were physically transferred for an in-person surgical consultation to confirm the opinion and to proceed with surgery. RT was typically recommended within a few weeks after recovery.
Duration of follow-up	Not reported
Sources of funding	Kerbel Research Fund.
Sample size	N=151; n=6 excluded as imaging could not be retrieved; n=20 excluded due to referral direct to spinal surgeon. n=46 had virtual consultation requested n=79 had no virtual consultation

Outcomes

Outcome	**Virtual consultation, Baseline, N = 46**	**No virtual consultation, Baseline, N = 79**
Overall survival – months	median 5.3 (95% CI 3.5 – 10.6)	median 3.9 (95% CI 2.0 – 4.9)
Access to services - number of candidates for surgery missed	n=0/46	5/79

Critical appraisal – ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Serious. *Patients were selected for virtual consultation or no virtual consultation based on the oncologist's judgement over whether they were potential candidates for surgery - therefore the two groups are not similar in terms of baseline characteristics.*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low
3. Bias in classification of interventions	Risk of bias judgement for classification of interven-	Low

Section	Question	Answer
	tions	
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low
5. Bias due to missing data	Risk of bias judgement for missing data	Low
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Moderate. *Outcome assessors were aware of the intervention received by study participants and methods of outcome assessment likely differed between groups.*
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Low
Overall bias	Risk of bias judgement	Serious. Serious risk of bias due to confounding and moderate risk of bias in measurement of outcomes.
Overall bias	Directness	Directly applicable

Guddati, 2017
Guddati A, Kumar K, Shapira I. Early intervention results in lower mortality in patients with cancer hospitalized for metastatic spinal cord compression. Journal of Investigative Medicine, 65, 787-793, 2017

Study details

Country/ies where study was carried out	USA
Study type	Retrospective cohort study
Study dates	2000-2011
Inclusion criteria	Adult patients (age ≥18 years) with metastatic cancer who were discharged with a primary diagnosis of metastatic spinal cord compression
Exclusion criteria	Unclear
Patient characteristics	N=13457 Age • 18–34 N=530 • 35–49 N=1962 • 50–64 N=4703 • 65–79 N=4789 • 80 and above N=1468

Sex
- Male N=7895

Race
- White N=7277
- Black N=1894
- Hispanic N=826
- Asian N=358
- Others N=276
- Unknown N=2826

Payer
- Private N=4771
- Medicare N=6131
- Medicaid N=1563
- Self N=609
- Other N=389

Hospital characteristics
- Teaching hospitals N=8890
- Non-teaching hospitals N=4567

Urban versus non-urban location
- Urban location N=12762

Hospital size
- Small N=816
- Medium N=2681
- Large N=9960

Hospital ownership
- Government—non-profit N=2091
- Private—non-profit N=10828
- Private—profit N=538

Hospital geographic location
- Northeast N=4397
- Midwest N=2925

	• South N=4097 • West N=2018
Intervention(s)/control	The usage and timing of interventions by RT or surgery was identified using ICD-9 codes. Intervention was classified as 'early' when provided within the first 48 hours and 'late' when provided after 48 hours of hospitalization.
Duration of follow-up	Unclear time, looked at discharge
Sources of funding	Unclear
Sample size	N=13457 Early intervention n=5035 Late intervention n=8422
Other information	Analysis of in-hospital mortality for early versus late intervention was adjusted for age, gender, race, insurance, Charlson's comorbidity index, hospital characteristics, individual cancers, use of mechanical ventilation and year of admission. The study reports hospital size and hospital ownership as risk factors for late intervention.

Outcomes

Outcome	**Early intervention, 11 day, n=5035**	**Late intervention, 11 day, n=8422**
Overall survival - In-hospital mortality	n=252/5035	n=581/8422
Length of stay, days, median (IQR)	6 (4 to 11)	11 (7 to 16)

Critical appraisal – ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Unclear. Some adjustment for confounders in analysis, however there were systematic differences between groups. Female gender, private-for-profit hospitals and higher comorbidity index were associated with lower rate of early intervention.
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Low
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low
5. Bias due to missing data	Risk of bias judgement for missing data	Low
6. Bias in measurement of out-	Risk of bias judgement for measurement of	Low

Section	Question	Answer
comes	outcomes	
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Low
Overall bias	Risk of bias judgement	Moderate. Potential for bias due to confounding.
Overall bias	Directness	Partially applicable. US healthcare setting.

Malik, 2020
Malik A, Baek J, Alexander J, et al. Orthopaedic vs. Neurosurgery – Does a surgeon's specialty have an influence on 90-day complications following surgical intervention of spinal metastases? Clinical Neurology and Neurosurgery 192, 105735, 2020

Study details

Country/ies where study was carried out	USA
Study type	Retrospective cohort study
Study dates	2007 - 2017
Inclusion criteria	Patients were identified from the Humana Administrative Claims (HAC) private payor dataset The HAC database is a research repository, containing billing/insurance claims from over 24 million individuals insured under Humana's Medicare Advantage, Commercial-only and/or Medicaid Managed Care plans across the USA. The 2007–2017 HAC database was queried using International Classification of Diseases 9th and 10th Edition (ICD-9/ICD-10) diagnosis codes 198.5, C79.5, C79.51 and C79.52 combined with procedure codes for laminectomy, osteotomy/corpectomy and/or fusion to identify patients undergoing surgical intervention for spinal metastases. ICD-9/10 diagnosis codes were used to identify the presence of a primary cancer (breast, lung, prostate, renal/kidney and other/ unspecified). Physician taxonomy codes were used to filter the cohort into two distinct groups: those who were operated on by an orthopaedic surgeon (207X00000X) or a neurological surgeon (207T00000X).
Exclusion criteria	Patients undergoing vertebroplasty and/or kyphoplasty were excluded from the study.
Patient characteristics	N=887 Age • <45 N=16 • 45-64 N=204 • 65-79 N=582 • ≥80 N=86 Gender

	• Female N=348 • Male N=539 Race • White N=560 • Black N=96 • Other N=13 • Unknown N=218 Region • Midwest N=230 • Northeast N=11 • South N=569 • West N=77 Plan • Medicare Advantage N=747 • Full-Insured/Commercial N=137 • Medicaid N=3 Primary cancer • Breast N=133 • Prostate N=190 • Lung N=232 • Renal N=133 • Other N=199 Surgery types • Fusion N=605 • Osteotomy/Corpectomy N=329 • Laminectomy N=628
Intervention(s)/control	Surgical intervention for spinal metastasis (laminectomy, osteotomy/corpectomy and/or fusion) performed by either a neurosurgeon or an orthopaedic surgeon.
Duration of follow-up	90 days
Sources of funding	None reported
Sample size	N=887. Orthopaedic surgeon group n=204; neurosurgeon group n=683

Other information	Analysis of complication rates was adjusted for for age, gender, region, plan, ECI, procedural characteristics (fusion, laminectomy and/or osteotomy) and type of primary cancer (breast, lung, prostate, renal and other).

Outcomes

Outcome	**Orthopaedic surgeon versus neurosurgeon, 90 day, n2=204; n1=683**
90-day mortality Odds ratio (95% CI)	0.92 (0.47 to 1.68)
Emergency department visits Odds ratio (95% CI)	1.01 (0.72 to 1.42)
90-day readmissions Odds ratio (95% CI)	1.2 (0.86 to 1.68)

Neurosurgeon is the reference - ORs greater than 1 indicate the outcome is more likely with orthopaedic surgeons

Critical appraisal – ROBINS-I

Section	**Question**	**Answer**
1. Bias due to confounding	Risk of bias judgement for confounding	Moderate. Analysis adjusted for age, gender, race, co-morbidity burden – but not extent of spinal disease.
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Low
3. Bias in classification of interventions	Risk of bias judgement for classification of interventions	Moderate. *Patients were identified from a database using procedure codes for spinal surgery however this would not have captured finer details about the procedure which could bias towards a neurosurgeon or orthopaedic surgeon carrying out the surgery.*
4. Bias due to deviations from intended interventions	Risk of bias judgement for deviations from intended interventions	Low
5. Bias due to missing data	Risk of bias judgement for missing data	Low
6. Bias in measurement of outcomes	Risk of bias judgement for measurement of outcomes	Low
7. Bias in selection of the reported result	Risk of bias judgement for selection of the reported result	Low
Overall bias	Risk of bias judgement	Moderate. Potential risk of bias due to confounding and classification of the interventions.
Overall bias	Directness	Directly applicable

Appendix E Forest plots

Forest plots for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

No meta-analysis was conducted for this review question and so there are no forest plots.

Appendix F GRADE tables

GRADE tables for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Table 6: Evidence profile for comparison between before and after upskilling MSCC service staff

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	After upskilling MSCC service staff	Before	Relative (95% CI)	Absolute		
Overall survival – patients with lung cancer												
Clatterbridge 2022	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	282	248	HR 0.72 [0.60 to 0.87]	Not estimable	VERY LOW	CRITICAL
Overall survival – patients with prostate cancer												
Clatterbridge 2022	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	390	291	HR 1.08 [0.90 to 1.30]	Not estimable	VERY LOW	CRITICAL
Overall survival – patients with breast cancer												
Clatterbridge 2022	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	225	178	HR 0.86 [0.65 to 1.14]	Not estimable	VERY LOW	CRITICAL
Overall survival – patients with unknown primary cancer												

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	After up-skilling MSCC service staff	Before	Relative (95% CI)	Absolute		
Clatterbridge 2022	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	328	184	HR 0.53 [0.67 to 0.84]	Not estimable	VERY LOW	CRITICAL
Overall survival – patients with other cancers												
Clatterbridge 2022	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	606	440	HR 0.84 [0.73 to 0.97]	Not estimable	VERY LOW	CRITICAL

CI: confidence interval; HR: hazard ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
2 95% CI crosses 1 MID

Table 7: Evidence profile for comparison between early intervention and late intervention

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early intervention	Late intervention	Relative (95% CI)	Absolute		
Overall survival - In-hospital mortality												
Guddati 2017	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	252/5035 (5%)	581/8422 (6.9%)	RR 0.73 (0.63 to 0.84)	19 fewer per 1000 (from 11 fewer to 26 fewer)	LOW	CRITICAL
Emergency admission to hospital and length of hospital stay - Length of stay, days												
Guddati 2017	observational studies	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	n=5035 Median 6 IQR 4 - 11	n=8422 Median 11 IQR 7 - 16	not estimable	5 days shorter with early intervention (p < 0.05)	MODERATE	CRITICAL

CI: confidence interval; IQR: interquartile range; RR: risk ratio

1 Serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
2 95% CI crosses 1 MID

Table 8: Evidence profile for comparison between surgery within 3 days and between 4 to 7 days

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Surgery within 3 days	Between 4 and 7 days	Relative (95% CI)	Absolute		
Neurological and functional status - Improvement at least 1 grade of AIS scale (injury, 6-point scale)												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/8 (75%)	10/14 (71.4%)	RR 1.05 (0.62 to 1.77)	36 more per 1000 (from 271 fewer to 550 more)	VERY LOW	CRITICAL
Neurological and functional status - Ambulatory status improvement												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/8 (25%)	5/14 (35.7%)	RR 0.7 (0.17 to 2.81)	107 fewer per 1000 (from 296 fewer to 646 more)	VERY LOW	CRITICAL
Emergency admission to hospital and length of hospital stay - Length of post-operative hospital stay, days												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	n=8 Median 13.5, range 6 to 44	n=15 Median 11.5, range 5 to 66	not estimable	2 days shorter with surgery between 4 and 7 days (p not reported)	VERY LOW	CRITICAL
Emergency admission to hospital and length of hospital stay - Length of hospital stay, days												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	n=8 Median 15, range 8 to 47	n=15 Median 14, range 10 to 68	not estimable	1 day shorter with surgery between 4 and 7 days (p not reported)	VERY LOW	CRITICAL

AIS: American Spinal Injury Association Impairment Scale; CI: confidence interval; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
2 95% CI crosses 2 MIDs
3 Sample size < 100

Table 9: Evidence profile for comparison between surgery within 3 days and after 7 days

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Surgery within 3 days	After 7 days	Relative (95% CI)	Absolute		
Neurological and functional status - Improvement at least 1 grade of AIS scale (injury, 6-point scale)												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/8 (75%)	25/53 (47.2%)	RR 1.59 (0.97 to 2.6)	278 more per 1000 (from 14 fewer to 755 more)	VERY LOW	CRITICAL
Neurological and functional status - Ambulatory status improvement												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	2/8 (25%)	29/53 (54.7%)	RR 0.46 (0.13 to 1.56)	295 fewer per 1000 (from 476 fewer to 306 more)	VERY LOW	CRITICAL
Emergency admission to hospital and length of hospital stay - Length of post-operative hospital stay, days												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	n=8 Median 13.5, range 6 to 44	n=53 Median 16, range 7 to 61	not estimable	2.5 days shorter with surgery within 3 days (P not reported)	VERY LOW	CRITICAL
Emergency admission to hospital and length of hospital stay – Total length of hospital stay, days												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	n=8 Median 15 Range 8 to 47	n=53 Median 22 Range 8 to 64	not estimable	7 days shorter with surgery within 3 days (P not reported)	VERY LOW	CRITICAL

AIS: American Spinal Injury Association Impairment Scale; CI: confidence interval; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
2 95% CI crosses 1 MID
3 95% CI crosses 2 MIDs
4 Sample size < 100

Table 10: Evidence profile for comparison between surgery within 4 to 7 days and after 7 days

Quality assessment	No. of patients	Effect	Quality	Importance

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Surgery between 4 and 7 days	After 7 days	Relative (95% CI)	Absolute		
Neurological and functional status - Improvement at least 1 grade of AIS scale (injury, 6-point scale)												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	10/14 (71.4%)	25/53 (47.2%)	RR 1.51 (0.98 to 2.34)	241 more per 1000 (from 9 fewer to 632 more)	VERY LOW	CRITICAL
Neurological and functional status - Ambulatory status improvement												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	5/14 (35.7%)	29/53 (54.7%)	RR 0.65 (0.31 to 1.37)	192 fewer per 1000 (from 378 fewer to 202 more)	VERY LOW	CRITICAL
Emergency admission to hospital and length of hospital stay - Length of post-operative hospital stay, days												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	N=14 Median 11.5 Range 5 to 66	N=53 Median 16 Range 7 to 61	not estimable	4.5 days shorter with surgery between 4 to 7 days (P not reported)	VERY LOW	CRITICAL
Emergency admission to hospital and length of hospital stay - Length of hospital stay, days												
Cui 2021	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	N=14 Median 14 Range 10 to 68	N=14 Median 22 Range 8 to 64	not estimable	8 days shorter with surgery between 4 to 7 days (P not reported)	VERY LOW	CRITICAL

AIS: American Spinal Injury Association Impairment Scale; CI: confidence interval; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
2 95% CI crosses 1 MID
3 95% CI crosses 2 MIDs
4 Sample size < 100

Table 11: Evidence profile for comparison between virtual consultation and no virtual consultation

Quality assessment	No. of patients	Effect	Quality	Importance

No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Virtual consultation	No virtual consultation	Relative (95% CI)	Absolute		
Overall survival - months												
Fitzpatrick 2012	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	N=46 Median 5.3 95% CI 3.5 - 10.6	N=79 Median 3.9 95% CI 2.0 – 4.9	not estimable	1.4 months longer with virtual consultation (p not reported)	VERY LOW	IMPORTANT
Access to services - number of candidates for surgery missed												
Fitzpatrick 2012	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/46 (0%)	5/79 (6.3%)	RR 0.15 (0.01 to 2.74)	54 fewer per 1000 (from 63 fewer to 110 more)	VERY LOW	IMPORTANT

CI: confidence interval; RR: risk ratio
1 Very serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Sample size < 100
3 95% CI crosses 2 MIDs

Table 12: Evidence profile for comparison between orthopaedic surgeon and neurosurgeon

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Orthopaedic surgeon	Neurosurgeon	Relative (95% CI)	Absolute		
Overall survival - 90-day mortality												
Malik 2020	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	15/204 (7.4%)	55/683 (8.1%)	OR 0.92 (0.5 to 1.68)	6 fewer per 1000 (from 39 fewer to 48 more)	VERY LOW	CRITICAL
Emergency admission to hospital and length of stay - emergency department visits												
Malik 2020	observational studies	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	82/204 (40.2%)	282/683 (41.3%)	OR 1.01 (0.72 to 1.42)	2 more per 1000 (from 77 fewer to 87 more)	VERY LOW	IMPORTANT
Emergency admission to hospital and length of hospital stay - 90-day readmissions												

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Orthopaedic surgeon	Neurosurgeon	Relative (95% CI)	Absolute		
Malik 2020	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	93/204 (45.6%)	382/683 (55.9%)	OR 1.2 (0.86 to 1.67)	69 more per 1000 (from 1 more to 154 more)	LOW	IMPORTANT

AIS: American Spinal Injury Association Impairment Scale; CI: confidence interval; OR: odds ratio
1 Serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I
2 95% CI crosses 2 MIDs
3 95% CI crosses 1 MID

Appendix G Economic evidence study selection

Study selection for: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

No economic evidence was identified which was applicable to this review question.

Appendix H Economic evidence tables

Economic evidence tables for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Table 13: Economic evidence tables

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
Author and year: NICE 2023 **Country:** UK **Type of economic analysis:** Cost utility **Source of funding:** Department of Health And Social Care For England	**Intervention**: Members of the MSCC team were upskilled to make more advanced clinical decisions on less complex referrals **Comparator:** MSCC service organised in accordance with the NICE 2008 guideline	**Population characteristic:** 3,173 people referred to a one UK MSCC centre with a spinal emergency expected to be MSCC. **Mean age**:69 years **Male**: 59.4% <u>Primary Cancer</u> Breast: 12.8% Lung: 16.9% Prostate: 21.5% Unknown: 15.8% Other: 33.0% **Modelling approach:** Before and after study and economic evaluation **Source of baseline**	**Life expectancy (days):** Before: 251.1 After: 304.0 **Mean cost per participant** Before: £1,265 After: £1,133 Difference: -£132 **Mean outcome per participant** Before: 0.2990 QALYs After: 0.3460 QALYs	**ICERs:** After approach both cost saving and health improving **Subgroup Analysis:** Subgrouped by deprivation quintile. All deprivation quintiles After approach cost saving and health improving apart from the least deprived quintile in which it was health decreasing and cost saving. Largest benefits were in the 2nd and 3rd least deprived quintils. **Sensitivity analysis:** Conclusions were robust	**Perspective:** UK NHS & PSS **Currency**: Pounds sterling (£) **Cost year:** 2021 **Time horizon:** 1 year **Discounting**: 3.5% per annum both costs and QALYs **Applicability**: Directly Applicable **Limitations**: Potentially serious limitations **Other comments:** Groups not randomised. Could not adjust for all potential confounders.

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
		data: Audit data from 1 UK MSCC centre **Source of effectiveness data:** Audit data from 1 UK MSCC centre. Quality of life from previously published economic evaluations of treatments of interest. **Source of cost data:** Previously published economic evaluations for treatments of interest.		to probabilistic sensitivity anlsysis	

1
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Appendix I Economic model

Economic model for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Upskilling staff in MSCC coordination to enable them to make decisions around people referred to a metastatic spinal cord compression service without senior clinician support. A 'before and after' study from one UK centre.

Introduction

Regional metastatic spinal cord compression (MSCC) services, coordinated through a specialist cancer centre, providing a single point of contact for confirmed metastatic spinal emergencies, have been created at a number of centres in the UK since the previous NICE MSCC guideline. These centres follow recommendations around the role of an MSCC co-ordinator. All people with a spinal emergency suspected to be MSCC, within the area covered by a regional service, should be referred to such places. It has been hypothesised that a regional co-ordinated service should lead to earlier diagnosis, consultant oncologist advice, and coordinated multi professional management. This will improve outcomes and potentially reduce costs.

Background

Clatterbridge Cancer Centre

Data for this economic analysis was obtained from the MSCC service at the Clatterbridge Cancer Centre. (CCC) CCC covers a population of 2.4 million people mostly located in the Merseyside and Cheshire area. The cancer incident rate is 1781 per 100,000 people and life expectancy is below the UK average. (Personal communication CCC) There are large inequalities between areas. Liverpool accounts for approximately 20% of the population covered by the CCC, a city where 10% of its lower layer super output areas (LSOAs) are in the bottom 1% for deprivation. (The English Indices of Deprivation 2019) Similar inequality is also identified across the larger Liverpool City Region which accounts for approximately 60% of CCC's population.

The MSCC service was created in January 2017 providing a single point of contact for confirmed metastatic spinal emergencies as well as other service configuration principles in the NICE 2008 MSCC guideline. The number of spinal metastases and MSCC for the region is about 2500 per year (Personal communication, CCC). In 2021, nearly 1200 patients presented with a suspected spinal emergency at this centrally coordinated pathway potentially benefitting from earlier diagnosis, consultant oncologist advice, and coordinated multi professional management.

Prior to this, surgical services were the 'gate keeper' for MSCC emergency referrals as surgery was seen as the best intervention associated with the best outcomes for patients. In approximately 97% of cases where the people referred were not suitable for surgery these were returned to the referrer who would then need to seek a second specialist opinion. This added days to the decision-making process to the detriment of outcomes of the people referred.

The CCC MSCC service pathway supports primary care, secondary care (8 Acute Trusts), urgent care pathways, 10 haematology teams, 9 hospices/ community teams, the oncology tertiary centre and spinal tertiary centre in the region. It operates as a 7-day service which has grown considerably in activity and resource since its creation.

The first 6 months of the service were used to identify activity levels, complexity of referred cases, the barriers to engaging with the service, the information required to inform clinical decision making as well as practical issues such as coordination and identifying education gaps in staff who worked in the service. The same period was used to identify any audit tool and data that needed to be captured to allow evaluation of the service (such as for this analysis) and outcomes for people referred to it.

The service was set-up during the last 6 months of 2017 based upon the MSCC service at The Christie NHS Foundation Trust in Manchester. Communication and engagement with CCC internal pathways and referral organisations by site visit were also undertaken delivering education through acute oncology teams and during relevant education events. The same period was used to create and distribute the regional MSCC guidelines and distribute the referral proforma and processes. The pathway was launched at the start of January 2018.

Audit Data

The audit data used starts 1st January 2018 when the service and pathway were fully implemented, and the toolkit and information needed for auditing and data collection were finalised. The audit data has records for all patients referred to the MSCC service through the MSCC pathway. The audit data covers all people referred up to and including the 31st May 2022 when this data was securely transferred to NICE.

The audit data was securely transferred to NICE for analysis in a pseudonymised format. The data variables that were shared for the purpose of this analysis, from the larger audit dataset, are presented and described in Table 14.

Table 14: Variables in the analysis dataset

Variable	Description
Patient ID	Unique code to identify different patients whilst maintaining anonymisation.
Date became aware of MSCC	The day the patient was identified as potentially having MSCC and being referred to the MSCC service.
Age	Chronological age in years at time of being referred to the MSCC service.
Sex	Sex of person referred.
Number of days until death	The number of days from referral to MSCC service until death. This field is blank for individuals who have not died within the timeframe of the analysis
Primary cancer location	This is the type of the primary cancer. It can take the values breast, lung, prostate, malignancy of undefined primary

	origin or other. The other group was used to prevent any possibility of identification of individuals with rare cancer types and covers a broad range of cancers.
Severity of MSCC	This could be one of 5 levels: • Advice- Where MSCC is not suspected but the service has been used for advice. • Nil/ Benign- Where an individual has been inappropriately referred for a non-malignant spinal cord compression. The symptoms between malignant and non-malignant are very similar and are often not picked up by more junior staff. This group also included those inappropriately referred with no compression of the spinal cord. • Metastasis- Where there is a metastatic tumour near to the spine but has not spread to or compressed on the spine or spinal cord. • Impending MSCC- Where the spinal cord is threatened by a tumour but is not yet compressed. This would usually be managed identically to MSCC. • MSCC – Where a cancerous tumour causes compression of the spinal cord or collapse of the spine.
Treatment plan	This was the treatment ultimately received by the individual. The following treatment plans were in the data set: • Radiotherapy: the radiotherapy dose and fractions were also recorded. • Palliative radiotherapy- a Consultant Radiographer lead palliative radiotherapy service whereby patients with MSCC or impending MSCC, needing urgent but not emergency treatment,

	could be referred. • Surgery – referral to the surgical team for treatment such as kyphoplasty, vertebroplasty, surgical stabilisation etc • SACT- referral to a consultant clinical oncologist to consider systemic anti-cancer therapies. • Local team/advice – Individuals with non-malignant spinal cord compression or referred to the service for advice are returned to the local referring team.
Index of multiple deprivation rank	A ranking of all LSOAs in England based on multiple indicators of deprivation. This measure is discussed later in this report. For the purposes of this analysis these have been converted into quintiles.

Length of stay (measured in days) in hospital was also included for about a third of the data set. This data was not available for some tertiary cancer centres and acute hospital trusts this data was missing for many treatments. It was also not missing at random and it was therefore difficult to impute values where there were blanks. Given these weaknesses, even though length of stay is a key driver of costs in many economic models, we did not include this cost in this analysis.

Whilst the audit data was considered a complete record of all people referred to the MSCC service, 7 individuals were dropped from the data set before the analysis. One induvial was dropped from the analysis as their age at referral was recorded as 119 years and 3 further individuals were dropped as their 'number of days until death' were negative values. Two further individuals were dropped as 'number of days until death' was recorded as zero. Whilst this is plausible (i.e. they died the same day as referral), death at time zero provides no information for the effectiveness of competing approaches. 6 of the 7 individuals removed from the analysis were in the 'before' group.

Case mix

As the pathway for referral to the MSCC centre was an emergency pathway and this had not changed over the lifetime of the service it is thought that the case mix should be similar across all years and in the before and after group. The main analysis therefore considered survival and other outcomes for the entire dataset. It was hypothesised though that in the first years of the service there had been a higher rate of inappropriate referrals for the following reasons:

- Signs and symptoms for non-malignant spinal cord compression (SCC) were similar to those of MSCC
- Junior and less experienced medical staff had difficulty distinguishing the differences between malignant and non-malignant SCC

- Education of the pathway had not been fully communicated to all referring centres
- Centres were encouraged to send people on for advice if they were unsure

This group of inappropriate referrals would almost certainly have a longer life expectancy than those with MSCC and would likely bias survival results in years with large numbers of such referrals.

Health inequalities

Potential health inequalities from MSCC have been highlighted in the equality impact assessment (EIA) completed for this guideline. The EIA identified socioeconomic factors being an equalities consideration for MSCC. In particular that incidence rates for most cancers and cancer deaths are higher in the most deprived groups compared to the least. It was therefore decided to look at outcomes in this analysis by deprivation score.

Differences in outcomes across different levels of deprivation were explored using the English Indices of Multiple deprivations (IMD) scores (The English Indices of Deprivation 2019) as published by UK government. The English indices of multiple deprivation (IMD) scores rate every LSOA in England. LSOAs split areas in England into smaller regions of approximately 1500 people or 650 households. The English IMD ranks all LSOAs in England from 1 (most deprived) to 32,844 (least deprived) based on 7 measures of deprivation involving 39 indicators. The 7 measures of deprivation are crime, education, employment, housing, income, health and living environment. A combined measure is also calculated weighting all these factors for one summary measure and ranking of deprivation. This value was used for ranking deprivation in this analysis although there is strong correlation between all measures.

The dataset recorded the deprivation scores for the majority of people going through the MSCC service based on their English postcode. The dataset did not record IMD for some individuals as they did not live in England and thus their area was not ranked by the English IMD (the MSCC service gets a number of referrals from Wales, the Isle of Man as well as international referrals). In total 96 people in the dataset did not have an IMD ranking as they lived in the Isle of Man and 58 people because they lived in Wales. Postcode or address data was missing for 59 people and 2 people had English postcodes which were not included in the IMD dataset most likely as they lived in newly built houses assigned new postcodes after the calculation of IMD indices.

These values were converted into quintiles (1= most deprived, 5=least deprived) based on the person's IMD ranking. The split of IMD quintiles and the percentage of the dataset assigned each quintile are presented in Table 15.

Table 15: Summary of Indices of multiple deprivation data included in the economic analysis

Quintile	Included English IMD ranks	Number in analysis dataset n (Percent)	Percent excluding missing
1 (Most deprived)	1-6,568	1098 (34.6)	37.0
2	6,569-13,137	395 (12.4)	13.3

3	13,138-19,706	513 (16.2)	17.3
4	19,707-26,275	510 (16.1)	17.2
5 (Least deprived)	26,276-32,844	450 (14.2)	15.2
Not applicable or missing		208 (6.6)	

Statistical Analysis

Interventions considered by the analysis

The guideline committee were interested in the effectiveness and cost effectiveness of the creation of a regionally coordinated MSCC services. However, the data available to them for this analysis was collected as part of the activities of a newly formed service of this type (in line with the standards set for services by the previous guideline) and thus data was not readily available for the period prior to the creation of the service. The committee hypothesised that as a newly formed service any changes in outcomes over time, such as year on year improvements in survival, could be as a result of its creation.

For this analysis a 'before and after' approach was taken. The date of 1st June 2020 was used as the cut point, with those referred to the service 31st May 2020 or earlier in the 'before' group with all others in the 'after' group. This date was chosen as the time the medical model at the MSCC service was changed to having a different consultant on call each day. COVID restrictions meant that multiple services, including consultant clinical opinions could be given remotely. This made it challenging to access consultants quickly for a clinical opinion. Other consultants were reluctant to make decisions on patients they were not going to treat or patients they did not make initial clinical decisions on. This resulted in the MSCC team needing to re-discuss cases more than once, delaying diagnosis and treatment which negatively impacted on outcomes for patients. During this period the service decided to upskill some MSCC team members from a range of medical specialities in MSCC coordination, to enable them to make initial clinical decisions on all but the most complex referrals. This upskilling was consistent with becoming a MSCC coordinator and was seen as strengthening that service configuration. This change resulted in approximately a 25% increase in decisions being made without the need for advice from a consultant. There was no wash-out period in this analysis as changes occurred over a short period of time.

In summary the 'after' intervention consists of the upskilling of members of the MSCC team to undertake the MSCC co-ordinator role, to make initial clinical decisions on referrals. This strengthens the MSCC co-ordinator model, through having more staff over a wider range of medical specialities able to perform the role. This is considered the primary intervention being considered by this analysis. The comparator is considered a 'weaker' form of the MSCC co-ordinator service delivery model because fewer staff can carry out the responsibilities of this role. The analysis therefore considers the effectiveness and cost effectiveness of strengthening the MSCC co-ordinator model as recommended in the previous guideline.

Analysis plan

The analysis used the entire Clatterbridge Audit data, apart from the removed observations discussed above, to compare survival in the before and after the upskilling of team members and changes in service delivery. Survival analysis was performed following Kaplan-Meier methods and unadjusted and adjusted curves were estimated for both the before and after group. The committee highlighted age, sex, race, socioeconomic status and primary cancer as factors which may lead to differing survival. The shared Clatterbridge audit data did not have race as a variable so this was not accounted for in any analysis. Separate Kaplan-Meier curves were also run for each primary cancer and each IMD quintile including where this was missing. Age and sex were adjusted for in the subgroup analyses apart from where the primary cancer was prostate cancer (and all people were male) where only age was adjusted for.

The data was considered a complete set and there was no missing data i.e. everyone referred to the centre during the relevant time period would be in the data set. Other than for the IMD quintile (where reasons for missing data are discussed above) all observations were present for all datasets. Censoring therefore only occurred when a patient did not experience the event of interest (death) before the end of the analysis timeframe, so called right censoring. We did not adjust for this censoring, given we did not have information beyond the end point of the analysis. There may however be some bias especially if people who were referred to the centre at a later date, and were therefore more likely to be censored, had different survival to those entering earlier. This potential difference in survival, occurring outside the analysis timeframe, would not be captured and would impact upon any estimate of overall survival for the economic analysis.

Adjusted overall survival and adjusted overall survival by IMD quintile were used to inform the outputs of the economic model. Other outcomes did not feed into the model but were useful in the consideration of the effectiveness of these service changes.

Software

All data cleansing, descriptive statistics and survival analysis were undertaken in STATA 13.1. (STATACorp 2013) Survival analysis was performed using the ‘sts’ package around survival functions to return a Kaplan-Meier survival curve, hazard ratio and area under the curve. The ‘adjustfor()’ option was used to adjust for age and sex where appropriate. This adjusts the Kaplan-Meier survival curve estimates to zero values of any covariates. Age was centred at 70 for this analysis, similar to the average age of the cohort. Separate survival curves were fitted for both male and females unless there was a small difference that was not statistically significant. The subgroup analyses around primary cancer and IMD quintile were estimated using the ‘by()’ option which fits separate Kaplan Meier functions, for before and after and for each unique value in the relevant variable.

The economic analyses and exploration of health inequalities were undertaken in Microsoft Excel 365 (Microsoft 2022) with survival outcomes from STATA reported in this analysis transferred to Excel as area under the survival curve values calculated with the ‘sts list’ command. This command returns the Kaplan-Meier curve in numerical form and allows for calculation of the area under the curve and therefore overall survival. The area under the curve was cut-off at 365 days for the purposes of the economic model given the longer analysis time and therefore longer survival function for the ‘before’ group. The STATA code for the statistical analysis is provided in Additional Information A.

Ethical Approval

The use of the audit data for this analysis was approved by the CCC NHS Foundation Trust Caldicott Guardian (medical director). The analysis did not require ethical approval as it used existing non-identifiable data collected for the purposes of evaluating the MSCC service.

Economic model

Population

Adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression referred to a MSCC centre as a spinal emergency.

Type of evaluation, time horizon, perspective

The analysis measures outcomes in quality-adjusted life years (QALYs). We express the incremental cost-effectiveness ratio (ICER) as a cost per QALY.

The model has a 365 day time horizon. The total possible time someone could spend in the analysis in the 'after' group, given the cut-off date for the before and after dates was 729 days. However, as not everyone will have joined the cohort at the first possible date most people had a lower possible total time in the cohort. Only 65% of the after cohort, who survived until the end date of the analysis, had more than 365 days of observations. Censoring after this time for this group was large and there were often small or no numbers for some of the subgroup analyses such as deprivation. As the intervention under consideration is relatively new and other data was not identified around this intervention it would be difficult to make evidence-based estimates of health outcomes such as survival beyond this time horizon and any estimate of differences in costs and outcomes would be very weak. 365 days was therefore chosen as the cut off. It should also reduce any potential biases cause by right censoring discussed above.

The analysis was conducted from the perspective of NHS and Personal Social Services (PSS) in the UK.

Discounting

QALYs were discounted at a rate of 3.5% per annum in the analysis in line with the NICE guidelines manual. All costs were applied at the first year of the model and where the estimated costs covered a period beyond one year these had already been discounted in the original analysis at a rate of 3.5% per annum. No further discounting was taken around costs.

Probabilistic Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) was conducted to assess the combined parameter uncertainty in the model. PSA replaces the values around costs and utility weights in the base-case with values drawn randomly from a probability distribution assigned to them. This was done for 1,000 iterations and the different outcomes of these iterations presented diagrammatically in the forms of a cost effectiveness plane and cost effectiveness acceptability curve. This was to reflect the uncertainty around the inputs and consequently the outcomes of the model. The distributions for all parameters used during the probabilistic sensitivity analysis are discussed in detail below presented in Table 16.

The distribution of values for the cost and utility weights for BSC and surgery were again taken from the guideline model. The PSA for this model estimated costs and QALYs (used as a proxy for utility weights) for 1000 iterations. Full discussion of the PSA for this model are presented in evidence report N. A random number generator draws from 1000 samples of costs and QALYs estimated in that model to give values for the costs and utility weights of BSC and surgery. Each iteration has 4 values in it, 1 costs and 1 utility weight, for each of BSC and surgery. Sampling sets of values preserves covariance between them. Each iteration has an identical probability of being chosen during this analysis. This non-parametric distribution was thought to best represent the variability around inputs for these 2 treatment plans.

Model parameterisation

Intervention effects

Overall survival and therefore the effect of the intervention was taken from the statistical analysis discussed above. Survival for the PSA was estimated using the hazard ratio for the after group relative to the before, adjusted for age and sex, to vary the survival curve for the after group (and consequently the area under the curve). The before group survival remained fixed. The usual proportional hazard assumptions were made about the hazard ratio for overall survival. The hazard ratio was varied, using a log-normal distribution, during PSA.

As the hazard ratio, confidence intervals and overall survival were estimated from the same data it was considered that altering both the hazard ratio and the before/baseline survival would significantly overestimate the amount of uncertainty around differences in survival. Whilst we did not vary the before group survival during the PSA, and therefore did not capture uncertainty around this parameter, this approach would capture uncertainty around the incremental survival between the two groups, which ultimately feeds into the outcomes of the model. It is acknowledged that there is some uncertainty around the before group survival and that lower estimates of survival in this group would lead to lower estimates of absolute survival differences in the after group. However, the committee highlighted that the estimates of survival were consistent with their clinical experience and that over estimating uncertainty would have a more detrimental effect on the applicability of the probabilistic sensitivity analysis results.

Costs

Quality adjusted life years

Differences in total costs and utility weights were estimated based on previous economic models both developed for this guideline and from the published literature. Estimates of total QALYs and costs were based on the treatment plan received. A cost and utility weight were assigned for every treatment plan considered by this analysis. The cost of the treatment plan received was assumed to be identical across all people in the data set regardless of estimated survival or other variables such as age, primary cancer or MSCC severity. The same was true for the utility weights other than this was multiplied by overall survival as estimated from the Kaplan–Meier survival curves.

The estimates for costs and utility weights for surgery and best supportive care (BSC) were taken directly from the economic model of kyphoplasty (surgery) versus best supportive care updated for this guideline and reported in Evidence report N. Deterministic results from the ‘as treated’ analysis without the extrapolation beyond 1 year were used for this analysis. It is thought the ‘as treated’ analysis would best re-

flect true costs and utility weights for these two groups given the large cross-over and much narrower results in the 'intention to treat' analysis. As the time horizon of the analysis was 1 year the total QALYs represented an average across the first year of treatment.

People referred back to their local team did not incur a cost in the model. Whilst this group would lead to a greater use of resources, approximately £405 based on NHS Cost Collection for a consultant led first multiprofessional Non-Admitted Face-to-Face Attendance at a spinal surgery service (Department of health 2021) it was assumed that this would be the only cost incurred by this group. As this first multiprofessional assessment is received by all people referred to the service, this cost would be incurred by everyone in the data set and thus excluding would not make any difference to incremental analyses. The cost of the 'advice' and 'local team' treatments plan were therefore set as zero and this was not varied during exploration of uncertainty. Utility weight for this group was set at 0.4392 for this group the baseline value in the economic model used to inform the estimates for surgery and BSC and taken from Chew 2013. It was considered that this group would present very similarly to those with non-cancerous SCC and have comparable quality of life. Costs and utility weights for this group were set to zero during sensitivity analysis essentially removing those without malignant MSCC from the analysis.

Systemic anti-cancer therapy plan was costed and assigned utility weights using values from the TRAPEZE randomised controlled study of chemotherapy with zoledronic acid, strontium-89 or both, in men with prostate cancer and bone metastases. (James 2016) The economic analysis was based on 707 patients who completed the questionnaires on resource use and quality of life (EQ-5D) at multiple UK hospitals. For this analysis the use of generic zoledronic acid came out as the preferable treatment and was used for the cost estimates for this analysis. The analysis estimated a cost of £13,766 (95% CIs £12,824 to £14,728) and a total QALY of 0.908. Costs were estimated for the cost year 2012 and were inflated to 2021 figures using the NHS Cost Inflation Index reported in the Unit Costs of Health and Social Care. (Jones 2021) As the costs in the analysis include both staff time and physical healthcare resources the combined inflation measure for both pay and prices was used. This calculated a figure in 2021 prices of £16,166 (95% CIs £15.060 to £17,296). QALYs were collected over a time horizon of 2 years (median survival in the analysis was 1.4 years). We therefore halved the total QALY gains to give a utility weighting for this group of 0.454. This is higher than for other treatment plans as expected given the reduced need for more invasive interventions in this group.

No economic analyses were identified for radiotherapy in this guideline that could be used for informing the costs and utility weights for this treatment plan. One study was identified, from a New Zealand health care perspective comparing different dosing regimens (single versus multiple fractions) for palliative radiotherapy in people with painful bone metastases from breast, lung and prostate cancer. (Collison 2016) The study estimated a quality of life weighting for people who had a pathological fracture as a result of the metastases to be 0.284. This group in our dataset was exclusively those with metastases or impending spinal cord compression. This group in the Collison trial was considered to be most similar to this population in this analysis. This guideline recommends 8 Gy single fraction palliative radiotherapy to people with spinal metastases causing non-mechanical spinal pain (without MSCC). For costs the values for single fraction radiotherapy were used form the analysis. This was considered most in line with recommendations in this guideline as well as current practice at both the Clatterbridge Cancer Centre and more widely in the NHS. This value was 1,458 New Zealand Dollars (NZ$) (95% CI NZ$1,126 - NZ$1,879) in 2011 prices. These were converted to UK Sterling using the IMF Purchasing Power Parities for

Healthcare and inflated to 2021 figures using the NHS Cost Inflation Index. (Jones 2021) This lead to a cost of £815 (95% CI £629-£1050) for palliative radiotherapy.

The cost and utility weights of radiotherapy were taken from the economic evaluation developed for the previous NICE MSCC guideline which estimated a cost of £1277 in 2007 prices. This was inflated to 2021 prices using identical methods to previous prices and gave a cost per person of £1587. Utility weights were also taken from the same study. Two scenarios were presented in the economic evaluation. In the ideal scenario the success rate of radiotherapy in terms of patients being ambulatory was assumed to be 100%. This gave an average QALY over the year of 0.67. A more conservative scenario was also presented where the success rate of the radiotherapy in terms of being ambulant was 74.3%. For those where radiotherapy was successful, people were assumed to retain the ability to walk for a mean 77.91 days and would become paraplegic before death. This scenario gave a utility weight over the year of 0.15. The average of both scenarios, 0.44 was used for this analysis.

Two people, both in the after group, died before they could be assigned a treatment plan. These two people were assigned costs and utility weights equal to zero. As this was a tiny proportion of the analysis, both true costs and QALYs were almost certainly small (mean survival of 10 days) and the changes to the service were unlikely to have impacted on survival. Therefore, no exploration of uncertainty was taken around this assumption.

Where evidence for costs and utility weights had not been identified from sources considering interventions not directly applicable to the intervention in the model a uniform distribution was assigned during the PSA, with upper and lower bounds of 50% and 150% of the point estimate, to reflect the large amount of uncertainty around these values.

Probability distributions for all parameters are presented in Table 16.

Table 16: Baseline costs and utility weights and distributions for the probabilistic sensitivity analysis

Treatment Plan	*Cost (£)*	*Utility weight*	*Source*	*PSA distribution cost*	*PSA distribution QALY weight*
Advice	*0*	*0.4392*	*Chew 2013*	*Fixed*	
Best supportive care	*336.65*	*0.4173*	*Economic model Evidence Report N*	*Random iteration of surgery model PSA in Evidence Report N*	
Local team	*0*	*0.4392*	*Chew 2013*	*Fixed*	

Palliative radiotherapy	*815.00*	*0.2840*	*Collison 2016*	*Gamma (57.59, 14.15)*	*Beta (6.2, 16)*
Systemic anticancer therapy	*16166.03*	*0.4540*	*James 2016*	*Gamma (28,662, 0.56)*	*Uniform (0.2270, 0.681)*
Surgery	*3047.87*	*0.4447*	*Economic model Evidence Report N*	*Random iteration of surgery model PSA in Evidence Report N*	
Radiotherapy	*1587.53*	*0.4400*	*NICE CG75*	*Uniform (793,2380)*	*Beta (6.2, 16)*

Statistical Analysis Results

Baseline characteristics

In total 3,174 individuals were included in the analysis, 1,343 in the before group and 1,831 in the after group. Differences in baseline characteristics between the before and after groups are shown in Table 17. The after group were on average 1 year older than the before group and were more likely to have cancer of unknown primary but less likely that their primary cancer was in the lung. All other variables were not statistically different between the before and after group at the time of referral.

Table 17: Mean baseline characteristics of the cohort before and after service change

	Before	After	p-value
Total number	1,342	1,831	
Age at referral (years)	68.5	69.5	P=0.02
Male (%)	59.3	59.4	P=0.96
Deprivation quintile (day)	2.4	2.5	P=0.38
Primary cancer (%)			

Breast	13.3	12.3	P=0.39
Lung	18.5	15.4	P=0.02
Prostate	21.7	21.3	P=0.78
Unknown primary	13.7	17.9	P=<0.01
Other	32.8	33.1	P=0.88

Inappropriate referrals

Table 18 shows that the number of inappropriate referrals were significant in all years of the MSCC service. The number of inappropriate referrals are higher in the first year of the MSCC service as hypothesised. However, despite falling by at least two thirds during the subsequent year we see a rise every year from 2020 to 2022 although this remains at least 10 percentage points lower than at its highest in the first year. Alongside the differences in baseline characteristics this suggest their may be some difference in case-mix between the before and after groups which would likely bias outcomes towards the before group.

Table 18: Total number and percentage of inappropriate referrals by year of referral

Year of referral	Number of inappropriate referrals	Percentage of all referrals
2018	187	35.2%
2019	58	10.6%
2020	110	14.7%
2021	177	19.7%
2022	107	23.8%

Changes in overall survival since the introduction of the MSCC service

Figure 2 presents the overall survival by year since the start of the MSCC service in January 2018. Data for people referred in 2022 has been excluded from the graph as the maximum number of days of information for people in this group was 150 days less that of other years. The year with the highest survival is 2021 with overall survival at 83%, 65% and 39% for 30, 90 and 360 days after referral respectively. This is markedly up on the worst year in the audit data 2019 where survival for the same time periods were 67%, 52% and 24%.

Figure 2: Overall survival by year

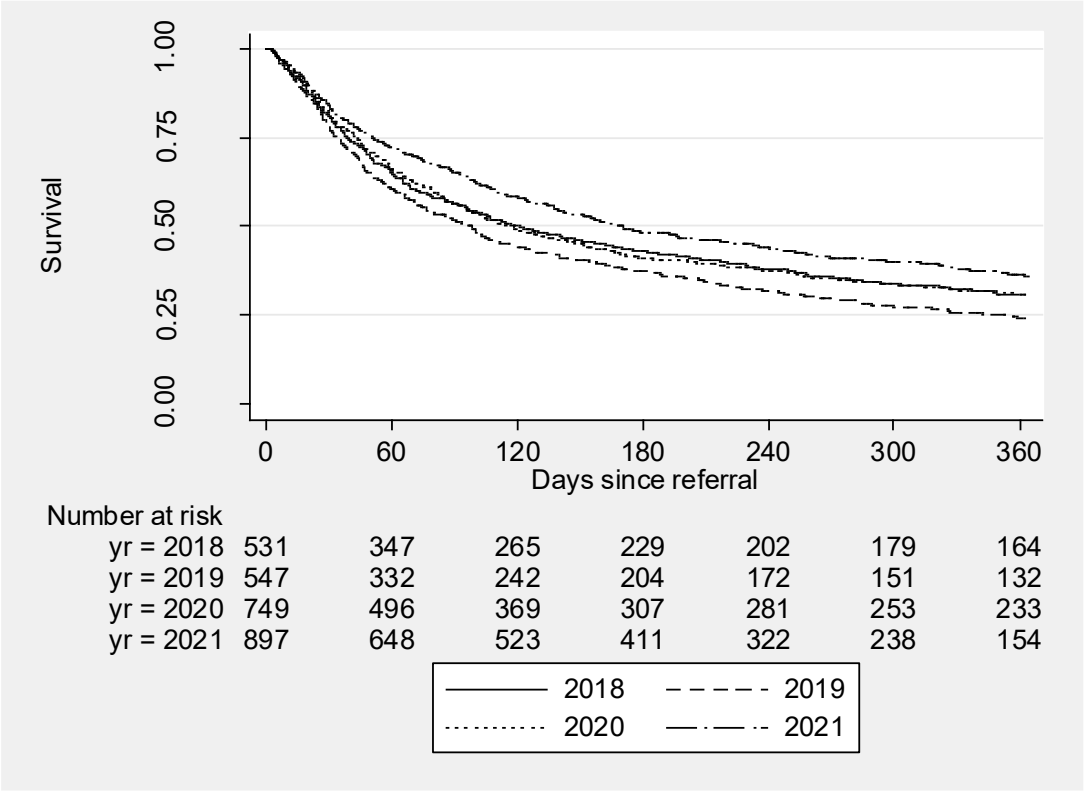
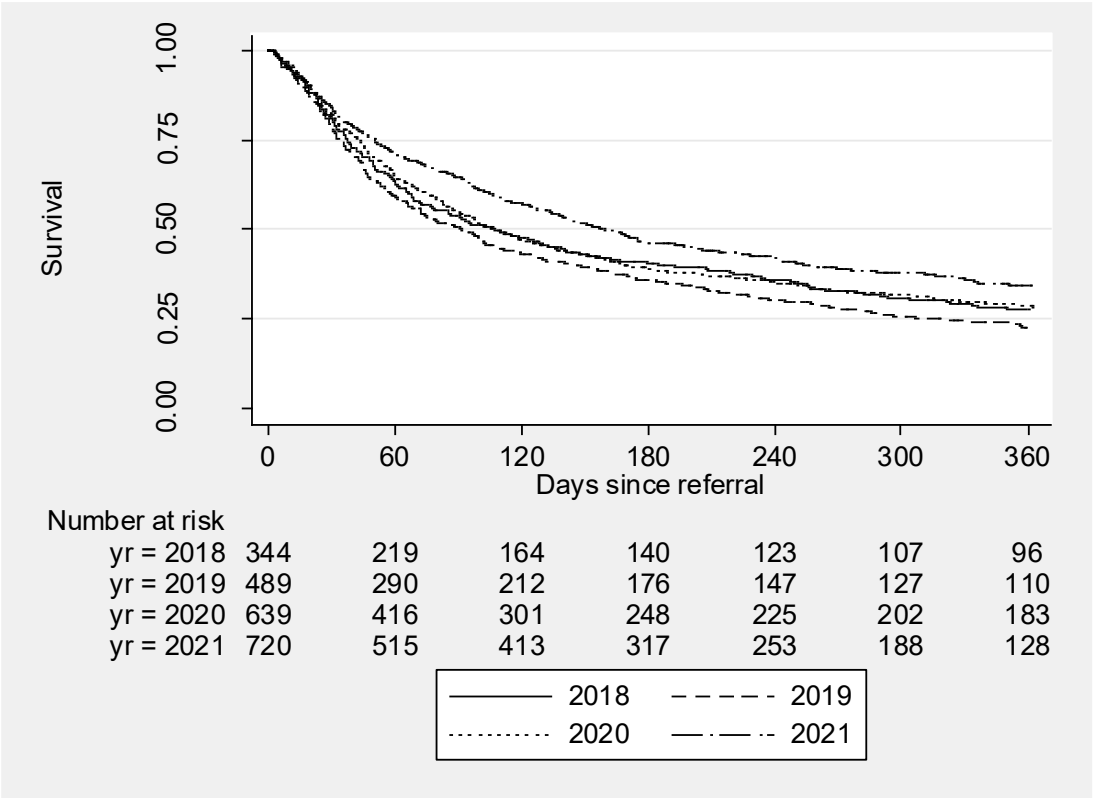


Figure 3 presents the same figures with those inappropriately referred removed from the analysis. The values for 2021 were broadly similar to those of the full data set at 3%, 65% and 37% for 30, 90 and 360 days after referral respectively reducing overall survival at 360 days by 2 percentage points. For 2019 the year with the lowest overall survival the figures were 77%, 50% and 23% for the same time periods. This shows a 10 percentage point increase for survival at 30 days but a 2 and 1 percentage point difference at 360 days. Differences between the full data set and that with inappropriate referrals removed were not statistically different and all subsequent analyses were undertaken on the full data set only.

Figure 3: Overall survival by year - inappropriate referrals removed



Overall survival before and after service configuration change

Figure 4 presents the overall survival between the before and after groups. The hazard ratio is 0.82 (0.76-0.90, p<0.01) favouring overall survival in the after group. Survival in the after group was 84%c, 64% and 43% at 30, 90 and 360 days respectively with a median survival of 184 days. For the before group survival was 79%, 54% and 28% at the same time periods with a median survival of 103 days, 81 days fewer than the before group.

Figure 4: Unadjusted overall survival before and after configuration changes

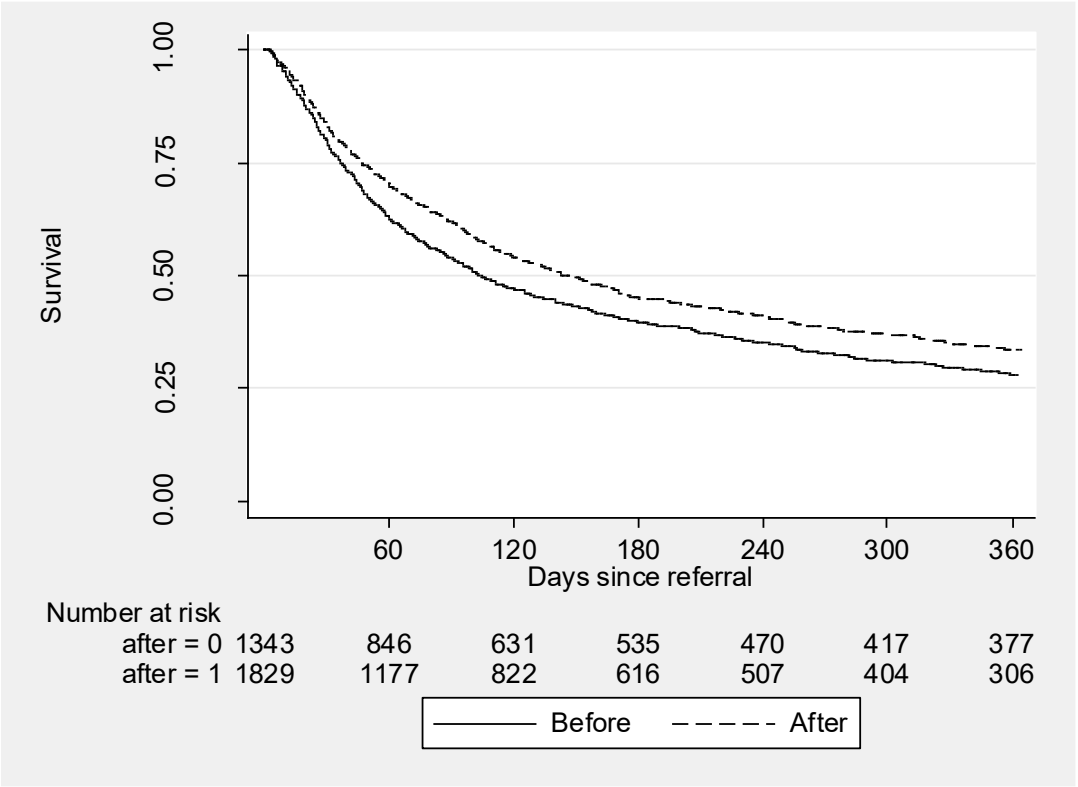
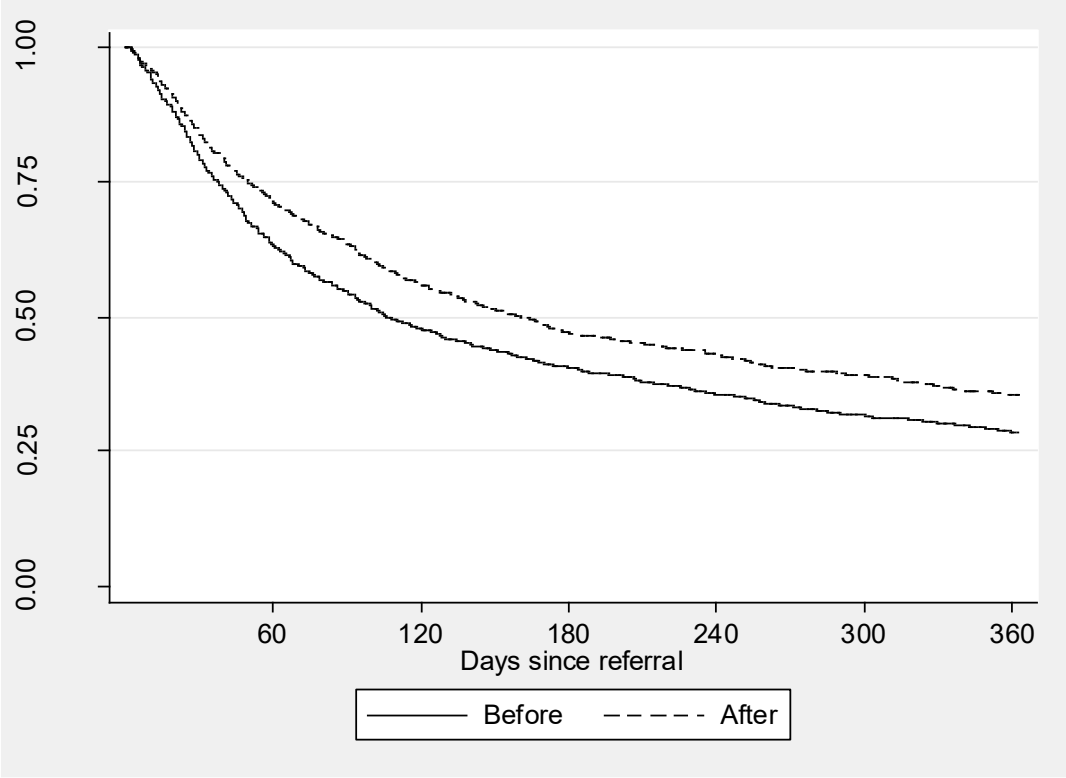


Figure 5 presents the overall survival before and after the service configuration change adjusted for age and sex. The age variable was centred to 70 years of age, similar to the average age of the cohort for the purposes of the analysis. The hazard ratio was slightly reduced to 0.81 (95% CI 0.75-0.89, p<0.001) making the adjusted analysis slightly more favourable to the after group compared to the unadjusted analysis. Adjusting for age impacted on overall survival with older populations having lower survival- HR=1.010 per year (95%CI 1.006-1.013, p<0.001). Whilst being male is weakly associated with lower survival this is not statistically significant at the 95% confidence level -HR=1.08 (95%CI-0.99-1.18). Given these results survival for the economic analysis was adjusted assuming an average age of 70 years but no adjustments were made for sex.

Figure 5: Overall survival for before and after configuration changes adjusted for age and sex



Survival by primary cancer

Rather than adjust for primary cancer in the analyses these were analysed in sub-group analyses. All analyses were adjusted for age and sex apart from where the primary cancer was in the prostate. Given this group is entirely male this analysis was only adjusted for age. All cancers apart from prostate and breast had a statistical difference at a 95% confidence level in survival between the before and after groups. The largest increase in survival was in the cancer of unknown primary group with a 10 and 17 percentage point difference in survival at 30 and 90 days respectively. Lung cancer which has the lowest rates of survival for the primary cancers investigated has shown an increase in survival following the service changes with an over 10 percentage point increase in survival 90 and 360 days after referral although increased survival is smaller than for other cancers 30 days post referral. Where the primary cancer was in the prostate survival was lower in the after group than the before although the difference was small and not statistically significant.

The hazard ratios and confidence intervals for each type of primary cancer are provided in Table 19.

Table 19: Hazard ratio and confidence intervals by primary cancer

Primary cancer	Hazard ratio	95% confidence interval	Figure
Lung	0.72	0.60-0.87	Figure 6

Prostate	1.08	0.90-1.30	Figure 7
Breast	0.86	0.65-1.14	Figure 8
Unknown primary	0.67	0.53-0.84	Figure 9
Other cancers	0.84	0.73-0.97	Figure 10

Figure 6: Overall survival in the before and after groups for people with primary lung cancer

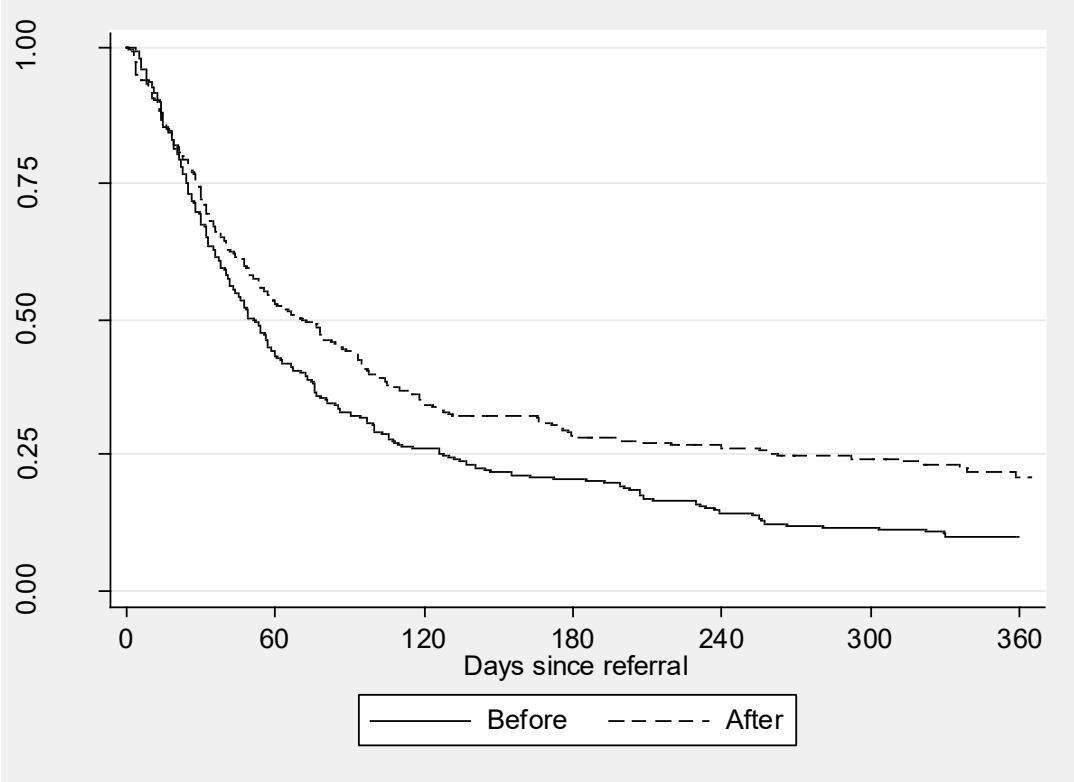


Figure 7: Overall survival in the before and after groups for people with primary prostate cancer

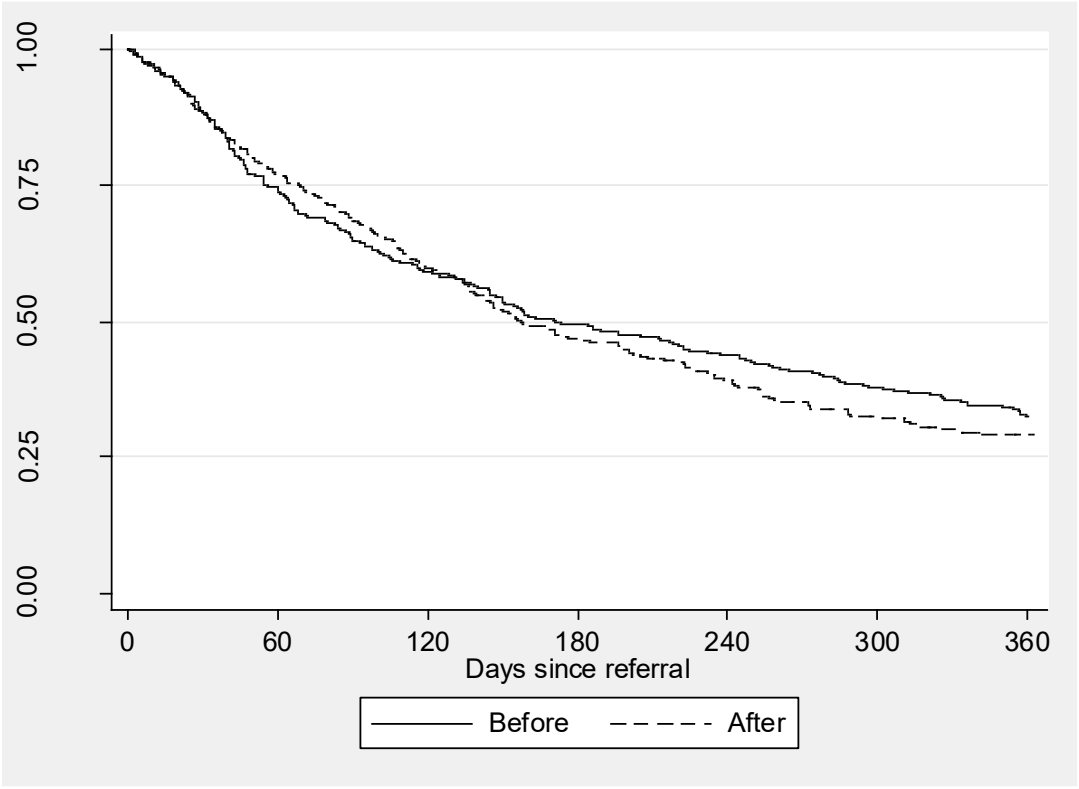


Figure 8: Overall survival in the before and after groups for people with primary breast cancer

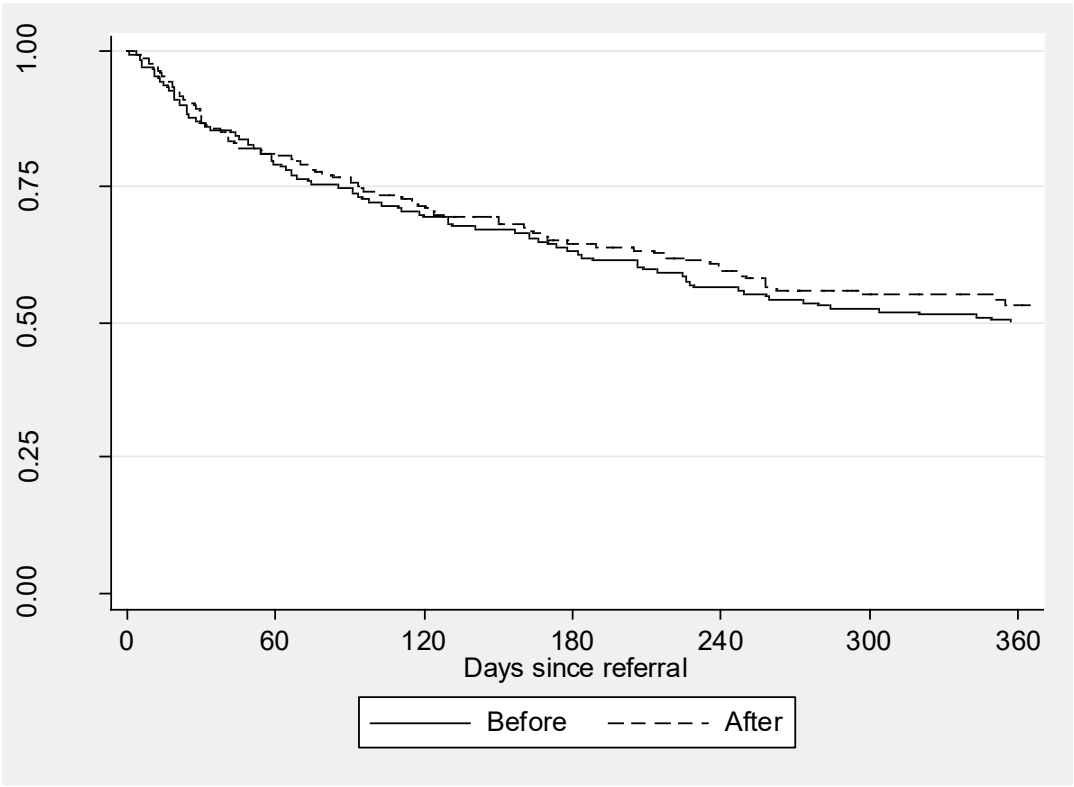


Figure 9: Overall survival in the before and after groups for people with cancer of unknown primary

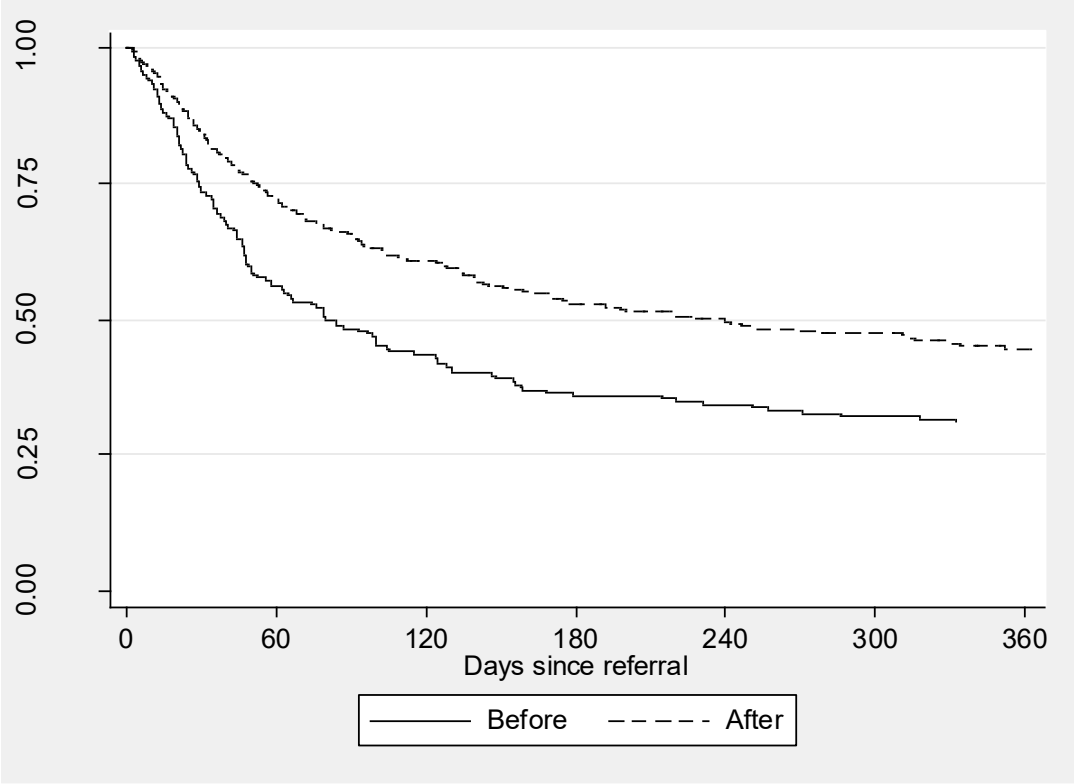
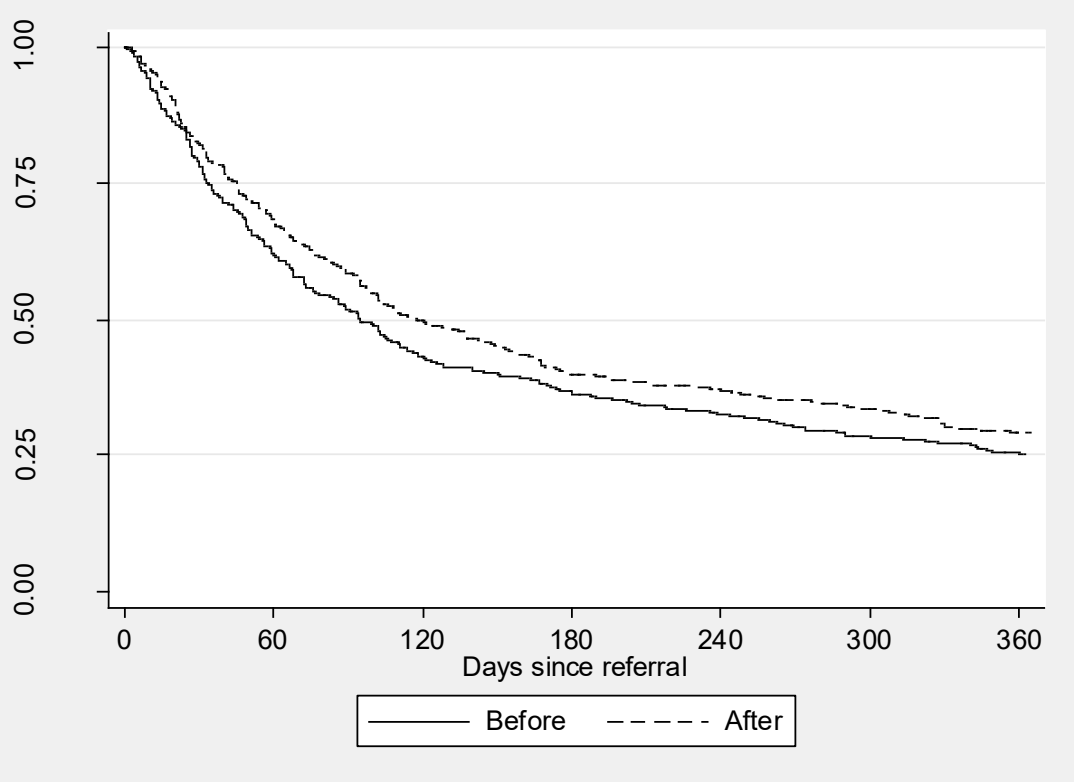


Figure 10: Overall survival in the before and after groups for people with other primary cancers



Change in treatment plan

Table 20 shows the changes in the percentage of people receiving each treatment plan between the before and after groups. There is weak evidence of changes in all treatment plans between the before and after group with stronger evidence for changes in all treatments other than surgery.

Table 20: Change in treatment plan between the before and after groups

	Before	After	p-value
Treatment plan (%)			
Best Supportive Care	3.0	10.4	P<0.01
Local Team	21.2	40.1	P<0.01
Radiotherapy through palliative Radiotherapy Clinic	2.8	14.2	P<0.01
Surgery	5.1	2.6	P=0.07
Radiotherapy	67.8	29.4	P<0.01

Cost effectiveness results

Deterministic Base Case Results

Table 21 presents the deterministic results of the cost effectiveness analysis based for the entire cohort of the model. The introduction of upskilling for staff (after) increased life expectancy in people referred to the service by just over 50 days and increased QALYs by just under 0.05 QALYs the equivalent of 18 days in full health. The approach was also found to be cost saving reducing costs per person referred by £132.

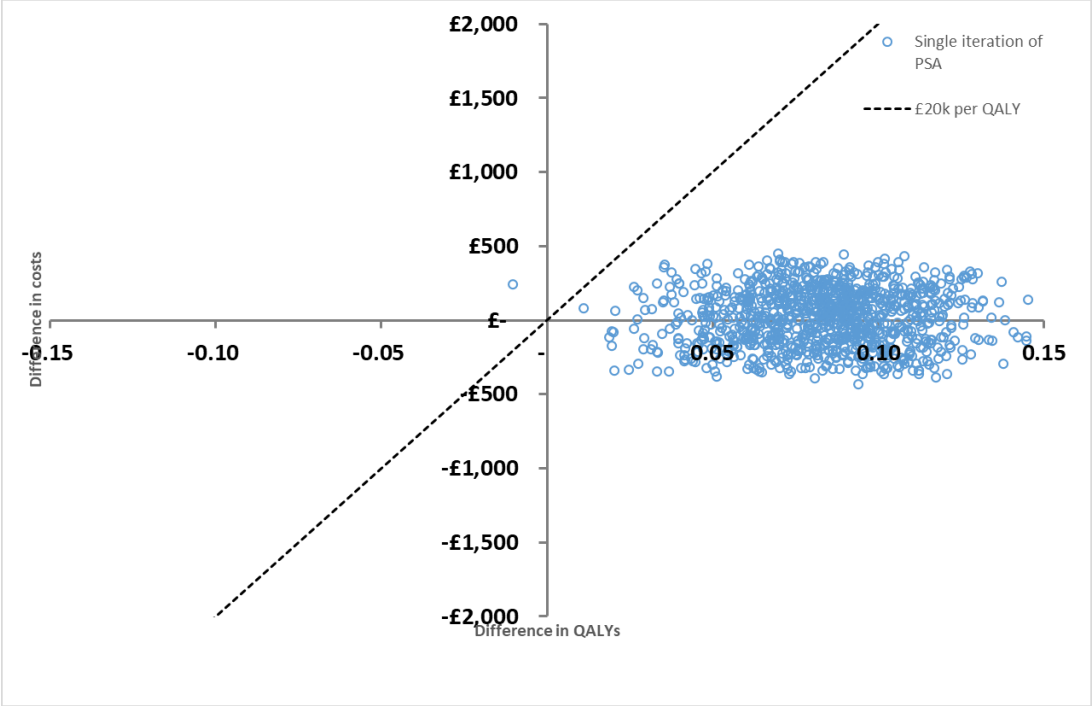
Table 21: Deterministic Cost Effectiveness Results

	Before	After
Life expectancy (days)	251.1	304.0
Incremental life expectancy		52.9
Total QALYs	0.2990	0.3460
Incremental QALY		0.0470
Cost	£1,265	£1,133
Incremental Cost		-£132
Incremental Net Monetary Benefit per person (£20,000 per QALY)		£1,073
Incremental Cost Effectiveness Ratio		**After strategy dominant (increases total QALYs and is cost saving)**

Probabilistic sensitivity analysis

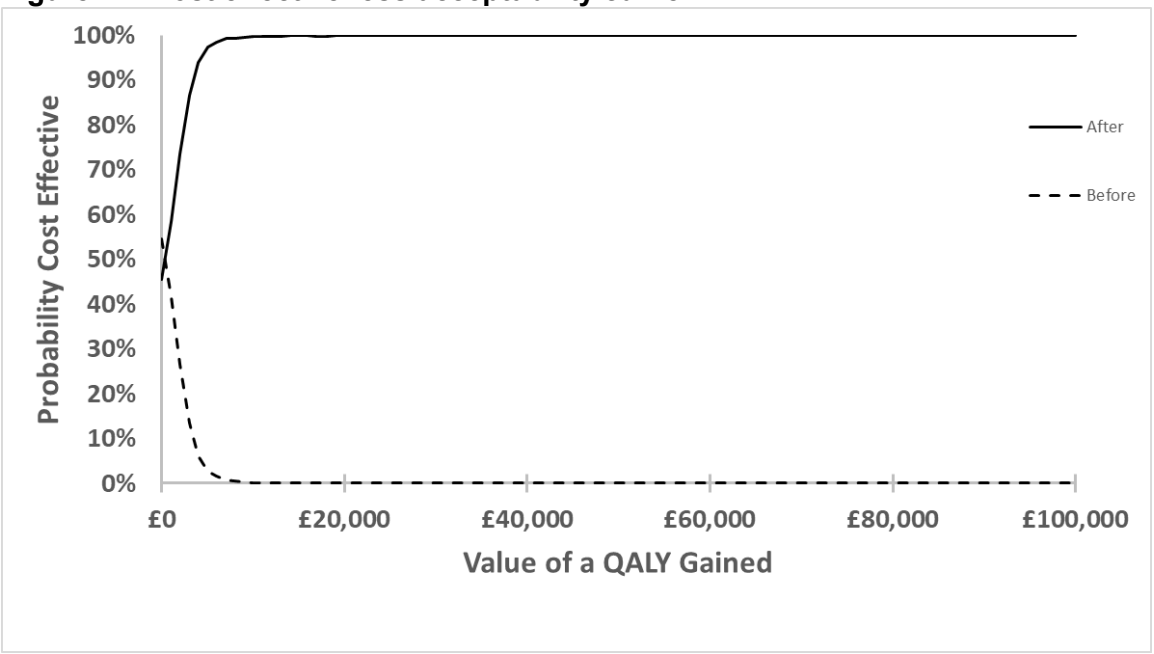
These results were robust to probabilistic sensitivity analysis. Figure 11 shows 1000 iterations of the probabilistic sensitivity analysis. All iterations were below £20,000 per QALY the value at which NICE usually recommend interventions. 46% of iterations were also cost saving with no iterations suggesting the after model for MSCC services led to a reduction in quality-adjusted life expectancy.

Figure 11: Cost effectiveness plane for after versus before



These results are echoed by the cost effectiveness acceptability curve which shows that even at willingness to pay per QALY values significantly less than those usually accepted by NICE that the 'after' approach remains the preferred option. (Figure 12) The after approach has a 100% probability of being cost effective at willingness to pay per QALY values above £9,000. At all values over £1,000 'after' has a higher probability of being cost effective than the 'before' approach.

Figure 12: Cost effectiveness acceptability curve.



Health inequalities

The cost effectiveness outcomes disaggregated by IMD quintile show that the 'after' strategy was both cost saving and health improving for all quintiles apart from quintile 5 (least deprived) which whilst showing a cost saving had a reduced life expectancy of 6.4 days and reduction in QALYs of -0.0194, equivalent to 7 days in full health (Table 22). QALY gains were largest in quintiles 3 and 4 with QALY gains 4 times higher and life expectancy gains at least twice as high as for any other quintile. Quintile 3 also had the largest cost saving with it being nearly twice as large as the next nearest quintile. Quintiles 3 and 4 make up only 36% of people referred to the MSCC centre but accrued 80% of the benefits when a QALY gained was valued at £20,000. (Figure 13) Comparatively the two most deprived quintiles 1 and 2 whilst making up 49% of the cohort only accrued 24% of the benefits of the after approach.

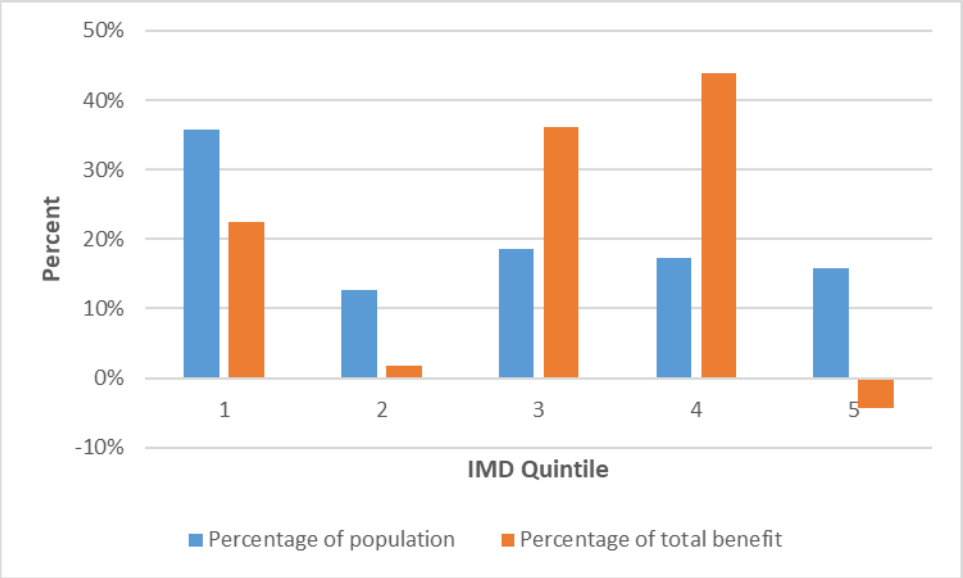
Table 22: Cost effectiveness result disaggregated by Index of Multiple Deprivation quintile

Deprivation Quintile	1 (most deprived)		2		3		4		5 (least deprived)	
	Before	After	Before	After	Before	After	Before	After	Before	After
% Total population (n=	39%	36%	14%	13%	16%	19%	17%	17%	14%	16%
Life expectancy (days)	221.8	254.0	260.1	273.4	304.8	384.6	207.4	319.2	332.2	338.5
Incremental life expectancy		32.2		13.3		79.7		111.8		6.4
Total QALYs	0.2641	0.2897	0.3107	0.3111	0.3594	0.4411	0.2481	0.3657	0.3970	0.3776
Incremental QALY		0.0256		0.0004		0.0817		0.1176		-0.0194
Cost	£1,240	£1,143	£1,329	£1,200	£1,356	£1,106	£1,168	£1,069	£1,346	£1,220
Incremental cost		-£97		-£129		-£250		-£99		-£126
Incremental cost effectiveness ratio		After dominant[1]		After dominant[1]		After dominant[1]		After dominant[1]		£6,495[2]
Incremental Net Monetary Benefit (£20,000 per		£609		£138		£1,884		£2,451		-£263

QALY)										
Total benefit (population*INMB)		£371,437		£29,780		£595,242		£725,391		-£70,713
Percentage over-all benefit		22%		2%		36%		44%		-4%
Difference benefit received and population		-11%		-10%		19%		28%		-19%

1. The strategy is both cost saving and health improving 2. As both incremental costs and QALYs are negative this value represents the savings from a QALY forgone. Higher values are more favourable to the intervention.

Figure 13: Percentage of population and percentage of health benefit received by IMD quintile



For comparison the results of those who have unknown IMD values are presented in Table 23. Compared to the reported quintiles, incremental life expectancy and incremental QALYs were only bettered by quintiles 3 and 4 with cost savings only bettered by quintile 3. It was also only bettered by quintiles 3 and 4 for incremental net monetary benefit.

Table 23: Cost effectiveness results for people with no reported Index of Multiple Deprivation in the cohort

Deprivation Quintile	**Not reported**	
	Before	After
% Total population	6%	7%
Life expectancy (days)	213.4	287.1
Incremental life expectancy		73.7
Total QALYs	0.2535	0.3260
Incremental QALY		0.0725
Cost	£1,142	£999
Incremental Cost		-£143
Incremental Net Monetary Benefit (£20,000 per QALY)		£1593

Conclusions

Upskilling staff to make initial decisions around referrals without senior clinician support, in line with the role of the MSCC co-ordinator, appears to be cost saving and health improving. Whilst this benefit was not evenly spread across all quintiles of deprivation all but the least deprived quintile had an improvement in both life expectancy and total QALYs. All quintiles resulted in cost savings. Differences in costs and outcomes were driven by people switching between treatments and living longer. More prompt referral and treatment, as is the aim of MSCC co-ordinator, should lead to higher quality of life and reduced costs from fewer adverse events even if the upskilling of staff did not result in a change of treatment plan.

There were a few weaknesses with our study. Firstly, being a before and after study it was difficult to control for outside factors which may have improved outcomes over the time frame. The most important one for this analysis was that restrictions as a result of the COVID pandemic occurred towards the end of the 'before' group and throughout most of the 'after' group time frame. It should be noted that the pandemic was partly the reason for implementing the changes, mostly as consultants started working remotely and became harder to contact for a clinical opinion. It also reduced any face-to-face appointments to only those that were clinically necessary. Treatment was also influenced by the reduction in available beds and the need to reduce hospital attendance unless clinically necessary. Treatment options were also altered with radiotherapy restricted to 1 fraction at 8GY unless clinically inappropriate. Case-mix was also likely to have changed between the before and after group. It was hypothesised that there would be more inappropriate referrals in the before group given that referring centres were likely to be unfamiliar with the new pathways. It is likely both of these would favour the before group suggesting that improvements in health are maybe underestimated.

Costs and QALYs were assigned to people in the cohort based on their received treatment and survival. We did not have the performance scores or resource use data to be able to accurately calculate these ourselves for each individual in the analysis. We would expect there to be variation in quality of life for people receiving the same intervention as outcomes and adverse events will not be identical for all. However, whilst it was difficult to estimate QALYs accurately there was an improvement in life expectancy between the 'before' and 'after' group. The committee considered it unlikely that this increased life expectancy would be as a result of reduced quality of life (i.e. through an increase in adverse events such as pain). The committee were therefore confident that the 'after' approach would lead to an increase in QALYs.

The analysis also missed some important costs not directly associated with treatment. For areas where an MSCC co-ordinated service is not already formed there will be large costs from setting this up. These costs will include recruiting members of the MSCC team including co-ordinators, setting up computer systems for recording patient information and auditing outcomes. There will also be costs incurred by having to set-up and disseminate pathways to referring centres. This may include site visits or organising training sessions which will divert time of attending clinicians away from other areas. Monitoring and feedback will also be needed during the first few months of the service to ensure that people are being referred quickly and in line with the relevant pathways. Clatterbridge Cancer Centre found a higher level of inappropriate referrals in the earlier years of the service potentially as a result of referrers being overly cautious. Returning these patients to the referring centre also takes up time and incurs costs. As with the Clatterbridge service it is expected that these referrals will decrease over time.

The economic model estimated that cost savings increased since the introduction of the service. The committee thought these one-off costs would be fully recouped over the first few years of the service operating although the exact timing would vary by centre based on the factors discussed above.

It is also not clear if similar or delayed costs would be incurred by other service configurations. For example, oversight systems will have to be in place and regularly updated for all medical service providers. It is therefore not expected that the omission of other costs will alter the conclusions of the model and that upskilling team members is likely to remain cost saving and health improving. Providing opportunities for professional development will also be budgeted for by providers of healthcare services.

Whilst the 'after' approach was cost effective the benefits were not distributed evenly across all deprivation quintiles or type of cancer. There was no observed difference in survival where the primary cancer was either breast or prostate although these groups already have higher survival than other primary cancers when adjusting for age. Attaining improvements in

this group maybe more difficult. The benefits of the ‘after’ approach were also heavily skewed towards the second and third least deprived quintiles. Given the data we have it was not possible to investigate why this was the case. It was hypothesised by the committee that there may be a ceiling effect with the least deprived quintile with early detection and quick referral already happening. The committee also hypothesised that the most deprived groups may get referred later especially when the symptom is back pain. There is a higher number of individuals in manual jobs in the most deprived quintiles and back pain may not be rapidly reported to health care practitioners or may be discounted as being caused by the physical nature of their job. Most deprived quintiles are also more likely to partake in behaviour associated with increased risk of cancer such as smoking. The committee accepted that improvements were smaller in the most deprived quintiles and made recommendations so that symptoms were more rapidly identified and not inappropriately discounted in this patient group.

Additional Information A

The Clatterbridge Cancer Centre NHS Foundation Trust are the owners of the data and the raw data cannot be shared as per the data sharing agreement between NICE and the Clatterbridge Cancer Centre. All variable names are consistent with those shared in the audit data and brief descriptions of them are provided in the code and in the report above.

STATA code for the statistical analysis.

```
clear all

insheet using "***File location removed****", comma clear

quiet

set more off

drop  if ageatreferral ==119 //outlier

gen dateaware=date( datemsccaware,"DMY") //change to date format

format dateaware %td

//negatives time to death removed

drop if daystodeathfrommsccknown <=0

//drop only occurence death before MRI

drop if  msccseverity=="RIP before MRI"

//change male/female to binary data

gen male=1

replace male=0 if mt_sex=="F"

label var male "male=1, female=0"

//Standardising terms tumour

replace tumourgroup="UnknownPrimary" if tumourgroup== "Unknown Primary"

replace tumourgroup="UnknownPrimary" if tumourgroup== "CUP"

replace tumourgroup="Skin&Melanoma" if tumourgroup== "Skin & Melanoma"

replace tumourgroup="Lung&Chest" if tumourgroup== "Lung & Chest"

replace tumourgroup="Lung&Chest" if tumourgroup== "Lung"

replace tumourgroup="Lung&Chest" if tumourgroup== "Chest"

replace tumourgroup="LowerGI" if tumourgroup== "Lower GI"

replace tumourgroup="UpperGI&HPB" if tumourgroup== "Upper GI & HPB"

replace tumourgroup="Gynaecological" if tumourgroup== "Gyane"

replace tumourgroup="Gynaecological" if tumourgroup== "Gynae"

replace tumourgroup="Head&Neck" if tumourgroup== "Head & Neck"
```

```
tab tumourgroup

//standardising severity

replace msccseverity="METS" if msccseverity== "METs"

replace msccseverity="METS" if msccseverity== "Mets"

replace msccseverity="NIL" if msccseverity== "nil"

replace msccseverity="NIL" if msccseverity== "Nil"

//Standardise plan variable

replace plan="LocalTeam" if plan== "Local Team"

replace plan="LocalTeam" if plan== "Local team"

replace plan="LocalTeam" if plan== "local Team"

replace plan="LocalTeam" if plan== "Advise"

replace plan="XRT" if plan=="XRT (Unable to tolerate)"

replace plan="XRT" if plan=="xrt"

drop if plan=="RIP"

//Missing mt_deceased data (assume those with positive values in daysdeceased are dead)

gen dead =1

replace dead=0 if daystodeathfrommsccknown==.

//Generate exit date for survivors

gen enddate1="31/05/2022"

gen enddate=date( enddate1 ,"DMY")

format enddate %td

drop enddate1

gen total_days=enddate-dateaware

label var total_days "total number of days in dataset either end time period or death"

replace total_days= daystodeathfrommsccknown if dead==1

//Generate year and other dates for subanalysis

generate yr=year(dateaware)

drop if yr==.

//generate 6 month and 12 month survival NOTE: does not censor for those not in dataset for less than this time. These values are not used in the analysis and are there for consistency checking

gen month6survival=0

label var month6survival "alive at 6 months after being aware"
```

```
replace month6survival=1 if total_days>182

gen month12survival=0

label var month12survival "alive at 12 months after being aware"

replace month12survival=1 if total_days>364

sort yr

by yr: sum month6survival if enddate-dateaware>182

by yr: sum month12survival if enddate-dateaware>364

// before after variable 1=after

gen after=1

label var after "1=after, 0=before"

//June 2020 set as year remote consultant and upskilled MSCC team to reduce rediscusses.

replace after =0 if dateaware <date("01062020","DMY")

//Set as time series data

stset total_days, failure(dead)

//adjust for age centre at mean 70

gen age70 = age-70

//combine palliative XRT with XRT

replace plan = "XRT" if plan=="XRT-Palliative"

//Quintiles for deprevation index multiple deprevation

gen deprevationquintile=0

label var deprevationquintile "quintiles for deprevation index multiple deprevation 1=most de-
prived 5=least deprived"

replace deprevationquintile=1 if indexofmultipledeprivationdecile==1

replace deprevationquintile=1 if indexofmultipledeprivationdecile==2

replace deprevationquintile=2 if indexofmultipledeprivationdecile==3

replace deprevationquintile=2 if indexofmultipledeprivationdecile==4

replace deprevationquintile=3 if indexofmultipledeprivationdecile==5

replace deprevationquintile=3 if indexofmultipledeprivationdecile==6

replace deprevationquintile=4 if indexofmultipledeprivationdecile==7

replace deprevationquintile=4 if indexofmultipledeprivationdecile==8

replace deprevationquintile=5 if indexofmultipledeprivationdecile==9

replace deprevationquintile=5 if indexofmultipledeprivationdecile==10
```

```
//Export outputs to Excel for economic evaluation
//Unadjusted
sts graph, by(after)
sts list, by(after)  saving(unadjusted, replace)
stcox after //Hazard Function
//adjusted age sex
sts graph, by(after) adjustfor(age70 male)
sts list, by(after) adjustfor(age70 male) saving(adjustedagesex, replace)
stcox after age70 male //Hazard Function
//by location adjusted for age but not sex due to perfect correlation male/prostate
sts graph, by(after primarycancerlocation) adjustfor(age70)
sts list, by(after primarycancerlocation) adjustfor(age70) saving(primarylocation, replace)
//health inequalities
sts graph, by(after deprevationquintile ) adjustfor(age70 male)
sts list, by(after deprevationquintile ) adjustfor(age70 male) saving(quintiles, replace)
//by year
sts graph, by (yr) adjustfor(age70 male)
sts list, by(yr) adjustfor(age70 male) saving(byyear, replace)
//by treatment plan
sts graph, by (after plan) adjustfor(age70 male)
sts list, by (after plan) adjustfor(age70 male) saving (plan, replace)
//by treatment plan and deprivation quintiles
sts graph, by (after plan deprevationquintile) adjustfor(age70 male)
sts list, by (after plan deprevationquintile) adjustfor(age70 male) saving (planDepr, replace)
//exporting files
use unadjusted, clear
export excel using unadjusted.xlsx, first(var) replace
use adjustedagesex, clear
export excel using adjustedagesex.xlsx, first(var) replace
use primarylocation, clear
export excel using primarylocation.xlsx, first(var) replace
use quintiles, clear
export excel using quintiles.xlsx, first(var) replace
```

```
use byyear, clear

export excel using byyear.xlsx, first(var) replace

use plan, clear

export excel using plan.xlsx, first(var) replace

use planDepr, clear

export excel using planDep.xlsx, first(var) replace
```

Appendix J Excluded studies

Excluded studies for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

Excluded effectiveness studies

Table 24: Excluded studies and reasons for their exclusion

Study	Reason for exclusion
Neurosurgical National Audit Programme (NNAP) https://www.nnap.org.uk/.	Publication type – does not match protocol - conference abstract
Ashcroft, J., Duran, I., Hoefeler, H. et al. (2018) Healthcare resource utilisation associated with skeletal-related events in European patients with multiple myeloma: Results from a prospective, multinational, observational study. European Journal of Haematology 100(5): 479-487	Population – does not match protocol
Barzilai, Ori, Boriani, Stefano, Fisher, Charles G et al. (2019) Essential Concepts for the Management of Metastatic Spine Disease: What the Surgeon Should Know and Practice. Global spine journal 9(1suppl): 98s-107s	Intervention – does not match protocol
Beiser, Erez, Soyfer, Viacheslav, Novikov, Ilyia et al. (2019) A critical assessment of the quality of radiation therapy in Israel: time to initiation of treatment of spinal cord compression as an index of efficiency. Journal of neuro-oncology 143(2): 329-335	Intervention – does not match protocol
Bollen, Laurens, Dijkstra, Sander P D, Bartels, Ronald H M A et al. (2018) Clinical management of spinal metastases-The Dutch national guideline. European journal of cancer (Oxford, England : 1990) 104: 81-90	Study design – does not match protocol
Brooks, F M, Ghatahora, Ameet, Brooks, M C et al. (2014) Management of metastatic spinal cord compression: awareness of NICE guidance. European journal of orthopaedic surgery & traumatology: orthopedie traumatologie 24suppl1: 255-9	Study design – does not match protocol
Charlton, P., Sabbagh, A., Shakir, R. et al. (2018) Implementation of the Oxford Acute Referral System (OARS) an Electronic System to Document and Manage the Acute Referral of Patients with Metastatic Spinal Cord Compression (MSCC). Clinical Oncology 30: 12-s13	Study design – does not match protocol
Chen, Albert C; Bonnen, Mark D; Mok, Henry (2017) Onsite versus offsite radiation treatment of malignant spinal cord compression: lessons from a safety net health system. The British journal of radiology 90(1072): 20160922	Study design – does not match protocol
Choy, W.J.; Phan, K.; Mobbs, R.J. (2019) Editorial on the integrated multidisciplinary algorithm for the management of spinal metastases. Translational Cancer Research 8(supplement2): 152-s155	Study design – does not match protocol
Curtin, Mark, Piggott, Robert P, Murphy, Evelyn P et al. (2017) Spinal Metastatic Disease: A Review of the Role of the Multidisciplinary Team. Orthopaedic surgery 9(2): 145-151	Intervention – does not match protocol
Dasenbrock, Hormuzdiyar H, Clarke, Michelle J, Thompson, Richard E et al. (2012) The impact of July hospital admission on outcome after surgery for spinal metastases at academic medical centers in the United States, 2005 to 2008. Cancer 118(5): 1429-38	Study design – does not match protocol
Dasenbrock, Hormuzdiyar H, Pradilla, Gustavo, Witham, Timothy F et	Study design – does not

Study	Reason for exclusion
al. (2012) The impact of weekend hospital admission on the timing of intervention and outcomes after surgery for spinal metastases. Neurosurgery 70(3): 586-93	match protocol
Debono, Bertrand, Braticevic, Cecile, Sabatier, Pascal et al. (2019) The "Friday peak" in surgical referrals for spinal metastases: lessons not learned. A retrospective analysis of 201 consecutive cases at a tertiary center. Acta neurochirurgica 161(6): 1069-1076	Study design – does not match protocol
Dhamija, B.; Batheja, D.; Balain, B. S. (2021) A systematic review of MIS and open decompression surgery for spinal metastases in the last two decades. Journal of clinical orthopaedics and trauma 22: 101596	Intervention – does not match protocol
Dunbar, E.M. (2020) Multidisciplinary spine oncology care across the disease continuum. Neuro-Oncology Practice 7: i1-i4	Study design – does not match protocol
Eleraky, Mohammed; Papanastassiou, Ioannis; Vrionis, Frank D (2010) Management of metastatic spine disease. Current opinion in supportive and palliative care 4(3): 182-8	Intervention – does not match protocol
Fenton, M. et al. An electronic proforma to improve documentation for cases of metastatic spinal cord compression: A quality-improvement project. Clinical Oncology, Volume 31, e6	Publication type - does not match protocol - conference abstract
Gao, Z. Y., Zhang, T., Zhang, H. et al. (2021) Effectiveness of preoperative embolization in patients with spinal metastases: a systematic review and meta-analysis. World neurosurgery	Intervention – does not match protocol
Gasbarrini, Alessandro, Li, Haomiao, Cappuccio, Michele et al. (2010) Efficacy evaluation of a new treatment algorithm for spinal metastases. Spine 35(15): 1466-70	Intervention – does not match protocol
Gebhardt, B.J., Rajagopalan, M.S., Gill, B.S. et al. (2015) Impact of dynamic changes to a bone metastases pathway in a large, integrated, National Cancer Institute-designated comprehensive cancer center network. Practical Radiation Oncology 5(6): 398-405	Publication type – does not match protocol - conference abstract
Greif, Dylan N, Ghasem, Alexander, Butler, Alexander et al. (2019) Multidisciplinary Management of Spinal Metastasis and Vertebral Instability: A Systematic Review. World neurosurgery 128: e944-e955	Intervention – does not match protocol
Groenen, Karlijn H J, van der Linden, Yvette M, Brouwer, Thea et al. (2018) The Dutch national guideline on metastases and hematological malignancies localized within the spine; a multidisciplinary collaboration towards timely and proactive management. Cancer treatment reviews 69: 29-38	Study design – does not match protocol
Gutt, R., Malhotra, S., Hagan, M.P. et al. (2021) Palliative Radiotherapy within the Veterans Health Administration: Barriers to Referral and Timeliness of Treatment. JCO Oncology Practice 17(12): e1913-e1922	Study design – does not match protocol
Guzik, Grzegorz (2018) Analysis of factors delaying the surgical treatment of patients with neurological deficits in the course of spinal metastatic disease. BMC palliative care 17(1): 44	Intervention – does not match protocol
Hanchanale S, Neoh K, Waldock J, et al MANAGEMENT OF METASTATIC SPINAL CORD COMPRESSION: AUDIT. BMJ Supportive & Palliative Care 2014;4:A54.	Publication type - does not match protocol - conference abstract
Hinojosa-Gonzalez, D. E., Roblesgil-Medrano, A., Villarreal-Espinosa, J. B. et al. (2021) Minimally Invasive versus Open Surgery for Spinal Metastasis: A Systematic Review and Meta-Analysis. Asian spine journal	Intervention – does not match protocol
Hsiue, Peter P, Kelley, Benjamin V, Chen, Clark J et al. (2020) Surgical treatment of metastatic spine disease: an update on national trends and clinical outcomes from 2010 to 2014. The spine journal : official journal of the North American Spine Society 20(6): 915-924	Intervention – does not match protocol

Study	Reason for exclusion
Huang, C.W.C., Ali, A., Chang, Y.-M. et al. (2019) Performance of on-call radiology residents in interpreting total spine MRI studies for the detection of spinal cord compression or cauda equina compression. American Journal of Roentgenology 213(6): 1341-1347	Population – does not match protocol
Khan, H.A., Rabah, N.M., Chakravarthy, V. et al. (2021) Predictors of nonelective surgery for spinal metastases: Insights from a national database. Spine 46(24): e1334-e1342	Population – does not match protocol
Kim, Ellen, McClelland, Shearwood 3rd, Jaboin, Jerry J et al. (2021) Disparities in Patterns of Conventional Versus Stereotactic Body Radiotherapy in the Treatment of Spine Metastasis in the United States. Journal of palliative care 36(2): 130-134	Outcomes – do not match protocol
Kumar, Naresh, Thomas, Andrew Cherian, Ramos, Miguel Rafael David et al. (2021) Readmission-Free Survival Analysis in Metastatic Spine Tumour Surgical Patients: A Novel Concept. Annals of surgical oncology 28(5): 2474-2482	Intervention – does not match protocol
Kurisunkal, Vineet; Gulia, Ashish; Gupta, Srinath (2020) Principles of Management of Spine Metastasis. Indian journal of orthopaedics 54(2): 181-193	Study design – does not match protocol
Lacey, Craig, Ockwell, Clare, Locke, Imogen et al. (2015) A prospective study comparing radiographer- and clinician-based localization for patients with metastatic spinal cord compression (MSCC) to assess the feasibility of a radiographer-led service. The British journal of radiology 88(1055): 20150586	Intervention – does not match protocol
Lawton, Andrew J, Lee, Kathleen A, Cheville, Andrea L et al. (2019) Assessment and Management of Patients With Metastatic Spinal Cord Compression: A Multidisciplinary Review. Journal of clinical oncology : official journal of the American Society of Clinical Oncology 37(1): 61-71	Study design – does not match protocol
Levack, P., Graham, J., Collie, D. et al. (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(6): 472-480	Comparator – does not match protocol
Lo, S.S.-M., Ryu, S., Chang, E.L. et al. (2015) ACR Appropriateness Criteria Metastatic Epidural Spinal Cord Compression and Recurrent Spinal Metastasis. Journal of Palliative Medicine 18(7): 573-584	Study design – does not match protocol
Lo, Wan-Yu and Yang, Shu-Hua (2017) Metastatic spinal cord compression (MSCC) treated with palliative decompression: Surgical timing and survival rate. PloS one 12(12): e0190342	Comparator – does not match protocol
Macdonald, A Graham, Lynch, Daniel, Garbett, Ian et al. (2019) Malignant spinal cord compression. The journal of the Royal College of Physicians of Edinburgh 49(2): 151-156	Comparator – does not match protocol
McLinton A, Hutchison C. Malignant spinal cord compression: a retrospective audit of clinical practice at a UK regional cancer centre. Br J Cancer. 2006 Feb 27;94(4):486-91	Comparator – does not match protocol
Newman, William Christopher, Patel, Ankur, Goldberg, Jacob L et al. (2020) The importance of multidisciplinary care for spine metastases: initial tumor management. Neuro-oncology practice 7(suppl1): i25-i32	Study design – does not match protocol
Paulino Pereira, N. R., Groot, O. Q., Verlaan, J. J. et al. (2021) Quality of Life Changes After Surgery for Metastatic Spinal Disease: A Systematic Review and Meta-analysis. Clinical spine surgery	Intervention – does not match protocol
Pease, N.J et al. Development and audit of a care pathway for the management of patients with suspected malignant spinal cord compression. Physiotherapy, Volume 90, Issue 1, 27 - 34	Other protocol criteria - duplicate publication.
Pease, N.J.; Harris, R.J.; Finlay, I.G. (2004) Development and audit of a care pathway for the management of patients with suspected ma-	Other protocol criteria - duplicate publication.

Study	Reason for exclusion
lignant spinal cord compression. Physiotherapy 90(1): 27-34	
Pennington, Zach, Porras, Jose L, Larry Lo, Sheng-Fu et al. (2021) International Variability in Spinal Metastasis Treatment: A Survey of the AO Spine Community. Global spine journal: 21925682211046904	Population – does not match protocol
Philipps, L. et al. An Audit of Metastatic Cord Compression Pathways. Clinical Oncology, Volume 30, S4	Publication type – does not match protocol - conference abstract
Pipola, Valerio, Terzi, Silvia, Tedesco, Giuseppe et al. (2018) Metastatic epidural spinal cord compression: does timing of surgery influence the chance of neurological recovery? An observational case-control study. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 26(9): 3181-3186	Intervention – does not match protocol
Rades, Dirk, Janssen, Stefan, Conde-Moreno, Antonio Jose et al. (2017) Role of the overall treatment time of radiotherapy with 10 x 3 Gy for outcomes in patients with metastatic spinal cord compression. Journal of medical imaging and radiation oncology 61(3): 388-393	Intervention – does not match protocol
Ratanatharathorn, V. and Powers, W.E. (1991) Epidural spinal cord compression from metastatic tumor: Diagnosis and guidelines for management. Cancer Treatment Reviews 18(1): 55-71	Study design – does not match protocol
Richards, Lena, Misra, Vivek, Verma, Rajat et al. (2017) 86 - Metastatic Spinal Cord Compression (MSCC) – Collaborative Work between the Tertiary Cancer Centre and the Specialist Spinal Centre Since the Introduction of the MSCC Coordinator Service Has Seen a Marked Increase in Surgical Rates, with 20% of Patients Who Presented with MSCC in the First 24 Months Having Spinal Surgery. This Has Resulted in Improved Survival Rates for MSCC Patients in Greater Manchester and Cheshire. Spine Journal 17: 30-s31	Publication type – does not match protocol - conference abstract
Rudra, Soumon, Lauman, Mary K, Stowe, Hayley et al. (2020) Evaluation of the Metastatic Spine Disease Multidisciplinary Working Group Algorithms as Part of a Multidisciplinary Spine Tumor Conference. Global spine journal 10(7): 888-895	Comparator – does not match protocol
Schilling, Andrew, Pennington, Zach, Ehresman, Jeff et al. (2021) Impact of Multidisciplinary Intraoperative Teams on Thirty-Day Complications After Sacral Tumor Resection. World neurosurgery 152: e558-e566	Population – does not match protocol
Services, NHS and Mike Hutton GIRFTClinical Lead for, Spinal (2019) Spinal Services GIRFT Programme National Specialty Report.	Population – does not match protocol
Shah, S. et al. (2021) Management of Metastatic Spinal Cord Compression in Secondary Care: A Practice Reflection from Medway Maritime Hospital, Kent, UK. J. Pers. Med.	Other protocol criteria - duplicate publication.
Shah, Sidrah, Kutka, Mikolaj, Lees, Kathryn et al. (2021) Management of Metastatic Spinal Cord Compression in Secondary Care: A Practice Reflection from Medway Maritime Hospital, Kent, UK. Journal of personalized medicine 11(2)	Comparator – does not match protocol
Souchon, R., Wenz, F., Sedlmayer, F. et al. (2009) DEGRO practice guidelines for palliative radiotherapy of metastatic breast cancer: BBBone metastases and metastatic spinal cord compression (MSCC). Strahlentherapie und Onkologie 185(7): 417-424	Study design – does not match protocol
Spratt, Daniel E, Beeler, Whitney H, de Moraes, Fabio Y et al. (2017) An integrated multidisciplinary algorithm for the management of spinal metastases: an International Spine Oncology Consortium report. The Lancet. Oncology 18(12): e720-e730	Study design – does not match protocol
Steinberger, Jeremy M, Yuk, Frank, Doshi, Amish H et al. (2020) Multidisciplinary management of metastatic spine disease: initial symptom-directed management. Neuro-oncology practice 7(suppl1): i33-i44	Study design – does not match protocol

Study	Reason for exclusion
Tabacof, L., Delgado, A., Dewil, S. et al. (2021) Safety and Feasibility of Outpatient Rehabilitation in Patients with Secondary Bone Cancer: A Preliminary Study. Rehabilitation Oncology 39(3): e42-e50	Comparator – does not match protocol
Tarawneh, Ahmad M; Pasku, Dritan; Quraishi, Nasir A (2021) Surgical complications and re-operation rates in spinal metastases surgery: a systematic review. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society 30(10): 2791-2799	Intervention – does not match protocol
Tsukada, Y., Nakamura, N., Ohde, S. et al. (2015) Factors that delay treatment of symptomatic metastatic extradural spinal cord compression. Journal of Palliative Medicine 18(2): 107-113	Intervention – does not match protocol - study shows treatment is delayed if patients present on weekend.
van Tol, Floris R, Choi, David, Verkooijen, Helena M et al. (2019) Delayed presentation to a spine surgeon is the strongest predictor of poor postoperative outcome in patients surgically treated for symptomatic spinal metastases. The spine journal : official journal of the North American Spine Society 19(9): 1540-1547	Intervention – does not match protocol - study shows poorer outcomes for patients where treatment was delayed.
van Tol, Floris R, Massier, Julie R A, Frederix, Geert W J et al. (2021) Costs Associated With Timely and Delayed Surgical Treatment of Spinal Metastases. Global spine journal: 2192568220984789	Intervention – does not match protocol
Vellayappan, B.A., Kumar, N., Chang, E.L. et al. (2018) Novel multidisciplinary approaches in the management of metastatic epidural spinal cord compression. Future Oncology 14(17): 1665-1668	Study design – does not match protocol
Wallace, Adam N, Robinson, Clifford G, Meyer, Jeffrey et al. (2019) The Metastatic Spine Disease Multidisciplinary Working Group Algorithms. The oncologist 24(3): 424	Study design – does not match protocol
White, B D, Stirling, A J, Paterson, E et al. (2008) Diagnosis and management of patients at risk of or with metastatic spinal cord compression: summary of NICE guidance. BMJ (Clinical research ed.) 337: a2538	Study design – does not match protocol
Zaveri, Gautam R, Jain, Reetu, Mehta, Nishank et al. (2021) An Overview of Decision Making in the Management of Metastatic Spinal Tumors. Indian journal of orthopaedics 55(4): 799-814	Study design – does not match protocol
Zehri, Aqib H, Peterson, Keyan A, Lee, Katriel E et al. (2022) National trends in the surgical management of metastatic lung cancer to the spine using the national inpatient sample database from 2005 to 2014. Journal of clinical neuroscience: official journal of the Neurosurgical Society of Australasia 95: 88-93	Intervention – does not match protocol

Excluded economic studies

No economic evidence was identified for this review. See supplement 2 for further information.

Appendix K Research recommendations – full details

Research recommendations for review question: What service configuration and delivery arrangements are effective in the management and early rehabilitation of adults with suspected or confirmed spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

No research recommendations were made for this review question.