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

Table 4: Evidence tables

Crnalic, 2013
Crnalic, Sead; Hildingsson, Christer; Bergh, Anders; Widmark, Anders; Svensson, Olle; Lofvenberg, Richard; Early diagnosis and treatment is crucial for neurological recovery after surgery for metastatic spinal cord compression in prostate cancer.; Acta oncologica (Stockholm, Sweden); 2013; vol. 52 (no. 4); 809-15

Study details

Country/ies where study was carried out	Sweden
Study type	Retrospective cohort study
Study dates	September 2003 to September 2010
Inclusion criteria	Men with prostate cancer referred for surgery as a result of neurological deficit due to metastatic spinal cord compression
Exclusion criteria	Not reported
Patient characteristics	N=68 Patients referred from local hospital (N = 55); directly presented to cancer centre (N = 13) Age at diagnosis of primary tumour, years (range): overall age not reported Hormone-naïve: 77 (60 – 88) Hormone refractory: 68 (45 – 86) Age at surgery for MSCC (years): Hormone-naive: 77 (60 – 88); hormone refractory: 71 (54 – 88)
Intervention(s)/control	Patients were either referred from local hospital or directly presented to cancer centre
Duration of follow-up	Functional outcome was assessed one month after surgery.
Sources of funding	This work was supported by grants from the Swedish Cancer Society and the County Council of Vasterbotten.
Sample size	N=68 Referred from local hospital N=55 Directly presented to cancer centre N=13

Outcomes

Outcome	Referred from local hospital, 1 month, n=55	Directly presented to cancer centre, 1 month, n=13
Access to services - delay to surgery, days, median (range). IQR not reported.	2 (0 – 24)	1 (0 – 4)
Access to services - delay to surgery from MRI diagnosis, days, median (range). IQR not reported.	1 (0 – 14)	0 (0 – 3)
Access to services - delay to surgery from loss of ambulation, days, median (range). IQR not reported.	1 (0 – 7)	1 (0 – 3)

Critical appraisal – ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Serious. *No adjusting for confounders.*
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 confounders).
Overall bias	Risk of bias variation across outcomes	None
Overall bias	Directness	Directly applicable

Mattes, 2020
Mattes M and Nieto J; Quality Improvement Initiative to Enhance Multidisciplinary Management of Malignant Extradural Spinal Cord Compression. JCO Oncology Practice, 16, e829-e83, 2020

Study details

Country/ies where study was carried out	United States.

Study type	Retrospective cohort study
Study dates	2015 - 2019.
Inclusion criteria	All patients diagnosed with malignant extradural spinal cord compression who were treated with radiotherapy to the spine between 2015 and 2017 at the West Virginia University department of radiation oncology.
Exclusion criteria	• Referred for radiotherapy from an outside hospital. • Referred for intramedullary metastasis, leptomeningeal carcinomatosis, or primary central nervous system tumour.
Patient characteristics	N=65 Age: not reported Sex: not reported Primary tumour type: *p* = .425 Lung - initial cohort n=9; follow-up cohort n=2. Prostate - initial cohort n=8; follow-up cohort n=5. Breast - initial cohort n=3; follow-up cohort n=3. Lymphoma - initial cohort n=5; follow-up cohort n=1. Multiple myeloma - initial cohort n=4; follow-up cohort n=5. Other - initial cohort n=11; follow-up cohort n=9. Setting: *p* = .686 Inpatient - initial cohort n=32; follow-up cohort n=21. Outpatient - initial cohort n=8; follow-up cohort n=4. Presenting symptoms: *p* = .118 Pain only - initial cohort n=21; follow-up cohort n=18. Pain plus other neurologic symptoms - initial cohort n=19; follow-up cohort n=7. Previously established diagnosis of malignancy: *p* = .564 Yes - initial cohort n=21; follow-up cohort n=15. No - initial cohort n=19; follow-up cohort n=10. Steroid use: *p* = .403 Yes - initial cohort n=32; follow-up cohort n=22. No - initial cohort n=8; follow-up cohort n=3. Surgical consultation: p = .568 Yes - initial cohort n=37; follow-up cohort n=24. No - initial cohort n=3; follow-up cohort n=1. Surgical management: *p* = .965

	Initial cohort n=11; follow-up cohort n=7. Initial cohort n=29; follow-up cohort n=18.
Intervention(s)/control	Quality improvement initiative/educational campaign aiming to expedite and improve multidisciplinary care for extradural spinal cord compression patients. A retrospective record review was conducted to record timescales of treatments. This was reviewed by a multidisciplinary group of clinicians who used the findings to develop an internal clinical pathway supported by National Comprehensive Cancer Network recommendations. The proposed clinical pathway, along with the data and practical information about how to consult relevant clinicians and expedite MRI and biopsy studies and their interpretations, was approved by the hospital cancer committee and presented to all relevant departments. Additional feedback was collected from these groups, and the finalized clinical pathway was then e-mailed to each department and published online to allow easy access at any time. This pathway was implemented between 2018 and 2019 and compared to previous years 2015 to 2017.
Duration of follow-up	N/A.
Sources of funding	Not reported.
Sample size	N=65. Initial cohort n=40; follow-up cohort n=25.

Outcomes

Outcome	**No care pathway (2015 - 2017 audit), n=40**	**Care pathway (2018 - 2019 audit), n=25**
Time from hospital admission to MRI, (initial MRI showing extradural spinal cord compression), days, median (IQR):	1 (0 – 1)	1 (0 – 1)
Time from MRI to steroid administration, (initial MRI showing extradural spinal cord compression), days, median (IQR):	0 (0 – 1)	1 (0 – 3)
Time from MRI to initial pathology obtained, (initial MRI showing extradural spinal cord compression), days, median (IQR):	2 (0.5 – 3)	2 (1 – 4.75)
Time from MRI to surgical consultation, (initial MRI showing extradural spinal cord compression), days, median (IQR):	0 (1 – 0)	0 (-1 – 1)
Time from MRI to radiation oncology consultation, (initial MRI showing extradural spinal cord compression), days, median (IQR):	3 (0.75 – 7)	1 (0 – 2)
Time from surgical consultation to surgery, (initial MRI showing extradural spinal cord compression), days, median (IQR):	3 (1.5 – 6.5)	4 (3.5 – 6)
Time from radiation oncology to first fraction, (initial MRI showing extradural spinal cord compression), days, median (IQR):	1 (0 – 2)	1 (1 – 1)

Critical appraisal – ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Critical *(Analysis method unlikely to control for all important confounders)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Moderate. *Control group were treated in 2015-2017, intervention group treated 2018-2019: other factors may explain differences in outcomes.*
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	Moderate. *Unclear whether data were available for all participants - or whether participants were selected because they had available data.*
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	Critical
Overall bias	Directness	Directly applicable

McGivern, 2014

McGivern, U M; Drinkwater, K J; Clarke, J I M; Locke, I; A royal college of radiologists national audit of radiotherapy in the treatment of metastatic spinal cord compression and implications for the development of acute oncology services.; Clinical oncology (Royal College of Radiologists (Great Britain)); 2014; vol. 26 (no. 8); 453-60

Study details

Country/ies where study was carried out	United Kingdom.
Study type	Retrospective cohort study.
Study dates	First audit - September 2008 - December 2008. Second audit- August 2012.
Inclusion criteria	First audit - all patients with a diagnosis of metastatic spinal cord compression receiving radiotherapy in all UK National Health Service cancer centres. Second audit - All patients presenting to radiotherapy centres with metastatic spinal cord compression.

Exclusion criteria	Not reported.
Patient characteristics	N=919 Age: not reported First audit - Male n=401; female n=195. Second audit - Male n=204 male; female n=92. Number of patients with a previous diagnosis of cancer: Total – 2008 n=448; 2012 n=246. Bladder - 2008 n=9; 2012 n=7. Breast - 2008 n=68; 2012 n=28. Central nervous system - 2008 n=0; 2012 n=2. Colorectal - 2008 n=24; 2012 n=6. GI (upper/lower) - 2008 n=20; 2012 n=8. Gynaecological - 2008 n=4; 2012 n=2. Head and neck - 2008 n=4; 2012 n=8. Lung - 2008 n=69; 2012 n=34. Lymphoma (including leukaemia and myeloma) - 2008 n=39; 2012 n=13. Prostate - 2008 n=146; 2012 n=95. Sarcoma - 2008 n=9; 2012 n=1. Skin - 2008 n=9; 2012 n=7. Unknown primary - 2008 n=6; 2012 n=8. Other (including renal, germ cell, etc.) - 2008 n=38; 2012 n=27. No information - 2008 n=3; 2012 n=0. Number of patients by initial referral source: Total – 2008 n=596; 2012 n=323. Cancer centre - 2008 n=89; 2012 n=67. Cancer unit - 2008 n=74; 2012 n=37. District general hospital (non-cancer unit) - 2008 n=179; 2012 n=70. GP - 2008 n=50; 2012 n=25. Haematology - 2008 n=16; 2012 n=3. Hospice - 2008 n=21; 2012 n=10. Medical oncology - 2008 n=43; 2012 n=16. Other hospital speciality - 2008 n=89; 2012 n=67. Other - 2008 n=11; 2012 n=16. No information – 2008 n=24; 2012 n=12. Number of patients by ECOG performance status: Total – 2008 n=596; 2012 n=323.

	0 - 2008 n=16; 2012 n=15. 1 - 2008 n=129; 2012 n=59. 2 - 2008 n=132; 2012 n=84. 3 - 2008 n=159; 2012 n=97. 4 - 2008 n=63; 2012 n=22. Number of patients by neurological status Total – 2008 n=596; 2012 n=323 Unaided - 2008 n=173; 2012 n=96. With help - 2008 n=261; 2012 n=153. Paraplegic - 2008 n=98; 2012 n=37. No information - 2008 n=64; 2012 n=37. No information - 2008 n=97; 2012 n=46. Place of discharge (number of patients): Total – 2008 n=596; 2012 n=323 Hospice - 2008 n=50; 2012 n=29. Nursing home - 2008 n=15; 2012 n=8. Own home - 2008 n=238; 2012 n=158. Referring hospital - 2008 n=102; 2012 n=31. Other - 2008 n=21; 2012 n=18. No information - 2008 n=170; 2012 n=79.
Intervention(s)/control	The audits assessed compliance with the following outcomes (derived from the Royal College of Radiation dose-fractionation guidance, based on the NICE guideline 2008) in particular: • Patients with symptoms suggestive of spinal cord compression should have access to an urgent MRI (within 24 h of presentation and referral for radiotherapy). • Patients immobile for <24 h or ambulant or performance status 0, 1 or 2 (‘good prognosis’) should be discussed with neuro/spinal surgeons. • Radiotherapy, if prescribed, should start within 24 h of diagnosis. • Fractionated treatment should be prescribed for patients immobile for <24 h or ambulant and performance status 0, 1 or 2. • Poor prognosis patients, for example, those with established paraplegia for >24 h should only receive radiotherapy for pain relief. Outcomes were measured before and after implementation of the NICE guideline (2008 compared to 2012)
Duration of follow-up	N/A.
Sources of funding	Not reported.
Sample size	First audit - data from n=596 cases received from 42/57 radiotherapy centres. The number of cases received from contributing centres varied from two to 41 (median 11). Second audit - data from n=323 cases received from 52/58 cancer centres. (No details reported regarding number of cases from each

	centre).
Other information	Second audit - An MSCC coordinator was available in just over 50% of cases (164/323) and involved in patient management in 26% of cases in 2012. No details reported regarding this in relation to the first audit.

Outcomes

Outcome	2012 audit, n=323	2008 audit, n=596
Access to services - number of patients who had an MRI scan within 24 hours of referral for radiotherapy	n = 205/212	n = 358/387
Access to services - number of patients where discussion with a surgeon took place	n = 94/228	n = 111/350
Access to services - number of patients where radiotherapy was started within 24 hours of referral for radiotherapy	n = 243/300	n = 369/512
Access to services - number of patients who received fractionated treatment	n = 132/153	n = 242/275
Access to services - number of patients who received radiotherapy for pain relief	n = 30/114	n = 50/227
Access to services - number of patients who had an MRI at the weekend or outside normal hours	n = 58/323	n = 86/596
Access to services - time between date of referral to oncology and first radiotherapy treatment, days, median (IQR)	1 (0 to 1)	1 (0 to 2)
Access to services - number of patients where discussion of surgical intervention with surgical team was included	n = 104/323	n = 148/596
Access to services - number of patients with ECOG performance status of 0 – 2 (potentially suitable for surgery) where discussion of surgical intervention was recorded	n = 56/158	n = 79/277
Access to services - number of patients with ECOG performance status of 3 – 4 (surgery unlikely to be beneficial) referred to surgical team	n = 43/119	n = 51/222
Access to services - number of patients whose case was discussed with surgical team who went on to have surgical intervention	n = 10/104	n=15/148

Compliance with audit criteria (derived from 2006 Royal College of Radiologists dose-fractionation guidance)

Critical appraisal – ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Critical *(Analysis method unlikely to control for all important confounders)*
2. Bias in selection of participants into the study	Risk of bias judgement for selection of participants into the study	Moderate (*Control group were treated in 2008, intervention group treated 2012: other factors (beyond service configuration) may explain differences in outcomes.)*
3. Bias in classification of inter-	Risk of bias judgement for classifica-	Low

Section	Question	Answer
ventions	tion of interventions	
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	Critical
Overall bias	Directness	Directly applicable

Pease, 2004
Pease, N, Development and audit of a care pathway for the management of patients with suspected malignant spinal cord compression. Physiotherapy, 90, 2004

Study details

Country/ies where study was carried out	United Kingdom.
Study type	Retrospective cohort study. Comparison of 2 audits.
Study dates	1997 and 2000.
Inclusion criteria	Inpatients with a diagnosis of cord compression. Patient identification was done via review of hospital physiotherapy records as all patients with cord compression are referred to the hospital physiotherapy team.
Exclusion criteria	Not reported.
Patient characteristics	N=148 Age, years, and months, median (range): No care pathway 66 years 6 months (37 – 82); care pathway 65 years, 6 months (27 – 88). Sex: No care pathway – female n=17, male n=36; care pathway female n=32, male n=62. Primary cancer site: Prostate - no care pathway n=16; care pathway n=27. Breast - no care pathway n=10; care pathway n=13. Lung/bronchus - no care pathway n=9; care pathway n=18. Gastro-intestinal - no care pathway n=4; care pathway n=7. Unknown - no care pathway n=7; care pathway n=15.

	Myeloma - no care pathway n=3; care pathway n=6. Other - no care pathway n=4; care pathway n=9. Number of patients on who mobility scores recorded in notes: no care pathway n=35; care pathway n=80. Length of stay, days, median (range): no care pathway 13 (2 – 35); care pathway 12 (1 – 105).
Intervention(s)/control	Care pathway versus no care pathway. The care pathway was implemented in June 1999 by a copy of the pathway being attached to the notes of each patient admitted with suspected cord compression. Decisions made at each stage were dated and signed by medical staff on the relevant section of the pathway, thereby facilitating its monitoring and use. The care pathway was designed to standardise the way in which patients with spinal cord compression were managed and in particular to: • Define the indications and timing for mobilising patients with malignant spinal cord compression. • Clarify who should be referred for an orthopaedic surgery opinion. • Minimise the potential risk of complication as a result of flat bed rest. The care pathway uses guidance from Campbell and Hotchkiss and The Welsh Assembly and was developed by physiotherapy and medical staff. Prior to implementation of the care pathway, patients were nursed supine until completion of their radiotherapy which lasted at least 5 days.
Duration of follow-up	1997 audit - 12 months duration. 2000 audit - 14 months duration. Patient outcomes measured at 60/78 weeks. The second audit did not include inpatients managed on the pathway for its first month of implementation (May 1999), to allow ward staff to become familiar with its use.
Sources of funding	Not reported.
Sample size	N=148.
Other information	**Results** Number of patients nursed flat: 2000 audit n=62/95 (65.3%); 1997 audit 44/52 (84.6%); $\chi 2=5.33$, p =0.021. Mortality rate: 2000 audit n=12/95 (12.6%); 1997 audit 18/53 (34%); $\chi 2=8.3$, p=0.0044. Mobility: Maintained - 2000 audit n=70/80 (91%); 1997 audit 30/35 (86%); p=0.79. Improved - 2000 audit n=3/80 (91%); 1997 audit 0/35 (86%); p=0.6. Deteriorated - 2000 audit n=7/80 (91%); 1997 audit 5/35 (86%); p=0.57.

Outcomes

Outcome	Care pathway (2000 audit), n=53	No care pathway (1997 audit), n=95
Overall survival - mortality rate (follow-up 60 weeks)	n=12	n=18
Neurological and functional status – mobility – maintained or improved (follow-up 60 weeks)	n=73	n=30

Outcome	Care pathway (2000 audit), n=53	No care pathway (1997 audit), n=95
Access to services - number of patients nursed flat	n=62	n=44

Critical appraisal – ROBINS-I

Section	Question	Answer
1. Bias due to confounding	Risk of bias judgement for confounding	Critical *(Analysis method unlikely to control for all important confounders)*
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	Moderate. *(Outcome data not available for all participants, unclear whether missingness is balanced between the 2 groups.)*
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	Critical
Overall bias	Directness	Directly applicable