Forest plots for review question: How effective is radiotherapy, including both fractionated and unfractionated radiotherapy, for the management of spinal metastases, direct malignant infiltration of the spine or associated spinal cord compression?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

Comparison 1: Spinal metastases patients - single fraction radiotherapy versus multiple fraction radiotherapy

Figure 2: Overall survival

0	Single fra	iction	Multifra	ction				Hazard Ratio	Hazard Ratio
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% CI	Exp[(O-E) / V], Fixed, 95% CI
Howell 2013	116	124	102	111	4.97	54.28	46.7%	1.10 [0.84, 1.43]	
Roos 2005	126	137	122	135	3.46	61.98	53.3%	1.06 [0.82, 1.36]	
Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect:	242 0.04, df = 1 Z = 0.78 (P	261 (P = 0.8 = 0.43)	224 35); I² = 09	246 %			100.0%	1.08 [0.90, 1.29]	0.1 0.2 0.5 1 2 5 10 Eavours single fraction. Eavours multifraction

Figure 3: Pain: Complete or partial pain response (follow-up 1 to 3 months)

	Single fraction Multiple fraction					Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Howell 2013	54	77	47	76	30.1%	1.13 [0.90, 1.43]	
Majumder 2012	25	31	27	33	16.7%	0.99 [0.78, 1.25]	-
Roos 2005	73	137	83	135	53.2%	0.87 [0.71, 1.06]	
Total (95% CI)		245		244	100.0%	0.97 [0.85, 1.11]	•
Total events	152		157				
Heterogeneity: Chi ² =	2.97, df = 2	(P = 0.2	3); I² = 33%				
Test for overall effect:	Z = 0.49 (P	= 0.62)					Favours multifraction Favours single fraction

Figure 4: Treatment related morbidity: Grade 2 to 4 adverse events

	Single frac	ction	Multiple fra	oction		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Howell 2013	3	124	5	111	31.2%	0.54 [0.13, 2.20]	
Majumder 2012	3	31	12	33	68.8%	0.27 [0.08, 0.85]	
T-1-1/054/ OB		455			400.00		
Total (95% CI)		155		144	100.0%	0.35 [0.14, 0.85]	
Total events	6		17				
Heterogeneity: Chi ² =	0.57, df = 1	(P = 0.4)	(5); I ² = 0%				
Test for overall effect:	Z = 2.32 (P	= 0.02)					Favours single fraction Favours multifraction

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	Single fra	ction	Multiple fra	ctions	Risk Ratio			Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl		M-H, Fixe	ed, 95% Cl	
Roos 2005	6	137	5	135	83.9%	1.18 [0.37, 3.78]				
Steenland 1999	4	165	1	177	16.1%	4.29 [0.48, 38.00]				_
Total (95% CI)		302		312	100.0%	1.68 [0.62, 4.53]		-		
Total events	10		6							
Heterogeneity: Chi ² =	1.06, df = 1	(P = 0.3)	30); I² = 6%					01		100
Test for overall effect:	Z=1.03 (P	= 0.30)					0.01	Favours single fraction	Favours multi. fraction	is

Figure 5: Spinal stability: Fractures (median follow-up 11 months)

Comparison 2: Patients with metastatic spinal cord compression - single fraction radiotherapy versus multiple (or short) fraction radiotherapy

Figure 6: Neurological and functional status: Ability to walk after treatment

	Single fraction Multiple fractions					Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% Cl
Hoskin 2019	115	166	128	176	49.1%	0.95 [0.83, 1.09]	+
Lee 2018	28	36	24	37	9.4%	1.20 [0.89, 1.61]	+•
Maranzano 2009	95	153	104	150	41.5%	0.90 [0.76, 1.05]	
Total (95% CI)		355		363	100.0%	0.95 [0.86, 1.05]	•
Total events	238		256				
Heterogeneity: Chi ² =	2.90, df = 2	(P = 0.2	23); I² = 31%				0.1 0.2 0.5 1 2 5 10
Test for overall effect:	Z=0.98 (P	= 0.33)					Favours multifraction Favours short course

Figure 7: Neurological and functional status: Normal bowel function after treatment

	Single fraction Mulitple fraction					Risk Ratio	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI		
Hoskin 2019	112	315	118	322	46.9%	0.97 [0.79, 1.19]	+		
Maranzano 2009	130	153	131	150	53.1%	0.97 [0.89, 1.06]	•		
Total (95% CI) Total events	242	468	249	472	100.0%	0.97 [0.87, 1.08]	• .		
Heterogeneity: Chi ² = Test for overall effect:	0.00, df = 1 Z = 0.52 (P	(P = 0.9 = 0.60)	18); I² = 0%				0.01 0.1 1 10 Favours multifraction Favours single fraction	100	

Figure 8: Overall survival

	Single fra	e fraction Multiple fraction				Hazard Ratio			Hazard Ratio				
Study or Subgroup	Events	Total	Events	Total	0-E	Variance	Weight	Exp[(O-E) / V], Fixed, 95% Cl		Exp[(O-E) /	V], Fixed,	95% CI	
Hoskin 2019	266	345	263	341	0.73	36.97	32.8%	1.02 [0.74, 1.41]		-	-		
Maranzano 2009	153	153	150	150	5.87	75.74	67.2%	1.08 [0.86, 1.35]					
Total (95% CI)		498		491			100.0%	1.06 [0.88, 1.28]			٠		
Total events	419		413										
Heterogeneity: Chi ² = 0.08, df = 1 (P = 0.77); I ² = 0%										0.2 0.6	-	1	± 10
Test for overall effect: Z = 0.62 (P = 0.53)									0.1	Favours single fraction	n Favou	rs multifractio	5 10 3n

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Figure 9: Treatment related morbidity: Grade 3 or 4 adverse events

	Single fra	ction	Multiple fra	ction		Peto Odds Ratio	Peto Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	Peto, Fixed, 95% Cl	Peto, Fixed, 95% Cl
Hoskin 2019	71	345	70	341	98.3%	1.00 [0.69, 1.45]	
Maranzano 2009	0	153	2	150	1.7%	0.13 [0.01, 2.12]	· • · · · · · · · · · · · · · · · · · ·
Total (95% CI)		498		491	100.0%	0.97 [0.67, 1.40]	↓ ◆
Total events	71		72				
Heterogeneity: Chi ² =	2.02, df = 1	(P = 0.1)	6); I² = 50%				
Test for overall effect:	Z=0.17 (P	= 0.86)					Favours single fraction Favours multifraction

Comparison 4: Spinal metastases patients – Stereotactic ablative body radiotherapy versus conventional radiotherapy

Figure 10: Pain: complete or partial pain response (6 months follow-up)

	SAB	R	EBR	Т		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
Sahgal 2021	47	114	36	115	83.9%	1.32 [0.93, 1.87]	
Sprave 2018 (SBRT trial)	14	27	7	28	16.1%	2.07 [0.99, 4.34]	
Total (95% CI)		141		143	100.0%	1.44 [1.05, 1.97]	◆
Total events	61		43				
Heterogeneity: Chi ² = 1.19,	df = 1 (P :	= 0.27)	; I ² = 16%	5			
Test for overall effect: Z = 2.	27 (P = 0	.02)					Eavours EBRT Favours SABR

Figure 11: Spinal stability: vertebral compression fracture of any grade - 6 months

	SABR E			Т		Risk Ratio		Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Randon	n, 95% Cl	
Sahgal 2021	12	114	20	115	51.2%	0.61 [0.31, 1.18]		+		
Sprave 2018 (SABR trial)	11	18	6	20	48.8%	2.04 [0.95, 4.37]		+	-	
Total (95% CI)		132		135	100.0%	1.09 [0.33, 3.66]				
Total events	23		26							
Heterogeneity: Tau ² = 0.62;	Chi ² = 5.	66, df =	: 1 (P = 0.	.02); I² =	= 82%		0.01	0.1 1	10	100
Test for overall effect: $Z = 0$.	15 (P = 0	.88)						Favours SABR F	avours EBRT	