GRADE 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 5: Evidence profile for comparison between referral from local hospital versus presented directly to cancer centre

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Referred from local hospital	Presented directly to cancer centre	Relative (95% CI)	Absolute		
Access to services - delay to surgery, days, median												
1 (Crnalic 2013)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	n=55 (Median 2, range 0 – 24)	n=13 (Median 1, range 0 – 4)	not estimable	1 day fewer with direct referral (p=0.004)	VERY LOW	IMPORTANT
Access to services - delay to surgery from MRI diagnosis, days, median												
1 (Crnalic 2013)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	n=55 (Median 1, range not reported)	n=13 (Median 0, range 0 – 3)	not estimable	1 day fewer with direct referral (p=0.017)	VERY LOW	IMPORTANT
Access to services - delay to surgery from loss of ambulation, days, median												
1 (Crnalic 2013)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	n=55 (Median 1, range 0 – 7)	n=13 (Median 1, range 0 – 3)	not estimable	0 days fewer with direct referral (p=0.107)	VERY LOW	IMPORTANT

CI: confidence interval; MID: minimal important difference; MRI: magnetic resonance imaging; n: number; SD: standard deviation.
1 Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I.
2 Sample size < 100

Table 6: Evidence profile for comparison between clinical care pathway versus no clinical care pathway

Quality assessment	No. of patients	Effect	Quali-	Importance

												ty	
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other consider-ations**	**Clinical care pathway**	**No clinical care path-way**	**Relative (95% CI)**	**Absolute**			
Access to services - time from hospital admission to MRI, days, median (initial MRI showing malignant extradural spinal cord compression)													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[2]	none	n=40 (Median 1, IQR 0 – 1)	n=25 (Median 1, IQR 0 – 1)	not esti-mable	0 days fewer with clinical care pathway (p=0.4)		VERY LOW	IM-PORTANT
Access to services - time from MRI to steroid administration, days, median (initial MRI showing malignant extradural spinal cord compression)													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[2]	none	n=40 (Median 0, IQR 0 – 1)	n=25 (Median 1, IQR 0 – 3)	not esti-mable	1 day fewer with clinical care pathway (p=0.2)		VERY LOW	IM-PORTANT
Access to services - time from MRI to initial pathology obtained, days, median (initial MRI showing malignant extradural spinal cord compression)													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[22]	none	n=40 (Median 2, IQR 0.5 – 3)	n=25 (Median 2, IQR 1 – 4.75)	not esti-mable	0 days fewer with clinical care pathway (p=0.71)		VERY LOW	IM-PORTANT
Access to services - time from MRI to surgical consultation, days, median (initial MRI showing malignant extradural spinal cord compression)													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[2]	none	n=40 (Median 0, IQR 1 – 0)	n=25 (Median 0, IQR −1 – 1)	not esti-mable	0 days fewer with clinical care pathway (p=0.38)		VERY LOW	IM-PORTANT
Access to services - time from MRI to radiation oncology consultation, days, median (initial MRI showing malignant extradural spinal cord compression)													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[2]	none	n=40 (Median 3, IQR 0.75 – 7)	n=25 (Median 1, IQR 0 – 2)	not esti-mable	2 days fewer with clinical care pathway (p=0.03)		VERY LOW	IM-PORTANT
Access to services - time from surgical consultation to surgery, days, median													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[2]	none	n=40 (Median 3, IQR 1.5 – 6.5)	n=25 (Median 4, IQR 3.5 – 6)	not esti-mable	1 day more with clinical care pathway (p=0.25)		VERY LOW	IM-PORTANT
Access to services - time from radiation oncology consultation to first fraction, days, median													
1 (Mattes 2020)	observational studies	very seri-ous[1]	no serious incon-sistency	no serious indirectness	very seri-ous[2]	none	n=40 (Median 1, IQR	n=25 (Median 1,	not esti-mable	0 days fewer with clinical care pathway (p=0.64)		VERY LOW	IM-PORTANT

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consider-ations	Clinical care pathway	No clinical care path-way	Relative (95% CI)	Absolute	Quali-ty	Importance
							0 – 2)	IQR 1 – 1)				

CI: confidence interval; IQR: interquartile range; MRI: magnetic resonance imaging; n: number; SD: standard deviation.

1 Very serious risk of bias in the evidence contributing to the outcomes as per ROBINS-I.
2 Sample size < 100

Table 7: Evidence profile for comparison between clinical care pathway (2000 audit) versus no clinical care pathway (1997 audit)

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Impreci-sion	Other consid-erations	Clinical care path-way (2000 audit)	No clinical care path-way (1997 audit)	Relative (95% CI)	Absolute	Quality	Im-portance
Overall survival – mortality rate (follow-up 60 weeks)												
1 (Pease 2004)	observational studies	very seri-ous[1]	no serious in-consistency	no serious indirectness	no seri-ous im-precision	none	n=12/95 (12.6%)	n=18/53 (34%)	RR 0.37 (0.19 to 0.71)	340 fewer per 1000 (from 340 fewer to 340 fewer)	LOW	CRITICAL
Neurological and functional status – mobility – maintained or improved (follow-up 60 weeks)												
1 (Pease 2004)	observational studies	very seri-ous[1]	no serious in-consistency	no serious indirectness	no seri-ous im-precision	none	n=73/80 (91.2%)	n=30/35 (85.7%)	RR 1.06 (0.92 to 1.24)	51 more per 1000 (from 69 fewer to 206 more)	LOW	CRITICAL
Access to services – number of patients nursed flat												
1 (Pease 2004)	observational studies	very seri-ous[1]	no serious in-consistency	no serious indirectness	serious[2]	none	n=62/95 (65.3%)	n=44/52 (84.6%)	RR 0.77 (0.64 to 0.93)	846 fewer per 1000 (from 846 fewer to 846 fewer)	VERY LOW	IM-PORTANT

CI: confidence interval; n: number; 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

Table 8: Evidence profile for comparison between 2008 audit versus 2012 audit

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	2012 audit (referral & care pathways implemented by cancer networks)	2008 audit	Relative (95% CI)	Absolute	Quality	Importance
Access to services - number of patients who had an MRI scan within 24 hours of referral for radiotherapy												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	205/212 (96.7%)	358/387 (92.5%)	RR 1.05 (1.01 to 1.09)	46 more per 1000 (from 9 more to 83 more)	LOW	IMPORTANT
Access to services - number of patients where discussion with a surgeon took place												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	94/228 (41.2%)	111/350 (31.7%)	RR 1.30 (1.05 to 1.62)	95 more per 1000 (from 16 more to 197 more)	VERY LOW	IMPORTANT
Access to services - number of patients where radiotherapy was started within 24 hours of referral for radiotherapy												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	243/300 (81%)	369/512 (72.1%)	RR 1.12 (1.04 to 1.21)	86 more per 1000 (from 29 more to 151 more)	LOW	IMPORTANT
Access to services - number of patients who received fractionated treatment												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132/153 (86.3%)	242/275 (88%)	RR 0.98 (0.91 to 1.06)	18 fewer per 1000 (from 79 fewer to 53 more)	LOW	IMPORTANT
Access to services - number of patients who received radiotherapy for pain relief												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	30/114 (26.3%)	50/227 (22%)	RR 1.19 (0.81 to 1.77)	42 more per 1000 (from 42 fewer to 170 more)	VERY LOW	IMPORTANT
Access to services - number of patients who had an MRI at the weekend or outside normal hours												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	58/323 (18%)	86/596 (14.4%)	RR 1.24 (0.92 to 1.69)	35 more per 1000 (from 12 fewer to 100 more)	VERY LOW	IMPORTANT

Quality assessment							No. of patients		Effect			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**2012 audit (referral & care pathways implemented by cancer networks)**	**2008 audit**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Access to services - time between date of referral to oncology and first radiotherapy treatment, days, median												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	N=311 (median 1 day, IQR 0 to 1 days)	N=512 (median 1 day, IQR 0 to 2 days)	not estimable	No difference (P not reported)	LOW	IMPORTANT
Access to services - number of patients where discussion of surgical intervention with surgical team was included												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	104/323 (32.2%)	148/596 (24.8%)	RR 1.30 (1.05 to 1.60)	74 more per 1000 (from 12 more to 149 more)	VERY LOW	IMPORTANT
Access to services - number of patients with ECOG performance status of 0 – 2 (potentially suitable for surgery) where discussion of surgical intervention was recorded												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	56/158 (35.4%)	79/227 (34.8%)	RR 1.02 (0.77 to 1.34)	7 more per 1000 (from 80 fewer to 118 more)	VERY LOW	IMPORTANT
Access to services - number of patients with ECOG performance status of 3 – 4 (surgery unlikely to be beneficial) referred to surgical team												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	43/119 (36.1%)	51/222 (23%)	RR 1.57 (1.12 to 2.21)	131 more per 1000 (from 28 more to 278 more)	VERY LOW	IMPORTANT
Access to services - number of patients whose case was discussed with surgical team who went on to have surgical intervention												
1 (McGivern 2014)	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	10/104 (9.6%)	15/148 (10.1%)	RR 0.95 (0.44 to 2.03)	5 fewer per 1000 (from 57 fewer to 104 more)	VERY LOW	IMPORTANT

CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; IQR: interquartile range; MID: minimal important difference; n: number; 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