

Ranking	Uncertainty	Additional notes	Source url:	Suggested Outcomes	Outcomes to be measured	Reference to up-to date systematic review	Reference to out of date SR	Reference to an up-to date, relevant and reliable SR which does not refer to uncertainty but could be extended	Protocol for a systematic review	Ongoing studies	Comparison	Health Topic	Health Topic	Uncertainty from Patient/Carer/Clinician/Research Recommendation or multiple sources	Age of patients/population
1	Does treatment (with neurosurgery or stereotactic radiosurgery) or no treatment improve outcome for people diagnosed with brain or spine cavernoma?	This question incorporates three others presented at the PSP workshop (11, 19 and 20, below). Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; acceptability to patients	Wang X, Mei G, Liu X, Dai J, Pan L, Wang E. The role of stereotactic radiosurgery in cavernous sinus hemangiomas: a systematic review and meta-analysis. <i>J Neuro-Oncol.</i> 2012;107(2):239-45. doi: 10.1007/s11060-011-0753-8. Epub 2011 Nov 16. Lu XY, Sun H, Xu JG, Li QY. Stereotactic radiosurgery of brainstem cavernous malformations: a systematic review and meta-analysis. <i>J Neurosurg.</i> 2014;120(4):982-7. doi: 10.3171/2013.12.JNS13990. Epub 2014 Feb 7. Badhiwala J.H. Ferrokhyar F, Alhazzani W, Varascavitch B, Ed Aref M, Algrd A, et al. Surgical outcomes and natural history of intramedullary spinal cord cavernous malformations: a single-center series and meta-analysis of individual patient data. <i>Journal of Neurosurgery: Spine.</i> 2014;21(4):662-76. doi: 10.3171/2014.6.SPINE13949. Epub 2014 Jul 25. Poorthuis M, Samarasekera N, Kontoh K, Stuart I, Cope B, Kitchen N, Al-Shahi Salman R. Comparative studies of the diagnosis and treatment of cerebral cavernous malformations in adults: Systematic review. <i>Acta Neurochirurg.</i> 2013;155(4):643-9. doi: 10.1007/s00701-013-1621-4. Epub 2013 Jan 31. Poorthuis MH, Klijn CJ, Algra A, Rinkel GJ, Al-Shahi Salman R. Treatment of cerebral cavernous malformations: a systematic review and meta-regression analysis. <i>J Neurol Neurosurg Psychiatr.</i> 2014; 85(12):1319-23. doi: 10.1136/jnnp-2013-307349. Epub 2014 Mar 25.	n/a	n/a	n/a	n/a	n/a	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Surgery, anaesthesia, perioperative and critical care	120 patients. 28 clinicians.	Any age
2	How do brain or spine cavernomas start and develop?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Aetiology	Aetiology	n/a	n/a	n/a	n/a	n/a	Aetiology	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	90 patients. 20 carers.	Any age
3	What is the risk of brain or spine cavernomas bleeding for the first and subsequent times?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Prognosis	Adverse effects or complications	n/a	n/a	n/a	n/a	n/a	Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	113 patients.	Any age
4	Could drugs targeted at cavernomas improve outcome for people with brain or spine cavernomas compared to no drug treatment?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms	n/a	n/a	n/a	n/a	n/a	Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions;	45 patients.	Any age
5	What mechanisms trigger bleeding or epileptic seizures in people with brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Aetiology	Adverse effects or complications; health related quality of life	n/a	n/a	n/a	n/a	n/a	Aetiology	Neurological conditions:Brain and spinal cavernomas; Neurological conditions:Epilepsy	Neurological conditions; Epilepsy	45 patients. 5 carers.	Any age
6	Are any features of brain or spine cavernoma on imaging associated with a higher or lower risk of bleeding?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Diagnostic; prognosis; change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; Adverse effects or complications; acceptability to patients or carers	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Diagnostics	12 patients.	Any age
7	Does the use of anticoagulant drugs increase the risk of bleeding from brain or spine cavernoma?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; acceptability to patients or carers	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Drug	45 patients. 7 clinicians.	Any age
8	Does regular monitoring of brain or spine cavernoma improve outcome compared to no monitoring?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Diagnostic; prognosis; change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms	n/a	n/a	n/a	n/a	n/a	Aetiology; Diagnostic; Prognosis; Service delivery	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; diagnostics	40 patients. 13 clinicians.	Any age
9	What features of brain cavernoma lead to the development of epilepsy, or influence the severity of existing epilepsy?	Existing guideline.	http://onlinelibrary.wiley.com/doi/10.1111/epi.12402/abstract;jsessionid=EE2DBD13C870DCFC3FAD26F1BEDD44BD.f01011	Aetiology; prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; health related quality of life	Rosenow F*, Alonso-Vanegas MA, Baumgartner C, Blümcke I, Carreño M, Gizewski ER, et al. Cavernoma related epilepsy: Review and recommendations for management—Report of the Surgical Task Force of the ILAE Commission on Therapeutic Strategies. <i>Epilepsia.</i> 2013;54(12): 2025-35. DOI: 10.1111/epi.12402	Moran NF, Fish DR, Kitchen N, Shorvon S, Kendall BE, Stevens JM. Supratentorial cavernous haemangiomas and epilepsy: a review of the literature and case series. <i>Neurosurg Psychiatr.</i> 1999; 66(5):561-8. http://jnnp.bmj.com/content/66/5/561.long	Al-Shahi Salman R. The outlook for adults with epileptic seizure(s) associated with cerebral cavernous malformations or arteriovenous malformations. <i>Epilepsia.</i> 2012;53 (SUPPL. 4):34-42. doi: 10.1111/j.1528-1167.2012.03611.x.	n/a	n/a	Neurological conditions:Brain and spinal cavernomas; Neurological conditions:Epilepsy	Neurological conditions; epilepsy	Research recommendation	Any age	
10	Do any specific activities undertaken by people with brain or spine cavernomas provoke bleeds or other symptoms?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Adverse effects or complications; acceptability to patients or carers; health related quality of life	n/a	n/a	n/a	n/a	n/a	Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Exercise	200 patients. 74 carers.	Any age

11	Is stereotactic radiosurgery or neurosurgery for brain or spine cavernomas better for improving outcome?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost		Badhiwala J.H, Farrokhfar F, Alhazzani W, Yarascavitch B, Ed Aref M, Algird A, et al. Surgical outcomes and natural history of intramedullary spinal cord cavernous malformations: a single-center series and meta-analysis of individual patient data. Journal of Neurosurgery: Spine. 2014;21(4):662-76. doi: 10.3171/2014.6.SPINE13949. Epub 2014 Jul 25. Poorthuis M, Samarasekera N, Kontoh K, Stuart I, Cope B, Kitchen N, Al-Shahi Salman R. Comparative studies of the diagnosis and treatment of cerebral cavernous malformations in adults: Systematic review. Acta Neurochirurg. 2013;155(4):643-9. doi: 10.1007/s00701-013-1621-4. Epub 2013 Jan 31. Poorthuis MH, Klijn CJ, Algra A, Rinkel GJ, Al-Shahi Salman R. Treatment of cerebral cavernous malformations: a systematic review and meta-regression analysis. J Neurol Neurosurg Psychiatr. 2014; 85(12):1319-23. doi: 10.1136/jnnp-2013-307349. Epub 2014 Mar 25.						Surgery; Service delivery	Neurological conditions:Brain and spinal cavernomas				
12	What is the impact of brain or spine cavernomas on life expectancy?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Prognosis	Adverse effects or complications; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	15 patients. 3 carers.	Any age	
13	When is the optimum time to start treatment of a brain or spine cavernoma diagnosed in an infant?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Timing of treatment: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; acceptability to patients or carers; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Service delivery	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	2 patients.	Child / Adolescent	
14	Why do only around half of people with a cavernoma gene mutation develop symptoms?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Prognosis	Adverse effects or complications; time in hospital and or needing health or social care services; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	60 patients. 28 carers.	Any age	
15	What causes brain or spine cavernomas arising following radiotherapy for brain tumours?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Aetiology: prognosis	Adverse effects or complications; acceptability to patients or carers	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Radiotherapy	4 patients.	Any age	
16	What causes single brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Aetiology	Aetiology	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	3 patients.	Any age	
17	Why do some patients develop multiple cavernomas even though they do not have any of the known genetic variations that can cause them?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Aetiology	Aetiology	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	4 patients. 1 clinician.	Any age	
18	What are the non-genetic causes of brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Aetiology	Aetiology	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	20 patients. 7 carers.	Any age	
19	Which behavioural or psychological therapies are effective in treating patients following neurosurgery for brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; acceptability to patients or carers; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Psychological therapy	Neurological conditions:Brain and spinal cavernomas; Mental Health	Neurological conditions;	2 clinicians.	Any age	
20	Which symptoms indicate that a brain or spine cavernoma is bleeding?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Diagnostic	Adverse effects or complications	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; diagnostics	20 patients.	Any age	
21	Can a care pathway improve outcome for patients with brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms	n/a	n/a	n/a	n/a	n/a	n/a	Service delivery	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Service delivery	3 clinicians.	Any age	
22	Which brain or spine cavernoma sites carry the highest risk of symptoms that impact on the life of patients?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Prognosis; health related quality of life	Adverse effects or complications; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions	5 patients. 3 carers.	Any age	
23	What kind of rehabilitation and support services have been shown to be effective for patients and their families / carers following diagnosis of, or treatment of, brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Prognosis; change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; time in hospital and or needing health or social care services; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Service delivery	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Social care	25 patients. 15 carers.	Any age	
24	What are the long-term effects of stereotactic radiosurgery for people with brain or spine cavernomas?	Existing systematic review.	http://jnnp.bmj.com/content/85/12/1319.long	Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; adverse effects or complications; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Surgery; Radiotherapy	Multiple sources.	Any age	
25	What proportion of brain or spine cavernoma bleeds are non-symptomatic?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-ssp-project/	Prognosis	Adverse effects or complications; health related quality of life	n/a	n/a	n/a	n/a	n/a	n/a	Prognosis	Neurological conditions:Brain and spinal cavernomas	Neurological conditions; Diagnostics	4 patients.	Any age	

26	Is it possible to identify signs and symptoms that are unique to brain or spine cavernomas?	Survey carried out by the Cavernom Alliance UK for this PSP.	http://cavernoma1.users40.interdns.co.uk/our-projects-and-campaigns/priority-setting-partnership-psp-project/	Diagnostic	Adverse effects or complications;	n/a	n/a	n/a	n/a	n/a	Aetiology; Prognosis	Neurological conditions: Brain and spinal cavernomas	Neurological conditions; diagnostics	8 patients. 8 clinicians.	Any age
27	What is the optimum radiation dose for use in stereotactic radiosurgery of brain or spine cavernomas?	Existing guideline.	http://cavernoma1.users40.interdns.co.uk/wp-content/uploads/2015/03/final-CCM-guidelines.pdf	Identification of optimum dose of radiation; change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost	Change of symptoms; acceptability to patients or carers	Genetic Alliance UK. Cavernoma Alliance UK. Guidelines for the management of cerebral cavernous malformations in adults. London; Cavernoma Alliance UK: 2014. http://cavernoma1.users40.interdns.co.uk/wp-content/uploads/2015/03/final-CCM-guidelines.pdf	n/a	n/a	n/a	n/a	Radiotherapy; Surgery	Neurological conditions: Brain and spinal cavernomas	Neurological conditions; Surgery; Radiotherapy	Research recommendation.	Any age
Deleted as merged with Q1 as agreed at the Workshop.															
Old19	Is surgical removal or no treatment better for improving outcome for people with cavernomas?	See uncertainty 1, above.		Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost							Prognosis; Surgery; Service delivery	Neurological conditions: Brain and spinal cavernomas			
Old 20	Is stereotactic radio surgery or no treatment better for improving outcome for people with cavernomas?	See uncertainty 1, above.		Prognosis: change in symptoms, or change in management of symptoms; adverse effects or complications; patient satisfaction; health related quality of life; service related issues; and health related cost							Prognosis; Surgery; Service delivery	Neurological conditions: Brain and spinal cavernomas			