

Metastatic spinal cord compression

[E] Recognition - MSCC

NICE guideline number tbc

Evidence reviews underpinning recommendations 1.3.1 and 1.3.2 as well as parts of box 1 (cancer and suspected cancer as well as symptoms and signs of cord compression) in the NICE guideline

March 2023

Draft for consultation

*These evidence reviews were developed by
NICE*

Disclaimer

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Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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1 Recognition - MSCC

2 Review question

3 In people who present with spinal cord compression what symptoms or signs, individually or
4 in combination, or validated clinical tools, indicate the presence of metastatic spinal disease
5 or direct malignant infiltration?

6 Introduction

7 The signs and symptoms of spinal cord compression are well known to include bladder or
8 bowel dysfunction, gait disturbance or difficulty walking, limb weakness, neurological signs of
9 spinal cord or cauda equina compression, numbness, paraesthesia or sensory loss and
10 radicular pain. This evidence review addressed whether there are particular signs or
11 symptoms that can differentiate spinal cord compression with a malignant cause from that
12 with non-malignant causes.

13 Summary of the protocol

14 See Table 1 for a summary of the Population, Index test, Reference standard and Outcome
15 (PIRO) characteristics of this review.

16 Table 1: Summary of the protocol (PIRO table)

17

Population	Adults presenting with symptoms or signs of spinal cord compression
Index test (Signs or symptoms)	Signs or symptoms alone or in combination: <ul style="list-style-type: none">• Pain location:<ul style="list-style-type: none">○ in the middle (thoracic) spine○ upper (cervical) spine○ lower (lumbar) spine○ bone pain elsewhere• Pain dynamics:<ul style="list-style-type: none">○ New onset spinal pain○ Progressive spinal pain○ Severe unremitting lower spinal pain• Spinal pain aggravated by straining (for example, at stool, or when coughing or sneezing) or weight bearing• Localised spinal tenderness• Nocturnal spinal pain preventing sleep.• Spinal deformity• Vertebral compression fractures• Neurological symptoms including:<ul style="list-style-type: none">○ radicular pain,○ any limb weakness,○ difficulty in walking○ inability to stand○ unsteadiness (ataxia)○ sensory loss or disturbance (for example tingling)○ bladder, bowel or sexual dysfunction• Neurological signs of spinal cord or cauda equina compression.

	<p>Any of the above in combination with potential symptoms of advanced cancer such as:</p> <ul style="list-style-type: none"> • Weight loss • Loss of appetite • Fatigue • Change in bowel habit • New and unexplained lumps • Frequent infections • Cough or hoarseness
Reference standard	<ul style="list-style-type: none"> • Metastatic disease • Malignant Infiltration <p>As determined by MRI, CT, PET-CT, or biopsy</p>
Outcome	<p>Critical</p> <ul style="list-style-type: none"> • Diagnostic accuracy: <ul style="list-style-type: none"> ○ Sensitivity, specificity ○ Positive and negative predictive value ○ Likelihood ratios • For clinical prediction tools <ul style="list-style-type: none"> ○ Calibration ○ Discrimination <p>Important</p> <ul style="list-style-type: none"> • Adverse events associated with measurement of the symptom or sign • Adverse events associated with radiology: <ul style="list-style-type: none"> ○ Contrast related ○ False positive / biopsy related adverse events

1 *CT: computed tomography; MRI: magnetic resonance imaging; PET-CT: positron emission tomography-computed*
2 *tomography.*

3 For further details see the review protocol in appendix A.

4 **Methods and process**

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

9 Declarations of interest were recorded according to [NICE's conflicts of interest policy](#).

10 **Diagnostic evidence**

11 **Included studies**

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

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

15 **Excluded studies**

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

1 **Summary of included studies**

2 No studies were identified which were applicable to this review question (and so there are no
3 evidence tables in Appendix D). No meta-analysis was conducted for this review (and so
4 there are no forest plots in Appendix E).

5 **Summary of the evidence**

6 No studies were identified which were applicable to this review question (and so there are no
7 GRADE tables in Appendix F).

8 **Economic evidence**

9 **Included studies**

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

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

14 **Excluded studies**

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

17 **Summary of included economic evidence**

18 No economic studies were identified which were applicable to this review question.

19 **Economic model**

20 No economic modelling was undertaken for this review because the committee agreed that
21 other topics were higher priorities for economic evaluation.

22 **Evidence statements**

23 No economic studies were identified which were applicable to this review question.

24 **The committee's discussion and interpretation of the evidence**

25 **The outcomes that matter most**

26 The committee agreed that diagnostic accuracy was a critical outcome for this evidence
27 review. This is because accurate classification of malignant and non-malignant spinal cord
28 compression will guide further investigations or treatments. Adverse events associated with
29 measurement of symptoms or signs or with radiological tests were important outcomes. This
30 is because tests and investigations could potentially have harmful effects on rare occasions
31 which need to be balanced against any benefits.

32 **The quality of the evidence**

33 There was a lack of evidence, so the committee based their recommendations completely on
34 their expertise and experience.

1 **Benefits and harms**

2 Even though no evidence was identified the committee agreed that there is a general
3 consensus in the clinical community about what the symptoms and signs of cord
4 compression are. Cord compression means that pressure is put on the spinal column and the
5 associated nerves around it. This results in neurological symptoms. The committee based on
6 their expertise, decided to list these:

- 7 • bladder or bowel dysfunction
- 8 • gait disturbance or difficulty walking
- 9 • limb weakness
- 10 • neurological signs of spinal cord or cauda equina compression
- 11 • numbness, paraesthesia or sensory loss
- 12 • radicular pain

13 Listing these symptoms and signs will enable clinicians to think about the possibility of MSCC
14 and to take the appropriate actions in a timely manner.

15 The committee agreed that a personal history of cancer in a person presenting with
16 symptoms or signs of spinal cord compression would increase the likelihood that the
17 compression was due to malignant causes. This should be treated as an oncological
18 emergency so that immediate action is taken.

19 The committee decided not to make a research recommendation because they thought that
20 their consensus recommendation reflect the most well-known symptoms and signs of MSCC.
21 They agreed that this would therefore not be a priority for further research.

22 **Cost effectiveness and resource use**

23 The committee agreed that the recommendations reflect current practice and that there will
24 be no change in resource use as a result of these recommendations.

25 **Other factors the committee took into account**

26 The committee was also aware that when there is a suspicion of cancer healthcare
27 professionals should refer to the [NICE guideline on suspected cancer](#) so that they can take
28 the appropriate action.

29 **Recommendations supported by this evidence review**

30 This evidence review supports recommendations 1.3.1 and 1.3.2 as well as parts of box 1
31 (cancer and suspected cancer as well as symptoms and signs of cord compression) in the
32 guideline.

33 **References – included studies**

34 No evidence was identified.

35

1 Appendices

2 Appendix A Review protocols

3 **Review protocol for review question: In people who present with spinal cord compression what symptoms or signs,**
4 **individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct**
5 **malignant infiltration?**

6 **Table 2: Review protocol**

ID	Field	Content
0.	PROSPERO registration number	CRD42022310721
1.	Review title	Symptoms or signs suggestive of the presence of spinal metastatic malignant disease or direct malignant infiltration of the spine in people with spinal cord compression.
2.	Review question	In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?
3.	Objective	To establish which symptoms or signs, or validated clinical tools suggest the presence of spinal metastatic malignant disease or direct malignant infiltration of the spine in people who present with spinal cord compression.
4.	Searches	The following databases will be searched: <ul style="list-style-type: none">• Cochrane Central Register of Controlled Trials (CENTRAL)• Cochrane Database of Systematic Reviews (CDSR)• Cumulative Index to Nursing and Allied Health Literature (CINAHL)• Embase• Epistemonikos• International Health Technology Assessment (INAHTA) database• MEDLINE & MEDLINE In-Process

ID	Field	Content
		<p>Searches will be restricted by:</p> <ul style="list-style-type: none"> • Date: 1990 onwards (see rationale under Section 10) • English language studies • Human studies <p>Other searches:</p> <ul style="list-style-type: none"> • Inclusion lists of systematic reviews <p>With the agreement of the guideline committee the searches will be re-run between 6-8 weeks before final submission of the review and further studies retrieved for inclusion.</p> <p>The full search strategies for MEDLINE database will be published in the final review.</p>
5.	Condition or domain being studied	Symptoms or signs that indicate spinal cord compression is due to spinal metastatic malignant disease or direct malignant infiltration of the spine rather than non-malignant causes.
6.	Population	<p>Inclusion:</p> <ul style="list-style-type: none"> • Adults presenting with symptoms or signs of spinal cord compression <p>Exclusion:</p> <ul style="list-style-type: none"> • Adults with primary bone tumours of the spinal column. • Children and young people under the age of 18
7.	Sign or symptom	<p>Symptoms alone or in combination:</p> <ul style="list-style-type: none"> • Pain location: <ul style="list-style-type: none"> ○ in the middle (thoracic) spine ○ upper (cervical) spine ○ lower (lumbar) spine ○ bone pain elsewhere • Pain dynamics:

ID	Field	Content
		<ul style="list-style-type: none"> ○ New onset spinal pain ○ Progressive spinal pain ○ Severe unremitting lower spinal pain ● Spinal pain aggravated by straining (for example, at stool, or when coughing or sneezing) or weight bearing ● Localised spinal tenderness ● Nocturnal spinal pain preventing sleep. ● Spinal deformity ● Vertebral compression fractures ● Neurological symptoms including: <ul style="list-style-type: none"> ○ radicular pain, ○ any limb weakness, ○ difficulty in walking ○ inability to stand ○ unsteadiness (ataxia) ○ sensory loss or disturbance (e.g. tingling) ○ bladder, bowel or sexual dysfunction ● Neurological signs of spinal cord or cauda equina compression. <p>Any of the above in combination with potential symptoms of advanced cancer such as:</p> <ul style="list-style-type: none"> ● Weight loss ● Loss of appetite ● Fatigue ● Change in bowel habit ● New and unexplained lumps ● Frequent infections ● Cough or hoarseness
8.	Reference standard	<ul style="list-style-type: none"> ● Metastatic disease

ID	Field	Content
		<ul style="list-style-type: none"> • Malignant Infiltration <p>As determined by MRI, CT, PET-CT, biopsy</p>
9.	Types of study to be included	<p>Diagnostic accuracy studies evaluating clinical outcomes:</p> <ul style="list-style-type: none"> • Cross-sectional studies • Cohort studies • Nested case-control
10.	Other exclusion criteria	<p>Inclusion:</p> <ul style="list-style-type: none"> • Full text papers <p>Exclusion:</p> <ul style="list-style-type: none"> • Conference abstracts • Articles published before 1990 (the date when MRI use became regular in this population). • 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	<p>Metastatic spinal cord compression in adults: risk assessment, diagnosis and management (2008) NICE guideline will be updated by this review question</p>
12.	Primary outcomes (critical outcomes)	<ul style="list-style-type: none"> • Diagnostic accuracy: <ul style="list-style-type: none"> ○ Sensitivity, specificity ○ Positive and negative predictive value ○ Likelihood ratios <p>For clinical prediction tools</p> <ul style="list-style-type: none"> • Calibration • Discrimination
13.	Secondary outcomes (important outcomes)	<ul style="list-style-type: none"> • Adverse events associated with measurement of the symptom or sign • Adverse events associated with radiology:

ID	Field	Content
		<ul style="list-style-type: none"> ○ Contrast related ○ False positive / biopsy related adverse events
14.	Data extraction (selection and coding)	<p>All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated.</p> <p>Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol.</p> <p>Dual sifting will be performed on at least 10% of records; 90% agreement is required. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. 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</p> <p>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.</p> <p>Draft excluded studies will be circulated to the Topic Group for their comments. Resolution of disputes will be by discussion between the senior reviewer, Topic Advisor and Chair. 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.</p>
15.	Risk of bias (quality) assessment	<p>Risk of bias of individual studies will be assessed using the preferred checklist as described in Developing NICE guidelines: the manual.</p> <p>Quality assessment of individual studies will be performed using the following checklists:</p> <ul style="list-style-type: none"> ● QUADAS-2 for diagnostic accuracy studies ● PROBAST tool for clinical prediction models

ID	Field	Content														
		The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.														
16.	Strategy for data synthesis	<p>Diagnostic / clinical prediction models review: Depending on the availability of the evidence, the findings will be summarised narratively or quantitatively. Where appropriate, meta-analysis of diagnostic test accuracy will be performed using the metandi and midas applications in STATA and Cochrane Review Manager. PPV with 95% CIs will be used as outcomes for diagnostic test usefulness. These diagnostic accuracy parameters will be obtained from the studies or calculated by the technical team using data from the studies.</p> <p>Validity 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/</p>														
17.	Analysis of sub-groups	<p>Evidence will be stratified by:</p> <ul style="list-style-type: none"> • Location in the spine of compression <p>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.</p>														
18.	Type and method of review	<table border="1"> <tbody> <tr> <td><input type="checkbox"/></td> <td>Intervention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Diagnostic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Prognostic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Qualitative</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Epidemiologic</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Service Delivery</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Other (please specify)</td> </tr> </tbody> </table>	<input type="checkbox"/>	Intervention	<input checked="" type="checkbox"/>	Diagnostic	<input type="checkbox"/>	Prognostic	<input type="checkbox"/>	Qualitative	<input type="checkbox"/>	Epidemiologic	<input type="checkbox"/>	Service Delivery	<input type="checkbox"/>	Other (please specify)
<input type="checkbox"/>	Intervention															
<input checked="" type="checkbox"/>	Diagnostic															
<input type="checkbox"/>	Prognostic															
<input type="checkbox"/>	Qualitative															
<input type="checkbox"/>	Epidemiologic															
<input type="checkbox"/>	Service Delivery															
<input type="checkbox"/>	Other (please specify)															
19.	Language	English														

ID	Field	Content		
20.	Country	England		
21.	Anticipated or actual start date	01 February 2022		
22.	Anticipated completion date	23 August 2023		
23.	Stage of review at time of this submission	Review stage	Started	Completed
		Preliminary searches	<input checked="" type="checkbox"/>	<input type="checkbox"/>
		Piloting of the study selection process	<input type="checkbox"/>	<input type="checkbox"/>
		Formal screening of search results against eligibility criteria	<input type="checkbox"/>	<input type="checkbox"/>
		Data extraction	<input type="checkbox"/>	<input type="checkbox"/>
		Risk of bias (quality) assessment	<input type="checkbox"/>	<input type="checkbox"/>
		Data analysis	<input type="checkbox"/>	<input type="checkbox"/>
24.	Named contact	<p>5a. Named contact National Guideline Alliance</p> <p>5b Named contact e-mail metastaticspinal@nice.org.uk</p> <p>5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Alliance</p>		
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		

ID	Field	Content	
		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	Not applicable	
30.	Reference/URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=310721	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: <ul style="list-style-type: none"> • 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 media channels, and publicising the guideline within NICE. 	
32.	Keywords	Recognising spinal metastases, identifying metastatic spinal disease	
33.	Details of existing review of same topic by same authors	Not applicable	
34.	Current review status	<input checked="" type="checkbox"/>	Ongoing
		<input type="checkbox"/>	Completed but not published
		<input type="checkbox"/>	Completed and published
		<input type="checkbox"/>	Completed, published and being updated
		<input type="checkbox"/>	Discontinued
35..	Additional information	[Provide any other information the review team feel is relevant to the registration of the review.]	

ID	Field	Content
36.	Details of final publication	www.nice.org.uk

1
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5

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: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

Database: Medline – OVID interface

#	Searches
1	Spinal Cord Compression/
2	exp Spinal Cord Neoplasms/ or Spinal Neoplasms/
3	((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) adj3 (infiltrat* or invad* or invasion or metast* or oligometast*)).ti,ab.
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	(mescc or msc).tw.
6	or/1-5
7	exp Back Pain/ or Spinal Fractures/
8	(backache or dorsalgia or lumbago or ((back or cauda equina or cervical* or cervicothoracic or coccyx or dorsal or lumbar or lumbosacral or lumbo sacral or spine or spinal or vertebra* or thoracic) adj2 (ache* or aching or abnormal* or anomal* or deform* or degenerat* or disorder* or displace* or fractur* or instabilit* or numb* or pain* or prolaps* or tender* or unstab*))).ti,ab.
9	(myelopath* or myeloradiculopath* or radiculopath* or radiculitis or radicular pain* or radiating pain* or sciatica or (sciatic adj2 pain*)).ti,ab.
10	exp "Bone and Bones"/ and Pain/
11	((bone* or musculoskelet* or skelet*) adj2 (ache* or aching or abnormal* or anomal* or deform* or degenerat* or disorder* or displace* or fractur* or instabilit* or numb* or pain* or tender* or unstab*)).ti,ab.
12	Neurologic Manifestations/ or exp Gait Disorders, Neurologic/ or exp Ataxia/ or Paralysis/ or Paresthesia/ or exp Paresis/ or Reflex, Abnormal/
13	(neurolog* adj3 (deficit* or disturb* or dysfunction* or impair*)).ti,ab.
14	(Babinski* or clonus or hyperreflex* or hyper reflex* or hyperactive reflex* or Lhermitte* or electric shock*).ti,ab.
15	(ataxia* or paraly* or par?esthesia* or pares?s or ((ambulat* or balanc* or arm*1 or feet or foot or gait* or hand*1 or leg*1 or limb*1 or locomot* or motor* or move or moving or sensation* or sensory or stand or standing or walk*) adj2 (coordinat* or co ordinat* or deficit* or difficult* or disturb* or heavy or heaviness or impair* or inability or lack* or lose or losing or loss or lost or "pins and needles" or prickling or tingling or tremo?r or unable or unsteadiness or unsteady or weak*))).ti,ab.
16	Fecal Incontinence/ or exp Urinary Incontinence/ or exp Sexual Dysfunction, Physiological/
17	((f?ecal* or f?ece* or anal or stool*1 or bowel*1 or def?ecat* or bladder* or urin*) adj2 (disorder* or disturb* or dysfunction* or incontinen* or urge* or leak* or seep* or soil*)) or (sphincter* adj2 (lose or losing or loss or lost)) or diarrh?ea*).ti,ab.
18	((sexual* or erecti*) adj2 (declin* or difficult* or disorder* or dysfunction* or impair* or impoten* or inability or lose or losing or loss or lost or pain* or problem* or symptom* or unable)) or dyspareunia).ti,ab.
19	or/7-18
20	6 and 19
21	exp "Signs and Symptoms"/ or Symptom Assessment/ or Diagnosis/
22	(presentation or red flag* or sign? or symptom*).ti,ab.
23	((clinical* or physical* or present*) adj3 (aspect* or characteristic* or feature* or finding* or manifest* or marker* or suspect* or suspicion*)).ti,ab.
24	(assess* or clinical tool* or criteria* or diagnos* or identif* or predict* or recogni*).ti,ab.
25	or/21-24
26	20 and 25
27	letter/ or editorial/ or news/ or exp historical article/ or Anecdotes as Topic/ or comment/ or case report/ or (letter or comment*).ti.
28	randomized controlled trial/ or random*.ti,ab.
29	27 not 28
30	(animals/ not humans/) or exp animals, laboratory/ or exp animal experimentation/ or exp models, animal/ or exp rodentia/ or (rat or rats or mouse or mice).ti.
31	29 or 30
32	26 not 31
33	limit 32 to english language
34	limit 33 to yr="1990 -Current"

Health economics search

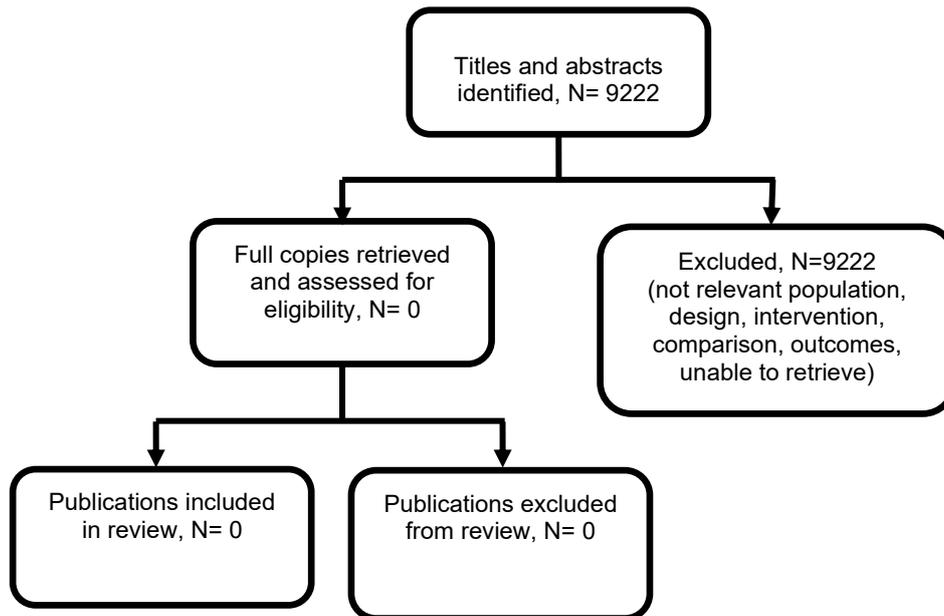
Database: Medline – OVID interface

#	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 msc).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
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"

Diagnostic evidence study selection

Study selection for: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

Figure 1: Study selection flow chart



Appendix C Evidence tables

Evidence tables for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

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

Appendix D Forest plots

Forest plots for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

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

Appendix E Modified GRADE tables

GRADE tables for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

No evidence was identified which was applicable to this review question so there are no modified GRADE tables.

Appendix F Economic evidence study selection

Study selection for: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

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

Appendix G Economic evidence tables

Economic evidence tables for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

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

Appendix H Economic model

Economic model for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

No economic analysis was conducted for this review question.

Appendix I Excluded studies

Excluded studies for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

Diagnostic effectiveness

There were no excluded studies.

Appendix J Research recommendations – full details

Research recommendations for review question: In people who present with spinal cord compression what symptoms or signs, individually or in combination, or validated clinical tools, indicate the presence of metastatic spinal disease or direct malignant infiltration?

No research recommendations were made for this review question.