National Institute for Health and Care Excellence

Brain tumours (primary) and brain metastases in adults

Evidence reviews for the investigation, management and follow-up of meningioma

NICE guideline NG99

Evidence Report B

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Final

These evidence reviews were developed by the National Guideline Alliance, hosted by the Royal College of Obstetricians and Gynaecologists

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Contents

Investigation, management and follow-up of meningioma

This Evidence Report contains information on 4 reviews relating to the investigation, management and follow-up of meningioma. The Evidence Report is split into 3 sections:

- investigation of suspected meningioma, which contains 1 review on imaging for suspected meningioma; this review is the second part of a similar review detailed in Evidence Report A on imaging for suspected glioma and meningioma, and therefore the results detailed are only those related to meningioma
- management of confirmed meningioma following surgery or if surgery is not possible, which contains 2 reviews; the first of these is on managing inoperable, incompletely excised or recurrent meningioma and the second is on techniques for radiotherapy for meningioma
- follow-up for meningioma which contains one review on follow-up for meningioma.

Investigation of suspected meningioma

Imaging for suspected meningioma

Review question

What is the most effective imaging strategy in newly diagnosed glioma and meningioma?

(Note that this review considers only the portion of the review question relating to meningioma; see Evidence Report A for details on the portion of the review relating to glioma)

Introduction

The purposes of imaging at tumour presentation are to:

- identify the anatomical extent of tumour
- identify tumour relationship to critical brain areas/structures
- exclude non-tumour diagnoses
- predict tumour grade/biology/genetics
- predict likely future behaviour to stratify treatment
- identify sites for biopsy.

This systematic review explores the evidence for imaging strategies for patients with radiologically suspected glioma or meningioma. Under consideration are the imaging techniques, or combination of techniques, that provide the information necessary to make an initial diagnosis and plan appropriate treatment. Magnetic resonance imaging (MRI) is the most commonly used imaging test after computerised tomography (CT). Standard structural MRI can be performed in a number of different ways, including the use of a number of advanced techniques.

PICO table

Table 1: Summary of the protocol (PICO table)

Population	Adults with a radiologically (by CT scan or MRI scan) suspected meningioma

Intervention	Standard MRI alone:
	• standard structural MRI (core protocol) +/- contrast (T1 pre and post contrast and T2)
	
	Plus one of the following advanced tests:
	• advanced MRI:
	  ○ MR Spectroscopy (chemical shift imaging)
	  ○ diffusion imaging (DWI/DTI) tensor imaging (DTI)
	  ○ perfusion imaging (DSC, DCE, ASL will not be looked at separately)
	  ○ structural imaging
	• PET-CT (including FDG: FET, MET, Choline-PET)
	• PET-MRI (including FDG: FET, MET, Choline-PET)

Reference standard (test)	Pathology (histology and, where appropriate molecular testing) or clinical /radiological follow-up if there is no biopsy
Outcome	Critical:

	• health-related quality of life (especially anxiety)
	• diagnostic accuracy, including:
	  ○ sensitivity
	  ○ specificity
	  ○ likelihood ratios
	For detecting:
	  ○ meningioma

ASL arterial spin labelling; CT computer tomography; DCE dynamic contrast-enhancement; DSC dynamic susceptibility contrast; DTI diffusion tensor imaging; DWI diffusion weighted imaging; FDG 2-deoxy-2-(18)fluoro-D-glucose; FET (18)F-fluoro-ethyl-l-tyrosine; MET (11)C-methionine; MRI magnetic resonance imaging; PET-CT positron emission tomography - computed tomography; PET-MRI positron emission tomography - magnetic resonance imaging..

For further details see the full review protocol in Appendix A.

Clinical evidence

The clinical evidence search identified no studies that met the inclusion criteria for the second part of this review (on meningioma).

For details on clinical evidence which met the inclusion criteria of the first part of this review (on glioma) see Evidence Report A.

Excluded studies

Full-text studies not included in this review with reasons for their exclusions are provided in Appendix K.

Economic evidence

The economic evidence search identified no studies that met the inclusion criteria for this review.

Resource Impact

No unit costs were presented to the committee as these were not prioritised for decision making purposes.

Evidence statements

No evidence was identified.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Diagnostic test accuracy outcomes, as reflected by the sensitivity and specificity of the diagnostic test, were considered critical for decision-making in this review. Sensitivity was used to evaluate imprecision, as an early accurate identification of meningioma confers benefits and reduces the harmful consequences of a misdiagnosis. Likelihood ratios were also considered to be critical diagnostic outcomes because they provide information about a test's usefulness in assisting the healthcare professional to make a diagnosis. Quality of life (especially anxiety) was also considered critical for decision-making because waiting for additional imaging tests may delay a diagnosis.

The quality of the evidence

The clinical evidence search identified no studies that met the inclusion criteria for this review.

Although no evidence was identified, the committee believed that they could use the evidence from the parallel review on imaging for glioma to inform their recommendations on this topic, as meningioma and glioma share some characteristics which make MRI scans appropriate for both.

For details on the evidence relating to glioma upon which the committee based some of their recommendations, see Evidence Report A.

The committee chose not to make a research recommendation as they believed standard practice in this area was clinically sufficient to inform the next stage of treatment of the meningioma.

Benefits and harms

Low to very low quality evidence from retrospective cohort studies relating to glioma show that standard structural MRI has excellent sensitivity and specificity at discriminating tumour from non-tumour. In the case of the papers related to glioma, the evidence was complex and demonstrated that optimal tumour characterisation depended on the exact parameters set on the MRI machine. The committee determined that these parameters should be left to the discretion of the operator, as it was not clear from the evidence whether the protocol used in the study would apply to all types of tumours across all types of machine, however the committee were satisfied that even without the careful optimisation done in these papers that MRI would have value at identifying clinically important features of the glioma. Based on their clinical experience, the committee therefore recommended MRI for use in meningioma, since techniques which can discriminate glioma from non-glioma should be able to discriminate meningioma from non-meningioma. Failing to offer MRI in this case would likely be harmful for patients, as it would make it difficult to plan subsequent treatment for surgeons and oncologists.

Following a consistent imaging protocol can reduce delays by reducing the need for repeat imaging. However this could not be demonstrated from published evidence (which should follow a consistent protocol by definition). To avoid ambiguity the committee recommended an imaging protocol they believed was the minimum standard for imaging acquisition.

In the experience of the committee, bone involvement by meningioma is common, and it can be difficult to accurately assess meningioma with bone involvement on MRI. The committee recommended using a CT scan to look for bone involvement in meningioma where this is suspected (particularly if the meningioma is near the base of the skull). This was based on their clinical experience that CT scans can be more accurate than MRI in these cases.

The imaging strategies outlined in this systematic review aimed to distinguish tumour from non-tumour. In any given diagnostic test, there is normally a trade-off between identifying all meningioma (sensitivity) and not identifying as meningioma too many cases of non-meningioma (specificity). For the purposes of this review, the committee prioritised test sensitivity, as they wanted to identify as many true cases of meningioma as possible.

The potential benefits associated with the recommendations made by the committee are that improved characterisation of meningiomas leads to different management strategies (for example, beginning treatment more quickly, and with different therapies). Other benefits include a better use of the resources available such as support groups or strategies to help cope with the symptoms. The committee believe a third benefit may be to empower the person with a meningioma, allowing them to participate in long-term planning and to help develop realistic expectations, which can reduce stress.

The potential harms associated with inaccurate diagnosis are: inappropriate interventions, such as a meningioma being treated more aggressively than necessary; or delay in treatment if a meningioma is not recognised. The concomitant morbidity and mortality may increase in both cases. These risks may occur through both the underuse and overuse of diagnostic imaging tests, and so represent a potential harm of the recommendations.

Overall, the committee believed that the balance of benefits and harms very much favours imaging in the case of meningioma, as the risks of misdiagnosis are low and the potential benefits of imaging are very high.

Cost effectiveness and resource use

A literature review of published cost effectiveness analyses did not identify any relevant studies for this topic.

There is currently variation in practice between radiologists, with different imaging protocols being used by different centres in different circumstances. For centres currently undertaking a reduced MR protocol when compared with the committee-recommended core sequences, there may be an increase in resource use through increased MR machine time, radiographer and radiologist time. However, these increases in resource use will be at least partially recouped through a clearer patient pathway reducing the need for repeat MR imaging, for example when initial imaging is not compatible with neuronavigational equipment. Reduction in resource use will also be made through a reduction in misdiagnoses (leading to reimaging, inappropriate treatment and greater costs of treating adverse events) given the high sensitivity and specificity of standard structural MRI.

The committee considered that recommendations around CT scans would only lead to small impact on resource use. This is already the standard of care for potential bone involvement and variation in practice is much smaller than for the other recommendations on this topic.

The committee believed that the recommendations around advanced imaging techniques, including MR perfusion and MR spectroscopy, may lead to minor, but not major, increases in resource use. There would be a large resource impact if hospitals without this technology were expected to provide it, but it is more likely that patients will be referred to appropriate specialist centres, where these techniques are usually available, and performed according to local expertise and experience. As the majority of these patients are already referred to specialist centres it was thought that any increase in referral would be minimal.

While it was unclear what the overall impact on resource use would be, more diagnostically accurate imaging protocols would lead to increases in both life expectancy and quality of life in this patient group. Missed diagnoses can lead to potential harmful effects on both length and quality of life and suboptimal of resources through inappropriate and potentially harmful interventions. Even if there were increases in resource use with these recommendations they would not be large. While no published cost effectiveness evidence was identified or bespoke economic modelling performed the committee believed that any calculated cost per additional QALY would be significantly below the £20,000 for which NICE conventionally recommends interventions.

Other factors the committee took into account

The committee was aware that imaging provision was variable at the moment. The recommendations should improve consistency in both specialist and non-specialist centres (for example district general hospitals).

References

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Management of confirmed meningioma following surgery or if surgery is not possible (or has been declined)

Managing inoperable, incompletely excised or recurrent meningioma

Review question

Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?

Introduction

For most people, complete surgical resection (Simpson grade 1 or 2 resection) of a meningioma is considered optimal treatment. However for many people their tumour is inoperable due to location (an attempt at resection would result in significant neurological deficit) or in such a position that resection would be incomplete to avoid neurological sequelae. For these people the optimal timing of radiotherapy is unclear. In addition it is unclear if patients who have residual disease after surgical resection should have immediate adjuvant radiotherapy or wait until progressive growth occurs.

If radiotherapy is thought appropriate, there is significant complexity to the choice of radiotherapy technique. This is due to the clinical complexity of selecting the schedule of radiation which has the best chance of controlling tumorous tissue while minimising dose to the normal brain, and also complex because of factors to do with the person with the tumour, such as their willingness to travel to receive treatment using a different kind of radiotherapy.

PICO table

Table 2: Summary of the protocol (PICO table)

Population	People with inoperable, incompletely excised meningioma or recurrent meningioma (subgrouped by clinical and disease characteristics).
	
	Sub-group:
	• inoperable versus incompletely excised
	• tumour grade I versus II versus III
	• anatomical tumour location:
	  ○ optic nerve
	  ○ cavernous sinus
	  ○ convexity and falx

Intervention	• No radiotherapy/observation • Radiotherapy • Observation followed by radiotherapy
Comparison	Each other
Outcome	Critical: • overall survival. • progression-free survival • cognitive function

	• neurological function:
	  ○ cranial neuropathy (e.g. optic neuropathy)
	Important:
	• treatment-related morbidity:
	  ○ radionecrosis
	  ○ oedema
	  ○ stroke
	  ○ second malignancy
	  ○ pituitary dysfunction
	  ○ epilepsy/seizures
	• health-related quality of life
	Of limited importance:
	• steroid use

For further details see the full review protocol in Appendix A.

Clinical evidence

Included studies

Twelve comparative observational studies were included in this review, 7 of which were conducted in the USA (Bagshaw, 2017; Hardesty, 2013; Lee 2013; McCarthy 1998; Peele 1996; Sun, 2013; Yoon 2015), 2 in Korea (Han, 2016; Park, 2013) and 1 in each of Sweden (Frostell, 2016), Canada (Alghamdi, 2017) and Taiwan (Wang, 2015).

The studies examined recurrence, survival and adverse events associated with subtotal resection with or without adjuvant radiotherapy for the following populations:

- patients with World Health Organization (WHO) grade I-III meningioma (Frostell, 2016)
- patients with atypical meningioma (Alghamdi, 2017; Bagshaw, 2017; Hardestry, 2013; Lee, 2013; McCarthy, 1998; Park, 2013; Sun 2013)
- patients with WHO grade II atypical meningioma located in the skull base (Wang, 2015)
- patients with recurrent atypical meningioma (Bagshaw, 2017)
- patients with benign meningioma (McCarthy, 1998)
- patients with malignant meningioma (McCarthy, 1998)
- patients with primary sphenoid wing meningioma (Peele 1996)
- patients with recurrent sphenoid wing meningioma (Peele, 1996)
- patients with grade II meningioma (not otherwise specified; Yoon, 2015)
- patients with intracranial meningioma involving the major venous sinus (Han, 2016).

A summary of these studies is provided in Table 3, and the results along with the quality of the evidence for each outcome are listed in Table 4 to Table 13 below.

For further details, see also the study selection flow chart in Appendix C, the evidence tables for the individual studies in Supplementary Material D and the full GRADE tables in Appendix F.

Excluded studies

Full-text studies not included in this review with reasons for their exclusions are provided in Appendix K.

Summary of clinical studies included in the evidence review

Table 3 provides a summary of the included studies.

Table 3: Summary of included studies

Study	Meningioma	Intervention group 1	Intervention group 2	Outcomes	Comments
Alghamdi, 2017	Atypical meningioma	Subtotal resection, no adjuvant radiotherapy (N = 30)	Subtotal resection + adjuvant radiotherapy (N = 6)	- Recurrence rate	Serious risk of bias: - uncontrolled confounders; small sample
Bagshaw, 2017	Atypical meningioma	Initial treatment Subtotal resection, no adjuvant radiotherapy (N = 9) Treatment at recurrence: Surgery alone (N = 10)	Initial treatment Subtotal resection + adjuvant radiotherapy (N = 2) Treatment at recurrence: Radiotherapy alone (N = 12)	- Recurrence rate/local failure rate - Survival	Serious risk of bias: - uncontrolled confounders; small sample
Frostell, 2016	Cerebral meningioma located in proximity to a venous structure (parasagittal, transverse, and sigmoid sinus)	Near total resection (NOS), no adjuvant stereotactic radiosurgery (N = 19); WHO grade I/II/III (N = 12/5/2)	Near total resection + adjuvant stereotactic radiosurgery (N = 21); WHO grade 1/2/3 (N = 19/5/5) SRS using stereotactic Leksell frame, MRI, and GammaKnife Perfexion (Gy median, (range)): Min dose: 15 (10-15); max dose: 31 (22-38); prescription dose: 15 (0-16); tumour volume: 1.07 (0-6) cm^3	- Overall survival - Progression-free survival - Retreatment rate - Time to retreatment - Oedema rate - Necrosis rate	Moderate risk of bias: - small sample/low event rates relative to the number of covariates - OS result not adjusted
Han, 2016	Intracranial meningioma involving the major venous sinus	Subtotal resection, no adjuvant radiotherapy (N = 7)	Subtotal resection + adjuvant radiotherapy (N = 7)	- Recurrence rate	Serious risk of bias: - uncontrolled confounders; small sample
Hardesty 2013	Atypical meningiomas	Subtotal resection (Simpson grade > II), no adjuvant radiotherapy (N = 54)	Subtotal resection with post-operative SRS (N = 22) RT: Median (range) radiation dose = 14 (11–16) Gy to the 50%	- Progression-free survival - Radiotherapy adverse events	Serious risk of bias: - uncontrolled confounders

Study	Meningioma	Intervention group 1	Intervention group 2	Outcomes	Comments
			isodose line for Gamma Knife-treated patients with the dose for CyberKnife-treated patients ranging from 14–16 Gy in 1 fraction, to 21–27 Gy in 3 fractions, to 25 Gy in 5 fractions. Subtotal resection with post-operative IMRT (N = 20) RT: Median (range) radiation dose = 54 (54–59) Gy in standard fractionation of 1.8–2 Gy per day		
Lee, 2013	Grade II atypical meningiomas	Subtotal resection (Simpson grade IV), no RT (N = 5) 14 of the 19 STR patients had also received pre-operative RT.	Subtotal resection with post-operative RT: (N = 14). RT: Fractionated stereotactic radiotherapy by linear accelerator (median dose 59.4 Gy, range 50.4–60.0 Gy) delivered to the tumour bed in 1.8- to 2.0-Gy fractions.	- Recurrence rate - Recurrence-free survival	Serious risk of bias: - uncontrolled confounders
Mc-Carthy 1998	Benign, atypical, or malignant (NOS)	Benign meningioma: Subtotal resection, no RT (N = 4577). Atypical meningioma: Subtotal resection, no RT (N = 86). Malignant meningioma: Subtotal resection, no RT: (N = 279).	Benign meningioma: Subtotal resection + RT (N = 238) Atypical meningioma: Subtotal resection with RT (N = 20) Malignant meningioma: Subtotal resection with RT (N = 169) RT defined as any form NOS.	- Overall survival	Serious risk of bias: - uncontrolled confounders All aspects of RT given is unclear
Park, 2013	WHO grade II atypical meningioma	Subtotal resection, no RT (N = 18).	Subtotal resection with RT (N = 10) RT: Median (range) dose = 61.2 (40–61.2) Gy) over 7 weeks with photon.	- Progression-free survival - Complications	Serious risk of bias: - uncontrolled confounders

Study	Meningioma	Intervention group 1	Intervention group 2	Outcomes	Comments
			Conventional RT until 2002 and three-dimensional conformal RT thereafter.		
Peele, 1996	Sphenoid wing meningiomas	Subtotal resection, no RT: Primary tumour (N = 38) Recurrent tumour (N = 6)	Subtotal resection + RT: Primary tumour (N = 31) Recurrent tumour (N = 11) RT: Mean dose = 180 cGy per fraction (range, 150-200 cGy) to a total dose of 4500 cGy (range, 4350-4850 cGy) with 6-MV photon beams, 5 days a week, 1 fraction per day.	- Recurrence - Operative complications - RT adverse events	Serious risk of bias: - uncontrolled confounders Patients treated 1981-1994, unclear how many treated 1981-85, that is, outside of our inclusion criterion of 1985 onwards
Sun 2013	Atypical meningioma	Subtotal resection, no RT (N = 27)	Subtotal resection + SRS (N = 7) RT: Median dose of 18 Gy (range, 14-18 Gy) - Subtotal resection with Subtotal resection + EBRT: (N = 25) RT: Median dose of 54 Gy (range, 52-60 Gy) delivered in 1.8- to 2.0-Gy fractions	- Local control - Progression-free survival - Overall survival - RT adverse events	Serious risk of bias: - uncontrolled confounders
Wang, 2015	Atypical meningioma, with tumours located in the skull base area.	Subtotal resection, no RT (N = 5)	Subtotal resection + RT (N = 9) RT: Total radiation dose = 54–60 Gy, delivered in 27–30 fractions.	- Recurrence rate - Operative complications - RT adverse events	Serious risk of bias: - uncontrolled confounders - small sample
Yoon, 2015	Grade II meningioma	Subtotal resection, no RT (N = 30)	Subtotal resection + RT (N = 12). RT: Mean adjuvant EBRT dose = 57 Gy, mean adjuvant SRS dose = 14 Gy.	- Recurrence rate - Progression-free survival - Overall survival	Serious risk of bias: - Uncontrolled confounders

cGy centi-Gray (unit of radiation); EBRT external beam radiotherapy; Gy Gray (unit of radiation); IMRT intensity modulated radiotherapy; MRI magnetic resonance imaging; MV mega volt; NOS not otherwise specified; OS overall survival; RT radiotherapy; SRS stereotactic radiosurgery; STR subtotal resection; WHO World Health Organization.

See Supplementary Material D for full evidence tables.

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in Table 4 to Table 13.

Table 4: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected WHO grade I-III meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Progression-free survival Follow-up: 4.7-5.3 years	Not estimable	Not estimable	Not estimable, but not significant	40 (1 study)	⊕⊖⊖⊖ very low[1,2]
Overall survival Follow-up: 4.7-5.3 years	211 per 1000	0 per 1000 (not estimable)	Not estimable, but significantly longer in the radiotherapy group	40 (1 study)	⊕⊖⊖⊖ very low[1,3]
Necrosis and oedema Follow-up: 4.7-5.3 years	None experienced the outcomes	None experienced the outcomes	Not estimable	40 (1 study)	⊕⊖⊖⊖ very low[1]

CI Confidence interval.
[1] Low event rate
[2]Event rates not clearly reported in study, so not included here
[3] Uncontrolled confounders/Unadjusted analyses

Table 5: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected benign meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Overall survival Follow-up: Median 10 months	Not estimable	Not estimable	Not estimable, but not significant	4815 (1 study)	⊕⊖⊖⊖ very low[1,2,3]

CI Confidence interval.
[1] Patient characteristics by intervention group not reported, unadjusted analyses.
[2] Radiotherapy was classified into yes/no depending on whether the patient had received any radiotherapy. No further details reported.
[3] Not enough information reported to estimate the absolute or relative effects.

Table 6: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected malignant meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Overall survival Follow-up: Median 10 months	Not estimable	Not estimable	Not estimable, but significantly shorter in the radiotherapy group compared to observation	448 (1 study)	⊕⊖⊖⊖ very low[1,2,3]

CI Confidence interval.
[1] Uncontrolled confounders/Unadjusted analyses
[2] Radiotherapy was classified into yes/no depending on whether the patient had received any radiotherapy. No further details reported.
[3] Not enough information reported to estimate the absolute or relative effects.

Table 7: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected II atypical meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Overall survival Follow-up: 12-67 months	Not estimable	Not estimable	RR 1.28 (0.65 to 2.53), 0.57 (0.36 to 0.88) and 1.23 (1.02 to 1.48)[1]	176 (3 studies)	⊕⊖⊖⊖ very low[1,2,3,4]
Recurrence Follow-up: 26-48.7 months	Not estimable	Not estimable	RR 0.53 (0.16 to 1.69), 0.66 (0.31 to 1.4) and 0.11 (0.02 to 0.51)[5]	66 (3 studies)	⊕⊖⊖⊖ very low[2,4,5]
Recurrence/progression-free survival Follow-up: 23-67 months	Study 1: 1/5 (20%) Study 2-4: Not reported	Study 1: 13/14 (92.9%) Study 2-4: Not reported	3 of the 4 studies found that recurrence/progression-free survival was	202 (4 studies)	⊕⊖⊖⊖ very low[2,4]

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
			longer in the radiotherapy group (p < 0.01)) whereas the 4th study found no difference between radiotherapy and observation.		
Treatment-related morbidity Follow-up: 23-67 months	Study 1: No severe acute side effects observed. Transient mild side effects, such as fatigue, headache, intermittent nausea, dizziness and skin irritation at portals observed in most patients. Cognitive disturbance and motor neuropathy were the most common late side effects. Others including memory disturbance, speech impairment, encephalopathy, seizures, and haemorrhage also observed. Study 2: No RT-related adverse events observed Study 3: 1 RT-related adverse event observed		Not estimable	185 (3 studies)	⊕⊖⊖⊖ very low[2,4]

CI Confidence interval; RT radiotherapy; RR risk ratio.
[1] I^2 = 88%, indicating very serious heterogeneity. Therefore the risk ratios were not combined.
[2] Uncontrolled confounders/unadjusted analyses
[3] Radiotherapy was classified into yes/no depending on whether the patient had received any radiotherapy. No further details reported.
[4] Low event rate
[5] I^2 = 60%, indicating substantial heterogeneity, which in combination with the fact that these were small observational studies with a number of limitations meant that the risk ratios were not combined.

Table 8: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected WHO grade II meningioma (not otherwise specified)

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Recurrence Follow-up: Median 32 months	267 per 1000	251 per 1000 (80 to 787)	Non-significant (p = 0.99)	42 (1 study)	⊕⊖⊖⊖ very low[1,2]
Progression-free survival Follow-up:	Mean = 47 months	Mean = 59 months	Non-significant (p = 0.4)	42 (1 study)	⊕⊖⊖⊖ very low[1,2]

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
Median 32 months					
Overall survival Follow-up: Median 32 months	833 per 1000	833 per 1000 (617 to 1000)	Non-significant (p = 0.98)	42 (1 study)	⊕⊖⊖⊖ very low[1,2]

CI confidence interval; NR not reported.
[1] Uncontrolled confounders/unadjusted analyses
[2] Low event rate

Table 9: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected WHO grade II atypical meningioma located in the skull base

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Recurrence Follow-up: Mean 57.4 months	5/5	NR/9	Non-significant	14 (1 study)	⊕⊖⊖⊖ very low[1,2]
Treatment-related morbidity Follow-up: Mean 57.4 months	1 complication observed after subtotal resection (facial palsy; tumour location petroclivus). "Following radiotherapy, self-limiting symptoms like dizziness, headache, and skin irritation were observed, but there were no severe acute side effects."			14 (1 study)	⊕⊖⊖⊖ very low[1,2]

CI confidence interval; NR not reported.
[1] Uncontrolled confounders/unadjusted analyses
[2] Low event rate

Table 10: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected primary sphenoid wing meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Recurrence Follow-up: 3.5-4.3 years	421 per 1000	0 per 1000 (not estimable)	Observation > Radio-therapy (p < 0.00005)	69 (1 study)	⊕⊖⊖⊖ very low[1,2,3]
Treatment-related morbidity Follow-up: 3.5-4.3 years	-Operative complications: Third cranial nerve palsy (N = 4), fifth cranial nerve dysfunction (N = 1), ptosis (N = 1), central retinal artery occlusion (N = 1), cerebrospinal fluid leak (N = 1), and pulmonary embolism (N = 1). -Serious morbidity (N = 0) or mortality (N = 0) -Anterior ischemic optic neuropathy (N = 3), central retinal vein occlusion (N = 1). "All events		Not estimable	86 (1 study)	⊕⊖⊖⊖ very low[1,2,3,4]

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	occurred at least 2 years postoperatively but ipsilateral to the previous frontotemporal craniotomy." -Radiation therapy (temporary) adverse events: Mild skin erythema and lateral brow alopecia, but no retinal or optic nerve complications, except possibly N = 1.				

CI confidence interval.
[1] Uncontrolled confounders/unadjusted analyses
[2] Patients treated 1981-1994, unclear how many treated 1981-1985, that is, outside of our inclusion criterion of 1985 onwards.
[3] Low event rate
[4] These data are not split by primary/recurrent group, but collapsed across them.

Table 11: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected meningioma involving the major venous sinus

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			
Recurrence Follow-up: median 26 months	429 per 1000	60 per 1000 (4 to 1000)	RR 0.14 (0.01 to 2.34)	14 (1 study)	⊕⊖⊖⊖ very low[1,2]

CI confidence interval; RR risk ratio.
[1] Uncontrolled confounders/unadjusted analyses
[2] Low event rate

Table 12: Summary clinical evidence profile for radiotherapy compared to surgery for patients with recurrent atypical meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Surgery	Radiotherapy			
Recurrence Follow-up: median 26 months	900 per 1000	747 per 1000 (513 to 1000)	RR 0.83 (0.57 to 1.23)	22 (1 study)	⊕⊖⊖⊖ very low[1,2]

CI confidence interval; RR risk ratio.
[1] Uncontrolled confounders/unadjusted analyses
[2] Low event rate

Table 13: Summary clinical evidence profile for radiotherapy compared to observation for patients with incompletely resected recurrent sphenoid wing meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Observation	Radiotherapy			

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
Recurrence Follow-up: 3.5-4.3 years	833 per 1000	0 per 1000 (not estimable)	Observation > Radio-therapy (p < 0.0012)	17 (1 study)	⊕⊖⊖⊖ very low[1,2,3]

CI: confidence interval.
[1] Uncontrolled confounders/unadjusted analyses
[2] Patients treated 1981-1994, unclear how many treated 1981-1985, that is, outside of our inclusion criterion of 1985 onwards.
[3] Low event rate

See Appendix F for full GRADE tables.

Economic evidence

The economic evidence search identified no studies that met the inclusion criteria for this review.

Resource Impact

No unit costs were presented to the committee as these were not prioritised for decision making purposes.

Evidence statements

Patients with incompletely resected WHO grade I-III meningioma

- One observational study (n=40) provided very low quality evidence that showed significantly longer overall survival in patients treated with radiotherapy, but no difference in progression-free survival or rates of necrosis and oedema between radiotherapy and observation.

Patients with incompletely resected benign meningioma

- One observational study (n=4815) provided very low quality evidence that showed no difference in overall survival between radiotherapy and observation.

Patients with incompletely resected malignant meningioma

- One observational study (n=448) provided very low quality evidence that showed shorter overall survival in patients treated with radiotherapy compared to observation.

Patients with incompletely resected WHO grade II atypical meningioma

- Three observational studies (n=176) provided very low quality evidence that showed that overall survival was either longer, shorter or similar in patients treated with radiotherapy compared to observation (RR1 = 1.28; 95% CI 0.65-2.53, RR2 = 0.57; 95% CI 0.36-0.88, and RR3 = 1.23; 95% CI 1.02-1.48; I^2 = 88%).Three observational studies (n=66) provided very low quality evidence that showed that the recurrence rate was either lower or similar in patients treated with radiotherapy compared to observation (RR1 = 0.53; 95% CI 0.16-1.69, RR2 = 0.66; 95% CI 0.31-1.4, and RR3 = 0.11; 95% CI 0.02-0.51; I^2 = 60%). Three observational studies (n=106) provided very low quality evidence that showed significantly longer recurrence/progression-free survival in patients treated with SRT+RT compared to STR alone, while a fourth study (n=96), also providing very low quality evidence, found no significant difference in progression-free survival between patients treated with SRT+RT

compared to STR alone. Three observational studies (n=183) provided very low quality evidence that showed that only 1 severe adverse event was observed in the STR+RT group after treatment with intensity-modulated radiotherapy.

Patients with incompletely resected WHO grade II meningioma (not otherwise specified)

- One observational study (n=42) provided very low quality evidence that showed no differences in recurrence rate, progression-free survival or overall survival between radiotherapy and observation.

Patients with incompletely resected WHO grade II atypical meningioma located in the skull base

- One observational study (n=14) provided very low quality evidence that showed no differences in recurrence rate between radiotherapy and observation.

Patients with incompletely resected primary sphenoid wing meningioma

- One observational study (n=69) provided very low quality evidence that showed that the recurrence rate was significantly lower after treatment with radiotherapy compared to observation, but no serious treatment-related morbidity or mortality.

Patients with incompletely resected meningioma involving the major venous sinus

- One observational study (n=14) provided very low quality evidence that showed that the recurrence rates did not differ between treatment with radiotherapy compared to observation (RR = 0.14; 95% CI 0.01-2.34).

Patients with recurrent atypical meningioma

- One observational study (n=22) provided very low quality evidence that showed that the recurrence rates did not differ between treatment with radiotherapy compared to surgery (RR = 0.83; 95% CI 0.57-1.23).

Patients with incompletely resected recurrent sphenoid wing meningioma

- One observational study (n=17) provided very low quality evidence that showed that the recurrence rate was significantly lower after treatment with radiotherapy compared to observation, but no serious treatment-related morbidity or mortality.

The committee's discussion of the evidence

See the committee's discussion of the evidence in the techniques for radiotherapy for meningioma section.

References

See the references in the techniques for radiotherapy for meningioma section.

Techniques for radiotherapy for meningioma

Review question

Which technique should be used for adults with meningioma who require radiotherapy?

Introduction

Though many meningiomas can be treated successfully with surgery, others require radiotherapy either following surgery as the sole modality of treatment or at recurrence. Over the past 20 years many new radiotherapy techniques have been developed which have the potential to improve effectiveness and reduce toxicity, especially late-effects. Historically treatment has used '3D conformal' radiotherapy, but newer techniques frequently used for radiotherapy include intensity modulated radiotherapy (IMRT), volumetrically modulated arc therapy (VMAT), stereotactic radiotherapy (either as single fraction, hypo-fractionated or conventionally fractionated). More experimental is proton beam and other particle therapies, such as carbon ions. This range of options creates uncertainty as to which technique and which fractionation schedule provides the highest level of tumour control with the lowest level of side effects. Therefore it would be helpful for clinical teams and patients to have an evaluation of the data to help selection of the optimal therapeutic option.

PICO table

Table 14: Summary of the protocol (PICO table)

Population	Adults with meningioma (not just recurrent meningioma) requiring/suitable for radiotherapy.
Intervention	• Conventionally fractionated 3D conformal radiotherapy • Conventionally fractionated IMRT/VMAT • Radiosurgery (1 fraction) • Stereotactic radiotherapy (2-5 fractions/hypofractionated) • Fractionated stereotactic radiotherapy (greater than 5 fractions) • Proton beam and other particle therapies
Comparison	• Each other • Combinations of interventions not possible Main comparisons to focus on: • fractionated radiotherapy: 1 fraction versus 2-20 fractions versus 21-35 fractions • 3D CRT versus FSRT versus IMRT/VMAT versus proton/particle
Outcome	• Critical: ○ progression-free survival/ local control ○ Karnofsky performance status ○ steroid (for example dexamethasone) use (duration and dose) • Important: ○ health-related quality of life ○ Neurological Function Scale ○ cognitive function • Of limited importance: ○ second malignancy

3D CRT 3D conformal radiotherapy; FSRT fractionated stereotactic radiotherapy; IMRT intensity modulated radiotherapy; VMAT volumetric modulated arc therapy;

For further details see the full review protocol in Appendix A.

Clinical evidence

Included studies

Seven comparative observational studies were included in this review, 3 of which were conducted in the USA (Han 2014; Hardesty, 2014; Torres, 2003), 2 in Germany (Fokas, 2014; Kaul, 2014), and 1 in each of France (Metellus, 2005) and Brazil (Correa, 2014). The studies examined progression-free survival, local control, steroid-use, cognitive function and radiation-induced malignancy rate after stereotactic radiosurgery (SRS), fractionated stereotactic radiotherapy (FSRT), hypo-fractionated stereotactic radiotherapy (hFSRT), or intensity modulated radiotherapy (IMRT) in patients with intracranial meningioma (Kaul, 2014; Torres, 2003), cavernous sinus meningioma (Correa, 2014; Metellus, 2005), grade I meningioma (Fokas, 2014), basal meningioma (Han, 2014), or atypical meningioma (Hardesty, 2013).

A summary of these studies is provided in Table 15, and the results along with the quality of the evidence for each outcome are listed in Table 16 to Table 21 below.

For further details, see also the study selection flow chart in Appendix C, the evidence tables for the individual studies in Supplementary Material D and the full GRADE tables in Appendix F.

Excluded studies

Full-text studies not included in this review with reasons for their exclusions are provided in Appendix K.

Summary of clinical studies included in the evidence review

Table 15 provides a summary of the included studies.

Table 15: Summary of included studies

Study	Meningioma	Intervention group 1	Intervention group 2	Outcomes	Comments
Correa, 2014	Cavernous sinus meningioma	SRS (N = 32)	FSRT (N = 57)	- Disease-free survival - Steroid use - Cognitive / dysthymic alteration - Radiation-induced malignancy	Serious risk of bias (uncontrolled confounders) Tumour size significantly larger in SRT group
Fokas, 2014	Grade I meningioma	FSRT (N = 253)	hFSRT (N = 49)	- Local control - Radiation-induced malignancy	Serious risk of bias (uncontrolled confounders) Target volume different between treatment groups; Some patients aged < 16 years, unclear how many
Han, 2014	Basal meningioma	SRS (N = 55)	FSRT (N = 143)	- Progression-free survival - Steroid use	Serious risk of bias (uncontrolled confounders) Tumour size significantly larger in FSRT group
Hardesty, 2013	Atypical meningioma	SRS (N = 32)	IMRT (N = 39)	- Progression-free survival	Serious risk of bias (likely uncontrolled confounders)

Study	Meningioma	Intervention group 1	Intervention group 2	Outcomes	Comments
					Tumour volume not reported, and target volume only for SRS Unequal lengths of follow up between treatment groups
Kaul, 2014	Intra-cranial meningioma	FSRT (N = 179)	hFSRT (N = 92)	- Progression-free survival	Serious risk of bias (likely uncontrolled confounders) Tumour size not reported, split by treatment groups
Metellus, 2005	Cavernous sinus meningioma	SRS (N = 36)	FSRT (N = 38)	- Progression-free survival - Radiation-induced malignancy	Serious risk of bias (uncontrolled confounders) Tumour size significantly larger in SRT group
Torres, 2003	Intra-cranial meningioma	SRS (N = 63)	FSRT (N = 72)	- Local control	Serious risk of bias (likely uncontrolled confounders) Unequal lengths of follow up between treatment groups

FSRT fractionated stereotactic radiotherapy; hFSRT hypo-fractionated stereotactic radiotherapy; IMRT intensity modulated radiotherapy SRS stereotactic radiosurgery; SRT stereotactic radiotherapy.

See Supplementary Material D for full evidence tables.

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in Table 16 to Table 21

No meta-analyses were performed either because there were only data from 1 study for the outcomes within each treatment comparison or – when more than 1 study contributed data to an outcome within a treatment comparison – because the data were not adequately reported to be able to undertake meta-analysis.

Table 16: Summary clinical evidence profile for stereotactic radiosurgery (SRS) compared to fractionated stereotactic radiotherapy (FSRT) for patients with cavernous sinus meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	FSRT	SRS			
Disease/ progression-free survival Follow-up: 63.6-88.6 months	Not estimable[1]	Not estimable[1]	Not estimable, but non-significant [2]	163 (2 studies)	⊕⊖⊖⊖ very low[3,4,5]
Cognitive / dysthymic improvement Follow-up: median 73 months	18 per 1000	94 per 1000 (10 to 864)	RR 5.34 (0.58 to 49.27)	89 (1 study)	⊕⊖⊖⊖ very low[3,4]

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
Steroid use Follow-up: median 73 months	Not estimable[6]	Not estimable[6]	RR 4.93 (1.89 to 12.87)	89 (1 study)	⊕⊖⊖⊖ very low[3,4]
Radiation-induced malignancy Follow-up: 63.6 months-15 years	Not estimable[7]	Not estimable[7]	Not estimable, but non-significant [7]	163 (2 studies)	⊕⊖⊖⊖ very low[3,4,5]

CI confidence interval; RR risk ratio.
[1] Event rate not reported in 1 of the studies. In the other study 2/38 and 2/36 patients, respectively, progressed in the FSRT and SRS groups.
[2] Disease-free survival rates in Correa 2014: SRS (5, 10 and 15 year = 100%, 95.7% and 90.3%) = SRT (5, 10 and 15 year = 98.1%, 90.3% and 90.3%; p = 0.567). Progression free survival rates in Metellus 2005: FSRT: 5- and 10-year = 94.7%;
SRS: 5- and 10-year = 94.4%.
[3] Uncontrolled confounders (SRS had smaller tumours than FSRT) in the included studies.
[4] Low event rates/low numbers of patients
[5] The time frames covering the 2 treatment group differed in 1 of the studies (FSRT: 1986-1999; SRS: 1994-1997)
[6] Event rates: SRS = 7/32; FSRT 0/57
[7] Event rates: SRS = 0/68; FSRT 0/95

Table 17: Summary clinical evidence profile for fractionated stereotactic radiotherapy (FSRT) compared to hypo-fractionated stereotactic radiotherapy (hFSRT) for patients with grade I meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	FSRT	hFSRT			
Local control Follow-up: median 50 months	Not estimable[1]	Not estimable[1]	Not estimable, but non-significant [1]	302 (1 study)	⊕⊖⊖⊖ very low[2,3,4]
Radiation-induced malignancy Follow-up: median 50 months	Not estimable[5]	Not estimable[5]	Not estimable, but non-significant [5]	302 (1 study)	⊕⊖⊖⊖ very low[2,3,4]

CI confidence interval; NR not reported; HR Hazard ratio.
[1] Event rate not reported
[2] Uncontrolled confounders (patient characteristics not reported split by radiotherapy group, but clear that at least target volume differ between the treatment groups)
[3] Some patients aged below 16 years, unclear how many
[4] Low event rates/low number of patients
[5] Event rates: FSRT = 0/253; hFSRT 0/49

Table 18: Summary clinical evidence profile for stereotactic radiosurgery (SRS) compared to fractionated stereotactic radiotherapy (FSRT) for patients with basal meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	SRS	FSRT			
Progression-free survival Follow-up: median 32 months	916 per 1000	870 per 1000 (779 to 980)	RR 0.95 (0.85 to 1.07)	198 (1 study)	⊕⊖⊖⊖ very low[1,2]
Steroid use Follow-up: median 32 months	109 per 1000	284 per 1000 (96 to 842)	RR 2.6 (0.88 to 7.72)	198 (1 study)	⊕⊖⊖⊖ very low[1,2]

CI confidence interval; FSRT fractionated stereotactic radiotherapy; RR risk ratio; SRS stereotactic radiosurgery.
[1] Uncontrolled confounders (SRS had significantly smaller tumours than FSRT)
[2] Low event rates/low numbers of patients

Table 19: Summary clinical evidence profile for stereotactic radiosurgery (SRS) compared to intensity-modulated radiotherapy (IMRT) for patients with atypical meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	SRS	IMRT			
Progression-free survival Follow-up: median 32 months	Not estimable[1]	Not estimable[1]	RR 0.72 (CI not reported)[2]	71 (1 study)	⊕⊖⊖⊖ very low[3,4]

CI Confidence interval; IMRT intensity modulated radiotherapy; RR relative risk; SRS stereotactic radiosurgery.
[1] Event rate not reported
[2] P = 0.52
[3] Uncontrolled confounders (tumour volume not reported, and target volume only reported for SRS)
[4] Low event rates/low numbers of patients

Table 20: Summary clinical evidence profile for fractionated stereotactic radiotherapy (FSRT) compared to hypo-fractionated stereotactic radiotherapy (hFSRT) for patients with intracranial meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	FSRT	hFSRT			
Progression-free survival Follow-up: mean 35 months	Not estimable[1]	Not estimable[1]	Not estimable, but non-significant [2]	271 (1 study)	⊕⊖⊖⊖ **very low**[3,4]

CI: confidence interval; FSRT fractionated stereotactic radiotherapy; hFSRT hypo-fractionated stereotactic radiotherapy; RR: relative risk.
[1] Event rate not reported
[2] FSRT (3-year = 92.7%; 5-year = 88.9%; 10-year = 86.9%) = hFSRT (3-year = 92.4%; 5-year = 80.9%; 10-year = NA; p = 0.81)

[3] Uncontrolled confounders (tumour size not reported split by treatment group, but likely to differ between them)
[4] Low event rates/low numbers of patients

Table 21: Summary clinical evidence profile for stereotactic radiosurgery (SRS) compared to fractionated stereotactic radiotherapy (FSRT) for patients with intracranial meningioma

Outcomes	Illustrative comparative risks (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	FSRT	SRS			
Local control Follow-up: 23.8-40.6 months	972 per 1000	924 per 1000 (846 to 1000)	RR 0.95 (0.87 to 1.03)	135 (1 study)	⊕⊖⊖⊖ very low[1,2,3]

CI confidence interval; FSRT fractionated stereotactic radiotherapy; RR risk ratio; SRS stereotactic radiosurgery.
[1] Uncontrolled confounders (not many patient characteristics reported split by treatment group; tumour volume may differ between the groups)
[2] Low event rates/low numbers of patients
[3] Unequal lengths of follow up between the treatment groups (Mean (range) = 40.6 (6-125) months and 23.8 (6-72) months for SRS and FSRT respectively.)

Economic evidence

The economic evidence search identified no studies that met the inclusion criteria for this review.

Resource Impact

No unit costs were presented to the committee as these were not prioritised for decision making purposes.

Evidence statements

Stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with cavernous sinus meningioma

- Two observational studies (n=163) provided very low quality evidence that showed that disease-/progression-free survival and 'rate of radiation-induced malignancy' did not differ between patients treated with stereotactic radiosurgery and fractionated stereotactic radiotherapy. One observational study (n=89) provided very low quality evidence that showed that the risk of steroid use was significantly higher in patients treated with stereotactic radiosurgery compared to patients treated with fractionated stereotactic radiotherapy (RR = 4.93; 95% CI 1.89-12.87), but that the risk of cognitive/dysthymic improvement did not differ between these treatment groups (RR = 5.34; 95% CI 0.58-49.27).

Fractionated stereotactic radiotherapy versus hypo-fractionated stereotactic radiotherapy for patients with grade I meningioma

- One observational study (n=302) provided very low quality evidence that showed that local control and 'rate of radiation-induced malignancy' did not differ between patients treated with fractionated stereotactic radiotherapy and hypo-fractionated stereotactic radiotherapy.

Stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with basal meningioma

- One observational study (n=198) provided very low quality evidence that showed that the risk of progression-free survival (RR = 0.95; 95% CI 0.85-1.07) and steroid use (RR = 2.6; 95% CI 0.88-7.72) did not differ between patients treated with stereotactic radiosurgery and fractionated stereotactic radiotherapy.

Stereotactic radiosurgery versus intensity-modulated radiotherapy for patients with atypical meningioma

- One observational study (n=71) provided very low quality evidence that showed that the risk of progression-free survival did not differ between patients treated with stereotactic radiosurgery and intensity-modulated stereotactic radiotherapy (RR = 0.715; 95% CI not reported).

Fractionated stereotactic radiotherapy versus hypo-fractionated stereotactic radiotherapy for patients with intracranial meningioma

- One observational study (n=271) provided very low quality evidence that showed that progression-free survival did not differ between patients treated with fractionated stereotactic radiotherapy and hypo-fractionated stereotactic radiotherapy.

Stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with intracranial meningioma

- One observational study (n=135) provided very low quality evidence that showed that the risk of local control (RR = 0.95; 95% CI 0.87-1.03) did not differ between patients treated with stereotactic radiosurgery and fractionated stereotactic radiotherapy.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

For the review on who should receive radiotherapy, the committee indicated the following 4 outcomes as critical for decision making: overall survival, progression-free survival, cognitive function and neurological function. These were seen as direct measures of the success or failure of a treatment. The committee additionally indicated health-related quality of life and a variety of treatment-related morbidities were important but not critical outcomes, since these either directly or indirectly measure side-effects of treatment. Steroid use was classified by the committee as being of limited importance, since although it is important as a measure of treatment effectiveness the impact on quality of life is already captured.

For the review on radiotherapy techniques, the committee indicated the following outcomes as critical for decision making: progression-free survival/ local control, Karnofsky performance status and steroid use as they are particularly important treatment outcomes when considering radiotherapy specifically. The committee also indicated health-related quality of life, neurological function and cognitive function were important but not critical, as they can be either a direct or secondary effect of treatment, and therefore the evidence is harder to interpret consistently. Secondary malignancy is a possibility, but the committee only prioritised the outcomes as being of limited importance as the relationship between secondary malignancy and treatment was not clear.

The quality of the evidence

The evidence on who should receive radiotherapy consisted of 9 comparative observational studies, 6 of which were conducted in the USA, and 1 each in Sweden, Korea and Taiwan. The studies examined recurrence, survival and adverse events associated with subtotal resection with or without adjuvant radiotherapy for the following populations:

- patients with WHO grade I-III meningioma
- patients with atypical meningioma
- patients with WHO grade II atypical meningioma located in the skull base
- patients with benign meningioma
- patients with malignant meningioma
- patients with primary sphenoid wing meningioma
- patients with recurrent sphenoid wing
- patients with grade II meningioma (not otherwise specified).
- patients with intracranial meningioma involving the major venous sinus.

The evidence was of very low quality for all the outcomes examined in all these subpopulations. This was due to high risk of bias and imprecision (low event rates) in all cases.

The evidence on radiotherapy techniques consisted of 7 observational studies, 3 of which were conducted in the USA, 2 in Germany and 1 each in Brazil and France. Comparisons were included for:

- stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with cavernous sinus meningioma
- fractionated stereotactic radiotherapy versus hypo-fractionated stereotactic radiotherapy for patients with grade I meningioma
- stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with basal meningioma
- stereotactic radiosurgery versus intensity-modulated radiotherapy for patients with atypical meningioma
- fractionated stereotactic radiotherapy versus hypo-fractionated stereotactic radiotherapy for patients with intracranial meningioma
- stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with intracranial meningioma

The evidence was of very low quality for all the outcomes examined in all these subpopulations. This was due to high risk of bias and imprecision (low event rates) in all cases. The risk of bias was due to all the studies being observational, with some design limitations meaning that it was possible for the data to be systematically trending to one direction.

The committee determined that it was difficult to make judgements about who should receive radiotherapy and how this should be performed, as studies did not always report a range of techniques for each population or a range of populations for each technique. For example a study reporting outcomes for stereotactic radiosurgery versus fractionated stereotactic radiotherapy for patients with intracranial meningioma would not also have a corresponding study for grade II atypical meningioma located in the skull base, making it difficult to compare techniques. However the committee did decide it could make some recommendations on the basis of the evidence, and additionally highlight that some combinations of technique and population were extremely risky and should not be undertaken (on the basis of their knowledge and understanding of that type of tumour).

The committee determined that due to the lack of evidence, a research recommendation would be appropriate to inform future clinical practice. They selected an area on which there was a significant lack of evidence, no strong clinical consensus and the possibility of greatly improving the outcomes of people with meningioma if results of the research were clinically implemented.

Benefits and harms

Completely excised (Simpson 1 to 3) grade I, II and III

No evidence on the management of completely excised grade I, II and III meningioma was available, and so the committee made recommendations based on common clinical practice and their judgement. The recommendation to offer more radiotherapy is based on a judgement of whether the risk of tumour recurrence justifies the potential harms from further treatment.

Incompletely excised (Simpson 4 to 5) grade I

For some people, incomplete resection may be the only surgical option. This is usually due to the location of the tumour. The committee identified no evidence on which method of management was likely to be more effective, and so recommended all three possible methods be considered.

Incompletely excised (Simpson 4 to 5) grade II and III

Based on very low quality evidence showing significantly longer overall survival in people having radiotherapy following subtotal resection compared to the people having subtotal resection only, the committee recommended that people with an incompletely resected grade II and III meningioma should have further treatment within a short time frame because of the high risk of disease progression. Further surgical resection should be considered before immediate adjuvant radiotherapy if possible, since outcomes for incompletely resected meningioma are poor.

No excision (radiological only diagnosis) grade I, II and III

A meningioma may be inoperable because of its location, the person's co-existing conditions or because the person with the tumour does not consent to surgery. In this case histological diagnosis will not be available and consequently treatment decisions must be taken on the basis of radiological diagnosis only. Since surgery is impossible, a decision between active monitoring and radiotherapy must be taken. Active monitoring would be more suitable in people with a tumour appearing to be less risky (that is, more likely to be grade I). However there are factors which might suggest radiotherapy in this group, for example radiotherapy might be preferred:

- for people who have symptoms that the radiotherapy might improve (for example, if they have a cavernous sinus meningioma that is causing double-vision)
- if tumour growth would result in different treatment options in future (for example a small meningioma could be treated with SRS now, but if significant growth then it will be treated with IMRT or VMAT)
- if tumour growth would cause significant complications (for example, if the tumour is already close to the optic apparatus).

In people with a tumour appearing to be more risky (that is, more likely to be grade II or III), the benefits of radiotherapy begin to outweigh the side effects, and radiotherapy might be more suitable. However the committee explained this was not a universal rule; for example in people with very limited life expectancy it would not be clinically appropriate to offer

radiotherapy (as the increase in length of life would not be worth the quality of life implications of the side effects associated with radiotherapy).

Overall the committee was unable to suggest firm guidelines in this group.

Recurrent grade I

The committee recommended people with recurrent grade I meningioma should be offered further treatment of either further surgical resection or radiotherapy on the basis of very low quality evidence showing no difference in outcome between these two techniques. The committee identified no evidence that would justify picking one over the other, but explained that active monitoring could be extremely harmful for the person with the tumour, and so justified an 'offer' recommendation on the basis that clinicians should – in ordinary circumstances – not actively monitor the tumour if there is any possibility of active intervention.

Recurrent grade II and III

For people with recurrent grade II and grade III meningioma further surgical resection should be considered based on the experience of the committee, since grade II and III meningioma are so fast-growing that treatment is very important to prevent negative outcomes. Though there was evidence on radiotherapy applying to other groups of tumour and the committee was able to make a strong recommendation to offer this if possible (people will usually have had radiotherapy in the initial treatment of their meningioma and so radiotherapy may be dangerous to repeat) they did not have any evidence on the value of surgical treatment for a recurrent grade II or III meningioma and so made a cautious recommendation on the basis of their clinical experience and judgement.

Applying to all types of tumour

The committee used their knowledge and experience to make recommendations on the management of different kinds of tumour, as the available evidence was limited and very low quality. This was true for both the review on who should be offered radiotherapy and the review on how they should receive it. The evidence was frequently very low quality, but the committee justified certain strong recommendations based on the risk of clinical negligence if treatment was not offered. The details of the discussion linking the evidence to the recommendations is below under separate headings for each tumour type.

Based on their experience, the committee highlighted several factors which were important to take into account before considering radiotherapy. Because of the very low quality of the evidence it was difficult to link these factors to the evidence, so the committee chose to highlight factors which – in their experience – were most likely to result in a change of treatment technique or modality.

No evidence for selecting one radiotherapy technique over another for people with meningiomas was available, but the committee was aware from their background knowledge that keeping the exposure of healthy tissue to radiation as low as possible improved outcomes provided efforts to induce local control were otherwise equal. The committee was also aware from their experience that several treatments may be options depending on factors such as tumour size, location and the person's preference. The committee therefore recommended that the radiotherapy technique selected should be the one which provides the least dose of radiation to the normal brain and the rest of the body, to reduce the risk of side effects of treatment, subject to that technique being appropriate in all other ways.

Because of the complexity of treatment, the committee recommended that if the multidisciplinary team decides radiotherapy is a treatment option, the person with the tumour should have the opportunity to meet the oncologist to discuss this in full. This was based on their experience that people with tumours found such a meeting reassuring and valuable in planning their care.

The standard treatment for meningioma is surgery. Where this is not possible, radiotherapy or active monitoring might be considered. The committee was aware that in most cases the balance of benefits and harms was complex once surgery had been performed, or been found impossible to perform. In general, the benefits of intervening are that the tumour is shrunk or removed, which the committee expected to have a positive effect on the quality of life of the person. However the harm of intervening is that the person with the tumour is exposed to the side-effects of treatment. Once a decision has been made to treat, the balance of benefits and harms between radiotherapy and surgery (alone or in combination) is extremely complex and depends on characteristics of the tumour and the preferences of the person with the tumour. In general, the committee think the best balance of benefits and harms is accomplished when higher-grade tumours (grade II and III) are treated with robust intervention such as radiotherapy, while lower grade tumours (grade I) are treated only with less risky interventions such as active monitoring. The recommendations the committee made reflect the balance of this benefit and harm shifting for different tumour types; in completely excised tumours it is reasonable to actively monitor a higher grade tumour than for recurrent tumours, for example, on the basis of a balance of these benefits and harms.

The committee discussed how the 'best' radiotherapy technique to use depended heavily on individual circumstances, and there were circumstances in which most widely-practiced techniques would be the clinically optimal one to use. Nevertheless, they pointed out that certain techniques such as VMAT/IMRT were likely to be superior to other techniques such as 3D-conformal radiotherapy in most cases and therefore the recommendation to minimise dose to normal brain tissue might result in people with tumours being offered treatment at a centre a long way away from their home. The committee determined that this represented a good option for people with tumours (even if they did not choose to travel for treatment) and so the balance of benefits and harms greatly favoured selecting the technique which minimised radiation dose to the normal brain and the rest of the body.

Cost effectiveness and resource use

A literature review of published cost effectiveness analyses did not identify any relevant studies for this topic.

These recommendations are unlikely to lead to any change in resource use given that they are standard of care in most parts of England. They will lead to more consistent treatment in centres which are currently practicing differently to these recommendations. This is likely to be a small number of centres and it would be difficult to estimate the direction of any change in resource use although it would likely be small.

It is not currently standard practice in many centres in England to offer an oncologist appointment prior to receiving radiotherapy. For the vast majority of people this is likely to mean an earlier first appointment and no overall increase in the overall number of appointments. Even if appointments with an oncologist were to increase in some centres, through scheduling of additional appointments rather than rescheduling appointments, this number was likely be small and would not result in a significant resource impact.

Other factors the committee took into account

The committee described how there were many different machines on the market for delivering doses of radiotherapy. These machines have different physical characteristics which could affect a decision to recommend one type of treatment over another. For example, some machines are able to conform the radiotherapy dose more closely to the tumour than others and so minimise the dose to the normal brain and rest of the body which may reduce the risk of late effects of treatment such as secondary tumours. The committee did not see any evidence to recommend one machine over another in general, so did not make a recommendation on this. However the committee added that consideration of the

specific characteristics of the machine could form part of selecting the radiotherapy technique that lowers dose to normal tissue and so should not be overlooked.

The committee described how for higher-grade meningiomas the effectiveness of treatment decreased and they can regrow rapidly. Consequently, early referral to palliative care services should be considered. They made recommendations about this in the section titled 'Follow-up for meningioma'.

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Follow-up for meningioma

Follow-up for meningioma

Review question

What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?

Introduction

Currently there is a large variation in the frequency and content of follow-up protocols for meningioma. After treatment, meningioma will recur in some patients. Some meningiomas grow quickly, while others relapse many years (sometimes decades) after initial treatment. Slow-growing meningioma recurrences often do not cause symptoms until they are very large, which may limit the therapeutic options. MRI of the brain (or CT in those unable to have an MRI) can identify asymptomatic recurrence, but it is unclear if the identification of asymptomatic recurrence improves outcomes. Given that there are harms due to excess scanning there is a need to investigate how these resources can be best targeted.

PICO table

Table 22: Summary of the protocol (PICO table)

Population	People treated for meningioma
Intervention	Follow-up protocol including duration, and frequency of tests (e.g., MRI/CT scans)
Comparison	• Any other follow-up protocol • No follow up (wait until patient reports symptoms of recurrence)

Outcome	Critical:
	• treatment for recurrence
	• overall survival.
	• cognition
	• symptomatic versus asymptomatic presentation
	Important:
	• health-related quality of life
	  ○ neurological outcome
	  ○ seizures

MRI magnetic resonance imaging; CT computerised tomography.

For further details see the full review protocol in Appendix A.

Clinical evidence

Included studies

The clinical evidence search identified no studies that met the inclusion criteria for this review.

Excluded studies

Full-text studies not included in this review with reasons for their exclusions are provided in Appendix K.

Economic evidence

The economic evidence search identified no studies that met the inclusion criteria for this review.

Resource impact

Table 23: Resource impact and unit costs associated with follow-up for meningioma

Resource	Unit costs	Source
Follow-Up Appointment	£188	NHS reference costs 2015-16 (WF01A)
MRI Scan	£145	NHS reference costs 2015-16 (RD01A)

Evidence statements

No evidence was identified.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee designated 4 outcomes as critical. These were cognitive function, treatment for recurrence, overall survival and the numbers of patients with symptomatic versus asymptomatic presentation. As the committee was unsure whether identifying early progression of a tumour would be clinically beneficial, they identified these outcomes as the easiest to interpret, so that the benefit or harm of treatment would be most obvious on review.

Health-related quality of life was also important, although not critical as the committee agreed the link between recurrence and health-related quality of life was not as direct.

The quality of the evidence

The clinical evidence search identified no studies that met the inclusion criteria for this review.

The committee decided that since the question was so important and the evidence so limited that they would make weak recommendations to provide guidance for clinicians based on their clinical knowledge.

The committee determined that a research recommendation was important to standardise practice in this area. They determined that the major outstanding clinical question was how valuable early detection of recurrence was compared to later detection. This was true for all 3 questions on follow-up the committee looked at (for glioma, meningioma and brain metastases) but the committee elected to prioritise glioma as treatment options for recurrence as the evidence for management options of recurrent glioma was higher quality, so it was more likely that findings would influence clinical practice. Therefore the committee did not make a research recommendation on the follow-up of meningioma. See Evidence Report A for details on the recommendation they made on the follow-up of glioma.

Benefits and harms

On the basis of experience and judgement, the committee recommended clinical review of a person with meningioma as this might be useful to detect recurrence, based on changes in

the person's symptoms and function. Clinical assessment can also lead to intervention or onward referral, if indicated. This may improve a person's quality of life by alleviating symptoms or helping the person develop adaptive strategies. Although the committee identified no evidence that early detection of changes in clinical status could improve outcomes, they agreed that failing to detect a change had happened at all could have severely negative consequences for the person with a tumour. Consequently they made a strong recommendation for offering a review that could detect recurrence or other changes in clinical condition, but weaker recommendations on what should be in that review.

The committee identified no evidence on which to make recommendations about when to arrange regular clinical review. From reviews on the management of the tumour, however, the committee believed it had indirect evidence of factors that would make a recurrence more dangerous. Consequently they made a weak recommendation to consider the factors that could alter the urgency of the review. The recommendation on taking into account the person's preferences was made on the basis of the committee's experience.

While there was no evidence for or against the use of MRI or other scans to detect recurrence, the committee recommended that MRI scanning could be useful to detect recurrence on the basis that it is standard practice to do this already and that unstandardised MRI is not as useful as standard structural MRI. The committee explained how under certain circumstances not all of the sequence would be necessary, for example if the tumour had very well-defined characteristics which could be adequately monitored with only some of the suggested sequence. Consequently they made a weaker recommendation than for the equivalent sequence in the investigation of the tumour, because in the investigation of the tumour it is not yet known what characteristics the tumour will have and therefore clinicians cannot determine if there are any aspects of the sequence which can be left out whereas in the follow up there is more scope for the use of clinical judgement in determining which steps were necessary.

Based on their experience, the committee recommended that clinicians be aware that routine imaging (and waiting for the result) may cause anxiety. The committee made this recommendation because in their experience the potential harms of scanning very frequently were sometimes not appreciated by all clinicians.

The committee recommended clinical review in response to new or changing neurological symptoms (outside the usual schedule of scans). This is based on the fact that the purpose of routine follow-up is to identify changes to the tumour in order to treat these before they become symptomatic (if this is possible). New or changing symptoms likely mean that the tumour has grown between scans, and therefore waiting until the next routine scan could limit treatment options. In addition, the review would represent an opportunity for the clinician to discuss how the change might affect the risk of negative effects (such as infection and swelling). The committee discussed how they had not reviewed the evidence for how long a clinical review could be delayed in the case of new or changing symptoms and therefore could not specifically recommend a timeframe for review, but discussed how similar clinical considerations would apply in the case of a changing symptom as a new cancer referral and that therefore the timing might be related to that in practice.

The committee suggested a schedule of scans for a person with meningioma as a possible guide to discuss with the person with the tumour. Although there was no evidence the committee felt that consensus recommendations would be valuable to help standardise practice and reduce inequity from clinical variation, and suggested a follow-up schedule that could be used as a guide. Detail on the link between the committee's judgement and the recommendations is given below.

Example schedule for grade I meningioma

For WHO grade I meningiomas the committee recommended scanning intervals that fit with their slow growth, with a scan 3 months after surgery to look for any residual tumour. The

scan can also help decide which treatment options to use and if more frequent follow-up scans may be needed.

The committee noted that whether or not there was residual tumour was impossible to establish until after an initial scan. While both of these types of tumours are less hazardous than a grade II or III meningioma, residual tumour is more hazardous than no residual tumour, based on the committee's experience. Consequently the committee suggested more follow-up contacts in the case of residual tumour.

Example schedule for grade II meningioma

Based on experience the committee agreed grade II meningiomas have a higher risk of relapse so recommended monitoring be relatively frequent to identify recurrence. This is especially the case in the first 2-3 years for those treated with surgery alone based on the experience of the committee. The risk of relapse after 10 years is small, especially in people treated with radiotherapy, so continuation of monitoring may not be needed.

Example schedule for grade III meningioma

The committee agreed that people with grade III meningioma have a very high risk of relapse, similar to those with WHO grade IV glioma, so the suggested monitoring protocol should be as intensive as for a glioblastoma. This was based on their experience that grade III meningioma could recur and grow very quickly and so the best possible outcome for the person with the tumour would be to identify the tumour as early as possible.

Example schedule for asymptomatic incidental meningioma

Based on their clinical experience and judgement the committee recommended that people who have asymptomatic incidental tumours have an initial scan at 1 year to assess if the tumour has a high growth velocity. If it does not, factors such as the size of the tumour, location and overall life expectancy of the person as well as their preference should be taken into account to determine if the person can be discharged or have a further scan at 5 years to identify slowly growing tumours.

Applying to all types of meningioma

The committee agreed that the overall benefits of the recommendations would be that more people who have been treated for meningioma will have longer overall survival because more recurrences will be picked up while they are still asymptomatic (which is when recurrences are easiest to treat). However, the committee also recognised that scanning is associated with psychological stress and anxiety for some people. The committee discussed whether more frequent scanning would provoke or reduce anxiety in people with brain tumours, but reached no consensus as it might be different for different people – for example reassurance of regular contact versus anxiety induction of worrying results (especially results of uncertain significance). While there was no absolute balance to be struck – the actual balance in all cases should depend on individual factors to do with the person – the committee believe their suggested follow-up schedule is a useful guide to balancing these benefits and harms.

Cost effectiveness and resource use

A literature review of published cost effectiveness analyses did not identify any relevant studies for this topic.

The committee believed these recommendations to be in line with current practice nationally and therefore did not think they would lead to any significant change in practice. The committee acknowledged that a small number of centres may not be using a follow up protocol similar or identical to the schedule recommended, and in these centres increased follow-up imaging and some service reconfiguration may be needed if the centre wishes to

implement this schedule. This would lead to increased costs and resource use although given the small number of centres this is unlikely to be significant. These additional cost may also be somewhat offset by quicker identification of recurrence and resultantly more effective treatment leading to reduced costs of treating adverse events.

Other factors the committee took into account

The committee decided against recommending advanced MRI scanning techniques for people with meningioma as these techniques are rarely used currently in this group and there was no evidence to support a change in practice. In the vast majority of cases, standard structural MRI can be used to make a diagnosis with a high degree of confidence. The committee was aware that MR spectroscopy may occasionally be useful to distinguish meningioma from other types of tumour.

The committee recognised that if the recommendations meant that follow-up scans had to be undertaken during the weekend then this would incur an additional cost. The committee therefore decided to use ranges of time for scanning that were at least 3 days long in order to ensure that weekend scanning could be minimised.

The committee also discussed that people with physical disabilities might find it difficult to attend very frequent scanning, and that consideration should therefore be given to alternative modalities of assessment for these people. They did not make a specific recommendation on this point as the types of physical disability experienced by people with brain tumours were very variable, and in not referring specifically to disability the committee believed they would make it clear that all people with tumours should be offered appropriate follow up, regardless of the presence of a disability.

References

The clinical evidence search identified no studies that met the inclusion criteria for this review.

Appendices

Appendix A – Review protocols

Review protocol for review 1a - imaging for suspected glioma and meningioma

Field (based on PRISMA-P)	Content
Key area in the scope	Diagnosing radiologically identified glioma, meningioma and brain metastases.
Actual review question	What is the most effective imaging strategy in newly diagnosed glioma and meningioma?
Type of review question	Diagnostic
Objective of the review	The purpose of this review is to identify the diagnostic accuracy of advanced MRI, PET-CT and PET-MRI for the characterisation of radiologically suspected glioma and meningioma in addition to standard MRI
Eligibility criteria – **population**/disease/condition/issue/domain	Adults with a radiologically (by CT scan or MRI scan) suspected glioma (high- or low-grade) or meningioma

Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)/ Index test	Standard MRI alone:
	• standard structured MRI (core protocol) +/- contrast (T1 pre and post contrast and T2)
	
	Standard MRI plus one of the following advanced tests:
	• advanced MRI:
	  ○ MR Spectroscopy (chemical shift imaging)
	  ○ diffusion imaging (DWI/DTI) tensor imaging (DTI)
	  ○ perfusion imaging (DSC, DCE, ASL will not be looked at separately)
	  ○ structural imaging
	
	• PET-CT (including FDG: FET, MET, Choline-PET)
	• PET-MRI (including FDG: FET, MET, Choline-PET)

Field (based on PRISMA-P)	Content
Eligibility criteria – **comparator(s)**/control or reference (gold) standard	• Pathology (histology and, where appropriate molecular testing) or clinical /radiological follow-up if there is not biopsy

Outcomes and prioritisation	Critical:
	• health-related quality of life (especially anxiety)
	• diagnostic accuracy, including:
	  ○ sensitivity
	  ○ specificity
	  ○ likelihood ratios
	For:
	• meningioma versus meningioma absent
	• high-grade glioma (WHO grade III and IV) versus high–grade glioma absent
	• low-grade glioma (WHO grade I and II) versus low-grade glioma absent

Eligibility criteria – **study design**	• Only published full text English language papers • Studies published from the year 2002 as it was when Standard structured MRI (core protocol) +/- contrast (T1 pre and post contrast and T2) was first used **Study design:** • cross-sectional studies (>20) • prospective comparative cohort studies (>20) • retrospective comparative cohort studies (>20) • nested case control (1 gate) studies (>20) Indirect comparisons will be considered, although direct comparisons will be preferred
Other **exclusion criteria**	• Recurrent meningioma, low-grade glioma or high-grade glioma • Children and young people (under 16 years old)

Field (based on PRISMA-P)	Content
	The following list of tumour types: ○ neuronal and mixed neuronal-glial tumours ○ tumours of the pineal region ○ embryonal tumours ○ tumours of the cranial and paraspinal nerves ○ melanocytic tumours ○ lymphomas ○ mesenchymal, histiocytic, germ cell, sellar originating and choroid plexus tumours. ○ brain metastases
Proposed sensitivity/**sub-group analysis**, or meta-regression	Stratification: • suspected low-grade glioma • suspected high-grade glioma (grade III or IV) • suspected meningioma • axial versus volume imaging
Selection process – duplicate screening/selection/analysis	Duplicate screening/selection/analysis will not be undertaken for this review as it was not prioritised for it. Included and excluded studies will be cross checked with the committee and with published systematic reviews when available.
Data management (software)	Pairwise meta-analyses were performed using STATA (statistical software). STAR will be used bibliographies/citations, text mining, and study sifting, data extraction and quality assessment/critical appraisal.
Information sources – databases and dates	See Appendix B for full list of databases. Sources to be searched: Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase Limits (e.g. date, study design): Limit to English language only (Medline and Embase). Limit to RCTs and systematic reviews and observational studies unless overall return is small Supplementary search techniques: No supplementary search techniques were used

Field (based on PRISMA-P)	Content
	Key papers: 1. Gliomas: Predicting Time to Progression or Survival with Cerebral Blood Volume Measurements at Dynamic Susceptibility-weighted Contrast-enhanced Perfusion MR Imaging. Meng Law, Robert J. Young, James S. Babb, Nicole Peccerelli, Sophie Chheang, Michael L. Gruber, Douglas C. Miller, John G. Golfinos, David Zagzag, and Glyn Johnson. Radiology 2008 247:2, 490-498 2. Multimodal MRI in the characterization of glial neoplasms: the combined role of single-voxel MR spectroscopy, diffusion imaging and echo-planar perfusion imaging. Zonari, P., Baraldi, P. & Crisi, G. Neuroradiology (2007) 49: 795. doi:10.1007/s00234-007-0253-x Cut-off date: 2002 as it was when Standard structured MRI (core protocol) +/- contrast (T1 pre and post contrast and T2) was first used
Identify if an update	Not an update
Author contacts	Developer: National Guideline Alliance (NGA-enquiries@rcog.org.uk)
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	See Appendix B for full list of databases.
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as Supplementary Material D.
Data items – define all variables to be collected	For details please see evidence tables in Supplementary Material D.
Methods for assessing bias at outcome/study level	Appraisal of methodological quality: The methodological quality of each study will be assessed using the following checklist: • QUADAS -II
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	The quality of the evidence for an outcome (i.e. across studies) will be assessed using QUADAS –II. Synthesis of data: Meta-analysis will be conducted where appropriate. Minimally important differences:

Field (based on PRISMA-P)	Content
	Default values will be used of: 0.8 and 1.25 for dichotomous outcomes; 0.5 times SD for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature. Data extraction and methodological quality assessment: Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer. Dual extraction and quality assessment was not performed for this review, as it was not prioritised for dual extraction, This was because the evidence base was complex, and required support from the committee, which served the same function as dual extraction and quality assessment.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review in the full guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and membership is given in Supplementary Material B in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see Supplementary Material C.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered in PROSPERO

ASL arterial spin labelling; CT computer tomography; DCE dynamic contrast-enhancement; DSC dynamic susceptibility contrast; DTI diffusion tensor imaging; DWI diffusion weighted imaging; FDG 2-deoxy-2-(18)fluoro-D-glucose; FET (18)F-fluoro-ethyl-l-tyrosine; MET (11)C-methionine; MR magnetic resonance; MRI magnetic resonance imaging; PET-CT positron emission tomography - computed tomography; PET-MRI magnetic resonance imaging - magnetic resonance imaging; QoL quality of life; RCT randomised control trial; SD standard deviation; WHO World Health Organization.

1 Review protocol for review 3a - managing inoperable, incompletely excised or recurrent meningioma

Field (based on PRISMA-P)	Content
Key area in the scope	Managing meningioma
Actual review question	Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?
Type of review question	Intervention
Objective of the review	Surgery is the well-established first-line treatment for most meningioma. If surgery is impossible to perform, or surgery is performed and the meningioma reoccurs, management is more complex. This review aims to identify which tumours can be treated with radiotherapy in this case.
Eligibility criteria – **population**/disease/condition/issue/domain	People with inoperable, incompletely excised meningioma or recurrent meningioma.
Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)	• Active monitoring alone • Radiotherapy • Active monitoring followed by radiotherapy • Surgery (for those with recurrence)
Eligibility criteria – **comparator(s)**/control or reference (gold) standard	The comparisons accepted for this review are any intervention versus any other intervention, except surgery versus active monitoring.

Outcomes and prioritisation	Critical:
	• overall survival.
	• progression-free survival
	• cognitive function
	• neurological function:
	  ○ cranial neuropathy (e.g. optic neuropathy)
	Important:
	• treatment-related morbidity:
	  ○ radionecrosis
	  ○ oedema
	  ○ stroke

Field (based on PRISMA-P)	Content
	○ second malignancy ○ pituitary dysfunction ○ epilepsy/ seizures • health-related quality of life Of limited importance: steroid use
Eligibility criteria – **study design**	Only published full text papers Systematic reviews RCTs Cohort or observational studies where RCTs are not available No size or date limits
Other inclusion **exclusion criteria**	• meningioma located elsewhere outside of brain • neurofibromatosis • radio-induced meningioma • children and young people (up to age 15)
Proposed sensitivity/**sub-group analysis**, or meta-regression	Results must be stratified in the following way or should be rejected on the grounds of too heterogeneous a population: Inoperable tumours should be stratified by location, which must be one of either: • Location: ○ anterior skull base (optic nerve/ cavernous sinus) ○ convexity and falx ○ other (not specified) Incompletely excised, recurrent and mixed-population tumours should be stratified by location and WHO grade: • Location: ○ anterior skull base (optic nerve/ cavernous sinus) ○ convexity and falx

Field (based on PRISMA-P)	Content
	○ other (not specified) • WHO Grade: ○ WHO Grade I ○ WHO Grade II ○ WHO Grade III
Selection process – duplicate screening/selection/analysis	Owing to high stakeholder interest in this question, a complete duplicate review was undertaken where both reviewers reviewed and extracted all papers. In addition to this formal method of validation, the excluded study list is checked by the committee prior to making recommendations.
Data management (software)	If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADEpro' will be used to assess the quality of evidence for each outcome. STAR will be used for bibliographies/citations and study sifting. Microsoft Word will be used for data extraction and quality assessment/critical appraisal
Information sources – databases and dates	See Appendix B for full details Sources to be searched: Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase Limits (e.g. date, study design): Limit to English language only (Medline and Embase). Limit to RCTs and systematic reviews and observational studies unless overall return is small Supplementary search techniques: No supplementary search techniques were used
Identify if an update	Not an update
Author contacts	Developer: National Guideline Alliance (NGA-enquiries@rcog.org.uk)
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see Appendix B

Field (based on PRISMA-P)	Content
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as Supplementary Material D.
Data items – define all variables to be collected	For details please see evidence tables in Supplementary Material D.
Methods for assessing bias at outcome/study level	Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: • ROBIS for systematic reviews • Cochrane risk of bias tool for randomised studies • Cochrane risk of bias tool for non-randomised studies For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence will 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
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	For details please see the methods chapter of the full guideline
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review in the full guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and membership is given in Supplementary Material B in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see Supplementary Material C.
Sources of funding/support	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The NGA is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists

Field (based on PRISMA-P)	Content
Roles of sponsor	NICE funds the NGA to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered in PROSPERO

1 Review protocol for review 3b – techniques for radiotherapy for meningioma

Field (based on PRISMA-P)	Content
Key area in the scope	Managing meningioma
Actual review question	Which technique should be used for adults with meningioma who require radiotherapy?
Type of review question	Intervention
Objective of the review	Though many meningioma can be successfully treated with surgery others require radiotherapy, either following surgery or as sole modality of treatment or at recurrence. Over the past twenty years many new radiotherapy techniques have been developed which have the potential to improve the effectiveness and reduce toxicity, especially late-effects. Therefore it would be helpful for clinical teams and patients to have an evaluation of the data to help selection of the optimal therapeutic option.
Eligibility criteria – **population**/disease/condition/issue/domain	Adults with meningioma (not just recurrent meningioma) requiring/suitable for radiotherapy.
Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)	• Conventionally fractionated 3D conformal radiotherapy • Conventionally fractionated IMRT/VMAT • Radiosurgery (1 fraction) • Stereotactic radiotherapy (2-5 fractions/hypofractionated) • Fractionated stereotactic radiotherapy (greater than 5 fractions) • Proton beam and other particle therapies
Eligibility criteria – **comparator(s)**/control or reference (gold) standard	• Each other • Combinations of interventions not possible Main comparisons to focus on: • Fractionated radiotherapy: 1 fraction v 2-20 fractions v 21-35 fractions • 3D CRT v FSRT v IMRT/VMAT v proton/particle
Outcomes and prioritisation	Preliminary classification of the outcomes for decision making:

Field (based on PRISMA-P)	Content

	• Critical:
	  ○ progression-free survival/ local control
	  ○ Karnofsky Performance status
	  ○ steroid (for example dexamethasone) use (duration and dose)
	• Important but not critical:
	  ○ health-related quality of life
	  ○ neurological Function Scale
	  ○ cognitive function
	• of limited importance:
	  ○ second malignancy

Eligibility criteria – **study design**	Only published full text papers Systematic reviews RCTs Comparative cohort (30 per arm) where RCTs are not available
Other inclusion **exclusion criteria**	Only studies including patients treated from 1985 onwards (due to radiotherapy technique advances after 1985 compared to before; treatment before 1985 not comparable to current RT treatment techniques).

Proposed sensitivity/**sub-group analysis**, or meta-regression	• Tumour size/volume
	• Tumour Grade 1 versus 2 versus 3
	• Anatomical tumour location:
	  ○ optic nerve
	  ○ cavernous sinus
	  ○ convexity and falx

Selection process – duplicate screening/selection/analysis	No duplicate screening/selection/analysis will be undertaken for this review as the topic is so technically complex that the clinical advisor is required to support the reviewer, and is therefore judged to be performing the quality assurance function of a conventional dual sift.

Field (based on PRISMA-P)	Content
	In order to ensure accuracy, all results are checked by a Senior Systematic Reviewer and the excluded study list is checked by the committee prior to making recommendations.
Data management (software)	If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADEpro' will be used to assess the quality of evidence for each outcome. STAR will be used for bibliographies/citations and study sifting. Microsoft Word will be used for data extraction and quality assessment/critical appraisal
Information sources – databases and dates	See Appendix B for details Sources to be searched: Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase Only studies including patients treated from 1985 onwards (due to radiotherapy technique advances after 1985 compared to before; treatment before 1985 not comparable to current RT treatment techniques). Limit to English language only (Medline and Embase). Limit to RCTs and systematic reviews and observational studies unless overall return is small Supplementary search techniques: No supplementary search techniques were used Key papers: • Litre et al Int J Rad Oncol Biol Phys 2009: 74 1012-1017 (on radiotherapy) • Santacroce A et al Neurosurgery 2012 :70 32-39 (on SRS)
Identify if an update	Not an update
Author contacts	Developer: National Guideline Alliance (NGA-enquiries@rcog.org.uk)
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see Appendix B of the full evidence review
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as Supplementary Material D
Data items – define all variables to be collected	For details please see evidence tables in Supplementary Material D
Methods for assessing bias at outcome/study level	Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist:

Field (based on PRISMA-P)	Content
	• ROBIS for systematic reviews • Cochrane risk of bias tool for randomised studies • Cochrane risk of bias tool for non-randomised studies For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence will 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
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	Synthesis of data: Meta-analysis will be conducted where appropriate using Review Manager. Minimally important differences Default values will be used of: 0.8 and 1.2 for dichotomous outcomes; 0.5 times SD for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review in the full evidence review/guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and membership is given in Supplementary Material B in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see Supplementary Material C.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists

Field (based on PRISMA-P)	Content
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered in PROSPERO

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2 **Review protocol for review 5b – follow-up for meningioma**

3

Field (based on PRISMA-P)	Content
Key area in the scope	Follow-up care after treatment for glioma, meningioma or brain metastases
Actual review question	5b – What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?
Type of review question	Intervention
Objective of the review	After treatment for meningioma some patients will recur. The speed of recurrence varies, some meningiomas grow quickly, others relapse many years, sometimes decades, after initial treatment. Slow growing meningioma recurrences often do not cause symptoms until they are very large which then limits the therapeutic options. MRI imaging of the brain (or CT in those unable to have MRI scan) identifies asymptomatic recurrence. Scanning routinely has costs to healthcare resources, patient time and potentially psychological health as well as excess radiation in those imaged with CT scan. However it is unclear if the identification of asymptomatic recurrence improves outcomes. Similarly, if routine imaging is recommended, the frequency and duration of scanning is also uncertain.
Eligibility criteria – **population**/disease/condition/issue/domain	Adults treated for meningioma (surgically or non-surgically)
Eligibility criteria – **intervention**(s)/exposure(s)/prognostic factor(s)	Any follow-up protocol including duration and frequency of any tests (e.g., MRI/CT scans)
Eligibility criteria – **comparator(s)**/control or reference (gold) standard	• Any other follow-up protocol • No follow up (wait until patient reports symptoms of recurrence)
Outcomes and prioritisation	Critical:

Field (based on PRISMA-P)	Content
	• cognitive function, • treatment for recurrence • overall survival, • numbers of patients with symptomatic versus asymptomatic presentation Important: • health-related quality of life
Eligibility criteria – **study design**	Only published full text papers Systematic reviews RCTs Comparative observational studies
Other inclusion **exclusion criteria**	We will include papers that have more than 90% of patients who have been treated for meningioma
Proposed sensitivity/**sub-group analysis**, or meta-regression	Adults treated for/after: • WHO grade I versus WHO grade II/III • initial treatment and after recurrence • Simpson grade 1/2 resection v > grade 2 resection Treatment with surgery versus radiotherapy/stereotactic radiosurgery versus both • radio-induced meningioma
Selection process – duplicate screening/selection/analysis	No duplicate screening/selection/analysis will be undertaken for this review as the topic is so technically complex that the clinical advisor is required to support the reviewer, and is therefore judged to be performing the quality assurance function of a conventional dual sift.
Data management (software)	If pairwise meta-analyses undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADEpro' will be used to assess the quality of evidence for each outcome.

Field (based on PRISMA-P)	Content
	STAR will be used for bibliographies/citations and study sifting. Microsoft Word will be used for data extraction and quality assessment/critical appraisal
Information sources – databases and dates	See Appendix B. Sources to be searched: Medline, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Cochrane Database of Abstracts of Reviews of Effectiveness, Health Technology Database, Embase Limits (e.g. date, study design): Limit to English language only (Medline and Embase). Limit to RCTs and systematic reviews and cohort studies unless overall return is small Date limit: 1990 (CT/MRI not available/comparable to present time before 1990) Supplementary search techniques: No supplementary search techniques were used
Identify if an update	Not an update
Author contacts	Developer: National Guideline Alliance (NGA-enquiries@rcog.org.uk)
Highlight if amendment to previous protocol	NA
Search strategy – for one database	For details please see Appendix B of the full evidence review
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as Supplementary Material D
Data items – define all variables to be collected	For details please see evidence tables in Supplementary Material D
Methods for assessing bias at outcome/study level	Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: • ROBIS for systematic reviews • Cochrane risk of bias tool for randomised studies • Cochrane risk of bias tool for non-randomised studies For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence will 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

Field (based on PRISMA-P)	Content
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual
Methods for quantitative analysis – combining studies and exploring (in)consistency	Synthesis of data: Meta-analysis will be conducted where appropriate using Review Manager. Minimally important differences Default values will be used of: 0.8 and 1.2 for dichotomous outcomes; 0.5 times SD for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature.
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual. No evidence was identified. No explorations of publication bias were therefore undertaken.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review in the full evidence review/guideline.
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and membership is given in Supplementary Material B in line with section 3 of Developing NICE guidelines: the manual. Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see Supplementary Material C.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered in PROSPERO

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Appendix B – Literature search strategies

Search strategy for review 1a - imaging for suspected glioma and meningioma

Date of initial search: 30/03/2017

Database: Embase 1974 to 2017 March 29, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Date of re-run: 05/09/2017
Database: Embase 1974 to 2017 Week 35, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	exp glioma/ or exp astrocytoma/ or oligodendroglioma/
2	exp Glioblastoma/
3	1 or 2 use ppez
4	exp glioma/ use oemezd or exp astrocytoma/ use oemezd
5	(glioma* or glioblastoma* or GBM or gliosarcoma* or astrocytoma* or oligoastrocytoma* or oligodendroglioma* or oligo?astrocytoma* or xanthoastrocytoma*).tw.
6	or/3-5
7	Meningioma/ use ppez
8	Meningeal Neoplasms/ use ppez
9	exp meningioma/ use oemezd
10	meningioma*.tw.
11	(mening* adj3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*)).tw.
12	or/7-11
13	6 or 12
14	Diagnostic Imaging/ use ppez
15	diagnostic imaging/ use oemezd
16	exp Neuroimaging/ use ppez
17	exp neuroimaging/ use oemezd
18	Multimodal Imaging/ use ppez
19	multimodal imaging/ use oemezd
20	Radionuclide Imaging/ use ppez
21	exp brain scintiscanning/ use oemezd
22	Perfusion Imaging/ use ppez
23	Neuronal Tract-Tracers/ use ppez
24	neuronal tract tracer/ use oemezd
25	exp Magnetic Resonance Imaging/ use ppez
26	exp nuclear magnetic resonance imaging/ use oemezd
27	Diffusion Magnetic Resonance Imaging/ use ppez
28	exp Magnetic Resonance Spectroscopy/ use ppez
29	proton nuclear magnetic resonance/ use oemezd
30	magnetic resonance.tw.
31	(MRI or MR*1 or NMR*1).tw.
32	(MR adj2 (imag* or neuroimag* or scan* or spectroscop* or elastogra* or examination)).tw.
33	(magnet* adj2 (imag* or neuroimag* or spectroscop* or scan* or elastogra* or examination)).tw.
34	(magneti?ation adj2 imaging).tw.
35	exp Positron-Emission Tomography/ use ppez
36	positron emission tomography/ use oemezd
37	computer assisted emission tomography/ use oemezd
38	(PET adj (scan* or imag* or examination)).tw.
39	positron emission tomogra*.tw.
40	(PET or PET-CT or PETCT or PET MR*1).tw.
41	(spin adj2 (imag* or neuroimag* or spectroscop* or resonance)).tw.
42	(advanced adj2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*)).tw.
43	(chemical shift adj2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*)).tw.
44	(structural adj2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*)).tw.

#	Searches
45	(functional adj2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*)).tw.
46	(diffusion adj2 (imag* or spectroscop* or tractogra* or neuroimag* or scan* or MR* or NMR*)).tw.
47	(perfusion adj2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR* or CT)).tw.
48	((axial or transverse) adj2 (imag* or neuroimag* or scan* or CT or tomogra*)).tw.
49	(T1W*1 or T2W*1).tw.
50	((T1 or T2) adj2 (imag* or neuroimag* or scan* or MR* or NMR*)).tw.
51	(DWI or DTI or DSC or DCE or ASL).tw.
52	exp nuclear magnetic resonance imaging agent/ use oemezd
53	dynamic contrast.tw.
54	Fluorodeoxyglucose F18/ use ppez
55	fluorodeoxyglucose f 18/ use oemezd
56	("18F fluorodeoxyglucose" or FDG).tw.
57	Tyrosine/ use ppez
58	"18F fluoro ethyl tyrosine".tw.
59	18F FET.tw.
60	Methionine/ use ppez
61	methionine c 11/ use oemezd
62	((11C or "carbon 11") adj methionine).tw.
63	MET PET.tw.
64	Gadolinium DTPA/ use ppez
65	gadolinium pentetate/ use oemezd
66	gadolinium.tw.
67	or/14-66
68	13 and 67
69	limit 68 to english language
70	limit 69 to yr="2002-Current"
71	Letter/ use ppez
72	letter.pt. or letter/ use oemezd
73	note.pt.
74	editorial.pt.
75	Editorial/ use ppez
76	News/ use ppez
77	exp Historical Article/ use ppez
78	Anecdotes as Topic/ use ppez
79	Comment/ use ppez
80	Case Report/ use ppez
81	case report/ or case study/ use oemezd
82	(letter or comment*).ti.
83	or/71-82
84	randomized controlled trial/ use ppez
85	randomized controlled trial/ use oemezd
86	random*.ti,ab.
87	or/84-86
88	83 not 87
89	animals/ not humans/ use ppez
90	animal/ not human/ use oemezd
91	nonhuman/ use oemezd
92	exp Animals, Laboratory/ use ppez
93	exp Animal Experimentation/ use ppez
94	exp Animal Experiment/ use oemezd
95	exp Experimental Animal/ use oemezd
96	exp Models, Animal/ use ppez
97	animal model/ use oemezd
98	exp Rodentia/ use ppez
99	exp Rodent/ use oemezd
100	(rat or rats or mouse or mice).ti.
101	or/88-100
102	70 not 101
103	Meta-Analysis/
104	Meta-Analysis as Topic/
105	systematic review/
106	meta-analysis/
107	(meta analy* or metanaly* or metaanaly*).ti,ab.
108	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
109	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
110	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
111	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
112	(search* adj4 literature).ab.

#	Searches
113	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
114	cochrane.jw.
115	((pool* or combined) adj2 (data or trials or studies or results)).ab.
116	or/103-104,107,109-114 use ppez
117	or/105-108,110-115 use oemezd
118	or/116-117
119	clinical Trials as topic.sh. or (controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or (placebo or randomi#ed or randomly).ab. or trial.ti.
120	119 use ppez
121	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
122	121 use ppez
123	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
124	123 use oemezd
125	120 or 122
126	124 or 125
127	Epidemiologic Studies/
128	Case Control Studies/
129	Retrospective Studies/
130	Cohort Studies/
131	Longitudinal Studies/
132	Follow-Up Studies/
133	Prospective Studies/
134	Cross-Sectional Studies/
135	or/127-134 use ppez
136	clinical study/
137	case control study/
138	family study/
139	longitudinal study/
140	retrospective study/
141	prospective study/
142	cohort analysis/
143	or/136-142 use oemezd
144	((retrospective$ or cohort$ or longitudinal or follow?up or prospective or cross section$) adj3 (stud$ or research or analys$)).ti.
145	135 or 143 or 144
146	118 or 126 or 145
147	102 and 146
148	remove duplicates from 147

Date of initial search: 05/07/2017

Database: The Cochrane Library, Issue 3 of 12, March 2017

Date of re-run: 05/09/2017

Database: The Cochrane Library, Issue 9 of 12, September 2017

ID	Search
#1	MeSH descriptor: [Glioma] explode all trees
#2	(glioma* or glioblastoma* or gliosarcoma* or astrocytoma* or astroblastoma* or oligodendroglioma* or oligodendrocytoma* or oligoastrocytoma* or GBM)
#3	(glial near/3 (neoplas* or cancer* or tumo* or carcin* or malign* or metasta*))
#4	{or #1-#3}
#5	MeSH descriptor: [Meningioma] explode all trees
#6	MeSH descriptor: [Meningeal Neoplasms] explode all trees
#7	meningioma*
#8	(mening* near/3 (neoplas* or cancer* or carcin* or tumo* or malign* or metasta*))
#9	{or #5-#8}
#10	#4 or #9
#11	MeSH descriptor: [Diagnostic Imaging] this term only
#12	MeSH descriptor: [Neuroimaging] explode all trees

ID	Search
#13	MeSH descriptor: [Multimodal Imaging] explode all trees
#14	MeSH descriptor: [Radionuclide Imaging] this term only
#15	MeSH descriptor: [Perfusion Imaging] explode all trees
#16	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#17	MeSH descriptor: [Diffusion Magnetic Resonance Imaging] explode all trees
#18	MeSH descriptor: [Magnetic Resonance Spectroscopy] explode all trees
#19	(MRI or MR*1 or NMR*1)
#20	(MR near/2 (imag* or neuroimag* or scan* or spectroscop* or elastogra* or examination))
#21	(magnet* near/2 (imag* or neuroimag* or spectroscop* or scan* or elastogra* or examination))
#22	(magneti?ation near/2 imaging)
#23	MeSH descriptor: [Positron-Emission Tomography] explode all trees
#24	(PET near (scan* or imag* or examination))
#25	positron emission tomogra*
#26	(PET or PET-CT or PETCT or PET MR*1)
#27	MeSH descriptor: [Spin Labels] explode all trees
#28	(spin near/2 (imag* or neuroimag* or spectroscop* or resonance))
#29	(advanced near/2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*))
#30	(chemical shift near/2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*))
#31	(structural near/2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*))
#32	(functional near/2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR*))
#33	(diffusion near/2 (imag* or spectroscop* or tractogra* or neuroimag* or scan* or MR* or NMR*))
#34	(perfusion near/2 (imag* or spectroscop* or neuroimag* or scan* or MR* or NMR* or CT))
#35	((axial or transverse) near/2 (imag* or neuroimag* or scan* or CT or tomogra*))
#36	(T1W*1 or T2W*1)
#37	((T1 or T2) near/2 (imag* or neuroimag* or scan* or MR* or NMR*))
#38	(DWI or DTI or DSC or DCE or ASL)
#39	dynamic contrast
#40	MeSH descriptor: [Fluorodeoxyglucose F18] explode all trees
#41	("18F fluorodeoxyglucose" or FDG)
#42	MeSH descriptor: [Tyrosine] this term only
#43	"18F fluoro ethyl tyrosine"
#44	18F FET
#45	MeSH descriptor: [Methionine] this term only
#46	((11C or "carbon 11") and methionine)
#47	MET PET
#48	MeSH descriptor: [Gadolinium DTPA] this term only
#49	gadolinium
#50	{or #11-#49}
#51	#10 and #50

Search strategy for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Date of initial search: 11/10/2016

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Date of re-run: 05/09/2017

Database: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	Meningioma/
2	Meningeal Neoplasms/
3	meningioma*.tw.
4	(mening* adj3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*)).tw.
5	or/1-4
6	exp radiotherapy/
7	radiotherapy.fs.
8	(radiotherap* or radiat* or irradiat* or tomotherap* or radiosurg* or brachytherap* or fractionat* or hyperfraction* or hypofraction* or gamma knife or cyber knife or cyberknife or xknife or arc therap*).tw.

#	Searches
9	(WBRT or WBI-IMRT or HA-WBRT or LINAC or IMRT or XRT or XBT or SRS or SRT or VMAT or 3DCRT or 3D CRT or CRT).tw.
10	Radiation Oncology/
11	(chemoradiotherap* or chemo-radiat* or chemo-irradiat*).tw.
12	or/6-11
13	Watchful Waiting/
14	Observation/
15	watchful wait*.tw.
16	((active or expect* or symptom* or watch*) adj2 (manag* or monitor* or surveill* or observ* or control*)).tw.
17	(best supportive care or BSC).tw.
18	or/13-17
19	12 and 18
20	Neurosurgery/
21	exp Neurosurgical Procedures/
22	Surgical Procedures, Operative/
23	exp Stereotaxic Techniques/
24	surgery.fs.
25	((brain or neuro* or intracereb* or intracrani* or crani*) adj2 (surg* or microsurg* or manipulat* or procedur* or operat* or resect* or debulk* or excis* or ablat* or biops*)).tw.
26	(neurosurg* or craniotom* or craniectom*).tw.
27	((intra-operat* or intraoperat*) adj3 (technolog* or modalit* or procedur* or technique* or method*)).tw.
28	or/20-27
29	Neoplasm Recurrence, Local/
30	recur*.tw.
31	29 or 30
32	28 and 31
33	12 or 18 or 19 or 32
34	5 and 33
35	limit 34 to english language
36	Epidemiologic Studies/
37	Case Control Studies/
38	Retrospective Studies/
39	Cohort Studies/
40	Longitudinal Studies/
41	Follow-Up Studies/
42	Prospective Studies/
43	Cross-Sectional Studies/
44	((retrospective$ or cohort$ or longitudinal or follow?up or prospective or cross section$) adj3 (stud$ or research or analys$)).ti.
45	or/36-44
46	Meta-Analysis/
47	Meta-Analysis as Topic/
48	(meta analy* or metanaly* or metaanaly*).ti,ab.
49	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
50	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
51	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
52	(search* adj4 literature).ab.
53	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
54	cochrane.jw.
55	or/46-54
56	randomized controlled trial.pt.
57	controlled clinical trial.pt.
58	pragmatic clinical trial.pt.
59	randomi#ed.ab.
60	placebo.ab.
61	drug therapy.fs.
62	randomly.ab.
63	trial.ab.
64	groups.ab.
65	or/56-64
66	Clinical Trials as topic.sh.
67	trial.ti.
68	or/56-60,62,66-67
69	45 or 55 or 68
70	35 and 69
71	Letter/
72	Editorial/
73	News/

#	Searches
74	exp Historical Article/
75	Anecdotes as Topic/
76	Comment/
77	Case Report/
78	(letter or comment* or abstracts).ti.
79	or/71-78
80	Randomized Controlled Trial/ or random*.ti,ab.
81	79 not 80
82	Animals/ not Humans/
83	exp Animals, Laboratory/
84	exp Animal Experimentation/
85	exp Models, Animal/
86	exp Rodentia/
87	(rat or rats or mouse or mice).ti.
88	or/81-87
89	70 not 88

Date of initial search: 11/10/2016

Database: Embase Classic+Embase 1947 to 2016 October 11

Date of re-run: 05/09/2017
Database: Embase Classic+Embase 1947 to 2017 Week 35

#	Searches
1	exp meningioma/
2	meningioma*.tw.
3	(mening* adj3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*)).tw.
4	or/1-3
5	exp radiotherapy/
6	radiotherapy.fs.
7	(radiotherap* or radiat* or irradiat* or tomotherap* or radiosurg* or brachytherap* or fractionat* or hyperfraction* or hypofraction* or gamma knife or cyber knife or cyberknife or xknife or arc therap*).tw.
8	(WBRT or WBI-IMRT or HA-WBRT or LINAC or IMRT or XRT or XBT or SRS or SRT or VMAT or 3DCRT or 3D CRT or CRT).tw.
9	(chemoradiotherap* or chemo-radiat* or chemo-irradiat*).tw.
10	or/5-9
11	watchful waiting/
12	conservative treatment/
13	clinical observation/
14	watchful wait*.tw.
15	((active or expect* or symptom* or watch*) adj2 (manag* or monitor* or surveill* or observ* or control*)).tw.
16	(best supportive care or BSC).tw.
17	or/11-16
18	10 and 17
19	exp neurosurgery/
20	exp cancer surgery/
21	exp stereotactic procedure/
22	surgery.fs.
23	((brain or neuro* or intracereb* or intracrani* or crani*) adj2 (surg* or microsurg* or manipulat* or procedur* or operat* or resect* or debulk* or excis* or ablat* or biops*)).tw.
24	(neurosurg* or craniotom* or craniectom*).tw.
25	((intra-operat* or intraoperat*) adj3 (technolog* or modalit* or procedur* or technique* or method*)).tw.
26	or/19-25
27	tumor recurrence/
28	cancer recurrence/
29	recur*.tw.
30	or/27-29
31	26 and 30
32	10 or 17 or 18 or 31
33	4 and 32
34	limit 33 to english language
35	random*.ti,ab.
36	factorial*.ti,ab.
37	(crossover* or cross over*).ti,ab.
38	((doubl* or singl*) adj blind*).ti,ab.

#	Searches
39	(assign* or allocat* or volunteer* or placebo*).ti,ab.
40	crossover procedure/
41	single blind procedure/
42	randomized controlled trial/
43	double blind procedure/
44	or/35-43
45	systematic review/
46	meta-analysis/
47	(meta analy* or metanaly* or metaanaly*).ti,ab.
48	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
49	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
50	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
51	(search* adj4 literature).ab.
52	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
53	((pool* or combined) adj2 (data or trials or studies or results)).ab.
54	cochrane.jw.
55	or/45-54
56	Clinical study/
57	Case control study/
58	family study/
59	longitudinal study/
60	retrospective study/
61	prospective study/
62	cohort analysis/
63	((retrospective* or cohort* or longitudinal or follow?up or prospective or cross section* or observation* or epidemiolog*) adj3 (stud* or research or analys*)).ti.
64	or/56-63
65	44 or 55 or 64
66	34 and 65
67	letter.pt. or letter/
68	note.pt.
69	editorial.pt.
70	case report/ or case study/
71	(letter or comment*).ti.
72	or/67-71
73	randomized controlled trial/ or random*.ti,ab.
74	72 not 73
75	animal/ not human/
76	nonhuman/
77	exp Animal Experiment/
78	exp Experimental Animal/
79	animal model/
80	exp Rodent/
81	(rat or rats or mouse or mice).ti.
82	or/74-81
83	66 not 82

Date of initial search: 11/10/2016

Database: The Cochrane Library, Issue 10 of 12, October 2016

Date of re-run: 05/09/2017

Database: The Cochrane Library, Issue 9 of 12, September 2017

ID	Search
#1	MeSH descriptor: [Meningioma] explode all trees
#2	MeSH descriptor: [Meningeal Neoplasms] explode all trees
#3	meningioma*
#4	(mening* near/3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*))
#5	{or #1-#4}
#6	MeSH descriptor: [Radiotherapy] explode all trees
#7	(radiotherap* or radiat* or irradiat* or tomotherap* or radiosurg* or brachytherap* or fractionat* or hyperfraction* or hypofraction* or gamma knife or cyber knife or cyberknife or xknife or arc therap*)

ID	Search
#8	(WBRT or WBI-IMRT or HA-WBRT or LINAC or IMRT or XRT or XBT or SRS or SRT or VMAT or 3DCRT or 3D CRT or CRT)
#9	MeSH descriptor: [Radiation Oncology] this term only
#10	(chemoradiotherap* or chemo-radiat* or chemo-irradiat*) .
#11	{or #6-#10}
#12	MeSH descriptor: [Watchful Waiting] explode all trees
#13	MeSH descriptor: [Observation] this term only
#14	watchful wait*
#15	((active or expect* or symptom* or watch*) near/2 (manag* or monitor* or surveill* or observ* or control*))
#16	(best supportive care or BSC)
#17	{or #12-#16}
#18	MeSH descriptor: [Neurosurgery] explode all trees
#19	MeSH descriptor: [Neurosurgical Procedures] explode all trees
#20	MeSH descriptor: [Surgical Procedures, Operative] explode all trees
#21	MeSH descriptor: [Stereotaxic Techniques] explode all trees
#22	((brain or neuro* or intracereb* or intracrani* or crani*) near/2 (surg* or microsurg* or manipulat* or procedur* or operat* or resect* or debulk* or excis* or ablat* or biops*))
#23	(neurosurg* or craniotom* or metastasectom*)
#24	((intra-operat* or intraoperat*) near/3 (technolog* or modalit* or procedur* or technique* or method*))
#25	{or #18-#24}
#26	MeSH descriptor: [Neoplasm Recurrence, Local] explode all trees
#27	recur*
#28	#26 or #27
#29	#25 and #28
#30	{or #11, #17, #29}
#31	#5 and #30

Search strategy for review 3b – techniques for radiotherapy for meningioma

Systematic reviews and RCTs

Date of initial search: 16/08/2017

Database(s): Embase 1980 to 2017 Week 33, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Date of re-run: 07/09/2017
Database(s): Embase 1980 to 2017 Week 36, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	Meningioma/
2	Meningeal Neoplasms/
3	1 or 2 use ppez
4	exp meningioma/ use emez
5	meningioma*.tw.
6	(mening* adj3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*)).tw.
7	or/3-6
8	exp Radiotherapy/ use ppez
9	exp radiotherapy/ use emez
10	radiotherapy.fs.
11	(radiotherap* or radiat* or irradiat* or radiosurg* or brachytherap* or fractionat* or hyperfraction* or hypofraction* or gamma knife or cyber knife or cyberknife or xknife or arc therap* or rapidarc).tw.
12	((proton* or particle* or neutron* or ion*) adj3 (therap* or treatment*)).tw.
13	(3DCRT or 3D CRT or CRT or FSRT or IMRT or XRT or XBT or SRS or SRT or VMAT).tw.
14	exp Stereotaxic Techniques/ use ppez
15	exp stereotactic procedure/ use emez
16	or/8-15

#	Searches
17	7 and 16
18	limit 17 to english language
19	limit 18 to yr="1985 -Current"
20	Letter/ use ppez
21	letter.pt. or letter/ use emez
22	note.pt.
23	editorial.pt.
24	Editorial/ use ppez
25	News/ use ppez
26	exp Historical Article/ use ppez
27	Anecdotes as Topic/ use ppez
28	Comment/ use ppez
29	Case Report/ use ppez
30	case report/ or case study/ use emez
31	(letter or comment*).ti.
32	or/20-31
33	randomized controlled trial/ use ppez
34	randomized controlled trial/ use emez
35	random*.ti,ab.
36	or/33-35
37	32 not 36
38	animals/ not humans/ use ppez
39	animal/ not human/ use emez
40	nonhuman/ use emez
41	exp Animals, Laboratory/ use ppez
42	exp Animal Experimentation/ use ppez
43	exp Animal Experiment/ use emez
44	exp Experimental Animal/ use emez
45	exp Models, Animal/ use ppez
46	animal model/ use emez
47	exp Rodentia/ use ppez
48	exp Rodent/ use emez
49	(rat or rats or mouse or mice).ti.
50	or/37-49
51	19 not 50
52	Meta-Analysis/
53	Meta-Analysis as Topic/
54	systematic review/
55	meta-analysis/
56	(meta analy* or metanaly* or metaanaly*).ti,ab.
57	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
58	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
59	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
60	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
61	(search* adj4 literature).ab.
62	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
63	cochrane.jw.
64	((pool* or combined) adj2 (data or trials or studies or results)).ab.
65	or/52-53,56,58-63 use ppez
66	or/54-57,59-64 use emez
67	or/65-66
68	clinical Trials as topic.sh. or (controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or (placebo or randomi#ed or randomly).ab. or trial.ti.
69	68 use ppez
70	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
71	70 use ppez
72	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
73	72 use emez
74	69 or 71
75	73 or 74
76	67 or 75
77	51 and 76
78	remove duplicates from 77

Observational studies

Date of initial search: 16/08/2017

Database: Embase 1980 to 2017 Week 33, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Date of re-run: 07/09/2017
Database(s): Embase 1980 to 2017 Week 36, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	Meningioma/
2	Meningeal Neoplasms/
3	1 or 2 use ppez
4	exp meningioma/ use emez
5	meningioma*.tw.
6	(mening* adj3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*)).tw.
7	or/3-6
8	exp Radiotherapy/ use ppez
9	exp radiotherapy/ use emez
10	radiotherapy.fs.
11	(radiotherap* or radiat* or irradiat* or radiosurg* or brachytherap* or fractionat* or hyperfraction* or hypofraction* or gamma knife or cyber knife or cyberknife or xknife or arc therap* or rapidarc).tw.
12	((proton* or particle* or neutron* or ion*) adj3 (therap* or treatment*)).tw.
13	(3DCRT or 3D CRT or CRT or FSRT or IMRT or XRT or XBT or SRS or SRT or VMAT).tw.
14	exp Stereotaxic Techniques/ use ppez
15	exp stereotactic procedure/ use emez
16	or/8-15
17	7 and 16
18	limit 17 to english language
19	limit 18 to yr="1985 -Current"
20	Letter/ use ppez
21	letter.pt. or letter/ use emez
22	note.pt.
23	editorial.pt.
24	Editorial/ use ppez
25	News/ use ppez
26	exp Historical Article/ use ppez
27	Anecdotes as Topic/ use ppez
28	Comment/ use ppez
29	Case Report/ use ppez
30	case report/ or case study/ use emez
31	(letter or comment*).ti.
32	or/20-31
33	randomized controlled trial/ use ppez
34	randomized controlled trial/ use emez
35	random*.ti,ab.
36	or/33-35
37	32 not 36
38	animals/ not humans/ use ppez
39	animal/ not human/ use emez
40	nonhuman/ use emez
41	exp Animals, Laboratory/ use ppez
42	exp Animal Experimentation/ use ppez
43	exp Animal Experiment/ use emez
44	exp Experimental Animal/ use emez
45	exp Models, Animal/ use ppez
46	animal model/ use emez
47	exp Rodentia/ use ppez
48	exp Rodent/ use emez
49	(rat or rats or mouse or mice).ti.
50	or/37-49

#	Searches
51	19 not 50
52	Epidemiologic Studies/
53	Case Control Studies/
54	Retrospective Studies/
55	Cohort Studies/
56	Longitudinal Studies/
57	Follow-Up Studies/
58	Prospective Studies/
59	Cross-Sectional Studies/
60	or/52-59 use ppez
61	clinical study/
62	case control study/
63	family study/
64	longitudinal study/
65	retrospective study/
66	prospective study/
67	cohort analysis/
68	or/61-67 use emez
69	((retrospective$ or cohort$ or longitudinal or follow?up or prospective or cross section$) adj3 (stud$ or research or analys$)).ti.
70	60 or 68 or 69
71	51 and 70
72	remove duplicates from 71

Other studies

Date of initial search: 16/08/2017

Database: The Cochrane Library, Issue 8 of 12, August 2017

Date of re-run: 07/09/2017

Database: The Cochrane Library, Issue 9 of 12, September 2017

ID	Search
#1	MeSH descriptor: [Meningioma] explode all trees
#2	MeSH descriptor: [Meningeal Neoplasms] explode all trees
#3	meningioma*
#4	(mening* near/3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*))
#5	{or #1-#4}
#6	MeSH descriptor: [Radiotherapy] explode all trees
#7	(radiotherap* or radiat* or irradiat* or radiosurg* or brachytherap* or fractionat* or hyperfraction* or hypofraction* or gamma knife or cyber knife or cyberknife or xknife or arc therap* or rapidarc)
#8	((proton* or particle* or neutron* or ion*) near/3 (therap* or treatment*))
#9	(3DCRT or 3D CRT or CRT or FSRT or IMRT or XRT or XBT or SRS or SRT or VMAT)
#10	{or #6-#9}
#11	#5 and #10

Search strategy for review 5b – follow-up for meningioma

Date of initial search: 22/03/2017

Database: Embase 1974 to 2017 March 21, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

Date of re-run: 07/09/2017

Database: Embase 1980 to 2017 Week 36, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present

#	Searches
1	exp Glioma/ use ppez
2	exp Glioma/ use oemezd
3	exp Astrocytoma/ use ppez
4	exp Astrocytoma/ use oemezd
5	Oligodendroglioma/ use ppez
6	exp Glioblastoma/ use ppez
7	(glioma* or glioblastoma* or GBM or gliosarcoma* or astrocytoma* or oligoastrocytoma* or oligodendroglioma* or oligo?astrocytoma* or xanthoastrocytoma*).tw.
8	or/1-7
9	Meningioma/ use ppez
10	Meningeal Neoplasms/ use ppez
11	exp Meningioma/ use oemezd
12	meningioma*.tw.
13	(mening* adj3 (neoplas* or cancer* or carcin* or tumo* or malign* or h?emangiopericytoma* or h?emangioblastoma*)).tw.
14	or/9-13
15	exp Brain Neoplasms/ use ppez
16	exp Brain Tumor/ use oemezd
17	exp Cerebral Cortex/ use ppez
18	exp Brain Cortex/ use oemezd
19	exp Brain/ use ppez
20	exp Brain/ use oemezd
21	exp Meninges/ use ppez
22	Meninx/ use oemezd
23	or/15-22
24	exp Neoplasm Metastasis/ use ppez
25	metastasis/ use oemezd
26	24 or 25
27	23 and 26
28	exp Brain Neoplasms/sc use ppez
29	Brain Metastasis/ use oemezd
30	Meningeal Metastasis/ use oemezd
31	or/28-30
32	27 or 31
33	((brain or cereb* or intracranial or mening* or brainstem*) adj3 (metasta* or micrometa* or macrometa* or spread* or carcinomatosis or carcinosis or secondar* or seeding or seeded or disseminat* or migrat*)).tw.
34	32 or 33
35	8 or 14 or 34
36	exp Recurrence/ use ppez
37	Neoplasm Recurrence, Local/ use ppez
38	Disease Progression/ use ppez
39	cancer recurrence/ use oemezd
40	recurrent disease/ use oemezd
41	tumor recurrence/ use oemezd
42	recurr*.ti.
43	or/36-42
44	35 and 43
45	exp Aftercare/ use ppez
46	exp aftercare/ use oemezd
47	(aftercare or "after care" or after-care or follow-up or "follow up" or followup or surveillance).tw.
48	(after treatment or after-treatment or posttreatment or post treatment or post-treatment or post-therap* or post therap*).ti,ab.
49	((post-surg* or post surg* or post-operat* or postoperat* or post operat*) adj1 (evaluat* or monitor* or care)).tw.
50	(post-hospital* or post hospital* or posthospital* or after hospital* or follow* hospital*).ti,ab.
51	disease surveillance/ use oemezd
52	periodic medical examination/ use oemezd
53	"medical record review"/ use oemezd
54	exp patient monitoring/ use oemezd
55	(re-examin* or reexamin or monitor* or periodic examin* or regular examin* or checkup* or check-up* or check up*).ti,ab.
56	follow*.ti.
57	or/45-56
58	44 and 57

#	Searches
59	limit 58 to english language
60	limit 59 to yr="1990 -Current"
61	Letter/ use ppez
62	letter.pt. or letter/ use oemezd
63	note.pt.
64	editorial.pt.
65	Editorial/ use ppez
66	News/ use ppez
67	exp Historical Article/ use ppez
68	Anecdotes as Topic/ use ppez
69	Comment/ use ppez
70	Case Report/ use ppez
71	case report/ or case study/ use oemezd
72	(letter or comment*).ti.
73	or/61-72
74	randomized controlled trial/ use ppez
75	randomized controlled trial/ use oemezd
76	random*.ti,ab.
77	or/74-76
78	73 not 77
79	animals/ not humans/ use ppez
80	animal/ not human/ use oemezd
81	nonhuman/ use oemezd
82	exp Animals, Laboratory/ use ppez
83	exp Animal Experimentation/ use ppez
84	exp Animal Experiment/ use oemezd
85	exp Experimental Animal/ use oemezd
86	exp Models, Animal/ use ppez
87	animal model/ use oemezd
88	exp Rodentia/ use ppez
89	exp Rodent/ use oemezd
90	(rat or rats or mouse or mice).ti.
91	or/78-90
92	60 not 91
93	Meta-Analysis/
94	Meta-Analysis as Topic/
95	systematic review/
96	meta-analysis/
97	(meta analy* or metanaly* or metaanaly*).ti,ab.
98	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
99	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
100	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
101	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
102	(search* adj4 literature).ab.
103	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
104	cochrane.jw.
105	((pool* or combined) adj2 (data or trials or studies or results)).ab.
106	or/93-94,97,99-104 use ppez
107	or/95-98,100-105 use oemezd
108	or/106-107
109	clinical Trials as topic.sh. or (controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or (placebo or randomi#ed or randomly).ab. or trial.ti.
110	109 use ppez
111	(controlled clinical trial or pragmatic clinical trial or randomized controlled trial).pt. or drug therapy.fs. or (groups or placebo or randomi#ed or randomly or trial).ab.
112	111 use ppez
113	crossover procedure/ or double blind procedure/ or randomized controlled trial/ or single blind procedure/ or (assign* or allocat* or crossover* or cross over* or ((doubl* or singl*) adj blind*) or factorial* or placebo* or random* or volunteer*).ti,ab.
114	113 use oemezd
115	110 or 112
116	112 or 114
117	Cohort Studies/ or Longitudinal Studies/ or Follow-Up Studies/ or Prospective Studies/ or Comparative Study/
118	117 use ppez
119	cohort analysis/ or longitudinal study/ or follow up/ or prospective study/ or comparative study/
120	119 use oemezd
121	((cohort* or follow-up or follow?up or inciden* or longitudinal or prospective) adj1 (stud* or research or analys*)).tw.
122	118 or 120 or 121

#	Searches
123	108 or 115 or 122
124	92 and 123
125	remove duplicates from 124

Date of initial search: 22/03/2017

Database: The Cochrane Library, Issue 3 of 12, March 2017

Date of re-run: 07/09/2017

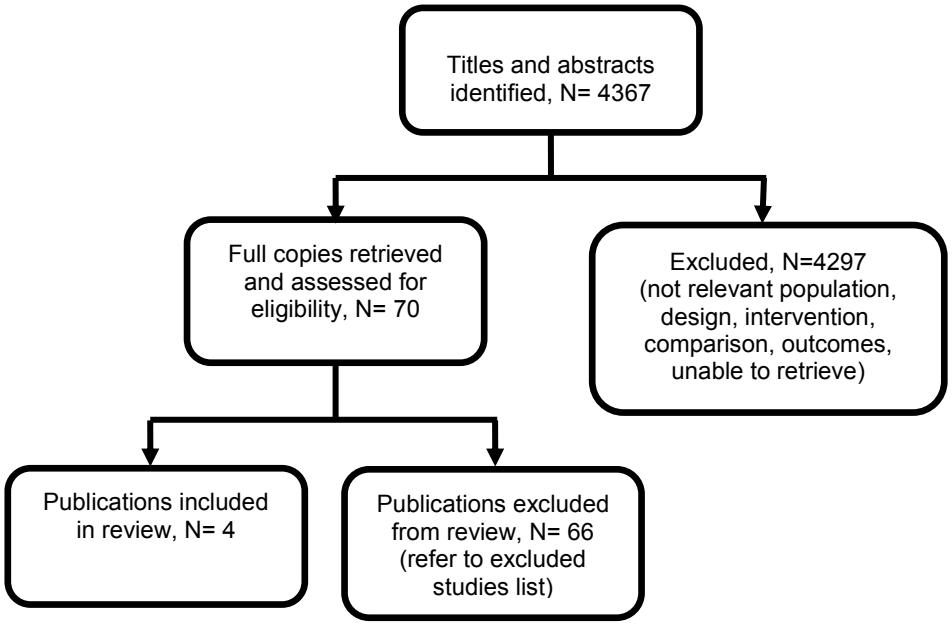
Database: The Cochrane Library, Issue 9 of 12, September 2017

ID	Search
#1	MeSH descriptor: [Glioma] explode all trees
#2	(glioma* or glioblastoma* or gliosarcoma* or astrocytoma* or astroblastoma* or oligodendroglioma* or oligodendrocytoma* or oligoastrocytoma* or GBM)
#3	(glial near/3 (neoplas* or cancer* or tumo* or carcin* or malign* or metasta*))
#4	{or #1-#3}
#5	MeSH descriptor: [Meningioma] explode all trees
#6	MeSH descriptor: [Meningeal Neoplasms] explode all trees
#7	meningioma*
#8	(mening* near/3 (neoplas* or cancer* or carcin* or tumo* or malign* or metasta*))
#9	{or #5-#8}
#10	MeSH descriptor: [Neoplasm Metastasis] explode all trees
#11	MeSH descriptor: [Brain Neoplasms] explode all trees
#12	MeSH descriptor: [Brain] explode all trees
#13	#11 or #12
#14	#10 and #13
#15	((brain or cereb* or intracranial or mening*) near/3 (metasta* or micometasta* or spread* or involvement or carcinosis or secondar*))
#16	#14 or #15
#17	#4 or #9 or #16
#18	MeSH descriptor: [Recurrence] explode all trees
#19	MeSH descriptor: [Neoplasm Recurrence, Local] explode all trees
#20	recurr*
#21	{or #18-#20}
#22	#17 and #21
#23	MeSH descriptor: [Aftercare] explode all trees
#24	(aftercare or "after care" or after-care or follow-up or "follow up" or followup or surveillance)
#25	("after treatment*" or after-treatment* or posttreatment* or "post treatment*" or post-treatment* or post-therap* or "post therap*")
#26	((post-surg* or "post surg*" or post-operat* or postoperat* or "post operat*") adj1 (evaluat* or monitor* or care))
#27	(post-hospital* or "post hospital*" or posthospital* or "after hospital*" or "follow* hospital*")
#28	{or #23-#27}
#29	#22 and #28 Publication Year from 1990 to 2017

Appendix C – Clinical evidence study selection

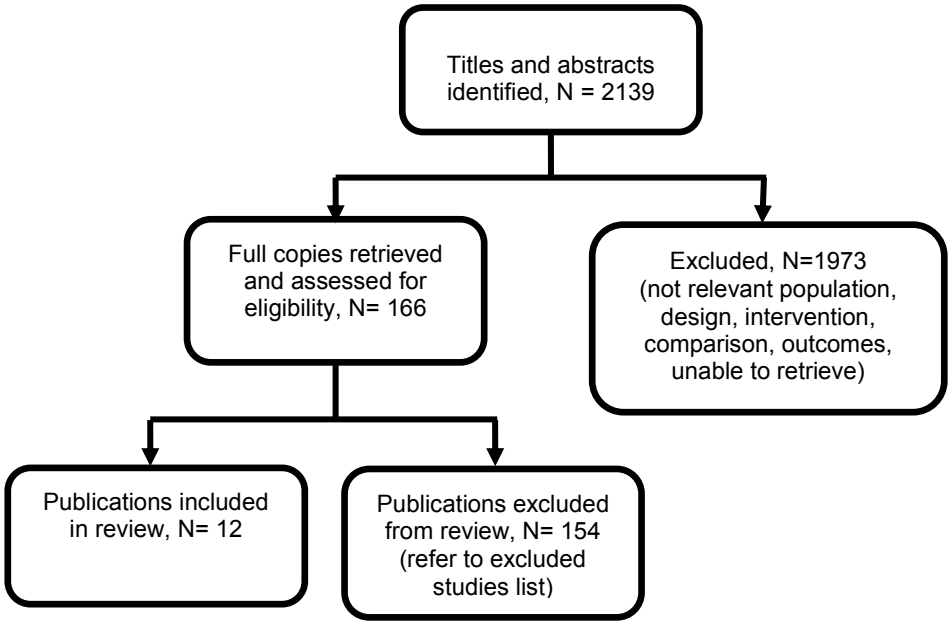
PRISMA flowchart for review 1a - imaging for suspected glioma and meningioma

Figure 1: Flow diagram of clinical article selection for review 1a - imaging for suspected glioma and meningioma



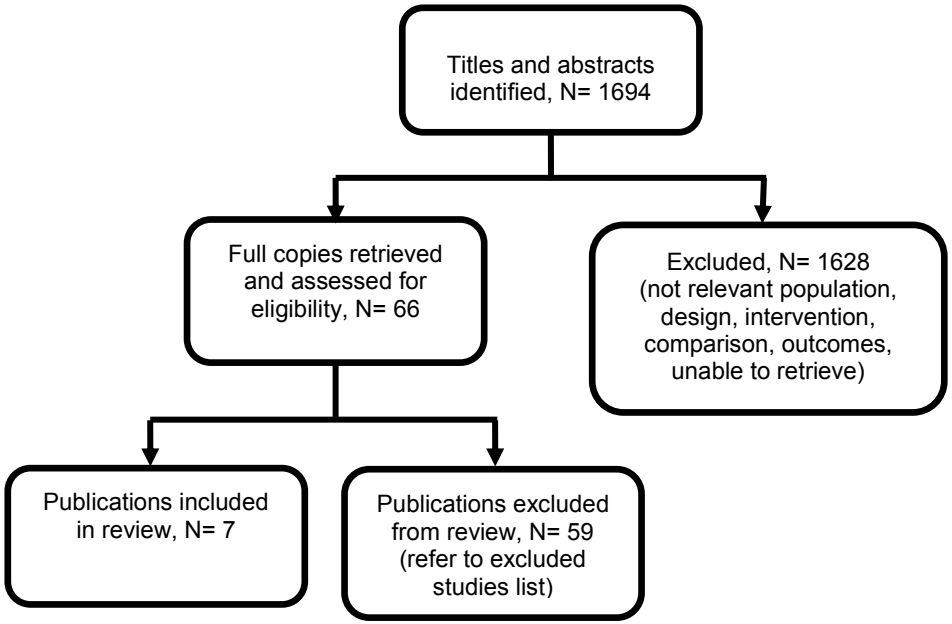
PRISMA flowchart for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Figure 2: Flow diagram of clinical article selection for review 3a – managing inoperable, incompletely excised or recurrent meningioma



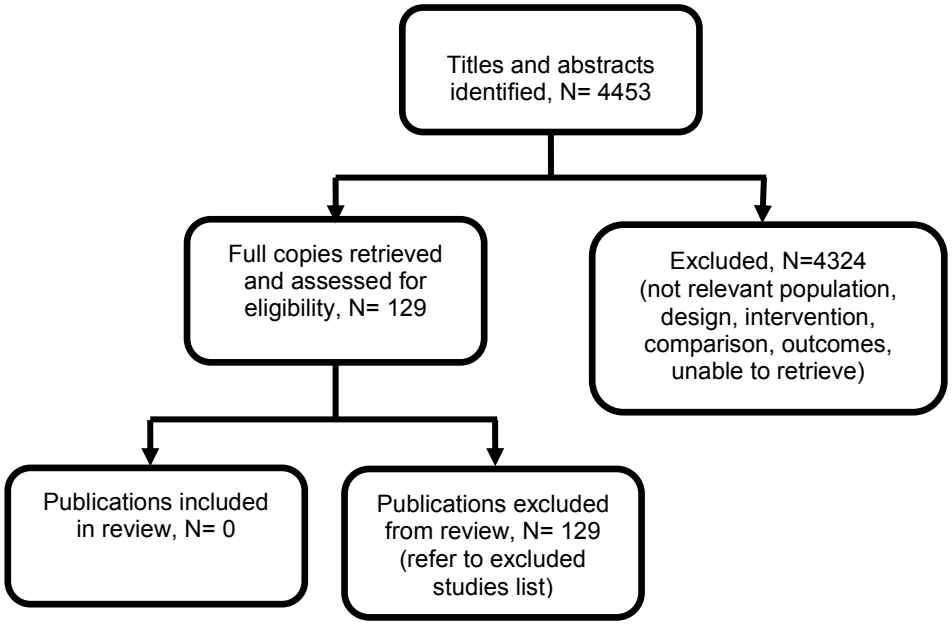
PRISMA flowchart for review 3b – techniques for radiotherapy for meningioma

Figure 3: Flow diagram of clinical article selection for review 3b – techniques for radiotherapy for meningioma



PRISMA flowchart for review 5b – follow-up for meningioma

Figure 4: Flow diagram of clinical article selection for 5a, 5b and 5c - follow up after treatment for glioma, meningioma and brain metastases (the searches for all three reviews were conducted simultaneously)



Appendix D – Clinical evidence tables

See Supplementary Material D.

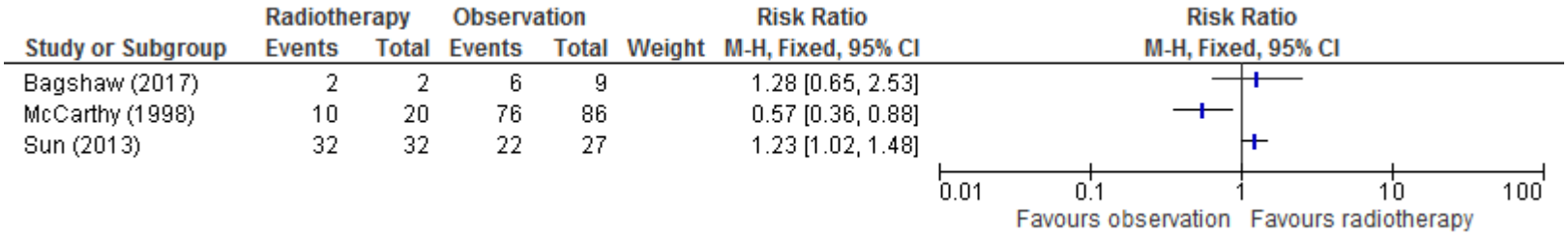
Appendix E – Forest plots

Forest plots for review 1a - imaging for suspected glioma and meningioma

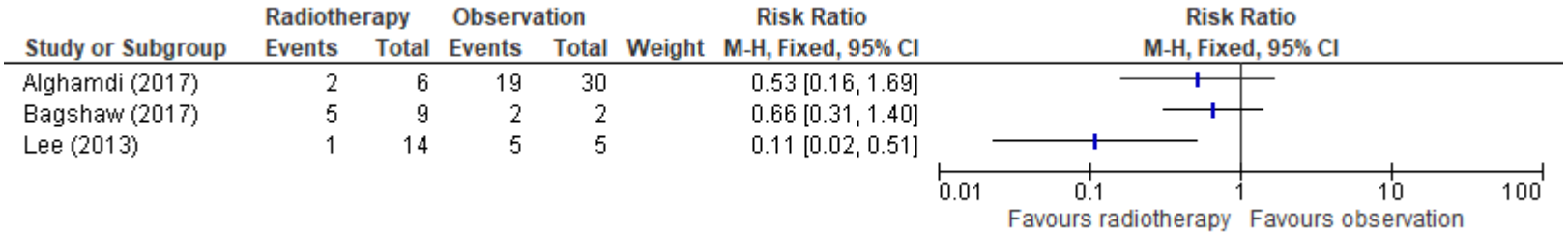
Not applicable - no evidence was identified.

Forest plots for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Forest plot for overall survival in patients with incompletely resected atypical meningioma



Forest plot for recurrence rate in patients with incompletely resected atypical meningioma



Forest plots for review 3b – techniques for radiotherapy for meningioma

Not applicable - there were only data from one study for the outcomes within each treatment comparison or, when more than one study contributed data to an outcome within a treatment comparison, because the data were not adequately reported to be able to undertake meta-analyses.

Forest plots for review 5b – follow-up for meningioma

Not applicable - no evidence was identified.

Appendix F – GRADE tables

GRADE tables for review 1a - imaging for suspected glioma and meningioma

Table 24: Clinical evidence profile: colour map images derived from PWI, MRS and the following cut-off data: 1.75 rCBV, 1.5 for Choline, 1.5 Cho/NAA (semi quantitative analysis from Caulo 2014)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
PWI and MRS	1	110	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision[2]	Very low

CI confidence interval
1 Unclear whether index test results were interpreted without knowledge of the results of the reference standard; unclear interval between index test and reference standard; unclear whether the study was free of commercial funding; data driven study: the threshold for a positive rest was not pre-specified but determined post-hoc after assessing the data
2 The difference between upper and lower 95% CI was >0.25 for sensitivity

Table 25: Clinical evidence profile: conventional MRI sequences (qualitative analysis from Caulo 2014)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Conventional MRI	1	110	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval
1 Interval between index test and reference standard unclear; unclear whether the study was free of commercial funding; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data

Table 26: Clinical evidence profile: DWI (ADC maps generated), DTI, MRS (Cho/Cr, NAA/Cr, Cho/NAA, lactate/Cr, and lipids/Cr) and PWI (blood volume and mean transit maps were generated) with a cut-off value of -0.3096 (quantitative analysis from Caulo 2014)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
DWI, DTI, MRS and WPI	1	110	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval
1 unclear whether index test results were interpreted without knowledge of the results of the reference standard; unclear interval between index test and reference standard; unclear whether the study was free of commercial funding; data driven study: the threshold for a positive rest was not pre-specified but determined post-hoc after assessing the data.

Table 27: Clinical evidence profile: DWI (ADC maps generated), DTI, MRS (Cho/Cr, NAA/Cr, Cho/NAA, lactate/Cr, and lipids/Cr) and PWI (blood volume and mean transit maps were generated) with a cut-off value of -0.3096 without including oligodendroglioma (ODG) (identification of high- versus low-grade glioma) (quantitative analysis from Caulo 2014)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
DWI, DTI, MRS and WPI	1	110	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval
1 unclear whether index test results were interpreted without knowledge of the results of the reference standard; unclear interval between index test and reference standard; unclear whether the study was free of commercial funding; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data.

Table 28: Summary clinical evidence profile: conventional MRI (Law 2003)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Conventional MRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval
1 unclear interval between index test and reference test; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data

Table 29: Clinical evidence profile: perfusion MRI (Law 2003)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Perfusion MRI – threshold values for rCBV with minimum C2 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for rCBV with minimum C1 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for same sensitivity as CMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for same specificity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval, rCBV relative cerebral blood volume
1 unclear interval between index test and reference test; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data

Table 30: Clinical evidence profile: threshold values for Cho/Cr from perfusion MRS (Law 2003)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Perfusion MRI – threshold values for Cho/Cr with minimum C2 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for Cho/Cr with minimum C1 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Perfusion MRI – threshold values for same sensitivity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for same specificity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval, rCBV relative cerebral blood volume, Cho/Cr choline [Cho] / creatine [Cr]; cMRI conventional MRI
1 unclear interval between index test and reference test; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data

Table 31: Clinical evidence profile: thresholds for Cho/NAA from perfusion MRI (Law 2003)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Perfusion MRI – threshold values for Cho/NAA with minimum C2 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for Cho/NAA with minimum C1 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Perfusion MRI – threshold values for same sensitivity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision[2]	Very low
Perfusion MRI – threshold values for same specificity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

Cho/NAA Cho/N-acetylaspartate [NAA], MRS magnetic resonance spectroscopy, CI confidence interval
1 unclear interval between index test and reference test; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data
2 The difference between the upper and lower 95% CI for sensitivity was >0.25

Table 32: Clinical evidence profile: threshold values for rCBV and Cho/NAA ratio together (Law 2003)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Threshold values for rCBV and Cho/NAA ratio together with minimum C2 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Threshold values for rCBV and Cho/NAA ratio together with minimum C1 error	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Threshold values for rCBV and Cho/NAA ratio together – threshold values for same sensitivity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low
Threshold values for rCBV and Cho/NAA ratio together – threshold values for same specificity as cMRI	1	160	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

Cho/NAA Cho/N-acetylaspartate [NAA], MRS magnetic resonance spectroscopy, CI confidence interval, rCBV relative cerebral blood volume
1 unclear interval between index test and reference test; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data

Table 33: Clinical evidence profile: conventional MRI (Zou 2011)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Conventional MRI	1	30	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision[2]	Very low

CI confidence interval; MRI magnetic resonance imaging
1 Unclear whether the results of the index test were interpreted without prior knowledge of the reference standard; the conduct or interpretation of the index test could have introduced bias; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data
2 The difference between upper and lower 95% CI was >0.25 for sensitivity

Table 34: Clinical evidence profile: combination of apparent diffusion coefficient (ADC) and N-acetylaspartate/choline ratio (NAA/Cho) (Zou 2011)

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Conventional MRI	1	30	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval; MRI magnetic resonance imaging
1 Unclear whether the results of the index test were interpreted without prior knowledge of the reference standard; the conduct or interpretation of the index test could have introduced bias; data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data

Table 35: Clinical evidence profile: T2 WI - FLAIR GLCM Cluster Shade

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Conventional MRI (T2 WI - FLAIR GLCM Cluster Shade)	1	66	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	Serious imprecision[2]	Very low

CI confidence interval; MRI magnetic resonance imaging
1 data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data; unclear whether patient flow could have introduced bias; unclear whether the study was free of commercial funding
2 The difference between upper and lower 95% CI was >0.25 for sensitivity

Table 36: Clinical evidence profile: T1W1-CE GLCM Entropy on the T1W1-CE sequence

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Conventional MRI (T1W1-CE GLCM Entropy on the T1W1-CE sequence)	1	66	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval; MRI magnetic resonance imaging
1 data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data; unclear whether patient flow could have introduced bias; unclear whether the study was free of commercial funding

Table 37: Clinical evidence profile: Summary clinical evidence profile for combined features of conventional MRI and DWI

Index test	Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Combined features of conventional MRI (T1W1-CE GLCM Entropy on the T1W1-CE sequence) and DWI (ADC homogeneity on the ADC map)	1	63	Very serious risk of bias[1]	No serious inconsistency	No serious indirectness	No serious imprecision	Low

CI confidence interval; MRI magnetic resonance imaging
1 data driven study: the threshold for a positive test was not pre-specified but determined post-hoc after assessing the data; unclear whether patient flow could have introduced bias; unclear whether the study was free of commercial funding

GRADE tables for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Table 52: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected WHO grade I-III meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Progression-free survival (follow-up 4.7-5.3 years)												
1 (Frostell 2016)	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	NR/21[2]	NR/19[2]	Not significant (uni- or multivariate)	474 fewer per 1000 (not estimable)	⊕OOO VERY LOW	CRITICAL
Overall survival (follow-up 4.7-5.3 years)												
1 (Frostell 2016)	observational studies	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	0/21 (0%)	4/19 (21.1%)	Observation < radiotherapy (p < 0.05)	211 fewer per 1000 (not estimable)	⊕OOO VERY LOW	CRITICAL
Necrosis and oedema (follow-up 4.7-5.3 years)												
1 (Frostell 2016)	observational studies	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	0/21 (0%)	0/19 (0%)	Not applicable	Not applicable	⊕OOO VERY LOW	CRITICAL

[1] *Low event rate*
[2] *Event rates not clearly reported in study, so not included here*
[3] *Uncontrolled confounders/Unadjusted analyses*

Table 53: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected benign meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Overall survival (follow-up median 10 months)												
1 (McCarthy 1998)	observational studies	serious[1,2]	no serious inconsistency	no serious indirectness[1]	no serious imprecision	none	155/238 (65.1%)	3447/4577 (75.3%)	Non-significant	753 fewer per 1000 (not estimable)	⊕OOO VERY LOW	CRITICAL

[1] *Radiotherapy was classified into yes/no depending on whether the patient had received any radiotherapy. No further details reported.*
[2] *Patient characteristics by intervention group not reported, unadjusted analyses.*

Table 54: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected malignant meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Overall survival (follow-up median 12 months)												
1 (McCarthy 1998)	observational studies	serious[1]	no serious inconsistency	no serious indirectness[2]	no serious imprecision	none	75/169 (44.4%)	178/279 (63.8%)	Observation > radiotherapy (p = 0.02, favours observation)	638 fewer per 1000 (not estimable)	⊕OOO VERY LOW	CRITICAL

[1] *Patient characteristics by intervention group not reported, unadjusted analyses*
[2] *Radiotherapy was classified into yes/no depending on whether the patient had received any radiotherapy. No further details reported.*

Table 55: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected atypical meningioma?

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute	Quality	Importance
Overall survival (follow-up 12-67 months)												
3 (Bagshaw 2017; McCarthy 1998; Sun 2013)	observational studies	serious [1]	very serious inconsistency[2]	no serious indirectness[3]	serious[4]	none	44/54 (81.5%)	104/122 (85.2%)	RR 1.28 (0.65 to 2.53), 0.57 (0.36 to 0.88) and 1.23 (1.02 to 1.48)[4]	-	⊕OOO VERY LOW	CRITICAL
Recurrence (follow-up 26-48.7 months)												
3 (Alghamdi 2017; Bagshaw 2017; Lee	observational studies	serious [1]	serious inconsistency[5]	no serious indirectness	serious[4]	none	8/29 (27.6%)	26/37 (70.3%)	RR 0.53 (0.16 to 1.69), 0.66 (0.31 to 1.4) and 0.11	-	⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
2013))									(0.02 to 0.51)[5]			
Recurrence/progression-free survival (follow-up 23-67 months)												
4 (Hardesty 2013; Lee 2013; Park 2013; Sun 2013)	observational studies	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	Hardesty (2013): Not reported Lee (2013): 13/14 (92.9%) Park (2013): Not reported Sun (2013): Not reported	Hardesty (2013): Not reported Lee (2013): 1/5 (20.0%) Park (2013): Not reported Sun (2013): Not reported	Hardesty (2013): Observation = Radiotherapy (p = 0.16-0.55) Lee (2013): Observation < Radiotherapy (p = 0.0016) Park (2013): Observation < Radiotherapy (p < 0.001) Sun (2013): Observation < Radiotherapy (ps < 0.008)		⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Treatment-related morbidity (follow-up 23-67 months)												
3 (Hardestry 2013; Park 2013; Sun 2013)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[4]	none	1/86 (1.2%)	0/99 (0.0%)	Study 1: No severe acute side effects observed. Transient mild side effects, such as fatigue, headache, intermittent nausea, dizziness and skin irritation at portals observed in most patients. Cognitive disturbance and motor neuropathy were the most common late side effects. Others including memory disturbance, speech impairment, encephalopathy, seizures, and aemorrhage also observed. Study 2: No RT-related adverse events observed		⊕OOO VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
									Study 3: 1 patient suffered cranial wound breakdown due to IMRT, requiring operative reconstruction.			

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *I^2 = 88%, indicating substantial heterogeneity. Therefore, the RRs were not combined.*
[3] *Radiotherapy was classified into yes/no depending on whether the patient had received any radiotherapy. No further details reported.*
[4] *Low event rate*
[5] *I^2 = 60%, indicating substantial heterogeneity, which in combination with the fact that these were small observational studies with a number of limitations meant that the risk ratios were not combined.*

Table 56: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected WHO grade II meningioma (NOS)?

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Recurrence (follow-up median 32 months)												
1 (Yoon 2015)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	3/12 (25.0%)	8/30 (26.7%)	Non-significant	16 fewer per 1000 (from 187	⊕OOO VER	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute	**Quality**	**Importance**
									(p = 0.99)	fewer to 520 more)	Y LOW	
Progression-free survival (follow-up median 32 months; Better indicated by higher values)												
1 (Yoon 2015)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	Mean = 59 months	Mean = 47 months	Non-significant (p = 0.4)	-	⊕OO O VERY LOW	CRITICAL
Overall survival (follow-up median 32 months)												
1 (Yoon 2015)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	Serious[2]	none	10/12 (83.3%)	25/30 (83.3%)	Non-significant (p = 0.98)	0 fewer per 1000 (from 217 fewer to to 292 more)	⊕OO O VERY LOW	CRITICAL

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *Low event rate*

Table 57: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected WHO grade II atypical meningioma located in the skull base

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute	Quality	Importance
Recurrence (follow-up mean 57.4 months)												
1 (Wang 2015)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	NR/9	5/5 (100%)	Non-significant	-	⊕OOO VERY LOW	CRITICAL
Treatment-related morbidity (follow-up mean 57.4 months)												
1 (Wang 2015)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	One complication observed after STR (facial palsy; tumour location petroclivus). "Following radiotherapy, self-limiting symptoms like dizziness, headache, and skin irritation were observed, but there were no severe acute side effects."				⊕OOO VERY LOW	CRITICAL

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *Low event rate*

Table 58: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected primary sphenoid wing meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Recurrence (follow-up 3.5-4.3 years)												
1 (Peele 1996)	observational studies	serious [1]	no serious inconsistency	no serious indirectness [2]	serious [3]	none	0/31 (0.0%)	16/38 (42.1%)	Observation > Radiotherapy (p < 0.00005)	421 fewer per 1000 (not estimable)	⊕OOO VERY LOW	CRITICAL
Treatment-related morbidity and mortality (follow-up 3.5-4.3 years)												
1 (Peele 1996)	observational studies	serious [1]	no serious inconsistency	no serious indirectness [2]	serious [3]	none	-Operative complications: Third cranial nerve palsy (N = 4), fifth cranial nerve dysfunction (N = 1), ptosis (N = 1), central retinal artery occlusion (N = 1), cerebrospinal fluid leak (N = 1), and pulmonary embolism (N = 1). -Serious morbidity (N = 0) or mortality (N = 0) -Anterior ischemic optic neuropathy (N = 3), central retinal vein occlusion (N = 1). "All events occurred at least 2 years postoperatively but ipsilateral to the previous frontotemporal craniotomy." -Radiation therapy (temporary) adverse events: Mild skin erythema and lateral brow alopecia, but no retinal or optic				⊕OOO VERY LOW	CRITICAL [4]

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
							nerve complications, except possibly N = 1.					

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *Patients treated 1981-1994, unclear how many treated 1981-1985, that is, outside of our inclusion criterion of 1985 onwards.*
[3] *Low event rate*
[4] *These data are not split by primary/recurrent group, but collapsed across them.*

Table 59: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected meningioma involving the major venous sinus

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Observation	Relative (95% CI)	Absolute		
Recurrence (follow-up median 60.2 months)												
1 (Han 2016)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/7 (0.0%)	3/7 (42.9%)	RR 0.14 (0.01 to 2.34)	369 fewer per 1000 (from 424 fewer to 574 more)	⊕OOO VERY LOW	CRITICAL

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *Low event rate*

Table 60: Clinical evidence profile: Radiotherapy versus surgery in patients with recurrent atypical meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Surgery	Relative (95% CI)	Absolute		
Recurrence (follow-up median 26 months)												
1 (Bagshaw 2017)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/12 (75.0%)	9/10 (90.0%)	RR 0.83 (0.57 to 1.23)	153 fewer per 1000 (from 387 fewer to 207 more)	⊕OOO VERY LOW	CRITICAL

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *Low event rate*

Table 61: Clinical evidence profile: Radiotherapy versus observation in patients with incompletely resected recurrent sphenoid wing meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiotherapy	Surgery	Relative (95% CI)	Absolute		
Recurrence (follow-up 3.5-4.4 years)												
1 (Peele 1996)	observational studies	serious [1]	no serious inconsistency	no serious indirectness[2]	serious[3]	none	0/11 (0.0%)	5/6 (83.3%)	Observation > Radiotherapy (p < 0.0012)	833 fewer per 1000 (not estimable)	⊕OOO VERY LOW	CRITICAL

[1] *Uncontrolled confounders/unadjusted analyses*
[2] *Patients treated 1981-1994, unclear how many treated 1981-1985, that is, outside of our inclusion criterion of 1985 onwards.*
[3] *Low event rate*

GRADE tables for review 3b – techniques for radiotherapy for meningioma

Table 62: Clinical evidence profile: Stereotactic radiosurgery (SRS) or fractionated stereotactic radiotherapy (FSRT) in patients with cavernous sinus meningioma

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SRS	FSRT	Relative (95% CI)	Absolute	**Quality**	**Importance**
Disease/progression-free survival (follow-up 63.6-88.6 months)												
2 (Correa 2014; Metellus 2005)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	yes[3]	68[4]	95[4]	Not estimable, but not signficant[4,5]	Not estimable[5]	⊕OOO VERY LOW	CRITICAL
Cognitive/dysthymic improvement (follow-up median 73 months)												
1 (Correa 2014)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	3/32 (9.4%)	1/57 (1.8%)	RR 5.34 (0.58 to 49.27)	76 more per 1000 (from 7 fewer to 847 more)	⊕OOO VERY LOW	IMPORTANT
Steroid use (follow-up median 73 months)												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SRS	FSRT	Relative (95% CI)	Absolute	**Quality**	**Importance**
1 (Correa 2014)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	7/32 (21.9%)	0/57 (0.0%)	RR 4.93 (1.89 to 12.87)	Not estimable	⊕OOO VERY LOW	CRITICAL
Radiation-induced malignancy (follow-up 63.6 months-15 years)												
2 (Correa 2014; Metellus 2005)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	yes[3]	0/68 (0.0%)	0/95 (0.0%)	Not estimable, but not significant	Not estimable	⊕OOO VERY LOW	NOT IMPORTANT

[1] *Uncontrolled confounders (SRS had smaller tumours than FSRT) in the included studies*
[2] *Low event rates/low numbers of patients*
[3] *The time frames covering the 2 treatment group differed in one of the studies (FSRT: 1986-1999; SRS: 1994-1997)*
[4] *Event rate not reported in one of the studies. In the other study 2/38 and 2/36 patients, respectively, progressed in the FSRT and SRS groups.*
[5] *Disease-free survival rates in Correa 2014: SRS (5, 10 and 15 year = 100%, 95.7% and 90.3%) = SRT (5, 10 and 15 year = 98.1%, 90.3% and 90.3%; p = 0.567). Progression free survival rates in Metellus 2005: FSRT: 5- and 10-year = 94.7%; SRS: 5- and 10-year = 94.4%.*

Table 63: Clinical evidence profile: Fractionated stereotactic radiotherapy (FSRT) versus hypo-fractionated stereotactic radiotherapy (hFRST) in patients with grade I meningioma

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FSRT	hFSRT	Relative (95% CI)	Absolute	**Quality**	**Importance**
Local control (follow-up median 50 months)												
1 (Fokas 2014)	observational studies	serious [1]	no serious inconsistency	serious[2]	serious[3]	none	253[4]	49[4]	Not estimable, but not significant	Not estimable[4]	⊕OOO VERY LOW	CRITICAL
Radiation-induced malignancy (follow-up median 50 months)												
1 (Fokas 2014)	observational studies	serious [1]	no serious inconsistency	serious[2]	serious[3]	none	0/253 (0.0%)	0/49 (0.0%)	Not estimable, but not significant	Not estimable	⊕OOO VERY LOW	NOT IMPORTANT

[1] *Uncontrolled confounders (patient characteristics not reported split by radiotherapy group, but clear that at least target volume differ between the treatment groups)*
[2] *Some patients aged below 16 years, unclear how many*
[3] *Low event rates/low numbers of patients*
[4] *Event rate not reported*

Table 64: Clinical evidence profile: Stereotactic radiosurgery (SRS) versus fractionated stereotactic radiotherapy (FRST) in patients with basal meningioma

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SRS	FSRT	Relative (95% CI)	Absolute	**Quality**	**Importance**
Progression-free survival (follow-up median 32 months)												
1 (Han 2014)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	48/55 (87.3%)	131/143 (91.6%)	RR 0.95 (0.85 to 1.07)	44 fewer per 1000 (from 131 fewer to 61 more)	⊕OOO VERY LOW	CRITICAL
Steroid use (follow-up median 32 months)												
1 (Han 2014)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/55 (10.9%)	6/143 (4.2%)	RR 2.6 (0.88 to 7.72)	175 more per 1000 (from 13 fewer to 733 more)	⊕OOO VERY LOW	CRITICAL

[1] Uncontrolled confounders (SRS had significantly smaller tumours than FSRT)
[2] Low event rates/low numbers of patients

Table 65: Clinical evidence profile: Stereotactic radiosurgery (SRS) versus intensity-modulated radiotherapy (IMRT) in patients with atypical meningioma

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SRS	IMRT	Relative (95% CI)	Absolute	**Quality**	**Importance**
Progression-free survival (follow-up median 32 months)												
1 (Hardesty 2013)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	32[3]	39[3]	RR 0.715 (not reported, but not significant)[3,4]	Not estimable	⊕OOO VERY LOW	CRITICAL

[1] Uncontrolled confounders (tumour volume not reported, and target volume only reported for SRS)
[2] Low event rates/low numbers of patients
[3] Event rate not reported
[4] P = 0.52

Table 66: Clinical evidence profile: Fractionated stereotactic radiotherapy (FSRT) versus hypo-fractionated stereotactic radiotherapy (hFSRT) in patients with intracranial meningioma

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FSRT	hFSRT	Relative (95% CI)	Absolute	**Quality**	**Importance**
Progression-free survival (follow-up median 35 months)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FSRT	hFSRT	Relative (95% CI)	Absolute		
1 (Kaul 2014)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none	179[3]	92[3]	Not estimable, but not significant[3,4]	Not estimable	⊕OOO VERY LOW	CRITICAL

[1] Uncontrolled confounders (tumour size not reported split by treatment group, but likely to differ between them)
[2] Low event rates/low numbers of patients
[1] Event rate not reported
[2] FSRT (3-year = 92.7%; 5-year = 88.9%; 10-year = 86.9%) = hFSRT (3-year = 92.4%; 5-year = 80.9%; 10-year = NA; p = 0.81)

Table 67: Clinical evidence profile: Stereotactic radiosurgery (SRS) versus fractionated stereotactic radiotherapy (FSRT) in patients with intracranial meningioma

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SRS	FSRT	Relative (95% CI)	Absolute		
Local control (follow-up 23.8-40.6 months)												
1 (Torres 2003)	observational studies	serious [1]	no serious inconsistency	no serious indirectness	serious[2]	none[3]	58/63 (92.1%)	70/72 (97.2%)	RR 0.95 (0.87 to 1.03)	49 fewer per 1000 (from 126 fewer to 29 more)	⊕OOO VERY LOW	CRITICAL

[1] Uncontrolled confounders (not many patient characteristics reported split by treatment group; tumour volume may differ between the groups)

[2] Low event rates/low numbers of patients
[3] Unequal lengths of follow up between the treatment groups (Mean (range) = 40.6 (6-125) months and 23.8 (6-72) months for SRS and FSRT respectively.)

GRADE tables for review 5b – follow-up for meningioma

Not applicable - no evidence was identified.

Appendix G – Economic evidence study selection

Economic evidence for review 1a - imaging for suspected glioma and meningioma

Economic study selection flowcharts are in Supplementary Material D.

Economic evidence for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Economic study selection flowcharts are in Supplementary Material D.

Economic evidence for review 3b – techniques for radiotherapy for meningioma

Economic study selection flowcharts are in Supplementary Material D.

Economic evidence for review 5b – follow-up for meningioma

Economic study selection flowcharts are in Supplementary Material D.

Appendix H – Economic evidence tables

Economic evidence tables for review 1a - imaging for suspected glioma and meningioma

Not applicable - no economic evidence was identified.

Economic evidence tables for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Not applicable - no economic evidence was identified.

Economic evidence tables for review 3b – techniques for radiotherapy for meningioma

Not applicable - no economic evidence was identified.

Economic evidence tables for review 5b – follow-up for meningioma

Not applicable - no economic evidence was identified.

Appendix I – Health economic evidence profiles

Health economic evidence profiles for review 1a - imaging for suspected glioma and meningioma

Not applicable - no economic evidence was identified.

Health economic evidence profiles for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Not applicable - no economic evidence was identified.

Health economic evidence profiles for review 3b – techniques for radiotherapy for meningioma

Not applicable - no economic evidence was identified.

Health economic evidence profiles for review 5b – follow-up for meningioma

Not applicable - no economic evidence was identified.

Appendix J – Health economic analysis

No de-novo economic analyses were carried out for these topics.

Appendix K – Excluded studies

Excluded studies for review 1a - imaging for suspected glioma and meningioma

Clinical studies

Excluded studies - What is the most effective imaging strategy in newly diagnosed glioma and meningioma?	
Study	**Reason for Exclusion**
Ahmad, N., Shaukat, A., Rehan, A., Rashid, S., Diagnostic Accuracy of Perfusion Computed Tomography in Cerebral Glioma Grading, Jcpsp, Journal of the College of Physicians & Surgeons - PakistanJ Coll Physicians Surg Pak, 26, 562-5, 2016	Standard MRI was not used
Bell, C., Dowson, N., Puttick, S., Gal, Y., Thomas, P., Fay, M., Smith, J., Rose, S., Increasing feasibility and utility of (18)F-FDOPA PET for the management of glioma, Nuclear Medicine & BiologyNucl Med Biol, 42, 788-95, 2015	Narrative review
Bulakbasi, N., Guvenc, I., Onguru, O., Erdogan, E., Tayfun, C., Ucoz, T., The added value of the apparent diffusion coefficient calculation to magnetic resonance imaging in the differentiation and grading of malignant brain tumors, J Comput Assist TomogrJournal of computer assisted tomography, 28, 735-46, 2004	Study did not provide the results of conventional MRI alone
Chawalparit, O., Sangruchi, T., Witthiwej, T., Sathornsumetee, S., Tritrakarn, S., Piyapittayanan, S., Chaicharoen, P., Direksunthorn, T., Charnchaowanish, P., Diagnostic performance of advanced MRI in differentiating high-grade from low-grade gliomas in a setting of routine service, Journal of the Medical Association of Thailand, 96, 1365-73, 2013	Study unavailable
Chen, Z., Ma, L., Lou, X., Zhou, Z., Diagnostic value of minimum apparent diffusion coefficient values in prediction of neuroepithelial tumor grading, Journal of Magnetic Resonance ImagingJ Magn Reson Imaging, 31, 1331-1338, 2010	Only advanced techniques were used
Collet, S., Valable, S., Constans, J. M., Lechapt-Zalcman, E., Roussel, S., Delcroix, N., Abbas, A., Ibazizene, M., Bernaudin, M., Barre, L., Derlon, J. M., Guillamo, J. S., [¹⁸F]-fluoro-l-thymidine PET and advanced MRI for preoperative grading of gliomas, NeuroImage: Clinical, 8, 448-454, 2015	No relevant outcomes were reported

Excluded studies - What is the most effective imaging strategy in newly diagnosed glioma and meningioma?	
Darwiesh, A. M. N., Maboud, N. M. A. E., Khalil, A. M. R., ElSharkawy, A. M., Role of magnetic resonance spectroscopy & diffusion weighted imaging in differentiation of supratentorial brain tumors, Egyptian Journal of Radiology and Nuclear Medicine, 47, 1037-1042, 2016	Sensitivity and specificity have not been provided
De Fatima Vasco Aragao, M., Law, M., Batista De Almeida, D., Fatterpekar, G., Delman, B., Bader, A. S., Pelaez, M., Fowkes, M., Vieira De Mello, R., Moraes Valenca, M., Comparison of perfusion, diffusion, and MR spectroscopy between low-grade enhancing pilocytic astrocytomas and high-grade astrocytomas, American Journal of Neuroradiology, 35, 1495-1502, 2014	Study did not provide the results of conventional MRI alone
Delgado, A. F., Delgado, A. F., Discrimination between Glioma Grades II and III Using Dynamic Susceptibility Perfusion MRI: A Meta-Analysis, Ajnr: American Journal of NeuroradiologyAJNR Am J Neuroradiol, 38, 1348-1355, 2017	Conventional MRI was not used as a comparison
Direksunthorn, T., Chawalparit, O., Sangruchi, T., Witthiwej, T., Tritrakarn, S. O., Piyapittayanan, S., Charnchaowanish, P., Pornpunyawut, P., Sathornsumetee, S., Diagnostic performance of perfusion MRI in differentiating low-grade and high-grade gliomas: advanced MRI in glioma, A Siriraj project, Journal of the Medical Association of Thailand, 96, 1183-90, 2013	Study unavailable
Dunet, V., Prior, J. O., Diagnostic accuracy of F-18-fluoroethyltyrosine PET and PET/CT in patients with brain tumor, Clinical and Translational Imaging, 1, 135-144, 2013	Index test not in protocol
Dunet, V., Rossier, C., Buck, A., Stupp, R., Prior, J. O., Performance of 18F-fluoro-ethyl-tyrosine (18F-FET) PET for the differential diagnosis of primary brain tumor: a systematic review and Metaanalysis, Journal of Nuclear MedicineJ Nucl Med, 53, 207-14, 2012	Index test not in protocol
Ellika, S. K., Jain, R., Patel, S. C., Scarpace, L., Schultz, L. R., Rock, J. P., Mikkelsen, T., Role of perfusion CT in glioma grading and comparison with conventional MR imaging features, 28, 1981-7, 2007	Index test not in protocol; low number of participants
El-Serougy, L., Abdel Razek, A. A., Ezzat, A., Eldawoody, H., El-Morsy, A., Assessment of diffusion tensor imaging metrics in differentiating low-grade from high-grade gliomas, Neuroradiology JournalNeuroradiol, 29, 400-7, 2016	Only advanced techniques were used

Excluded studies - What is the most effective imaging strategy in newly diagnosed glioma and meningioma?	
Falk, A., Fahlstrom, M., Rostrup, E., Berntsson, S., Zetterling, M., Morell, A., Larsson, H. B., Smits, A., Larsson, E. M., Discrimination between glioma grades II and III in suspected low-grade gliomas using dynamic contrast-enhanced and dynamic susceptibility contrast perfusion MR imaging: a histogram analysis approach, NeuroradiologyNeuroradiology, 56, 1031-8, 2014	Index test not in protocol
Ferda, J., Kastner, J., Mukensnabl, P., Choc, M., Horemuzova, J., Ferdova, E., Kreuzberg, B., Diffusion tensor magnetic resonance imaging of glial brain tumors, Eur J RadiolEuropean journal of radiology, 74, 428-436, 2010	Only advanced techniques have been reported
Floeth, F. W., Pauleit, D., Wittsack, H. J., Langen, K. J., Reifenberger, G., Hamacher, K., Messing-Junger, M., Zilles, K., Weber, F., Stummer, W., Steiger, H. J., Woebker, G., Muller, H. W., Coenen, H., Sabel, M., Multimodal metabolic imaging of cerebral gliomas: positron emission tomography with [18F]fluoroethyl-L-tyrosine and magnetic resonance spectroscopy, J NeurosurgJournal of neurosurgery, 102, 318-27, 2005	Index test not in PICO
Fouke, S. J., Benzinger, T., Gibson, D., Ryken, T. C., Kalkanis, S. N., Olson, J. J., The role of imaging in the management of adults with diffuse low grade glioma: A systematic review and evidence-based clinical practice guideline, Journal of Neuro-Oncology, 125, 457-479, 2015	Only advanced techniques were used
Garibotto, V., Forster, S., Haller, S., Vargas, M. I., Drzezga, A., Molecular neuroimaging with PET/MRI, Clinical and Translational Imaging, 1, 53-63, 2013	Narrative review
Hakyemez, B., Erdogan, C., Ercan, I., Ergin, N., Uysal, S., Atahan, S., High-grade and low-grade gliomas: differentiation by using perfusion MR imaging, Clinical RadiologyClin Radiol, 60, 493-502, 2005	Study did not provide the results of conventional MRI alone
Hatakeyama, T., Kawai, N., Nishiyama, Y., Yamamoto, Y., Sasakawa, Y., Ichikawa, T., Tamiya, T., ¹¹C-methionine (MET) and ¹⁸F-fluorothymidine (FLT) PET in patients with newly diagnosed glioma, Eur J Nucl Med Mol ImagingEuropean journal of nuclear medicine and molecular imaging, 35, 2009-2017, 2008	Index test not in protocol
Hilario, A., Ramos, A., Perez-Nunez, A., Salvador, E., Millan, J. M., Lagares, A., Sepulveda, J. M., Gonzalez-Leon, P., Hernandez-Lain, A., Ricoy, J. R., The added value of apparent diffusion coefficient to cerebral blood volume in the preoperative grading of diffuse gliomas, 33, 701-7, 2012	Only advanced techniques were used

Excluded studies - What is the most effective imaging strategy in newly diagnosed glioma and meningioma?	
Hollingworth, W., Medina, L. S., Lenkinski, R. E., Shibata, D. K., Bernal, B., Zurakowski, D., Comstock, B., Jarvik, J. G., A systematic literature review of magnetic resonance spectroscopy for the characterization of brain tumors, American Journal of Neuroradiology, 27, 1404-1411, 2006	Only advanced techniques have been reported
Hutterer, M., Nowosielski, M., Putzer, D., Jansen, N. L., Seiz, M., Schocke, M., McCoy, M., Gobel, G., la Fougere, C., Virgolini, I. J., Trinka, E., Jacobs, A. H., Stockhammer, G., [18F]-fluoro-ethyl-L-tyrosine PET: a valuable diagnostic tool in neuro-oncology, but not all that glitters is glioma, Neuro OncolNeuro-oncology, 15, 341-51, 2013	Index test not in protocol
Jansen, N. L., Graute, V., Armbruster, L., Suchorska, B., Lutz, J., Eigenbrod, S., Cumming, P., Bartenstein, P., Tonn, J. C., Kreth, F. W., La Fougere, C., MRI-suspected low-grade glioma: Is there a need to perform dynamic FET PET?, Eur J Nucl Med Mol ImagingEuropean journal of nuclear medicine and molecular imaging, 39, 1021-1029, 2012	Index test not in protocol
Kim, H. S., Goh, M. J., Kim, N., Choi, C. G., Kim, S. J., Kim, J. H., Which combination of MR imaging modalities is best for predicting recurrent glioblastoma? Study of diagnostic accuracy and reproducibility, RadiologyRadiology, 273, 831-43, 2014	Recurrent glioblastoma is not part of the population of interest
Liang, R., Wang, X., Li, M., Yang, Y., Luo, J., Mao, Q., Liu, Y., Potential role of fractional anisotropy derived from diffusion tensor imaging in differentiating high-grade gliomas from low-grade gliomas: A meta-analysis, International journal of clinical and experimental medicineInt J Clin Exp Med, 7, 3647-3653, 2014	Only advanced techniques have been reported
Nguyen, T. B., Cron, G. O., Perdrizet, K., Bezzina, K., Torres, C. H., Chakraborty, S., Woulfe, J., Jansen, G. H., Sinclair, J., Thornhill, R. E., Foottit, C., Zanette, B., Cameron, I. G., Comparison of the diagnostic accuracy of DSC- and dynamic contrast-enhanced MRI in the preoperative grading of astrocytomas, American Journal of Neuroradiology, 36, 2017-2022, 2015	The study looked at the different types of perfusion imaging and did not compare the results with conventional MRI
Pauleit, D., Floeth, F., Hamacher, K., Riemenschneider, M. J., Reifenberger, G., Muller, H. W., Zilles, K., Coenen, H. H., Langen, K. J., O-(2-[18F]fluoroethyl)-L-tyrosine PET combined with MRI improves the diagnostic assessment of cerebral gliomas, BrainBrain, 128, 678-87, 2005	Index test not in protocol
Rapp, M., Heinzel, A., Galldiks, N., Stoffels, G., Felsberg, J., Ewelt, C., Sabel, M., Steiger, H. J., Reifenberger, G., Beez, T., Coenen, H. H., Floeth, F. W.,	Index test not in protocol

Excluded studies - What is the most effective imaging strategy in newly diagnosed glioma and meningioma?	
Langen, K. J., Diagnostic performance of 18F-FET PET in newly diagnosed cerebral lesions suggestive of glioma, Journal of Nuclear MedicineJ Nucl Med, 54, 229-35, 2013	
Sahoo, P., Gupta, R. K., Gupta, P. K., Awasthi, A., Pandey, C. M., Gupta, M., Patir, R., Vaishya, S., Ahlawat, S., Saha, I., Diagnostic accuracy of automatic normalization of CBV in glioma grading using T1- weighted DCE-MRI, Magnetic Resonance ImagingMagn Reson Imaging, 44, 32-37, 2017	Index test (ROI placement) not in protocol
Saito, T., Yamasaki, F., Kajiwara, Y., Abe, N., Akiyama, Y., Kakuda, T., Takeshima, Y., Sugiyama, K., Okada, Y., Kurisu, K., Role of perfusion-weighted imaging at 3 T in the histopathological differentiation between astrocytic and oligodendroglial tumors, Eur J RadiolEuropean journal of radiology, 81, 1863-1869, 2012	Only advanced techniques were used
Server, A., Graff, B. A., Orheim, T. E. D., Schellhorn, T., Josefsen, R., Gadmar, O. B., Nakstad, P. H., Measurements of diagnostic examination performance and correlation analysis using microvascular leakage, cerebral blood volume, and blood flow derived from 3T dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging in glial tumor grading, NeuroradiologyNeuroradiology, 53, 435-447, 2011	Only advanced techniques were used
Song, Pj, Lu, Qy, Li, My, Li, X, Shen, F, Comparison of effects of 18F-FDG PET-CT and MRI in identifying and grading gliomas, J Biol Regul Homeost AgentsJournal of biological regulators and homeostatic agents, 30, 833-838, 2017	Index tests were not compared to histology
Sui, Y., Xiong, Y., Jiang, J., Karaman, M. M., Xie, K. L., Zhu, W., Zhou, X. J., Differentiation of Low- and High-Grade Gliomas Using High b-Value Diffusion Imaging with a Non-Gaussian Diffusion Model, 37, 1643-9, 2016	Only advanced techniques were used
Testart Dardel, N., Gomez-Rio, M., Trivino-Ibanez, E., Llamas-Elvira, J. M., Clinical applications of PET using C-11/F-18-choline in brain tumours: a systematic review, Clinical and Translational Imaging, 5, 101-119, 2017	Only advanced techniques were used
Tomura, N., Mizuno, Y., Saginoya, T., PET/CT findings for tumors in the base of the skull: Comparison of 18 F-FDG with 11 C-methionine, Acta RadiologicaActa Radiol, 57, 325-332, 2016	Sensitivity and specificity have not been reported
Tong, T., Yang, Z., Chen, J. W., Zhu, J., Yao, Z., Dynamic ¹H-MRS assessment of brain tumors: A novel approach for differential diagnosis of glioma, OncotargetOncotarget, 6, 32257-32265, 2015	Only advanced techniques were used

Excluded studies - What is the most effective imaging strategy in newly diagnosed glioma and meningioma?	
van den Bent, M. J., Wefel, J. S., Schiff, D., Taphoorn, M. J., Jaeckle, K., Junck, L., Armstrong, T., Choucair, A., Waldman, A. D., Gorlia, T., Chamberlain, M., Baumert, B. G., Vogelbaum, M. A., Macdonald, D. R., Reardon, D. A., Wen, P. Y., Chang, S. M., Jacobs, A. H., Response assessment in neuro-oncology (a report of the RANO group): assessment of outcome in trials of diffuse low-grade gliomas, Lancet OncologyLancet Oncol, 12, 583-93, 2011	Did not provide any analysis or study related with the added value of an imaging strategy over standard MRI
Verburg, N., Hoefnagels, F. W. A., Barkhof, F., Boellaard, R., Goldman, S., Guo, J., Heimans, J. J., Hoekstra, O. S., Jain, R., Kinoshita, M., Pouwels, P. J. W., Price, S. J., Reijneveld, J. C., Stadlbauer, A., Vandertop, W. P., Wesseling, P., Zwinderman, A. H., De Witt Hamer, P. C., Diagnostic Accuracy of Neuroimaging to Delineate Diffuse Gliomas within the Brain: A Meta-Analysis, American Journal of Neuroradiology, 2017	Advanced MRI techniques were not used in combination with conventional MRI
Wakabayashi, T., Iuchi, T., Tsuyuguchi, N., Nishikawa, R., Arakawa, Y., Sasayama, T., Miyake, K., Nariai, T., Narita, Y., Hashimoto, N., Okuda, O., Matsuda, H., Kubota, K., Ito, K., Nakazato, Y., Kubomura, K., Diagnostic Performance and Safety of Positron Emission Tomography Using ¹⁸F-Fluciclovine in Patients with Clinically Suspected High- or Low-grade Gliomas: A Multicenter Phase IIb Trial, Asia Oceania Journal of Nuclear Medicine & BiologyAsia ocean, 5, 10-21, 2017	The outcome was to locate the presence versus absence of (any) tumour grade
Wang, Q., Zhang, H., Zhang, J., Wu, C., Zhu, W., Li, F., Chen, X., Xu, B., The diagnostic performance of magnetic resonance spectroscopy in differentiating high-from low-grade gliomas: A systematic review and meta-analysis, European Radiology, 26, 2670-84, 2016	Only advanced techniques have been reported
Zikou, A., Alexiou, G. A., Goussia, A., Kosta, P., Xydis, V., Voulgaris, S., Kyritsis, A. P., Argyropoulou, M. I., The role of diffusion tensor imaging and dynamic susceptibility perfusion MRI in the evaluation of meningioma grade and subtype, Clinical Neurology and Neurosurgery, 146, 109-115, 2016	Only advanced techniques were used
Zonari, P., Baraldi, P., Crisi, G., Multimodal MRI in the characterization of glial neoplasms: the combined role of single-voxel MR spectroscopy, diffusion imaging and echo-planar perfusion imaging, Neuroradiology, 49, 795-803, 2007	Study did not provide the results of conventional MRI alone

Economic studies

Not applicable – health economic inclusion / exclusion detailed in Supplementary Material D.

Excluded studies for review 3a – managing inoperable, incompletely excised or recurrent meningioma

Clinical studies

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Study	**Reason for Exclusion**
Abdelaziz, Osama S., Kandil, Alaa, El-Assaal, Shaaban, Abdelaziz, Amro, Rostom, Yosry, Rashed, Yaser, Linear accelerator-based stereotactic radiosurgery of intracranial meningiomas: results of the first 5 years of clinical practice, Neurosurgical ReviewNeurosurg Rev, 34, 87-99, 2011	Non-comparative study
Aboukais, R., Zairi, F., Lejeune, J. P., Le Rhun, E., Vermandel, M., Blond, S., Devos, P., Reyns, N., Grade 2 meningioma and radiosurgery, Journal of NeurosurgeryJ Neurosurg, 122, 1157-1162, 2015	Non-comparative study
Agarwal, V., McCutcheon, B. A., Hughes, J. D., Carlson, M. L., Glasgow, A. E., Habermann, E. B., Nguyen, Q. B., Link, M. J., Van Gompel, J. J., Trends in Management of Intracranial Meningiomas: Analysis of 49,921 Cases from Modern Cohort, World Neurosurgery, 106, 145-151, 2017	Analyses not in PICO
Aichholzer, M., Bertalanffy, A., Dietrich, W., Roessler, K., Pfisterer, W., Ungersboeck, K., Heimberger, K., Kitz, K., Gamma knife radiosurgery of skull base meningiomas, Acta NeurochirurgicaActa Neurochir (Wien), 142, 647-52; discussion 652-3, 2000	Observational study; comparisons not in PICO
Arvold,N.D., Lessell,S., Bussiere,M., Beaudette,K., Rizzo,J.F., Loeffler,J.S., Shih,H.A., Visual outcome and tumor control after conformal radiotherapy for patients with optic nerve sheath meningioma, International Journal of Radiation Oncology, Biology, Physics, 75, 1166-1172, 2009	Non-comparative retrospective study
Azar, M., Kazemi, F., Chanideh, I., Amirjamshidi, A., Amini, E., Ghanavati, P., Gamma Knife Radiosurgery in Sphenopetroclival Meningiomas: Preliminary Experience at the Iran Gamma Knife Center, World NeurosurgeryWorld Neurosurg, 93, 39-43, 2016	Non-comparative retrospective study
Azar, M., Kazemi, F., Jahanbakhshi, A., Chanideh, I., Jalessi, M., Amini, E., Geraily, G., Farhadi, M., Gamma Knife Radiosurgery for Cavernous Sinus Meningiomas: Analysis of Outcome in 166 Patients, Stereotactic and Functional Neurosurgery, 259-267, 2017	Analyses not in PICO

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Balasubramanian, S. K., Sharma, M., Silva, D., Karivedu, V., Schmitt, P., Stevens, G. H., Barnett, G. H., Prayson, R. A., Elson, P., Suh, J. H., Murphy, E. S., Chao, S. T., Longitudinal experience with WHO Grade III (anaplastic) meningiomas at a single institution, Journal of Neuro-Oncology, 131, 555-563, 2017	N = 3 received STR; analyses not in PICO
Barbaro, N. M., Gutin, P. H., Wilson, C. B., Sheline, G. E., Boldrey, E. B., Wara, W. M., Radiation therapy in the treatment of partially resected meningiomas, NeurosurgeryNeurosurgery, 20, 525-8, 1987	Years of treatment 1968-1978
Bassiouni, Hischam, Asgari, Siamak, Stolke, Dietmar, Tuberculum sellae meningiomas: functional outcome in a consecutive series treated microsurgically, Surgical NeurologySurg Neurol, 66, 37-44; discussion 44-5, 2006	Non-comparative retrospective study
Brell, Marta, Villa, Salvador, Teixidor, Pilar, Lucas, Anna, Ferran, Enric, Marin, Susanna, Acebes, Juan Jose, Fractionated stereotactic radiotherapy in the treatment of exclusive cavernous sinus meningioma: functional outcome, local control, and tolerance, Surgical NeurologySurg Neurol, 65, 28-33; discussion 33-4, 2006	Non-comparative retrospective study
Bria, Carley, Wegner, Rodney E., Clump, David A., Vargo, John A., Mintz, Arlan H., Heron, Dwight E., Burton, Steven A., Fractionated stereotactic radiosurgery for the treatment of meningiomas, Journal of Cancer Research & TherapeuticsJ Cancer Res Ther, 7, 52-7, 2011	Non-comparative retrospective study
Brokinkel, B., Holling, M., Spille, D. C., Hess, K., Sauerland, C., Bleimuller, C., Paulus, W., Wolfer, J., Stummer, W., Surgery for meningioma in the elderly and long-term survival: Comparison with an age- and sex-matched general population and with younger patients, Journal of Neurosurgery, 126, 1201-1211, 2017	Analyses/comparisons not in PICO
Buglione, M., De Bari, B., Trevisan, F., Ghirardelli, P., Pedretti, S., Triggiani, L., Magrini, S. M., Role of external beam radiotherapy in the treatment of relapsing meningioma, Medical OncologyMed Oncol, 31 (3) (no pagination), 2014	Non-comparative study
Cain, S. A., Smoll, N. R., Van Heerden, J., Tsui, A., Drummond, K. J., Atypical and malignant meningiomas: Considerations for treatment and efficacy of radiotherapy, Journal of Clinical NeuroscienceJ Clin Neurosci, 22, 1742-1748, 2015	46/58 patients received gross total resection.
Cao, Xiaoyu, Hao, Shuyu, Wu, Zhen, Wang, Liang, Jia, Guijun, Zhang, Liwei, Zhang, Junting, Treatment Response and Prognosis After Recurrence of Atypical Meningiomas, World NeurosurgeryWorld Neurosurg, 84, 1014-9, 2015	Non-comparative retrospective study
Celtikci, Emrah, Kaymaz, A. Memduh, Akgul, Gulsah, Karaaslan, Burak, Emmez, O. Hakan, Borcek, Alp, Retrospective Analysis of 449 Intracranial Meningioma Patients Operated between years 2007 - 2013 in a Single Institute, 2016	Non-comparative retrospective study
Chang, S. D., Adler, J. R., Jr., Treatment of cranial base meningiomas with linear accelerator radiosurgery, NeurosurgeryNeurosurgery, 41, 1019-25; discussion 1025-7, 1997	Non-comparative retrospective study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Chin, Lawrence S., Szerlip, Nicholas J., Regine, William F., Stereotactic radiosurgery for meningiomas, Neurosurgical FocusNeurosurg, 14, e6, 2003	Narrative review
Cohen-Inbar, O., Lee, C. C., Schlesinger, D., Xu, Z., Sheehan, J. P., Long-term results of stereotactic radiosurgery for skull base meningiomas, Clinical NeurosurgeryClin Neurosurg, 79, 58-68, 2016	Non-comparative retrospective study
Cohen-Inbar, O., Lee, C. C., Sheehan, J. P., The Contemporary Role of Stereotactic Radiosurgery in the Treatment of Meningiomas, Neurosurgery Clinics of North AmericaNeurosurg Clin N Am, 27, 215-228, 2016	Narrative review
Combs, S. E., Hartmann, C., Nikoghosyan, A., Jakel, O., Karger, C. P., Haberer, T., von Deimling, A., Munter, M. W., Huber, P. E., Debus, J., Schulz-Ertner, D., Carbon ion radiation therapy for high-risk meningiomas, Radiotherapy and Oncology, 95, 54-59, 2010	Non-comparative retrospective study
Combs, Stephanie E., Edler, Lutz, Burkholder, Iris, Rieken, Stefan, Habermehl, Daniel, Jakel, Oliver, Haberer, Thomas, Unterberg, Andreas, Wick, Wolfgang, Debus, Jurgen, Haselmann, Renate, Treatment of patients with atypical meningiomas Simpson grade 4 and 5 with a carbon ion boost in combination with postoperative photon radiotherapy: the MARCIE trial, BMC CancerBMC Cancer, 10, 615, 2010	Trial protocol
Combs, Stephanie E., Sterzing, Florian, Uhl, Matthias, Habl, Gregor, Schubert, Kai, Debus, Jurgen, Herfarth, Klaus, Helical tomotherapy for meningiomas of the skull base and in paraspinal regions with complex anatomy and/or multiple lesions, TumoriTumori, 97, 484-91, 2011	Non-comparative retrospective study
Correa, Sebastiao Francisco Miranda, Marta, Gustavo Nader, Teixeira, Manoel Jacobsen, Neurosymptomatic carvenous sinus meningioma: a 15-years experience with fractionated stereotactic radiotherapy and radiosurgery, Radiation OncologyRadiat, 9, 27, 2014	Observational study; comparison not in PICO (radiotherapy vesus radiotherapy)
de Almeida, A. N., Pereira, B. J. A., Pires Aguiar, P. H., Paiva, W. S., Cabrera, H. N., da Silva, C. C., Teixeira, M. J., Marie, S. K. N., Clinical Outcome, Tumor Recurrence, and Causes of Death: A Long-Term Follow-Up of Surgically Treated Meningiomas, World Neurosurgery, 102, 139-143, 2017	Analyses not in PICO
De Jesus, O., Sekhar, L. N., Parikh, H. K., Wright, D. C., Wagner, D. P., Long-term follow-up of patients with meningiomas involving the cavernous sinus: recurrence, progression, and quality of life, NeurosurgeryNeurosurgery, 39, 915-9; discussion 919-20, 1996	Non-comparative retrospective study
Debus, J., Wuendrich, M., Pirzkall, A., Hoess, A., Schlegel, W., Zuna, I., Engenhart-Cabillic, R., Wannenmacher, M., High efficacy of fractionated stereotactic radiotherapy of large base-of-skull meningiomas: long-term results, Journal of Clinical OncologyJ Clin Oncol, 19, 3547-53, 2001	Non-comparative retrospective study
Ding, D., Starke, R. M., Kano, H., Nakaji, P., Barnett, G. H., Mathieu, D., Chiang, V., Omay, S. B., Hess, J., McBride, H. L., Honea, N., Lee, J. Y. K., Rahmathulla, G., Evanoff, W. A., Alonso-Basanta, M., Lunsford, L.	Non-comparative retrospective study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
D., Sheehan, J. P., Gamma knife radiosurgery for cerebellopontine angle meningiomas: A multicenter study, NeurosurgeryNeurosurgery, 75, 398-407, 2014	
Ding, Dale, Starke, Robert M., Hantzmon, John, Yen, Chun-Po, Williams, Brian J., Sheehan, Jason P., The role of radiosurgery in the management of WHO Grade II and III intracranial meningiomas, Neurosurgical FocusNeurosurg, 35, E16, 2013	Review, but not systematic review
Ding, Dale, Xu, Zhiyuan, McNeill, Ian T., Yen, Chun-Po, Sheehan, Jason P., Radiosurgery for parasagittal and parafalcine meningiomas, Journal of NeurosurgeryJ Neurosurg, 119, 871-7, 2013	Non-comparative retrospective study
Dufour, H., Muracciole, X., Metellus, P., Regis, J., Chinot, O., Grisoli, F., Long-term tumor control and functional outcome in patients with cavernous sinus meningiomas treated by radiotherapy with or without previous surgery: Is there an alternative to aggressive tumor removal?, NeurosurgeryNeurosurgery, 48, 285-296, 2001	Observational study, comparison not in PICO (surgery + radiotherapy versus radiotherapy)
Eldebawy, Eman, Mousa, Amr, Reda, Wael, Elgantiry, Mahmoud, Stereotactic radiosurgery and radiotherapy in benign intracranial meningioma, Journal of Egyptian National Cancer InstituteJ, 23, 89-93, 2011	Non-comparative retrospective study
El-Khatib, M., Majdoub, F. E., Hoevels, M., Kocher, M., Muller, R. P., Steiger, H. J., Sturm, V., Maarouf, M., Stereotactic LINAC radiosurgery for incompletely resected or recurrent atypical and anaplastic meningiomas, Acta NeurochirurgicaActa Neurochir (Wien), 153, 1761-1767, 2011	Non-comparative study
El-Khatib, Mustafa, El Majdoub, Faycal, Hunsche, Stefan, Hoevels, Mauritius, Kocher, Martin, Sturm, Volker, Maarouf, Mohammad, Stereotactic LINAC radiosurgery for the treatment of typical intracranial meningiomas. Efficacy and safety after a follow-up of over 12 years, Strahlentherapie und OnkologieStrahlenther Onkol, 191, 921-7, 2015	Non-comparative study
Flickinger, John C., Kondziolka, Douglas, Maitz, Ann H., Lunsford, L. Dade, Gamma knife radiosurgery of imaging-diagnosed intracranial meningioma, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 56, 801-6, 2003	Non-comparative study
Freeman, J. L., Davern, M. S., Oushy, S., Sillau, S., Ormond, D. R., Youssef, A. S., Lillehei, K. O., Spheno-Orbital Meningiomas: A 16-Year Surgical Experience, World Neurosurgery, 99, e39, 2017	Analyses not in PICO
Gallagher, M. J., Jenkinson, M. D., Brodbelt, A. R., Mills, S. J., Chavredakis, E., WHO grade 1 meningioma recurrence: Are location and Simpson grade still relevant?, Clinical Neurology & NeurosurgeryClin Neurol Neurosurg, 141, 117-21, 2016	Comparison/analyses not in PICO
Ganz, J. C., Reda, W. A., Abdelkarim, K., Gamma Knife surgery of large meningiomas: early response to treatment, Acta NeurochirurgicaActa Neurochir (Wien), 151, 1-8, 2009	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Garzon-Muvdi, T., Yang, W., Lim, M., Brem, H., Huang, J., Atypical and anaplastic meningioma: outcomes in a population based study, Journal of Neuro-Oncology, 1-10, 2017	Analyses not in PICO
Glaholm, J., Bloom, H. J., Crow, J. H., The role of radiotherapy in the management of intracranial meningiomas: the Royal Marsden Hospital experience with 186 patients, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 18, 755-61, 1990	Non-comparative study; analyses not in PICO
Gorman, L., Ruben, J., Myers, R., Dally, M., Role of hypofractionated stereotactic radiotherapy in treatment of skull base meningiomas, Journal of Clinical NeuroscienceJ Clin Neurosci, 15, 856-862, 2008	Non-comparative study
Gudjonsson, O., Blomquist, E., Nyberg, G., Pellettieri, L., Montelius, A., Grusell, E., Dahlgren, C., Isacsson, U., Lilja, A., Glimelius, B., Stereotactic irradiation of skull base meningiomas with high energy protons, Acta NeurochirurgicaActa Neurochir (Wien), 141, 933-40, 1999	Non-comparative study
Hadelsberg, Uri, Nissim, Uzi, Cohen, Zvi R., Spiegelmann, Roberto, LINAC radiosurgery in the management of parasagittal meningiomas, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 93, 10-6, 2015	Non-comparative study
Hahn, B. M., Schrell, U. M. H., Sauer, R., Fahlbusch, R., Ganslandt, O., Grabenbauer, G. G., Prolonged oral hydroxyurea and concurrent 3d-conformal radiation in patients with progressive or recurrent meningioma: Results of a pilot study, Journal of Neuro-OncologyJ Neurooncol, 74, 157-165, 2005	Non-comparative retrospective study
Halasz, L. M., Bussire, M. R., Dennis, E. R., Niemierko, A., Chapman, P. H., Loeffler, J. S., Shih, H. A., Proton stereotactic radiosurgery for the treatment of benign meningiomas, International Journal of Radiation Oncology Biology Physics, 81, 1428-1435, 2011	Non-comparative retrospective study
Hamm, K., Henzel, M., Gross, M. W., Surber, G., Kleinert, G., Engenhart-Cabillic, R., Radiosurgery/stereotactic radiotherapy in the therapeutical concept for skull base meningiomas, Zentralblatt fur NeurochirurgieZentralbl Neurochir, 69, 14-21, 2008	Non-comparative retrospective study
Han, Jeannie, Girvigian, Michael R., Chen, Joseph C. T., Miller, Michael J., Lodin, Kenneth, Rahimian, Javad, Arellano, Alonzo, Cahan, Benjamin L., Kaptein, John S., A comparative study of stereotactic radiosurgery, hypofractionated, and fractionated stereotactic radiotherapy in the treatment of skull base meningioma, American Journal of Clinical OncologyAm J Clin Oncol, 37, 255-60, 2014	Observational study, comparison not in PICO: radiotherapy versus radiotherapyversus radiotherapy
Han, Jung Ho, Kim, Dong Gyu, Chung, Hyun-Tai, Park, Chul-Kee, Paek, Sun Ha, Kim, Chae-Yong, Jung, Hee-Won, Gamma knife radiosurgery for skull base meningiomas: long-term radiologic and clinical outcome, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 72, 1324-32, 2008	Non-comparative retrospective study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Hanakita, Shunya, Koga, Tomoyuki, Igaki, Hiroshi, Murakami, Naoya, Oya, Soichi, Shin, Masahiro, Saito, Nobuhito, Role of gamma knife surgery for intracranial atypical (WHO grade II) meningiomas, Journal of NeurosurgeryJ Neurosurg, 119, 1410-4, 2013	Non-comparative study with multivariate analyses
Hasegawa, Toshinori, Kida, Yoshihisa, Yoshimoto, Masayuki, Iizuka, Hiroshi, Ishii, Dai, Yoshida, Kouta, Gamma Knife surgery for convexity, parasagittal, and falcine meningiomas, Journal of NeurosurgeryJ Neurosurg, 114, 1392-8, 2011	Non-comparative study
Hodes, J. E., Sanders, M., Patel, P., Patchell, R. A., Radiosurgical management of meningiomas, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 66, 15-8, 1996	Non-comparative study
Huffmann, Beate C., Reinacher, Peter C., Gilsbach, Joachim M., Gamma knife surgery for atypical meningiomas, Journal of NeurosurgeryJ Neurosurg, 102 Suppl, 283-6, 2005	Non-comparative retrospective study
Hug, E. B., Devries, A., Thornton, A. F., Munzenride, J. E., Pardo, F. S., Hedley-Whyte, E. T., Bussiere, M. R., Ojemann, R., Management of atypical and malignant meningiomas: role of high-dose, 3D-conformal radiation therapy, Journal of Neuro-OncologyJ Neurooncol, 48, 151-60, 2000	Non-comparative study (21/23 patients received subtotal resection + radiotherapyversus 2/23 patients who received biopsy only and radiotherapy)
Igaki, Hiroshi, Maruyama, Keisuke, Koga, Tomoyuki, Murakami, Naoya, Tago, Masao, Terahara, Atsuro, Shin, Masahiro, Nakagawa, Keiichi, Ohtomo, Kuni, Stereotactic radiosurgery for skull base meningioma, Neurologia Medico-ChirurgicaNeurol Med Chir (Tokyo), 49, 456-61, 2009	Non-comparative retrospective study
Iwai, Yoshiyasu, Yamanaka, Kazuhiro, Ikeda, Hidetoshi, Gamma Knife radiosurgery for skull base meningioma: long-term results of low-dose treatment, Journal of NeurosurgeryJ Neurosurg, 109, 804-10, 2008	Non-comparative retrospective study
Iwai, Yoshiyasu, Yamanaka, Kazuhiro, Ishiguro, Tomoya, Gamma knife radiosurgery for the treatment of cavernous sinus meningiomas, NeurosurgeryNeurosurgery, 52, 517-24; discussion 523-4, 2003	Non-comparative study
Iwai, Yoshiyasu, Yamanaka, Kazuhiro, Morikawa, Toshie, Adjuvant gamma knife radiosurgery after meningioma resection, J Clin Neurosci, 11, 715-8, 2004	Non-comparative study
Jenkinson, M. D., Waqar, M., Farah, J. O., Farrell, M., Barbagallo, G. M. V., McManus, R., Looby, S., Hussey, D., Fitzpatrick, D., Certo, F., Javadpour, M., Early adjuvant radiotherapy in the treatment of atypical meningioma, J Clin Neurosci, 28, 87-92, 2016	Observational study; comparisons/analyses not in PICO
Jenkinson, M. D., Waqar, M., Farah, J. O., Farrell, M., Barbagallo, G. M. V., McManus, R., Looby, S., Hussey, D., Fitzpatrick, D., Certo, F., Javadpour, M., Early adjuvant radiotherapy in the treatment of atypical meningioma, Journal of Clinical NeuroscienceJ Clin Neurosci, 28, 87-92, 2016	Duplicate

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Jeremic, B., Pitz, S., Primary optic nerve sheath meningioma: Stereotactic fractionated radiation therapy as an emerging treatment of choice, Cancer, 110, 714-722, 2007	Narrative review
Kaley, T., Barani, I., Chamberlain, M., McDermott, M., Panageas, K., Raizer, J., Rogers, L., Schiff, D., Vogelbaum, M., Weber, D., Wen, P., Historical benchmarks for medical therapy trials in surgery-and radiation-refractory meningioma: A RANO review, Neuro-OncologyNeuro-oncol, 16, 829-840, 2014	Intervention (medical systemic therapies) not in PICO
Kano, Hideyuki, Takahashi, Jun A., Katsuki, Takahisa, Araki, Norio, Oya, Natsuo, Hiraoka, Masahiro, Hashimoto, Nobuo, Stereotactic radiosurgery for atypical and anaplastic meningiomas, J Neurooncol, 84, 41-7, 2007	Observational study; comparison not in PICO (radiotherapy versus radiotherapy)
Kaul, David, Budach, Volker, Wurm, Reinhard, Gruen, Arne, Graaf, Lukas, Habbel, Piet, Badakhshi, Harun, Linac-based stereotactic radiotherapy and radiosurgery in patients with meningioma, Radiation OncologyRadiat, 9, 78, 2014	Observational study; comparison not in PICO (radiotherapy versus radiotherapy)
Kessel, K. A., Fischer, H., Oechnser, M., Zimmer, C., Meyer, B., Combs, S. E., High-precision radiotherapy for meningiomas: Long-term results and patient-reported outcome (PRO), Strahlentherapie und Onkologie, 1-10, 2017	Comparison not in PICO
Kim, J. W., Kim, D. G., Se, Y. B., Kim, S. K., Chung, H. T., Paek, S. H., Jung, H. W., Gamma Knife Radiosurgery for Petroclival Meningioma: Long-Term Outcome and Failure Pattern, Stereotactic and Functional Neurosurgery, 209-215, 2017	Non-comparative study
Kim, M., Cho, Y. H., Kim, J. H., Kim, C. J., Kwon, D. H., Analysis the causes of radiosurgical failure in intracranial meningiomas treated with radiosurgery, Clinical Neurology and Neurosurgery, 154, 51-58, 2017	Non-comparative study
Kim, M., Lee, D. H., Kim, Rn H. J., Cho, Y. H., Kim, J. H., Kwon, D. H., Analysis of the results of recurrent intracranial meningiomas treated with re-radiosurgery, Clinical Neurology and Neurosurgery, 153, 93-101, 2017	Non-comparative study
Kim, Dong Gyu, Kim, Ch Heon, Chung, Hyun-Tai, Paek, Sun Ha, Jeong, Sang Soon, Han, Dae Hee, Jung, Hee-Won, Gamma knife surgery of superficially located meningioma, J Neurosurg, 102 Suppl, 255-8, 2005	Non-comparative study
Kim, Y. H., Kim, D. G., Han, J. H., Chung, H. T., Kim, I. K., Song, S. W., Park, J. H., Kim, J. W., Kim, Y. H., Park, C. K., Kim, C. Y., Paek, S. H., Jung, H. W., Radiosurgery for para-IAC meningiomas: The effect of radiation dose to the cochlea on hearing outcome, International Journal of Radiation Oncology Biology Physics, 84, 675-680, 2012	Non-comparative retrospective study
Kimball, M. M., Friedman, W. A., Foote, K. D., Bova, F. J., Chi, Y. Y., Linear accelerator radiosurgery for cavernous sinus meningiomas, Stereotactic and Functional Neurosurgery, 87, 120-127, 2009	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Klinger, Daniel R., Flores, Bruno C., Lewis, Jeremy J., Hatanpaa, Kimmo, Choe, Kevin, Mickey, Bruce, Barnett, Samuel, Atypical Meningiomas: Recurrence, Reoperation, and Radiotherapy, World NeurosurgeryWorld Neurosurg, 84, 839-45, 2015	Non-comparative retrospective study
Knosp, E., Perneczky, A., Koos, W. T., Fries, G., Matula, C., Meningiomas of the space of the cavernous sinus, NeurosurgeryNeurosurgery, 38, 434-42; discussion 442-4, 1996	Non-comparative retrospective study
Kobayashi, T., Kida, Y., Mori, Y., Long-term results of stereotactic gamma radiosurgery of meningiomas, Surgical NeurologySurg Neurol, 55, 325-31, 2001	Non-comparative study
Kollova, Aurelia, Liscak, Roman, Novotny, Josef, Jr., Vladyka, Vilibald, Simonova, Gabriela, Janouskova, Ladislava, Gamma Knife surgery for benign meningioma, Journal of NeurosurgeryJ Neurosurg, 107, 325-36, 2007	Non-comparative study (mixed population, unclear who has received which treatment)
Komotar, R. J., Bryan Lorgulescu, J., Raper, D. M. S., Holland, E. C., Beal, K., Bilsky, M. H., Brennan, C. W., Tabar, V., Sherman, J. H., Yamada, Y., Gutin, P. H., The role of radiotherapy following gross-total resection of atypical meningiomas, Journal of NeurosurgeryJ Neurosurg, 117, 679-686, 2012	Population not in PICO
Kondziolka, Douglas, Mathieu, David, Lunsford, L. Dade, Martin, Juan J., Madhok, Ricky, Niranjan, Ajay, Flickinger, John C., Radiosurgery as definitive management of intracranial meningiomas, NeurosurgeryNeurosurgery, 62, 53-8; discussion 58-60, 2008	Non-comparative retrospective study
Korah, Mariam P., Nowlan, Adam W., Johnstone, Peter A. S., Crocker, Ian R., Radiation therapy alone for imaging-defined meningiomas, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 76, 181-6, 2010	Non-comparative retrospective study
Koutourousiou, M., Vaz Guimaraes Filho, F., Fernandez-Miranda, J. C., Wang, E. W., Stefko, S. T., Snyderman, C. H., Gardner, P. A., Endoscopic Endonasal Surgery for Tumors of the Cavernous Sinus: A Series of 234 Patients, World Neurosurgery, 103, 713-732, 2017	Analyses not in PICO
Kreil, W., Luggin, J., Fuchs, I., Weigl, V., Eustacchio, S., Papaefthymiou, G., Long term experience of gamma knife radiosurgery for benign skull base meningiomas, Journal of Neurology, Neurosurgery & PsychiatryJ Neurol Neurosurg Psychiatry, 76, 1425-30, 2005	Non-comparative retrospective study
Kuhn, Elizabeth N., Taksler, Glen B., Dayton, Orrin, Loganathan, Amritraj G., Vern-Gross, Tamara Z., Bourland, J. Daniel, Laxton, Adrian W., Chan, Michael D., Tatter, Stephen B., Patterns of recurrence after stereotactic radiosurgery for treatment of meningiomas, Neurosurgical FocusNeurosurg, 35, E14, 2013	Non-comparative retrospective study
Kumar, N., Kumar, R., Khosla, D., Salunke, P. S., Gupta, S. K., Radotra, B. D., Survival and failure patterns in atypical and anaplastic meningiomas: A single-center experience of surgery and postoperative radiotherapy, Journal of Cancer Research & TherapeuticsJ Cancer Res Ther, 11, 735-9, 2015	Analyses not in PICO

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Lagman, C., Bhatt, N. S., Lee, S. J., Bui, T. T., Chung, L. K., Voth, B. L., Barnette, N. E., Pouratian, N., Lee, P., Selch, M., Kaprealian, T., Chin, R., McArthur, D. L., Mukherjee, D., Patil, C. G., Yang, I., Adjuvant Radiosurgery Versus Serial Surveillance Following Subtotal Resection of Atypical Meningioma: A Systematic Analysis, World Neurosurgery, 98, 339-346, 2017	Systematic review with different inclusion criteria to the current review; included studies checked for relevance
Lagman, C., Bhatt, N., Pelargos, P., Lee, S., Mukherjee, D., Yang, I., A meta-analysis of published literature on adjuvant radiosurgery and surveillance following subtotal resection of atypical meningioma, Neuro-Oncology, 18, vi101, 2016	Conference abstract of Lagman 2017 (full text)
Lee, J. Y., Kondziolka, D., Flickinger, J. C., Lunsford, L. D., Radiosurgery for intracranial meningiomas, Progress in Neurological SurgeryProg, 20, 142-149, 2007	Non-comparative retrospective study
Lee, John Y. K., Niranjan, Ajay, McInerney, James, Kondziolka, Douglas, Flickinger, John C., Lunsford, L. Dade, Stereotactic radiosurgery providing long-term tumor control of cavernous sinus meningiomas, Journal of NeurosurgeryJ Neurosurg, 97, 65-72, 2002	Non-comparative retrospective study
Liscak, R., Kollova, A., Vladyka, V., Simonova, G., Novotny, J., Jr., Gamma knife radiosurgery of skull base meningiomas, Acta Neurochirurgica - SupplementActa Neurochir Suppl, 91, 65-74, 2004	Non-comparative retrospective study
Liscak, R., Simonova, G., Vymazal, J., Janouskova, L., Vladyka, V., Gamma knife radiosurgery of meningiomas in the cavernous sinus region, Acta NeurochirurgicaActa Neurochir (Wien), 141, 473-80, 1999	Non-comparative retrospective study
Liu, A. Li, Wang, Chungcheng, Sun, Shibing, Wang, Meihua, Liu, Peng, Gamma knife radiosurgery for tumors involving the cavernous sinus, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 83, 45-51, 2005	Non-comparative study
Liu, Ren-Shyan, Chang, Chen-Pei, Guo, Wen-You, Pan, David H. C., Ho, Donald Ming-Tak, Chang, Chi-Wei, Yang, Bang-Hung, Wu, Liang-Chi, Yeh, Shin-Hwa, 1-11C-acetate versus 18F-FDG PET in detection of meningioma and monitoring the effect of gamma-knife radiosurgery, Journal of Nuclear MedicineJ Nucl Med, 51, 883-91, 2010	Not in PICO
Lo, Simon S., Cho, Kwan H., Hall, Walter A., Kossow, Ronald J., Hernandez, Wilson L., McCollow, Kim K., Gerbi, Bruce J., Higgins, Patrick D., Lee, Chung K., Dusenbery, Kathryn E., Single dose versus fractionated stereotactic radiotherapy for meningiomas.[Erratum appears in Can J Neurol Sci. 2003 Feb;30(1):85], Canadian Journal of Neurological SciencesCan J Neurol Sci, 29, 240-8, 2002	Observational study, comparison not in PICO (radiotherapy versus radiotherapy)
Maire, J. P., Caudry, M., Guerin, J., Celerier, D., San Galli, F., Causse, N., Trouette, R., Dautheribes, M., Fractionated radiation therapy in the treatment of intracranial meningiomas: local control, functional efficacy, and tolerance in 91 patients, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 33, 315-21, 1995	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Malik, I., Rowe, J. G., Walton, L., Radatz, M. W. R., Kemeny, A. A., The use of stereotactic radiosurgery in the management of meningiomas, British Journal of NeurosurgeryBr J Neurosurg, 19, 13-20, 2005	Non-comparative study
Marcus, H. J., Price, S. J., Wilby, M., Santarius, T., Kirollos, R. W., Radiotherapy as an adjuvant in the management of intracranial meningiomas: Are we practising evidence-based medicine?, British Journal of NeurosurgeryBr J Neurosurg, 22, 520-528, 2008	Systematic review with no meta-analysis, not reporting on target patients with recurrence, all relevant included studies have been included individually in the current review instead
Maruyama, K., Shin, M., Kurita, H., Kawahara, N., Morita, A., Kirino, T., Proposed treatment strategy for cavernous sinus meningiomas: A prospective study, NeurosurgeryNeurosurgery, 55, 1068-1075, 2004	Observational study, comparison not in PICO ((radiotherapy versus radiotherapy + surgery)
Mendenhall, William M., Morris, Christopher G., Amdur, Robert J., Foote, Kelly D., Friedman, William A., Radiotherapy alone or after subtotal resection for benign skull base meningiomas, CancerCancer, 98, 1473-82, 2003	Non-comparative study
Meskal, I., Gehring, K., Rutten, G. J. M., Sitskoorn, M. M., Cognitive functioning in meningioma patients: a systematic review, Journal of Neuro-OncologyJ Neurooncol, 128, 195-205, 2016	Systematic review; included studies not in PICO
Metellus, Philipe, Regis, Jean, Muracciole, Xavier, Fuentes, Stephane, Dufour, Henry, Nanni, Isabelle, Chinot, Oliver, Martin, Pierre-Marie, Grisoli, Francois, Evaluation of fractionated radiotherapy and gamma knife radiosurgery in cavernous sinus meningiomas: treatment strategy, NeurosurgeryNeurosurgery, 57, 873-86; discussion 873-86, 2005	Observational study; comparison not in PICO (radiotherapy versus radiotherapy)
Metellus, Philippe, Batra, Sachin, Karkar, Siddharth, Kapoor, Sumit, Weiss, Stephanie, Kleinberg, Lawrence, Rigamonti, Danielle, Fractionated conformal radiotherapy in the management of cavernous sinus meningiomas: long-term functional outcome and tumor control at a single institution, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 78, 836-43, 2010	Non-comparative study
Milker-Zabel, Stefanie, Zabel, Angelika, Schulz-Ertner, Daniela, Schlegel, Wolfgang, Wannenmacher, Michael, Debus, Jurgen, Fractionated stereotactic radiotherapy in patients with benign or atypical intracranial meningioma: long-term experience and prognostic factors, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 61, 809-16, 2005	Non-comparative study
Milosevic, M. F., Frost, P. J., Laperriere, N. J., Wong, C. S., Simpson, W. J., Radiotherapy for atypical or malignant intracranial meningioma, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 34, 817-22, 1996	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Minniti, G., Clarke, E., Cavallo, L., Osti, M. F., Esposito, V., Cantore, G., Cappabianca, P., Enrici, R. M., Fractionated stereotactic conformal radiotherapy for large benign skull base meningiomas, Radiation OncologyRadiat, 6 (1) (no pagination), 2011	Non-comparative study
Minniti, Giuseppe, Amichetti, Maurizio, Enrici, Riccardo Maurizi, Radiotherapy and radiosurgery for benign skull base meningiomas, Radiation OncologyRadiat, 4, 42, 2009	Narrative review
Navarria, Pierina, Pessina, Federico, Cozzi, Luca, Clerici, Elena, Villa, Elisa, Ascolese, Anna Maria, De Rose, Fiorenza, Comito, Tiziana, Franzese, Ciro, D'Agostino, Giuseppe, Lobefalo, Francesca, Fogliata, Antonella, Reggiori, Giacomo, Fornari, Maurizio, Tomatis, Stefano, Bello, Lorenzo, Scorsetti, Marta, Hypofractionated stereotactic radiation therapy in skull base meningiomas, Journal of Neuro-OncologyJ Neurooncol, 124, 283-9, 2015	Non-comparative study
Nicolato, A., Ferraresi, P., Foroni, R., Pasqualin, A., Piovan, E., Severi, F., Masotto, B., Gerosa, M., Gamma Knife radiosurgery in skull base meningiomas. Preliminary experience with 50 cases, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 66 Suppl 1, 112-20, 1996	Observational study; comparisons not in PICO (radiotherapy versus radiotherapy)
Nicolato, A., Foroni, R., Pellegrino, M., Ferraresi, P., Alessandrini, F., Gerosa, M., Bricolo, A., Gamma knife radiosurgery in meningiomas of the posterior fossa. Experience with 62 treated lesions, Minimally Invasive NeurosurgeryMinim Invasive Neurosurg, 44, 211-7, 2001	Observational study; comparisons not in PICO (radiotherapy versus radiotherapy)
Nutting, C., Brada, M., Brazil, L., Sibtain, A., Saran, F., Westbury, C., Moore, A., Thomas, D. G., Traish, D., Ashley, S., Radiotherapy in the treatment of benign meningioma of the skull base, Journal of NeurosurgeryJ Neurosurg, 90, 823-7, 1999	Non-comparative study
Oermann, E. K., Bhandari, R., Chen, V. J., Lebec, G., Gurka, M., Lei, S., Chen, L., Suy, S., Azumi, N., Berkowitz, F., Kalhorn, C., McGrail, K., Collins, B. T., Jean, W. C., Collins, S. P., Five fraction image-guided radiosurgery for primary and recurrent meningiomas, Frontiers in Oncology, 3 AUG (no pagination), 2013	Non-comparative study
Ohba, Shigeo, Kobayashi, Masahito, Horiguchi, Takashi, Onozuka, Satoshi, Yoshida, Kazunari, Ohira, Takayuki, Kawase, Takeshi, Long-term surgical outcome and biological prognostic factors in patients with skull base meningiomas, Journal of NeurosurgeryJ Neurosurg, 114, 1278-87, 2011	Mixed population, unclear what treatments which patients got
Ohta, K., Yasuo, K., Morikawa, M., Nagashima, T., Tamaki, N., Treatment of tuberculum sellae meningiomas:a long-term follow-up study, Journal of Clinical NeuroscienceJ Clin Neurosci, 8 Suppl 1, 26-31, 2001	Observational study; comparisons not in PICO (surgery versus surgery)
Ojemann, S. G., Sneed, P. K., Larson, D. A., Gutin, P. H., Berger, M. S., Verhey, L., Smith, V., Petti, P., Wara, W., Park, E., McDermott, M. W., Radiosurgery for malignant meningioma: results in 22 patients, Journal of NeurosurgeryJ Neurosurg, 93 Suppl 3, 62-7, 2000	Non-comparative study (mixed population/mixed treatments)

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Onodera, Shunsuke, Aoyama, Hidefumi, Katoh, Norio, Taguchi, Hiroshi, Yasuda, Kouichi, Yoshida, Daisuke, Surtherland, Ken, Suzuki, Ryusuke, Ishikawa, Masayori, Gerard, Bengua, Terasaka, Shunsuke, Shirato, Hiroki, Long-term outcomes of fractionated stereotactic radiotherapy for intracranial skull base benign meningiomas in single institution, Japanese Journal of Clinical OncologyJpn J Clin Oncol, 41, 462-8, 2011	Non-comparative study
Otero, A., Tabernero, M. D., Munoz, M. C., Sousa, P., Miranda, D., Pascual, D., Goncalves, J. M., Ruiz, L., Relevance of Simpson's grading system for resections in WHO grade I meningiomas, Neurocirugia, 28, 176-182, 2017	Comparison/analyses not in PICO
Pamir, M. N., Peker, S., Kilic, T., Sengoz, M., Efficacy of gamma-knife surgery for treating meningiomas that involve the superior sagittal sinus, Zentralblatt fur NeurochirurgieZentralbl Neurochir, 68, 73-8, 2007	Non-comparative study
Pan, D. H., Guo, W. Y., Chang, Y. C., Chung, W. Y., Shiau, C. Y., Wang, L. W., Wu, S. M., The effectiveness and factors related to treatment results of gamma knife radiosurgery for meningiomas, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 70 Suppl 1, 19-32, 1998	Observational study, comparison not in PICO (radiotherapy versus radiotherapy)
Paulsen, F., Doerr, S., Wilhelm, H., Becker, G., Bamberg, M., Classen, J., Fractionated stereotactic radiotherapy in patients with optic nerve sheath meningioma, International Journal of Radiation Oncology Biology Physics, 82, 773-778, 2012	Non-comparative study
Pendl, G., Eustacchio, S., Unger, F., Radiosurgery as alternative treatment for skull base meningiomas, Journal of Clinical NeuroscienceJ Clin Neurosci, 8 Suppl 1, 12-4, 2001	Non-comparative study
Pollock, B. E., Radiosurgery for intracranial meningiomas, Neurosurgery Quarterly, 13, 77-86, 2003	Non-comparative study
Pollock, B. E., Stafford, S. L., Link, M. J., Brown, P. D., Garces, Y. I., Foote, R. L., Single-fraction radiosurgery of benign intracranial meningiomas, NeurosurgeryNeurosurgery, 71, 604-612, 2012	Non-comparative study
Pollock, Bruce E., Stafford, Scott L., Link, Michael J., Garces, Yolanda I., Foote, Robert L., Stereotactic radiosurgery of World Health Organization grade II and III intracranial meningiomas: treatment results on the basis of a 22-year experience, CancerCancer, 118, 1048-54, 2012	Non-comparative study
Pollock, Bruce E., Stafford, Scott L., Link, Michael J., Garces, Yolanda I., Foote, Robert L., Single-fraction radiosurgery for presumed intracranial meningiomas: efficacy and complications from a 22-year experience, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 83, 1414-8, 2012	Non-comparative study
Pollock, Bruce E., Stafford, Scott L., Link, Michael J., Garces, Yolanda I., Foote, Robert L., Single-fraction radiosurgery of benign cavernous sinus meningiomas, Journal of NeurosurgeryJ Neurosurg, 119, 675-82, 2013	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Poon, M. T. C., Fung, L. H. K., Pu, J. K. S., Leung, G. K. K., Outcome of elderly patients undergoing intracranial meningioma resection - A systematic review and meta-analysis, British Journal of NeurosurgeryBr J Neurosurg, 28, 303-309, 2014	Non-comparative study
Przybylowski, C. J., Raper, D. M. S., Starke, R. M., Xu, Z., Liu, K. C., Sheehan, J. P., Stereotactic radiosurgery of meningiomas following resection: Predictors of progression, Journal of Clinical NeuroscienceJ Clin Neurosci, 22, 161-165, 2015	Non-comparative study
Roche, P. H., Regis, J., Dufour, H., Fournier, H. D., Delsanti, C., Pellet, W., Grisoli, F., Peragut, J. C., Gamma knife radiosurgery in the management of cavernous sinus meningiomas, Journal of NeurosurgeryJ Neurosurg, 93 Suppl 3, 68-73, 2000	Non-comparative study
Sajja, R., Barnett, G. M., Lee, S. Y., Harnisch, G., Stevens, G. H. J., Lee, J., Suh, J. H., Intensity-modulated radiation therapy (IMRT) for newly diagnosed and recurrent intracranial meningiomas: Preliminary results, Technology in Cancer Research and Treatment, 4, 675-682, 2005	Non-comparative study/any comparisons not in PICO
Salvetti, David J., Nagaraja, Tara G., Levy, Carl, Xu, Zhiyaun, Sheehan, Jason, Gamma Knife surgery for the treatment of patients with asymptomatic meningiomas, Journal of NeurosurgeryJ Neurosurg, 119, 487-93, 2013	Non-comparative study
Samblas, Jose, Luis Lopez Guerra, Jose, Bustos, Jose, Angel Gutierrez-Diaz, Jose, Wolski, Michael, Peraza, Carmen, Marsiglia, Hugo, Sallabanda, Kita, Stereotactic radiosurgery in patients with multiple intracranial meningiomas, Journal of B.U.On.J, 19, 250-5, 2014	Non-comparative study
Santacroce, A., Walier, M., Regis, J., Liscak, R., Motti, E., Lindquist, C., Kemeny, A., Kitz, K., Lippitz, B., Alvarez, R. M., Pedersen, P. H., Yomo, S., Lupidi, F., Dominikus, K., Blackburn, P., Mindermann, T., Bundschuh, O., Van Eck, A. T. C. J., Fimmers, R., Horstmann, G. A., Long-term tumor control of benign intracranial meningiomas after radiosurgery in a series of 4565 patients, NeurosurgeryNeurosurgery, 70, 32-39, 2012	Non-comparative study
Selch, Michael T., Ahn, Eugene, Laskari, Ashkan, Lee, Steve P., Agazaryan, Nhzde, Solberg, Timothy D., Cabatan-Awang, Cynthia, Frighetto, Leonardo, Desalles, Antonio A. F., Stereotactic radiotherapy for treatment of cavernous sinus meningiomas, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 59, 101-11, 2004	Non-comparative study
Shan, B., Zhang, J., Song, Y., Xu, J., Prognostic factors for patients with World Health Organization grade III meningiomas treated at a single center, MedicineMedicine (Baltimore), 96, e7385, 2017	Analyses not in PICO
Sheehan, Jason P., Starke, Robert M., Kano, Hideyuki, Kaufmann, Anthony M., Mathieu, David, Zeiler, Fred A., West, Michael, Chao, Samuel T., Varma, Gandhi, Chiang, Veronica L. S., Yu, James B., McBride,	Non-comparative study with multivariate analyses, however, on the multivariate

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Heyoung L., Nakaji, Peter, Youssef, Emad, Honea, Norissa, Rush, Stephen, Kondziolka, Douglas, Lee, John Y. K., Bailey, Robert L., Kunwar, Sandeep, Petti, Paula, Lunsford, L. Dade, Gamma Knife radiosurgery for sellar and parasellar meningiomas: a multicenter study, Journal of NeurosurgeryJ Neurosurg, 120, 1268-77, 2014	analysis MVA, patient characteristics unclear in any that may be relevant
Shen, X., Andrews, D. W., Sergott, R. C., Evans, J. J., Curran, W. J., Machtay, M., Fragoso, R., Eldredge, H., Champ, C. E., Witek, M., Mishra, M. V., Dicker, A. P., Werner-Wasik, M., Fractionated stereotactic radiation therapy improves cranial neuropathies in patients with skull base meningiomas: A retrospective cohort study, Radiation OncologyRadiat, 7 (1) (no pagination), 2012	Non-comparative study
Slater, Jerry D., Loredo, Lilia N., Chung, Arthur, Bush, David A., Patyal, Baldev, Johnson, Walter D., Hsu, Frank P. K., Slater, James M., Fractionated proton radiotherapy for benign cavernous sinus meningiomas, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 83, e633-7, 2012	Non-comparative study
Solda, F., Wharram, B., De Ieso, P. B., Bonner, J., Ashley, S., Brada, M., Long-term efficacy of fractionated radiotherapy for benign meningiomas, Radiotherapy and Oncology, 109, 330-334, 2013	Non-comparative study
Solda, F., Wharram, B., Gunapala, R., Brada, M., Fractionated Stereotactic Conformal Radiotherapy for Optic Nerve Sheath Meningiomas, Clinical OncologyClin Oncol (R Coll Radiol), 24, e106-e112, 2012	Non-comparative study
Soyuer, S., Chang, E. L., Selek, U., Shi, W., Maor, M. H., DeMonte, F., Radiotherapy after surgery for benign cerebral meningioma, Radiotherapy and Oncology, 71, 85-90, 2004	Years of treatment: 1953-2001 – N = 92; N = 44 underwent STR (N = 48 GTR); not clear how many of these patients treated after 1985 and no subgroup analyses for them
Stafford, S. L., Pollock, B. E., Foote, R. L., Link, M. J., Gorman, D. A., Schomberg, P. J., Leavitt, J. A., Meningioma radiosurgery: tumor control, outcomes, and complications among 190 consecutive patients, NeurosurgeryNeurosurgery, 49, 1029-37; discussion 1037-8, 2001	Non-comparative study
Starke, Robert M., Nguyen, James H., Rainey, Jessica, Williams, Brian J., Sherman, Jonathan H., Savage, Jesse, Yen, Chun Po, Sheehan, Jason P., Gamma Knife surgery of meningiomas located in the posterior fossa: factors predictive of outcome and remission, Journal of NeurosurgeryJ Neurosurg, 114, 1399-409, 2011	Non-comparative study, with multivariate analyses; however, on the multivariate analysis patient characteristics unclear in any that may be relevant
Starke, Robert M., Przybylowski, Colin J., Sugoto, Mukherjee, Fezeu, Francis, Awad, Ahmed J., Ding, Dale, Nguyen, James H., Sheehan, Jason P., Gamma Knife radiosurgery of large skull base meningiomas, Journal of NeurosurgeryJ Neurosurg, 122, 363-72, 2015	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
Starke, Robert, Kano, Hideyuki, Ding, Dale, Nakaji, Peter, Barnett, Gene H., Mathieu, David, Chiang, Veronica, Yu, James B., Hess, Judith, McBride, Heyoung L., Honea, Norissa, Lee, John Y. K., Rahmathulla, Gazanfar, Evanoff, Wendi A., Alonso-Basanta, Michelle, Lunsford, L. Dade, Sheehan, Jason P., Stereotactic radiosurgery of petroclival meningiomas: a multicenter study, Journal of Neuro-OncologyJ Neurooncol, 119, 169-76, 2014	Non-randomised trial; unclear what treatments which patients had in potentially relevant comparative analyses
Steinvorth, S., Welzel, G., Fuss, M., Debus, J., Wildermuth, S., Wannenmacher, M., Wenz, F., Neuropsychological outcome after fractionated stereotactic radiotherapy (FSRT) for base of skull meningiomas: A prospective 1-year follow-up, Radiotherapy and Oncology, 69, 177-182, 2003	Non-comparative study
Takanashi, Masami, Fukuoka, Seiji, Hojyo, Atsufumi, Sasaki, Takehiko, Nakagawara, Jyoji, Nakamura, Hirohiko, Gamma knife radiosurgery for skull-base meningiomas, Progress in Neurological SurgeryProg, 22, 96-111, 2009	Observational study, comparison not in PICO (surgery + radiotherapy versus radiotherapy))
Tanzler, Emily, Morris, Christopher G., Kirwan, Jessica M., Amdur, Robert J., Mendenhall, William M., Outcomes of WHO Grade I meningiomas receiving definitive or postoperative radiotherapy, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 79, 508-13, 2011	Non-comparative study/comparisons not in PICO
Torres, R. C., Frighetto, L., De Salles, A. A., Goss, B., Medin, P., Solberg, T., Ford, J. M., Selch, M., Radiosurgery and stereotactic radiotherapy for intracranial meningiomas, Neurosurgical FocusNeurosurg, 14, e5, 2003	Observational study, comparison not in PICO (radiotherapy versus radiotherapy)
van Nieuwenhuizen, D., Ambachtsheer, N., Heimans, J. J., Reijneveld, J. C., Peerdeman, S. M., Klein, M., Neurocognitive functioning and health-related quality of life in patients with radiologically suspected meningiomas, Journal of Neuro-OncologyJ Neurooncol, 113, 433-40, 2013	Population/intervention not in PICO
Vermeulen, S., Young, R., Li, F., Meier, R., Raisis, J., Klein, S., Kohler, E., A comparison of single fraction radiosurgery tumor control and toxicity in the treatment of basal and nonbasal meningiomas, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 72 Suppl 1, 60-6, 1999	Non-comparative study
Wang, W. H., Lee, C. C., Yang, H. C., Liu, K. D., Wu, H. M., Shiau, C. Y., Guo, W. Y., Pan, D. H. C., Chung, W. Y., Chen, M. T., Gamma Knife Radiosurgery for Atypical and Anaplastic Meningiomas, World Neurosurg, 87, 557-564, 2016	Non-comparative study (unclear which patients had which treatments)
Wara, W. M., Sheline, G. E., Newman, H., Townsend, J. J., Boldrey, E. B., Radiation therapy of meningiomas, American Journal of Roentgenology, Radium Therapy & Nuclear MedicineAm J Roentgenol Radium Ther Nucl Med, 123, 453-8, 1975	Years of treatment: 1942-1972
Wenkel, E., Thornton, A. F., Finkelstein, D., Adams, J., Lyons, S., De La Monte, S., Ojeman, R. G., Munzenrider, J. E., Benign meningioma: Partially resected, biopsied, and recurrent intracranial tumors treated	Non-comparative study

Excluded studies - Which adults with inoperable or incompletely excised or recurrent meningioma should be offered radiotherapy?	
with combined proton and photon radiotherapy, International Journal of Radiation Oncology Biology Physics, 48, 1363-1370, 2000	
Yang, C. C., Tsai, C. C., Chen, S. J., Chiang, M. F., Lin, J. F., Hu, C. K., Chan, Y. K., Lin, H. Y., Cheng, S. Y., Factors Associated with Recurrence of Intracranial Meningiomas After Surgical Resection: A Retrospective Single-Center Study, International Journal of Gerontology., 22, 2017	Analyses not in PICO
Zachenhofer, I., Wolfsberger, S., Aichholzer, M., Bertalanffy, A., Roessler, K., Kitz, K., Knosp, E., Gamma-knife radiosurgery for cranial base meningiomas: Experience of tumor control, clinical course, and morbidity in a follow-up of more than 8 years, NeurosurgeryNeurosurgery, 58, 28-36, 2006	Non-comparative study
Zada, G., Pagnini, P. G., Yu, C., Erickson, K. T., Hirschbein, J., Zelman, V., Apuzzo, M. L. J., Long-term outcomes and patterns of tumor progression after Gamma Knife radiosurgery for benign meningiomas, NeurosurgeryNeurosurgery, 67, 322-328, 2010	Non-comparative study
Zamorano, L., Saenz, A., Matter, A., Buciuc, R., Gaspar, L., Fontanesi, J., Garzon, A., Diaz, F., Radiosurgical treatment of meningiomas, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 69, 156-61, 1997	Observational study. Comparison not in PICO (radiotherapy versus radiotherapy)
Zeiler, F. A., McDonald, P. J., Kaufmann, A. M., Fewer, D., Butler, J., Schroeder, G., West, M., Gamma Knife radiosurgery of cavernous sinus meningiomas: an institutional review, Canadian Journal of Neurological SciencesCan J Neurol Sci, 39, 757-62, 2012	Non-comparative study
Zenonos, Georgios, Kondziolka, Douglas, Flickinger, John C., Gardner, Paul, Lunsford, L. Dade, Gamma Knife surgery in the treatment paradigm for foramen magnum meningiomas, Journal of NeurosurgeryJ Neurosurg, 117, 864-73, 2012	Non-comparative study
Zhang, M, Ho, Al, D'Astous, M, Pendharkar, Av, Choi, Cyh, Thompson, Pa, Tayag, At, Soltys, Sg, Gibbs, Ic, Chang, Sd, CyberKnife Stereotactic Radiosurgery for Atypical and Malignant Meningiomas, World NeurosurgeryWorld Neurosurg, 91, 574-581.e1, 2016	Non-comparative study
Zhang, H., Ma, L., Wang, Y. B., Shu, C., Kuang, W., Huang, Y. A., Dong, L. Q., Cheng, G. G., Intracranial Clear Cell Meningiomas: Study on Clinical Features and Predictors of Recurrence, World Neurosurgery, 97, 693-700, 2017	11/47 patients who received subtotal resection were children; relevant analyses reported only for the whole subtotal resection group, not for the adults separately.

Economic studies

Not applicable - health economic inclusion / exclusion detailed in Supplementary Material D.

Excluded studies for review 3b – techniques for radiotherapy for meningioma

Clinical studies

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Study	**Reason for Exclusion**
Meningiomas: Knowledge base, treatment outcomes, and uncertainties. A RANO review, Journal of Neurosurgery. 122 (1) (pp 4-23), 2015. Date of Publication: 01 Jan 2015., 2015	Semi-systematic review with different inclusion criteria to the present review and no meta-analyses
Australian, Safety, Efficacy, Register of New Interventional Procedures Surgical, Proton beam therapy for the treatment of neoplasms involving (or adjacent to) cranial structures (Structured abstract), Health Technology Assessment Database, 2007	Systematic review without meta-analysis. Included studies checked for relevance
Bhattacharjee, M., Bose, I., Sarkar, P., Banerjee, C., Dutta, S., Ghosh, A., Mukherjee, J., Acharya, S., Goswami, S., Mazumdar, A., Chaudhuri, S., Chaudhuri, S., A sequential scanning of the immune efficiency in astrocytoma (Grade I to Grade Iii), meningioma and secondary glioma patients with and without therapeutic scheduling, Cancer Investigation, 24, 502-13, 2006	N < 30 in all treatment groups
Celtikci, E., Kaymaz, A. M., Akgul, G., Karaaslan, B., Emmez, O. H., Borcek, A., Retrospective Analysis of 449 Intracranial Meningioma Patients Operated between years 2007 - 2013 in a Single Institute, Turkish Neurosurgery, 05, 05, 2016	Non-comparative study
Chandralekha, K., Shanmughakumar, S., Balasubramaniam, P., Retrospective study of meningiomas at BIRO, Journal of Cancer Research and Therapeutics, 8, S146, 2012	Published as abstract only, not enough information to ascertain relevance although it does not seem to be in PICO
Chung, L. K., Mathur, I., Lagman, C., Bui, T. T., Lee, S. J., Voth, B. L., Chen, C. H. J., Barnette, N. E., Spasic, M., Pouratian, N., Lee, P., Selch, M., Chin, R., Kaprealian, T., Gopen, Q., Yang, I., Stereotactic radiosurgery versus fractionated stereotactic radiotherapy in benign meningioma, Journal of Clinical Neuroscience, 36, 1-5, 2017	Systematic review with different inclusion criteria to this review; included studies checked for relevance

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Combs, S. E., Farzin, M., Bohmer, J., Oehlke, O., Molls, M., Debus, J., Grosu, A. L., Clinical outcome after high-precision radiotherapy for skull base meningiomas: Pooled data from three large German Centers of Radiation Oncology, Strahlentherapie und Onkologie, 191, S38, 2015	Comparative observational study published as abstract only, not enough information available to evaluate the study (e.g., to compare the groups at baseline etc)
Detti, B., Scoccianti, S., Di Cataldo, V., Monteleone, E., Cipressi, S., Bordi, L., Pellicano, G., Gadda, D., Saieva, C., Greto, D., Pecchioli, G., Buccoliero, A., Ceroti, M., Ammannati, F., Biti, G., Atypical and malignant meningioma: Outcome and prognostic factors in 68 irradiated patients, Journal of Neuro-OncologyJ Neurooncol, 115, 421-427, 2013	N > 30 in only one treatment group
DiBiase, S. J., Kwok, Y., Yovino, S., Arena, C., Naqvi, S., Temple, R., Regine, W. F., Amin, P., Guo, C., Chin, L. S., Factors predicting local tumor control after gamma knife stereotactic radiosurgery for benign intracranial meningiomas, International Journal of Radiation Oncology Biology Physics, 60, 1515-1519, 2004	All patients treated with gamma knife stereotactic radiosurgery; authors state that "dose" was analysed, but provide no further details.
Ding, D., Starke, R. M., Hantzmon, J., Yen, C. P., Williams, B. J., Sheehan, J. P., The role of radiosurgery in the management of WHO Grade II and III intracranial meningiomas, Neurosurgical FocusNeurosurg, 35, E16, 2013	Systematic review with different inclusion criteria to the present review and no meta-analyses
Ding, D., Starke, R. M., Kano, H., Nakaji, P., Barnett, G. H., Mathieu, D., Chiang, V., Omay, S. B., Hess, J., McBride, H. L., Honea, N., Lee, J. Y. K., Rahmathulla, G., Evanoff, W. A., Alonso-Basanta, M., Lunsford, L. D., Sheehan, J. P., Gamma knife radiosurgery for cerebellopontine angle meningiomas: A multicenter study, NeurosurgeryNeurosurgery, 75, 398-407, 2014	Non-comparative study
Estall, V., Treece, S. J., Jena, R., Jefferies, S. J., Burton, K. E., Parker, R. A., Burnet, N. G., Pattern of relapse after fractionated external beam radiotherapy for meningioma: experience from Addenbrooke's Hospital, Clinical OncologyClin Oncol (R Coll Radiol), 21, 745-52, 2009	Comparison not in PICO (different doses of fractionated external beam radiotherapy)
Flickinger, J. C., Kondziolka, D., Maitz, A. H., Lunsford, L. D., Gamma knife radiosurgery of imaging-diagnosed intracranial meningioma, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 56, 801-6, 2003	Comparison not in PICO (different doses of gamme knife radiosurgery)
Fokas, E., Henzel, M., Surber, G., Hamm, K., Engenhart-Cabillic, R., Stereotactic radiotherapy of benign meningioma in the elderly: clinical outcome and toxicity in 121 patients, Radiotherapy & OncologyRadiother Oncol, 111, 457-62, 2014	All the patients also included in Fokas 2014 (Stereotactic Radiation Therapy for Benign Meningioma: Long-Term Outcome in 318 Patients)
Garzon-Muvdi, T., Yang, W., Lim, M., Brem, H., Huang, J., Atypical and anaplastic meningioma: outcomes in a population based study, Journal of Neuro-Oncology, 1-10, 2017	Analyses not in PICO (radiotherapy versus radiotherapy)

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Goldsmith, B. J., Wara, W. M., Wilson, C. B., Larson, D. A., Postoperative irradiation for subtotally resected meningiomas. A retrospective analysis of 140 patients treated from 1967 to 1990, Journal of NeurosurgeryJ Neurosurg, 80, 195-201, 1994	N = 140, aged 3-80 years, treated from 1967-1990; unclear how many were in PICO (i.e., aged 16 or above and treated from 1985 onwards); no subgroup analyses presented for the population in PICO
Han, J. H., Kim, D. G., Chung, H. T., Park, C. K., Paek, S. H., Kim, C. Y., Jung, H. W., Gamma knife radiosurgery for skull base meningiomas: long-term radiologic and clinical outcome, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 72, 1324-32, 2008	Comparison not in PICO (different doses of gramme knife radiosurgery)
Henzel, M., Gross, M. W., Hamm, K., Surber, G., Kleinert, G., Failing, T., Strassmann, G., Engenhart-Cabillic, R., Significant tumor volume reduction of meningiomas after stereotactic radiotherapy: Results of a prospective multicenter study, NeurosurgeryNeurosurgery, 59, 1188-1194, 2006	Comparison not in PICO (different doses of SRT)
Henzel, M., Gross, M. W., Hamm, K., Surber, G., Kleinert, G., Failing, T., Strassmann, G., Engenhart-Cabillic, R., Stereotactic radiotherapy of meningiomas: symptomatology, acute and late toxicity, Strahlentherapie und Onkologie, 182, 382-8, 2006	Observational study of patients treated with SRS and SRT; all data and results presented are collapsed across the treatments; the only comparative results presented are unclear and lack details (e.g., "There were no differences between SRT, hSRT, or SRS" with no further details provided by group)
Kaprealian, T., Raleigh, D. R., Sneed, P. K., Nabavizadeh, N., Nakamura, J. L., McDermott, M. W., Parameters influencing local control of meningiomas treated with radiosurgery, Journal of Neuro-OncologyJ Neurooncol, 128, 357-364, 2016	Comparison not in PICO (SRS upfrontversus SRS after recurrence after surgery versus SRS after recurrence after RT)
Kaur, G., Sayegh, E. T., Larson, A., Bloch, O., Madden, M., Sun, M. Z., Barani, I. J., James, C. D., Parsa, A. T., Adjuvant radiotherapy for atypical and malignant meningiomas: A systematic review, Neuro-OncologyNeuro-oncol, 16, 628-636, 2014	Systematic review without meta-analysis; checked for relevant studies
Kollova, A., Liscak, R., Novotny, J., Jr., Vladyka, V., Simonova, G., Janouskova, L., Gamma Knife surgery for benign meningioma, Journal of Neurosurgery, 107, 325-36, 2007	Comparison not in PICO (same data as Novotny 2006)
Kollova, A., Liscak, R., Novotny, J., Jr., Vladyka, V., Simonova, G., Janouskova, L., Gamma Knife surgery for benign meningioma, Journal of Neurosurgery, 107, 325-36, 2007	Duplicate
Kuhn, E. N., Taksler, G. B., Dayton, O., Loganathan, A. G., Vern-Gross, T. Z., Bourland, J. D., Laxton, A. W., Chan, M. D., Tatter, S. B., Patterns of recurrence after stereotactic radiosurgery for treatment of meningiomas, Neurosurgical FocusNeurosurg, 35, E14, 2013	Comparison not in PICO (different doses of SRS)

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Kuhn, E. N., Taksler, G. B., Dayton, O., Loganathan, A., Bourland, D., Tatter, S. B., Laxton, A. W., Chan, M. D., Is there a tumor volume threshold for postradiosurgical symptoms? a single-institution analysis, NeurosurgeryNeurosurgery, 75, 536-544, 2014	Comparison not in PICO (different doses of SRS)
Leavitt, J. A., Stafford, S. L., Link, M. J., Pollock, B. E., Long-term evaluation of radiation-induced optic neuropathy after single-fraction stereotactic radiosurgery, International Journal of Radiation Oncology Biology Physics, 87, 524-527, 2013	Comparison not in PICO (different doses of SRS)
Lee, S. R., Yang, K. A., Kim, S. K., Kim, S. H., Radiation-induced intratumoral necrosis and peritumoral edema after Gamma knife radiosurgery for intracranial meningiomas, Journal of Korean Neurosurgical SocietyJ, 52, 98-102, 2012	Comparison not in PICO (different doses of SRS)
Lee, J. W., Wernicke, A. G., Risk and survival outcomes of radiation-induced CNS tumors, Journal of Neuro-Oncology, 129, 15-22, 2016	Systematic review without meta-analysis, checked included studies for relevance
Liscak, R., Kollova, A., Vladyka, V., Simonova, G., Novotny, J., Jr.Gamma knife radiosurgery of skull base meningiomas. Acta Neurochirurgica - SupplementActa Neurochir Suppl 2004 91 p.65-74	Comparison not in PICO (GKRS dose)
Liu, Y., Xiao, S., Liu, M., Li, G., Wang, D., He, J., Hu, B., Zu, D., Analysis of related factors in complications of stereotactic radiosurgery in intracranial tumors, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 75, 129-32, 2000	N = 19 with meningioma
Lopes, Vv, Chan, A, Loeffler, J, Munzenrider, J, A randomized radiation dose escalation trial in patients with recurrent or incompletely resected benign meningiomas treated with proton-photon irradiation, International Journal of Radiation Oncology Biology Physics, 57, S323-4, 2003	Abstract of the trial reported in the full paper by Sanford 2014
Lozada, D., Brau, R. H., Stereotactic radiosurgery for intracranial tumors: Puerto Rico experience, Puerto Rico Health Sciences JournalP R Health Sci J, 29, 286-92, 2010	(Narrative?) review; no relevant analyses
Lunsford, L. D., Kondziolka, D. S., Flickinger, J. C.Radiosurgery of tumors of the cerebellopontine angle. Clinical Neurosurgery 1994 41 p.168-84	N = 19 with meningioma
Mahmood, A., Qureshi, N. H., Malik, G. M., Intracranial meningiomas: analysis of recurrence after surgical treatment, Acta NeurochirurgicaActa Neurochir (Wien), 126, 53-8, 1994	N = 21 received RT
Mair, R., Morris, K., Scott, I., Phil, D., Path, F. R. C., Carroll, T. A., Radiotherapy for atypical meningiomas: Clinical article, Journal of Neurosurgery, 115, 811-819, 2011	N = 31 received RT
Maranzano, E., Draghini, L., Casale, M., Arcidiacono, F., Anselmo, P., Trippa, F., Giorgi, C., Long-term outcome of moderate hypofractionated stereotactic radiotherapy for meningiomas, Strahlentherapie und Onkologie, 191, 953-60, 2015	Comparison not in PICO (14 × 3 Gy versus 15 × 3 Gy).

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Marta, G., Correa, S. F. M., Teixeira, M. J., Long-term outcome fractionated stereotactic radiotherapy and radiosurgery for treatment of symptomatic cavernous sinus meningioma: A 15-year experience, European Journal of CancerEur J Cancer, 49, S784, 2013	Retrospective cohort study published as abstract only, not enough information available to evaluate the study
Mozes, P., Dittmar, J. O., Habermehl, D., Tonndorf-Martini, E., Hideghety, K., Dittmar, A., Debus, J., Combs, S. E., Volumetric response of intracranial meningioma after photon or particle irradiation, Acta Oncologica, 56, 431-437, 2017	N < 30 in all treatment groups
Novotny, J., Jr., Kollova, A., Liscak, R., Prediction of intracranial edema after radiosurgery of meningiomas, Journal of Neurosurgery, 105 Suppl, 120-6, 2006	Comparison not in PICO (Observational comparative study addressing radiation dose after treatment with Leksell Gamma Knife)
Ojemann, R. G., Thornton, A. F., Harsh, G. R. Management of anterior cranial base and cavernous sinus neoplasms with conservative surgery alone or in combination with fractionated photon or stereotactic proton radiotherapy. Clinical NeurosurgeryClin Neurosurg 1995 42 p.71-98	N < 30 in all the treatment groups
Pan, D. H., Guo, W. Y., Chang, Y. C., Chung, W. Y., Shiau, C. Y., Wang, L. W., Wu, S. M., The effectiveness and factors related to treatment results of gamma knife radiosurgery for meningiomas, Stereotactic & Functional NeurosurgeryStereotact Funct Neurosurg, 70 Suppl 1, 19-32, 1998	Comparison not in PICO (different doses of gamma knife radiosurgery)
Pasquier, D., Bijmolt, S., Veninga, T., Rezvoy, N., Villa, S., Krengli, M., Weber, D. C., Baumert, B. G., Canyilmaz, E., Yalman, D., Szutowicz, E., Tzuk-Shina, T., Mirimanoff, R. O., Atypical and Malignant Meningioma: Outcome and Prognostic Factors in 119 Irradiated Patients. A Multicenter, Retrospective Study of the Rare Cancer Network, International Journal of Radiation Oncology Biology Physics, 71, 1388-1393, 2008	Analyses not in PICO
Pintea, B., Kinfe, T. M., Baumert, B. G., Bostrom, J., Earlier and sustained response with incidental use of cardiovascular drugs among patients with low- to medium-grade meningiomas treated with radiosurgery (SRS) or stereotactic radiotherapy (SRT), Radiotherapy and Oncology, 111, 446-450, 2014	N > 30 in only one treatment group
Sanford, N. N., Yeap, B. Y., Larvie, M., Daartz, J., Munzenrider, J. E., Liebsch, N. J., Fullerton, B., Pan, E., Loeffler, J. S., Shih, H. A., Prospective, Randomized Study of Radiation Dose Escalation With Combined Proton-Photon Therapy for Benign Meningiomas, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 12, 12, 2017	Comparison not in PICO (different doses of proton-photon treatment)
Schmieder, K., Engelhardt, M., Wawrzyniak, S., Borger, S., Becker, K., Zimolong, A., The impact of microsurgery, stereotactic radiosurgery and radiotherapy in the treatment of meningiomas depending on different localizations, GMS Health Technology AssessmentGMS Health Technol Assess, 6, Doc02, 2010	No relevant results included

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Sethi, R. A., Rush, S. C., Liu, S., Sethi, S. A., Parker, E., Donahue, B., Narayana, A., Silverman, J., Kondziolka, D., Golfinos, J. G., Dose-response relationships for meningioma radiosurgery, American Journal of Clinical Oncology: Cancer Clinical Trials, 38, 600-604, 2015	Comparison not in PICO (different doses of SRS)
Sheehan, J. P., Cohen-Inbar, O., Ruangkanchanasetr, R., Bulent Omay, S., Hess, J., Chiang, V., Iorio-Morin, C., Alonso-Basanta, M., Mathieu, D., Grills, I. S., Lee, J. Y. K., Lee, C. C., Dade Lunsford, L., Post-radiosurgical edema associated with parasagittal and parafalcine meningiomas: a multicenter study, Journal of Neuro-OncologyJ Neurooncol, 125, 317-324, 2015	Comparison not in PICO (different doses of single-session SRS)
Sheehan, J. P., Lee, C. C., Xu, Z., Przybylowski, C. J., Meimer, P. D., Schlesinger, D., Edema following Gamma Knife radiosurgery for parasagittal and parafalcine meningiomas, Journal of NeurosurgeryJ Neurosurg, 123, 1287-1293, 2015	Comparison not in PICO (different doses of SRS)
Sheehan, J. P., Starke, R. M., Kano, H., Kaufmann, A. M., Mathieu, D., Zeiler, F. A., West, M., Chao, S. T., Varma, G., Chiang, V. L., Yu, J. B., McBride, H. L., Nakaji, P., Youssef, E., Honea, N., Rush, S., Kondziolka, D., Lee, J. Y., Bailey, R. L., Kunwar, S., Petti, P., Lunsford, L. D., Gamma Knife radiosurgery for sellar and parasellar meningiomas: a multicenter study, Journal of Neurosurgery, 120, 1268-77, 2014	Comparison not in PICO (different doses of SRS)
Shih, H. A., Niu, N. N., Pan, E., Daartz, J., Yeap, B. Y., Munzenrider, J. E., Loeffler, J. S., Mixed proton and photon therapy for benign meningiomas: Longterm results of a prospective randomized dose escalation study, International Journal of Radiation Oncology Biology Physics, 1), S158-S159, 2013	Abstract of the same trial as Sanford 2014.
Singh, V. P., Kansai, S., Vaishya, S., Julka, P. K., Mehta, V. S., Early complications following gamma knife radiosurgery for intracranial meningiomas, Journal of NeurosurgeryJ Neurosurg, 93 Suppl 3, 57-61, 2000	Non-comparative study
Spiegelmann, R., Cohen, Z. R., Nissim, O., Alezra, D., Pfeffer, R., Cavernous sinus meningiomas: A large LINAC radiosurgery series, Journal of Neuro-OncologyJ Neurooncol, 98, 195-202, 2010	Non-comparative study
Stafford, S. L., Pollock, B. E., Foote, R. L., Link, M. J., Gorman, D. A., Schomberg, P. J., Leavitt, J. A., Meningioma radiosurgery: tumor control, outcomes, and complications among 190 consecutive patients, NeurosurgeryNeurosurgery, 49, 1029-37; discussion 1037-8, 2001	Comparison not in PICO (different doses of radiosurgery)
Stafford, S. L., Pollock, B. E., Leavitt, J. A., Foote, R. L., Brown, P. D., Link, M. J., Gorman, D. A., Schomberg, P. J., A study on the radiation tolerance of the optic nerves and chiasm after stereotactic radiosurgery, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 55, 1177-81, 2003	Comparison not in PICO (different doses of SRS)
Starke, R. M., Nguyen, J. H., Rainey, J., Williams, B. J., Sherman, J. H., Savage, J., Yen, C. P., Sheehan, J. P., Gamma Knife surgery of meningiomas located in the posterior fossa: Factors predictive of outcome and remission: Clinical article, Journal of Neurosurgery, 114, 1399-1409, 2011	Comparison not in PICO (different doses of gamma knife surgery)

Excluded studies – Which technique should be used for adults with meningioma who require radiotherapy?	
Starke, R. M., Przybylowski, C. J., Sugoto, M., Fezeu, F., Awad, A. J., Ding, D., Nguyen, J. H., Sheehan, J. P., Gamma Knife radiosurgery of large skull base meningiomas, Journal of Neurosurgery, 122, 363-72, 2015	Comparison not in PICO (different doses of single-session gamma knife radiosurgery)
Starke, R. M., Williams, B. J., Hiles, C., Nguyen, J. H., Elsharkawy, M. Y., Sheehan, J. P., Gamma knife surgery for skull base meningiomas: Clinical article, Journal of NeurosurgeryJ Neurosurg, 116, 588-597, 2012	Comparison not in PICO (different doses of gamma knife surgery)
Starke, R., Kano, H., Ding, D., Nakaji, P., Barnett, G. H., Mathieu, D., Chiang, V., Yu, J. B., Hess, J., McBride, H. L., Honea, N., Lee, J. Y., Rahmathulla, G., Evanoff, W. A., Alonso-Basanta, M., Lunsford, L. D., Sheehan, J. P., Stereotactic radiosurgery of petroclival meningiomas: a multicenter study, Journal of Neuro-Oncology, 119, 169-76, 2014	Comparison not in PICO (different doses of SRS)
Williams, B. J., Yen, C. P., Starke, R. M., Basina, B., Nguyen, J., Rainey, J., Sherman, J. H., Schlesinger, D., Sheehan, J. P., Gamma Knife surgery for parasellar meningiomas: Long-term results including complications, predictive factors, and progression-free survival: Clinical article, Journal of NeurosurgeryJ Neurosurg, 114, 1571-1577, 2011	Comparison not in PICO (different doses of gamma knife surgery)

Economic studies

Not applicable - health economic inclusion / exclusion detailed in Supplementary Material D.

Excluded studies for review 5b – follow-up for meningioma

Clinical studies

Excluded studies (search conducted together for all three follow up questions): - What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma? - What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma? - What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?	
Study	**Reason for Exclusion**
Albert, F. K., Forsting, M., Sartor, K., Adams, H. P., Kunze, S., Salcman, M., Wilson, C. B., Early postoperative magnetic resonance imaging after resection of malignant glioma: Objective evaluation of residual tumor and its influence on regrowth and prognosis, Neurosurgery, 34, 45-61, 1994	Not follow up protocol

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Aukema, T. S., Valdes Olmos, R. A., Korse, C. M., Kroon, B. B. R., Wouters, M. W. J. M., Vogel, W. V., Bonfrer, J. M. G., Nieweg, O. E., Utility of fDG PET/CT and brain MRI in melanoma patients with increased serum S-100B level during follow-up, Annals of Surgical Oncology, 17, 1657-1661, 2010	Population not in PICO (melanoma patients without symptoms and signs of recurrent disease were referred for total body PET/CT and MRI of the brain because of an increased S-100B); not follow up protocol
Aukema, T. S., Valdes Olmos, R. A., Korse, T. M., Kroon, B. B., Wouters, M. W., Vogel, W. V., Bonfrer, J. M., Nieweg, O. E., Increased serum S-100B level in melanoma patients during followup and utility of FDG PET/CT and brain MRI, Annals of Surgical Oncology, 17, S114-S115, 2010	Abstract only; same study as excluded Aukema (2010)
Baker, J. J., Meyers, M. O., Frank, J., Amos, K. D., Stitzenberg, K. B., Ollila, D. W., Routine restaging PET/CT and detection of initial recurrence in sentinel lymph node positive stage III melanoma, American Journal of SurgeryAm J Surg, 207, 549-554, 2014	Population not in PICO
Baker, J. J., Meyers, M. O., Yeh, J. J., Frank, J., Amos, K. D., Stitzenberg, K. B., Long, P., Ollila, D. W., Routine restaging PET/CT and detection of recurrence in sentinel lymph node positive stage III melanoma, Annals of Surgical Oncology, 18, S114, 2011	Population not in PICO
Becker, G., Hofmann, E., Woydt, M., Hulsmann, U., Maurer, M., Lindner, A., Becker, T., Krone, A., Postoperative neuroimaging of high-grade gliomas: Comparison of transcranial sonography, magnetic resonance imaging, and computed tomography, Neurosurgery, 44, 469-478, 1999	Outcomes not in PICO and non-comparative study
Becker, G., Krone, A., Schmitt, K., Woydt, M., Hofmann, E., Lindner, A., Bogdahn, U., Gahnl, G., Roosen, K., Preoperative and postoperative follow-up in high-grade gliomas: Comparison of transcranial color-coded real-time sonography and computed tomography findings, Ultrasound in Medicine and Biology, 21, 1123-1135, 1995	Outcomes not in PICO, unclear follow up protocol (“Contrast CT scans, TCCS and neurological follow-up examinations were performed at the same time within a time interval of 6 weeks to 3 months, coinciding with the protocol of adjuvant tumor therapy”.), N = 20

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Belohlavek, O., Simonova, G., Kantorova, I., Novotny Jr, J., Liscak, R., Brain metastases after stereotactic radiosurgery using the Leksell gamma knife: Can FDG PET help to differentiate radionecrosis from tumour progression?, European Journal of Nuclear Medicine and Molecular Imaging, 30, 96-100, 2003	Outcomes not in PICO
Caresia, A. P., Castell-Conesa, J., Negre, M., Mestre, A., Cuberas, G., Manes, A., Maldonado, X., Thallium-201SPECT assessment in the detection of recurrences of treated gliomas and ependymomas, Clinical and Translational Oncology, 8, 750-754, 2006	Population not in PICO (patients received SPECT if they had equivocal CT or RM images)
Casalino, D. D., Remer, E. M., Bishoff, J. T., Coursey, C. A., Dighe, M., Harvin, H. J., Heilbrun, M. E., Majd, M., Nikolaidis, P., Preminger, G. M., Raman, S. S., Sheth, S., Vikram, R., Weinfeld, R. M., ACR appropriateness criteria post-treatment follow-Up of renal cell carcinoma, Journal of the American College of Radiology, 11, 443-449, 2014	Guideline for asymptomatic patients who have been treated for renal cell carcinoma (RCC) by radical nephrectomy or nephron-sparing surgery.
Chabert, I., Belladjou, I., Poisson, F., Dhermain, F., Martin, V., Ammari, S., Vauclin, S., Pineau, P., Buvat, I., Deutsch, E., Robert, C., Correlation between MRI-based hyper-perfused areas and tumor recurrence in high-grade gliomas, Radiotherapy and Oncology, 119, S885, 2016	Published as abstract only, not enough information available to ascertain relevance although it appears to not be relevant
Chang, J. H., Kim, C. Y., Choi, B. S., Kim, Y. J., Kim, J. S., Kim, I. A., Pseudoprogression and pseudoresponse in the management of high-grade glioma: Optimal decision timing according to the response assessment of the neuro-oncology working group, Journal of Korean Neurosurgical Society, 55, 5-11, 2014	Non-comparative study
Chang, P. D., Chow, D. S., Yang, P. H., Filippi, C. G., Lignelli, A., Predicting glioblastoma recurrence by early changes in the apparent diffusion coefficient value and signal intensity on FLAIR images, American Journal of Roentgenology, 208, 57-65, 2017	Population not in PICO ("Only patients for whom follow-up MRI examinations performed at Columbia University Medical Center showed definitive contrast-enhancing recurrent tumor were included in the study.")
Chow, D. S., Qi, J., Guo, X., Miloushev, V. Z., Iwamoto, F. M., Bruce, J. N., Lassman, A. B., Schwartz, L. H., Lignelli, A., Zhao, B., Filippi, C. G., Semiautomated volumetric measurement on postcontrast MR imaging for analysis of recurrent and residual disease in glioblastoma multiforme, American Journal of Neuroradiology, 35, 498-503, 2014	Not follow up protocol; outcomes not in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Christensen, M., Kamson, D. O., Snyder, M., Kim, H., Robinette, N. L., Mittal, S., Juhasz, C., Tryptophan PET-defined gross tumor volume offers better coverage of initial progression than standard MRI-based planning in glioblastoma patients, Journal of Radiation Oncology, 3, 131-138, 2014	Non-comparative study, N = 11
Darcourt, J., Dufour, M., Mondot, L., Bourg, V., Bondiau, P., Almairac, F., Saada, E., Fontaine, D., Fauchon, F., Vandenbos, F., Ouvrier, M., Sapin, N., Role of 18F-DOPA in the management of patients suspected of brain tumour recurrence, European Journal of Nuclear Medicine and Molecular Imaging, 41, S312, 2014	Published as abstract only, with not enough information to ascertain relevance
Datta, Niloy Ranjan, Pasricha, Rajesh, Gambhir, Sanjay, Prasad, Shambhu Nath, Phadke, Rajendra Vishnu, Comparative evaluation of 201Tl SPECT and CT in the follow-up of irradiated brain tumors, International Journal of Clinical Oncology, 9, 51-8, 2004	Unclear follow up protocol; outcomes/analyses not in PICO
De Paepe, A., Vandeneede, N., Strens, D., Specenier, P., The economics of the treatment and follow-up of patients with glioblastoma, Value in Health, 18 (7), A448, 2015	Published as abstract only, with not enough information to ascertain relevance
Deng, S. M., Zhang, B., Wu, Y. W., Zhang, W., Chen, Y. Y., Detection of glioma recurrence by 11C-methionine positron emission tomography and dynamic susceptibility contrast-enhanced magnetic resonance imaging: A meta-analysis, Nuclear Medicine Communications, 34, 758-766, 2013	Outcomes (and possibly population) not in PICO
Dong, Y., Hou, H., Wang, C., Li, J., Yao, Q., Amer, S., Tian, M., The diagnostic value of 18F-FDG PET/CT in association with serum tumor marker assays in breast cancer recurrence and metastasis, BioMed Research International, 2015, no pagination, 2015	Population not in PICO (breast cancer patients who have received modified radical mastectomy and "The patients were diagnosed as suspicion of recurrence and referred to for whole-body 18F-FDG PET/CT scanning at the PET Center fromJuly 2013 to January 2014.")
D'Souza, M. M., Sharma, R., Jaimini, A., Panwar, P., Saw, S., Kaur, P., Mondal, A., Mishra, A., Tripathi, R. P., 11C-MET PET/CT and advanced MRI in the evaluation of tumor recurrence in high-grade gliomas, Clinical Nuclear Medicine, 39, 791-798, 2014	Not follow up protocol; outcomes not in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Ekinci, G., Akpinar, I. N., Baltacioglu, F., Erzen, C., Kilic, T., Elmaci, I., Pamir, N., Early-postoperative magnetic resonance imaging in glial tumors: Prediction of tumor regrowth and recurrence, European Journal of Radiology, 45, 99-107, 2003	Not follow up protocol (only pre-operative scan and early-postoperative magnetic resonance scan)
Ellingson, B. M., Cloughesy, T. F., Lai, A., Nghiemphu, P. L., Pope, W. B., Nonlinear registration of diffusion-weighted images improves clinical sensitivity of functional diffusion maps in recurrent glioblastoma treated with bevacizumab, Magnetic Resonance in Medicine, 67, 237-245, 2012	Not follow up protocol ("Baseline scans were obtained approximately 1.5 weeks before treatment, and follow-up scans were obtained at approximately 6 weeks after the initiation of bevacizumab.")
Fields, R. C., Coit, D. G., Evidence-based follow-up for the patient with melanoma, Surgical Oncology Clinics of North America, 20, 181-200, 2011	Guideline/narrative review
Fink, J. R., Carr, R. B., Matsusue, E., Iyer, R. S., Rockhill, J. K., Haynor, D. R., Maravilla, K. R., Comparison of 3 Tesla proton MR spectroscopy, MR perfusion and MR diffusion for distinguishing glioma recurrence from posttreatment effects, Journal of Magnetic Resonance Imaging, 35, 56-63, 2012	Not follow up protocol; Population not in PICO ("All patients who underwent advanced physiologic 3T MRI, including MRS, DSC, and DWI, for evaluation of suspected malignant glioma recurrence at our institution between October 2006 and December 2008 were identified.")
Forsting, M., Albert, F. K., Kunze, S., Adams, H. P., Zenner, D., Sartor, K., Extirpation of glioblastomas: MR and CT follow-up of residual tumor and regrowth patterns, American Journal of Neuroradiology, 14, 77-87, 1993	Non-comparative study
Fouke, S. J., Benzinger, T., Gibson, D., Ryken, T. C., Kalkanis, S. N., Olson, J. J., The role of imaging in the management of adults with diffuse low grade glioma: A systematic review and evidence-based clinical practice guideline, Journal of Neuro-Oncology, 125, 457-479, 2015	Outcomes not in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Gietema, J. A., Meinardi, M. T., Sleijfer, D. T., Hoekstra, H. J., van der Graaf, W. T. A., Routine chest X-rays have no additional value in the detection of relapse during routine follow-up of patients treated with chemotherapy for disseminated non-seminomatous testicular cancer, Annals of Oncology, 13, 1616-1620, 2002	Non-comparative study; unclear population (not reported how many patients had had brain metastases at study entry)
Goenka, A., Kumar, A., Sharma, R., Seith, A., Kumar, R., Julka, P., Differentiation of glioma progression or recurrence from treatment-induced changes using a combination of diffusion, perfusion and 3D-MR spectroscopy: A prospective study, Journal of Neuroimaging, 20, 99-100, 2010	Published as abstract only, so little information available to use to ascertain relevance; but population appears to not be in PICO
Gomez-Rio, M., Del Valle Torres, D. M., Rodriguez-Fernandez, A., Llamas-Elvira, J. M., Lozano, S. O., Font, C. R., Ramirez, E. L., Katati, M., 201Tl-SPECT in low-grade gliomas: Diagnostic accuracy in differential diagnosis between tumour recurrence and radionecrosis, European Journal of Nuclear Medicine and Molecular Imaging, 31, 1237-1243, 2004	Not follow up protocol/population not in PICO (patients with suspected tumour recurrence)/outcomes not in PICO
Gourcerol, D., Scherpereel, A., Debeugny, S., Porte, H., Cortot, A. B., Lafitte, J. J., Relevance of an extensive follow-up after surgery for nonsmall cell lung cancer, European Respiratory JournalEur Respir J, 42, 1357-1364, 2013	Population not in PICO (only 2 patients had stage 4 lung cancer)
Grigolato, D., Locantore, L., Cucca, M., Zuffante, M., Ferdeghini, M., 18F-DOPA PET/CT imaging in brain tumors, European Journal of Nuclear Medicine and Molecular Imaging, 43, S264, 2016	Published as abstract only, not enough information available to ascertain relevance, but population appears not to be in PICO
Grosu, A. L., Astner, S. T., Riedel, E., Nieder, C., Wiedenmann, N., Heinemann, F., Schwaiger, M., Molls, M., Wester, H. J., Weber, W. A., An interindividual comparison of O-(2-[18F]fluoroethyl)-L- tyrosine (FET)- and L-[methyl-11C]methionine (MET)-PET in patients with brain gliomas and metastases, International Journal of Radiation Oncology Biology Physics, 81, 1049-1058, 2011	Population not in PICO (All patients had previously been treated for gliomas or brain metastases and now presented with MRI findings suggesting the presence of residual or recurrent tumor tissue)
Hamdan, A., Kane, P., Uncertainty and variability in surveillance imaging after completion of primary treatment in glioblastoma multiforme, Neuro-Oncology, 16, ii80, 2014	Published as abstract only, not enough information available to ascertain relevance

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Hamdan, A., Kane, P., Variability in follow up imaging guidelines after the completion of primary therapy in glioblastoma multiforme, Neuro-Oncology, 16, vi1-vi2, 2014	Published as abstract only, not enough information available to ascertain relevance
Hawighorst, H., Essig, M., Debus, J., Knopp, M. V., Engenhart-Cabilic, R., Schonberg, S. O., Brix, G., Zuna, I., van Kaick, G., Serial MR imaging of intracranial metastases after radiosurgery, Magnetic Resonance ImagingMagn Reson Imaging, 15, 1121-32, 1997	Non-comparative study
Hodgson, T. J., Kingsley, D. P. E., Moseley, I. F., The role of imaging in the follow up of meningiomas, Journal of Neurology Neurosurgery and Psychiatry, 59, 545-547, 1995	Not follow up protocol/unclear when/what the patients had (as) follow up
Hojer, C., Hildebrandt, G., Lanfermann, H., Schroder, R., Haupt, W. F., Pilocytic astrocytomas of the posterior fossa - A follow-up study in 33 patients, Acta Neurochirurgica, 129, 131-139, 1994	Not follow up protocol/unclear which patients received what follow up
Hu, X., Ma, L., Li, W., Sun, X., Sun, J., Yu, J., 11C-choline PET/CT detecting tumour recurrence and predicting survival in post-treatment patients with high-grade Glioma, European Journal of Nuclear Medicine and Molecular Imaging, 40, S351, 2013	Published as abstract only, not enough information available to ascertain relevance
Hu, X., Wong, K. K., Young, G. S., Guo, L., Wong, S. T., Support vector machine multiparametric MRI identification of pseudoprogression from tumor recurrence in patients with resected glioblastoma, Journal of Magnetic Resonance Imaging, 33, 296-305, 2011	Population not in PICO (patients with confirmed radiation necrosis or recurrence)
Huber, P. E., Hawighorst, H., Fuss, M., van Kaick, G., Wannenmacher, M. F., Debus, J., Transient enlargement of contrast uptake on MRI after linear accelerator (linac) stereotactic radiosurgery for brain metastases, International Journal of Radiation Oncology, Biology, PhysicsInt J Radiat Oncol Biol Phys, 49, 1339-49, 2001	Not follow up protocol
Ikeda, H., Tsuyuguchi, N., Kunihiro, N., Ishibashi, K., Goto, T., Ohata, K., Analysis of progression and recurrence of meningioma using 11C-methionine PET, Annals of Nuclear Medicine, 27, 772-780, 2013	Not follow up protocol

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Ion-Margineanu, A., Van Cauter, S., Sima, D. M., Maes, F., Van Gool, S. W., Sunaert, S., Himmelreich, U., Van Huffel, S., Tumour Relapse Prediction Using Multiparametric MR Data Recorded during Follow-Up of GBM Patients, BioMed Research InternationalBiomed Res Int, 2015 (no pagination), 2015	Not follow up protocol
Jansen, N., Suchorska, B., Graute, V., Lutz, J., Schwarz, S., Bartenstein, P., Kreth, F. W., La Fougere, C., [18F]FET-PET based therapy monitoring after stereotactic 125iodine brachytherapy in patients with recurrent high grade glioma, NuklearMedizin, 51, A14, 2012	Published as abstract only, with not enough information reported to ascertain relevance
Jora, C., Mattakarottu, J. J., Aniruddha, P. G., Mudalsha, R., Singh, D. K., Pathak, H. C., Sharma, N., Sarin, A., Prince, A., Singh, G., Comparative evaluation of 18F-FDOPA, 13N-AMMONIA, 18F-FDG PET/CT and MRI in primary brain tumors - A pilot study, Indian Journal of Nuclear Medicine, 26, 78-81, 2011	Population not in PICO (15/23 were postoperative cases with suspected recurrence or residual tumor tissue)
Jostel, A., Mukherjee, A., Hulse, P. A., Shalet, S. M., Adult growth hormone replacement therapy and neuroimaging surveillance in brain tumour survivors, Clinical EndocrinologyClin Endocrinol (Oxf), 62, 698-705, 2005	Population not in PICO/mixed population
Juhasz, C., Mittal, S., Muzik, O., Chugani, D. C., Chakraborty, P. K., Bahl, G., Barger, G. R., Accurate identification of recurrent gliomas by kinetic analysis of alpha-methyl-l-tryptophan unidirectional uptake on PET, Neuro-Oncology, 12, iv113, 2010	Published as abstract only, not enough information reported to ascertain relevance, but it seems that population/outcomes not in PICO
Jung, B. H., Hwang, S., Moon, D. B., Ahn, C. S., Kim, K. H., Ha, T. Y., Song, G. W., Jung, D. H., Lee, S. G., Surveillance protocol for hepatocellular carcinoma recurrence after living donor liver transplantation, HPB, 16, 578-579, 2014	Published as abstract only, not enough information reported to ascertain relevance, but it seems that population not in PICO
Kaplan, M. A., Inal, A., Kucukoner, M., Urakci, Z., Ekici, F., Firat, U., Zincircioglu, S. B., Isikdogan, A., Cranial magnetic resonance imaging in the staging of HER2-positive breast cancer patients, Onkologie, 36, 176-181, 2013	Population not in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Kelly, J, Does the addition of positron emission tomography/computed tomography (PET/CT) to the routine investigation and assessment of patients with melanoma yield clinical and economic benefits? (Structured abstract), Health Technology Assessment Database, 2013	Unavailable/cannot source paper
Klesse, L., Bezner, S., Gargan, L., Leonard, D., Bowers, D., Utility of long term neuro-imaging in patients with cerebellar pilocytic astrocytomas, Pediatric Blood and Cancer, 56, 963, 2011	Population not in PICO (mean age at diagnosis < 10 years)
Klutmann, S., Bohuslavizki, K. H., Brenner, W., Behnke, A., Tietje, N., Kroger, S., Hugo, H. H., Mehdorn, H. M., Clausen, M., Henze, E., Somatostatin receptor scintigraphy in postsurgical follow-up examinations of meningioma, Journal of Nuclear MedicineJ Nucl Med, 39, 1913-7, 1998	Not follow up protocol
Lagman, C, Bhatt, N, Pelargos, P, Lee, S, Mukherjee, D, Yang, I, A meta-analysis of published literature on adjuvant radiosurgery and surveillance following subtotal resection of atypical meningioma, Neuro-oncology. Conference: 21st annual scientific meeting and education day of the society for neuro-oncology. United states. Conference start: 20161117. Conference end: 20161120, 18, vi101, 2017	Duplicate
Lagman, C., Bhatt, N., Pelargos, P., Lee, S., Mukherjee, D., Yang, I., A meta-analysis of published literature on adjuvant radiosurgery and surveillance following subtotal resection of atypical meningioma, Neuro-Oncology, 18, vi101, 2016	Published as abstract only, not enough information available to ascertain relevance (checked for topic 3a)
Lagman, Carlito, Bhatt, Nikhilesh S., Lee, Seung J., Bui, Timothy T., Chung, Lawrance K., Voth, Brittany L., Barnette, Natalie E., Pouratian, Nader, Lee, Percy, Selch, Michael, Kaprealian, Tania, Chin, Robert, McArthur, David L., Mukherjee, Debraj, Patil, Chirag G., Yang, Isaac, Adjuvant Radiosurgery Versus Serial Surveillance Following Subtotal Resection of Atypical Meningioma: A Systematic Analysis, World Neurosurgery, 98, 339-346, 2017	Checked for topic 3a; all included studies checked for relevance for topic 3a
Law, A., Loh, N., Francis, R., Bynevelt, M., McCarthy, M., Segard, T., Morandeau, L., Maton, P., Nowak, A., Atkinson, J., 11C-Methionine and 18F-fluorothymidine PET-CT imaging in suspected residual or recurrent glioma, Journal of Medical Imaging and Radiation Oncology, 56, 32, 2012	Published as abstract only and not enough information is reported to ascertain relevance, although it appears not to be a follow up protocol

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Le Jeune, F. P., Dubois, F., Blond, S., Steinling, M., Sestamibi technetium-99m brain single-photon emission computed tomography to identify recurrent glioma in adults: 201 studies, Journal of Neuro-Oncology, 77, 177-183, 2006	Outcomes not in PICO
Lee, J. W., Kang, K. W., Park, S. H., Lee, S. M., Paeng, J. C., Chung, J. K., Lee, M. C., Lee, D. S., 18F-FDG PET in the assessment of tumor grade and prediction of tumor recurrence in intracranial meningioma, European Journal of Nuclear Medicine and Molecular Imaging, 36, 1574-1582, 2009	Not follow up protocol
Leimgruber, Antoine, Ostermann, Sandrine, Yeon, Eun Jo, Buff, Evelyn, Maeder, Philippe P., Stupp, Roger, Meuli, Reto A., Perfusion and diffusion MRI of glioblastoma progression in a four-year prospective temozolomide clinical trial, International journal of radiation oncology, biology, physics, 64, 869-75, 2006	Not follow up protocol
Lemasson, B., Chenevert, T. L., Mikkelsen, T., Boes, J. L., Johnson, T. D., Galban, S., Rehemtulla, A., Galban, C., Ross, B. D., Novel MRI-based biomarker for early assessment of glioma recurrence, Cancer Research, 72, no pagination, 2012	Published as an abstract only, not enough information reported to ascertain relevance. N = 14.
Li, Wanhu, Ma, Li, Wang, Xiaoyue, Sun, Jujie, Wang, Suzhen, Hu, Xudong, (11)C-choline PET/CT tumor recurrence detection and survival prediction in post-treatment patients with high-grade gliomas, Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine, 35, 12353-60, 2014	Population not in PICO (suspicion of recurrence)
Lorberboym, D., Baram, J., Feibel, M., Hercbergs, A., Lieberman, L., A prospective evaluation of thallium-201 single photon emission computerized tomography for brain tumor burden, International Journal of Radiation Oncology Biology Physics, 32, 249-254, 1995	Unclear follow up protocol/outcomes not in PICO
Loreti, F., Trippa, F., Costa, M., Conti, S., Francesconi, E., Giorgi, C., Carletti, S., Maranzano, E., 99mTc-MIBI SPECT/CT in brain metastases treated with stereotactic radiosurgery (SRS): Experience of the Terni Hospital neuro-oncology group, Clinical and Translational Imaging, 1, S40, 2013	Published as an abstract only, not enough information reported to ascertain relevance.
Madhavi, T., Raunak, V., Rajnish, S., Jaspriya, B., Abhinav, J., Maria, S. M. D., Pandey Santosh, K., Jyotika, J., Puja, P., Mishra Anil, K., Anupam, M., Comparative evaluation of C-11 methionine (METPET) and F-18	Published as abstract only, not enough information reported to ascertain relevance,

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
flurodeoxyglucose (FDG) PET/CT for detection of recurrent brain tumors, Indian Journal of Nuclear Medicine, 25, 90, 2010	but study does not seem to be follow up protocol
Makita, Masujiro, Sakai, Takehiko, Ogiya, Akiko, Kitagawa, Dai, Morizono, Hidetomo, Miyagi, Yumi, Iijima, Kotaro, Iwase, Takuji, Optimal surveillance for postoperative metastasis in breast cancer patients, Breast cancer (Tokyo, Japan), 23, 286-94, 2016	Population not in PICO
Massager, N., De Smedt, F., Devriendt, D., Long-term tumor control of benign intracranial tumors after Gamma Knife radiosurgery in 280 patients followed more than 5 years, Acta Neurologica Belgica, 113, 463-467, 2013	Not follow up protocol
Matsuo, M., Miwa, K., Shinoda, J., Tanaka, O., Krishna, M., Impact Of C11-methionine positron emission tomography (PET) for malignant glioma in radiation therapy: Is C11-methionine PET a superior to magnetic resonance imaging?, International Journal of Radiation Oncology Biology Physics, 81, S182, 2011	Published as abstract only, not enough information reported to ascertain relevance
Menoux, I., Armspach, J. P., Noel, G., Antoni, D., Imaging methods used in the differential diagnosis between brain tumour relapse and radiation necrosis after stereotactic radiosurgery of brain metastases: Literature review, Cancer/Radiotherapie, 20, 837-845, 2016	Narrative review
Meyers, S. P., Wildenhain, S., Chess, M. A., Tarr, R. W., Postoperative evaluation for intracranial recurrence of medulloblastoma: MR findings with gadopentetate dimeglumine, AJNR. American journal of neuroradiology, 15, 1425-34, 1994	Not follow up protocol/population not in PICO (mean age 8.3 years, range 1-42 years; no further details)
Mori, H., Kunimatsu, A., Abe, O., Sasaki, H., Takao, H., Nojo, T., Kawai, K., Saito, N., Ohtomo, K., Diagnostic ability of fluid-attenuated inversion recovery MR imaging to detect remnant or recurrent meningiomas after resection, Neuroradiology Journal, 25, 163-171, 2012	Not follow up protocol
Mori, H., Kunimatsu, A., Abe, O., Sasaki, H., Takao, H., Nojo, T., Ohtomo, K., Resected meningiomas: Diagnostic performance of fluid-attenuated inversion recovery MR imaging for detection of remnant or recurrence, Neuroradiology Journal, 23, 419-420, 2010	Published as abstract only, not enough information reported to ascertain relevance, but study does not seem to be follow up protocol

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Nayeri, A., Prablek, M. A., Brinson, P. R., Weaver, K. D., Thompson, R. C., Chambless, L. B., Short-term postoperative surveillance imaging may be unnecessary in elderly patients with resected WHO Grade i meningiomas, Journal of Clinical NeuroscienceJ Clin Neurosci, 26, 101-104, 2016	Not follow up protocol
Nesbitt, D., Hendry, G., Scoones, D., Kane, P., Routine follow-up imaging after treatment for glioblastoma: How useful is it?, Neuro-Oncology, 12, iii34, 2010	Published as abstract only; non-comparative study
Nihashi, T., Dahabreh, I. J., Terasawa, T., PET in the clinical management of glioma: Evidence map, American Journal of Roentgenology, 200, W654-W660, 2013	Outcomes not in PICO
Niyazi, M., Schnell, O., Suchorska, B., Schwarz, S. B., Ganswindt, U., Geisler, J., Bartenstein, P., Kreth, F. W., Tonn, J. C., Eigenbrod, S., Belka, C., La Fougere, C., FET-PET assessed recurrence pattern after radio-chemotherapy in newly diagnosed patients with glioblastoma is influenced by MGMT methylation status, Radiotherapy and Oncology, 104, 78-82, 2012	Not follow up protocol
Nowosielski, M., Hutterer, M., Tinkhauser, G., Irschick, R., Waitz, D., Putzer, D., Stockhammer, G., Recheis, W., Jaschke, W., Gotwald, T., Bevacizumab/irinotecan in recurrent malignant glioma: A retrospective analysis of MRI, FET-PET, and clinical performance, Journal of Clinical Oncology, 28, no pagination, 2010	Published as abstract only, not enough information reported to ascertain relevance
Nozawa, A, Rivandi, Ah, Kanematsu, M, Hoshi, H, Piccioni, D, Kesari, S, Hoh, Ck, Glucose-corrected standardized uptake value in the differentiation of high-grade glioma versus post-treatment changes, Nuclear Medicine CommunicationsNucl Med Commun, 36, 573-81, 2015	Not follow up protocol
Nozawa, Asae, Rivandi, Ali Hosseini, Kanematsu, Masayuki, Hoshi, Hiroaki, Piccioni, David, Kesari, Santosh, Hoh, Carl K., Glucose-corrected standardized uptake value in the differentiation of high-grade glioma versus post-treatment changes, Nuclear Medicine Communications, 36, 573-81, 2015	Duplicate
Nuutinen, J., Sonninen, P., Lehikoinen, P., Sutinen, E., Valavaara, R., Eronen, E., Norrgard, S., Kulmala, J., Teras, M., Minn, H., Radiotherapy treatment planning and long-term follow-up with [11C]methionine PET in patients with low-grade astrocytoma, International Journal of Radiation Oncology Biology Physics, 48, 43-52, 2000	Outcomes/analyses not in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Park, Ji Eun, Kim, Ho Sung, Park, Kye Jin, Kim, Sang Joon, Kim, Jeong Hoon, Smith, Seth A., Pre- and Posttreatment Glioma: Comparison of Amide Proton Transfer Imaging with MR Spectroscopy for Biomarkers of Tumor Proliferation, Radiology, 278, 514-23, 2016	Not follow up protocol
Patel, P., Baradaran, H., Delgado, D., Askin, G., Christos, P., Tsiouris, A. J., Gupta, A., MR perfusion-weighted imaging in the evaluation of high-grade gliomas after treatment: A systematic review and meta-analysis, Neuro-Oncology, 19, 118-127, 2017	Population and outcomes not in PICO
Patel, S. H., Robbins, J. R., Gore, E. M., Bradley, J. D., Gaspar, L. E., Germano, I., Ghafoori, P., Henderson, M. A., Lutz, S. T., McDermott, M. W., Patchell, R. A., Robins, H. I., Vassil, A. D., Wippold, F. J., Videtic, G. M., ACR appropriateness criteria follow-up and retreatment of brain metastases, American Journal of Clinical Oncology: Cancer Clinical Trials, 35, 302-306, 2012	Narrative review/guideline
Pavlicek, R., Garcia, J. R., Baquero, M., Soler, M., Fernandez, Y., Fuertes, S., Carrio, I., Lomena, F., Contribution of 11C-methionine PET to MRI in the differentiation of recurrent brain tumor from radiation necrosis, European Journal of Nuclear Medicine and Molecular Imaging, 38, S342, 2011	Published as abstract only, not enough information reported to ascertain relevance, but study does not seem to be follow up protocol, appears to be non-comparative with n = 14
Potzi, C., Becherer, A., Marosi, C., Karanikas, G., Szabo, M., Dudczak, R., Kletter, K., Asenbaum, S., [11C] methionine and [18F] fluorodeoxyglucose PET in the follow-up of glioblastoma multiforme, Journal of Neuro-Oncology, 84, 305-314, 2007	Outcomes or analyses not in PICO
Prat, R., Galeano, I., Lucas, A., Martinez, J. C., Martin, M., Amador, R., Reynes, G., Relative value of magnetic resonance spectroscopy, magnetic resonance perfusion, and 2-(18F) fluoro-2-deoxy-D-glucose positron emission tomography for detection of recurrence or grade increase in gliomas, Journal of Clinical Neuroscience, 17, 50-53, 2010	Population not in PICO; outcomes not in PICO
Prigent-Le Jeune, F., Dubois, F., Perez, S., Blond, S., Steinling, M., Technetium-99m sestamibi brain SPECT in the follow-up of glioma for evaluation of response to chemotherapy: First results, European Journal of Nuclear Medicine and Molecular Imaging, 31, 714-719, 2004	Not follow up protocol

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Pronin, I., Dolgushin, M., Fadeeva, L., Podoprigora, A., Serkov, S., Golanov, A., Nikitin, K., Kornienko, V., CT perfusion in diagnosis of Radiation Necrosis, Neuroradiology Journal, 23, 354, 2010	Published as abstract only, not enough information reported to ascertain relevance, but outcomes do not appear to be in PICO
Pungavkar, S., Gupta, T., Moiyadi, A., Shetty, P., Shridhar, E., Chinnaswamy, G., Godashastri, J., Jalali, R., 3D arterial spin labeling - A novel, non-invasive technique to assess perfusion in brain tumors - Experience of over 200 cases, European Journal of Cancer, 54, S38, 2016	Published as abstract only, not enough information reported to ascertain relevance
Rachinger, W., Goetz, C., Popperl, G., Gildehaus, F. J., Kreth, F. W., Holtmannspotter, M., Herms, J., Koch, W., Tatsch, K., Tonn, J. C., Positron emission tomography with O-(2-[18F]flouroethyl)-L- tyrosine versus magnetic resonance imaging in the diagnosis of recurrent gliomas, Neurosurgery, 57, 505-511, 2005	Outcomes not in PICO
Radbruch, Alexander, Lutz, Kira, Wiestler, Benedikt, Baumer, Philipp, Heiland, Sabine, Wick, Wolfgang, Bendszus, Martin, Relevance of T2 signal changes in the assessment of progression of glioblastoma according to the Response Assessment in Neurooncology criteria, Neuro-Oncology, 14, 222-9, 2012	Not follow up protocol; unclear when patients had scans
Reiche, W., Schaefer, A., Schmidt, S., Moringlane, J. R., Feiden, W., Kirsch, C. M., Piepgras, U., 18FDG-SPECT imaging of brain tumours: Results in 41 patients, Rivista di Neuroradiologia, 11, 149-160, 1998	Not follow up protocol
Reijneveld, J. C., van der Grond, J., Ramos, L. M. P., Bromberg, J. E. C., Taphoorn, M. J. B., Proton MRS imaging in the follow-up of patients with suspected low-grade gliomas, Neuroradiology, 47, 887-91, 2005	Population not in PICO; non-comparative study with n = 14
Roberts, S., Jones, L., Exley, C., CT follow up after surgery for lung cancer-should the availability of radio-surgery prompt a change in screening protocol to detect early intracerebral recurrence?, Thorax, 70, A159, 2015	Population not in PICO
Rodriguez-Bel, L., Gamez-Cenzano, C., Garciagarzon, J., Sabate-Llobera, A., Vercher-Conejero, J., Gracia-Sanchez, L., Linares-Tello, E. L., Majos-Torro, C., Lucas-Calduch, A., Macia-garau, M., Bruna-Escuer, J., Diagnostic accuracy for F18-FDG-PET/CT and C11-METHIONINEPET/ CT Co-registered with MRI for differentiation of recurrent brain tumor from radiation injury, European Journal of Nuclear Medicine and Molecular Imaging, 43, S260, 2016	Published as abstract only, not enough information reported to ascertain relevance, but population and outcomes appear not to be in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
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Rubinstein, R., Karger, H., Pietrzyk, U., Siegal, T., Gomori, J. M., Chisin, R., Use of 201Thallium brain SPECT, image registration, and semi-quantitative analysis in the follow-up of brain tumors, European Journal of Radiology, 21, 188-95, 1996	Outcomes not in PICO
Sadeghi, N., Lebrun, J. C., Absil, J., Metens, T., Goldman, S., Dynamic susceptibility contrast enhanced (DSC) MR based perfusion imaging to differentiate recurrence from stable disease in brain gliomas, Neuroradiology, 56, 233, 2014	Published as abstract only, not enough information reported to ascertain relevance, but outcomes appear not to be in PICO
Samnick, S., Bader, J. B., Hellwig, D., Moringlane, J. R., Alexander, C., Romeike, B. F. M., Feiden, W., Kirsch, C. M., Clinical value of iodine-123-alpha-methyl-L-tyrosine single-photon emission tomography in the differential diagnosis of recurrent brain tumor in patients pretreated for glioma at follow-up, Journal of Clinical Oncology, 20, 396-404, 2002	Population not in PICO, not follow up protocol
Santoni, M., Berardi, R., Bittoni, A., Paccapelo, A., Nanni, C., Fanti, S., Burattini, L., Cascinu, S., Clinical impact of [11C]-methionine positron emission tomography on the treatment of primary and recurrent gliomas, Annals of Oncology, 23, ix148, 2012	Published as abstract only, not enough information reported to ascertain relevance
Santoni, M., Nanni, C., Bittoni, A., Polonara, G., Paccapelo, A., Trignani, R., De Lisa, M., Rychlicki, F., Burattini, L., Berardi, R., Fanti, S., Cascinu, S., [11C]-Methionine positron emission tomography in the postoperative imaging and followup of patients with primary and recurrent gliomas, ISRN Oncology, 2014, no pagination, 2014	Not follow up protocol/outcomes not in PICO
Seeger, A., Braun, C., Skardelly, M., Paulsen, F., Schittenhelm, J., Ernemann, U., Bisdas, S., Comparison of Three Different MR Perfusion Techniques and MR Spectroscopy for Multiparametric Assessment in Distinguishing Recurrent High-Grade Gliomas from Stable Disease, Academic Radiology, 20, 1557-1565, 2013	Population not in PICO (patients with the presence of new enhancing lesions after chemoradiotherapy)

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Shan, Y., Chen, X., Lin, Y., Wang, Y., Zhong, S., Gong, Y., Value of magnetic resonance spectroscopy and perfusion-weighted imaging in distinguishing glioma recurrence from PTRE: A meta-analysis, International Journal of Clinical and Experimental Medicine, 9, 10006-10017, 2016	Unavailable/we cannot source paper
Sharma, R., D'Souza, M., Jaimini, A., Hazari, P. P., Saw, S., Pandey, S., Singh, D., Solanki, Y., Kumar, N., Mishra, A. K., Mondal, A., A comparison study of 11 C-methionine and 18 F-fluorodeoxyglucose positron emission tomography-computed tomography scans in evaluation of patients with recurrent brain tumors, Indian Journal of Nuclear Medicine, 31, 93-102, 2016	Not follow up protocol (one scan); outcomes not in PICO
Shin, K. E., Ahn, K. J., Choi, H. S., Jung, S. L., Kim, B. S., Jeon, S. S., Hong, Y. G., DCE and DSC MR perfusion imaging in the differentiation of recurrent tumour from treatment-related changes in patients with glioma, Clinical Radiology, 69, e264-e272, 2014	Population not in PICO ("patients who subsequently developed new enhancing lesions on follow-up contrast-enhanced MRI")
Simpson, J. R., Mendenhall, W. M., Schupak, K. D., Larson, D., Bloomer, W. D., Buckley, J. A., Gaspar, L. E., Gibbs, F. A., Lewin, A. A., Loeffler, J. S., Malcolm, A. W., Schneider, J. F., Shaw, E. G., Wharam Jr, M. D., Gutin, P. H., Rogers, L., Leibel, S., Follow-up and retreatment of brain metastasis. American College of Radiology. ACR Appropriateness Criteria, Radiology, 215 Suppl, 1129-1135, 2000	Unavailable/cannot source paper
Skvortsova, T., Savintseva, Z., Brodskaya, Z., Medvedev, S. V., Bechtereva, N. P., Direct comparison of [11C]methionine PET with perfusion magnetic resonance imaging for detection of recurrent brain tumors, European Journal of Nuclear Medicine and Molecular Imaging, 39, S381, 2012	Published as abstract only, not enough information reported to ascertain relevance, but population does not appear to be in PICO
Smets, T., Lawson, T. M., Grandin, C., Jankoversuski, A., Raftopoulos, C., Immediate post-operative MRI suggestive of the site and timing of glioblastoma recurrence after gross total resection: A retrospective longitudinal preliminary study, European Radiology, 23, 1467-1477, 2013	Population not in PICO (22/24 were selected to have/had recurrence)
Smith, J. S., Cha, S., Mayo, M. C., McDermott, M. W., Parsa, A. T., Chang, S. M., Dillon, W. P., Berger, M. S., Serial diffusion-weighted magnetic resonance imaging in cases of glioma: distinguishing tumor recurrence from postresection injury, Journal of Neurosurgery, 103, 428-438, 2005	Not follow up protocol; outcomes not in PICO

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Steele, J., Sibtain, A., Brada, M., The content and efficacy of conventional methods of follow-up in neuro-oncology: The need for new strategies, Clinical Oncology, 9, 168-171, 1997	Unclear follow up protocol, non-comparative study, outcomes not in PICO
Stenberg, L., Englund, E., Wirestam, R., Siesjo, P., Salford, L. G., Larsson, E. M., Dynamic susceptibility contrast-enhanced perfusion magnetic resonance (MR) imaging combined with contrast-enhanced MR imaging in the follow-up of immunogene-treated glioblastoma multiforme, Acta radiologica (Stockholm, Sweden : 1987), 47, 852-861, 2006	Unclear follow up protocol, non-comparative study, N = 8
Stupp, R., Brada, M., van den Bent, M. J., Tonn, J. C., Pentheroudakis, G., High-grade glioma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up, Annals of Oncology, 25, 93-101, 2014	Guideline/narrative review
Thapa, P. K., Tripathi, M., Jaimini, A., D'Souza, M., Chouttani, K., Pandey, S., Sehar, R., Rawat, H., Mishra, A. K., Sharma, R., Mondal, A., Comparative study between Tc-99m labelled Methionine and C-11 Methionine in detection of low grade astrocytoma, Indian Journal of Nuclear Medicine, 26, S29, 2011	Published as abstract only, not enough information reported to ascertain relevance, but population/outcomes do not appear to be in PICO
Tripathi, M., Sharma, R., Varshney, R., Jaimini, A., Jain, J., Souza, M. M. D., Bal, J., Pandey, S., Kumar, N., Mishra, A. K., Mondal, A., Comparison of F-18 FDG and C-11 methionine PET/CT for the evaluation of recurrent primary brain tumors, Clinical Nuclear Medicine, 37, 158-163, 2012	Population not in PICO (patients referred for evaluation of recurrence); not follow up protocol
Ueki, K., Higuchi, F., Ohtani, R., Udzuka, T., Sakamoto, S., Kim, P., 11C-methionin-pet enables early detection and subsequent intervention of recurrence in 1p/ 19q co-deleted gliomas, Neuro-Oncology, 17, v169, 2015	Published as abstract only, not enough information reported to ascertain relevance, but study appears to be non-comparative
Unterrainer, M., Schweisthal, F., Suchorska, B., Wenter, V., Schmid-Tannwald, C., Fendler, W. P., Schuller, U., Bartenstein, P., Tonn, J. C., Albert, N. L., Serial 18F-FET PET imaging of primarily 18F-FET-negative glioma: Does it make sense?, Journal of Nuclear Medicine, 57, 1177-1182, 2016	Outcomes not in PICO
Van Laere, K., Ceyssens, S., Van Calenbergh, F., De Groot, T., Menten, J., Flamen, P., Bormans, G., Mortelmans, L., Direct comparison of 18F-FDG and 11C-methionine PET in suspected recurrence of glioma:	Not follow up protocol: data obtained in a single session in patients with a history of previously treated primary brain tumours

Excluded studies (search conducted together for all three follow up questions): **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma?** **- What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?**	
Sensitivity, inter-observer variability and prognostic value, European Journal of Nuclear Medicine and Molecular Imaging, 32, 39-51, 2005	were referred to the PET centre to differentiate between radiation necrosis and recurrence/progression
Vassilyadi, M., Shamji, M. F., Tataryn, Z., Keene, D., Ventureyra, E., Postoperative surveillance magnetic resonance imaging for cerebellar astrocytoma, Canadian Journal of Neurological Sciences, 36, 707-712, 2009	Population not in PICO (children)
Verburg, N., Hoefnagels, F., Pouwels, P., Boellaard, R., Barkhof, F., Hoekstra, O., Wesseling, P., Reijneveld, J., Heimans, J., Vandertop, P., Zwinderman, K., De Witt Hamer, H., The diagnostic accuracy of neuro-imaging to detect infiltrative glioma within the brain: A meta-analysis based on 1598 patients in 58 publications, Neuro-Oncology, 15, iii194, 2013	Published as abstract only, not enough information available to ascertain relevance, although it appears not to be follow up protocol and outcomes not in PICO
Vigil, C., Caicedo, C., Hernandez, M., Rodriguez-ruiz, M., Olarte, A., Valtuena, G., Moreno-jimenez, M., Penuelas, I., Aristu, J., Arbizu, J., 11C-Methionine-Positron Emission Tomography as prognostic factor of recurrence in glioblastoma, Reports of Practical Oncology and Radiotherapy, 18, S186, 2013	Published as abstract only, not enough information reported to ascertain relevance, but does not appear to be follow up
Vos, M J, Tony, B N, Hoekstra, O S, Postma, T J, Heimans, J J, Hooft, L, Systematic review of the diagnostic accuracy of 201-Tl single photon emission computed tomography in the detection of recurrent glioma (Structured abstract), Nuclear Medicine Communications, 28, 431-439, 2007	Population not in PICO (patients who were clinically suspected of recurrent tumour growth); outcomes not in PICO
Vos, M. J., Hoekstra, O. S., Barkhof, F., Berkhof, J., Heimans, J. J., Van Groeningen, C. J., Vandertop, W. P., Slotman, B. J., Postma, T. J., Thallium-201 single-photon emission computed tomography as an early predictor of outcome in recurrent glioma, Journal of Clinical Oncology, 21, 3559-3565, 2003	Not follow up protocol/analyses not in PICO
Vos, Mj, Berkhof, J, Hoekstra, Os, Bosma, I, Sizoo, Em, Heimans, Jj, Reijneveld, Jc, Sanchez, E, Lagerwaard, Fj, Buter, J, Noske, Dp, Postma, Tj, MRI and thallium-201 SPECT in the prediction of survival in glioma, Neuroradiology, 54, 539-46, 2012	Not follow up protocol/analyses not in PICO
Vrabec, M., Van Cauter, S., Himmelreich, U., Van Gool, S. W., Sunaert, S., De Vleeschouwer, S., Suput, D., Demaerel, P., MR perfusion and diffusion imaging in the follow-up of recurrent glioblastoma treated with dendritic cell immunotherapy: A pilot study, Neuroradiology, 53, 721-731, 2011	N = 8, outcomes not in PICO, not follow up protocol

Excluded studies (search conducted together for all three follow up questions): - What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for glioma? - What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for meningioma? - What is the most effective follow-up protocol (including duration, frequency and tests) to detect recurrence after treatment for brain metastases?	
Wang, X, Hu, X, Xie, P, Li, W, Li, X, Ma, L, Comparison of magnetic resonance spectroscopy and positron emission tomography in detection of tumor recurrence in posttreatment of glioma: a diagnostic meta-analysis (Provisional abstract), Database of Abstracts of Reviews of Effects, epub, 2014	Unavailable/cannot source paper
Weber, M. A., Lichy, M. P., Gunther, M., Delorme, S., Thilmann, C., Bachert, P., Schad, L., Debus, J., Schlemmer, H. P., Monitoring of Irradiated Brain Metastases Using Arterial Spin-Labeling MR-Perfusion Imaging and 1H MR Spectroscopy, Rivista di Neuroradiologia, 16, 1118-1122, 2003	Outcomes not in PICO
Weizman, Lior, Sira, Liat Ben, Joskowicz, Leo, Rubin, Daniel L., Yeom, Kristen W., Constantini, Shlomi, Shofty, Ben, Bashat, Dafna Ben, Semiautomatic segmentation and follow-up of multicomponent low-grade tumors in longitudinal brain MRI studies, Medical physics, 41, 052303, 2014	Population not in PICO (children)
Winterstein, Marianne, Munter, Marc W., Burkholder, Iris, Essig, Marco, Kauczor, Hans-Ulrich, Weber, Marc-Andre, Partially resected gliomas: diagnostic performance of fluid-attenuated inversion recovery MR imaging for detection of progression, Radiology, 254, 907-16, 2010	Outcomes not in PICO
Yokoi, K., Miyazawa, N., Arai, T., Brain metastasis in resected lung cancer: value of intensive follow-up with computed tomography, The Annals of thoracic surgery, 61, 546-551, 1996	Population not in PICO (patients treated for lung cancer without brain metastasis)
Yondorf, M. Z., Wernicke, A. G., Parashar, B., Schwartz, T. H., Boockvar, J. A., Stieg, P., Pannullo, S., Nori, D., Chao, K. S. C., Kovanlikaya, I., Impact of Serial DWI and ADC Measurements in Assessment of Brain Metastases Treated With Neurosurgical Resection and Intraoperative Cesium- 131 Brachytherapy: Results of a Prospective Trial, Oncology. Conference: 96th Annual Meeting of the American Radium Society, ARS, 28, 2014	Published as abstract only, not enough information reported to ascertain relevance, but does not appear to be follow up

Economic studies

Not applicable - health economic inclusion / exclusion detailed in Supplementary Material D.

Appendix L – Research recommendations

R5. Is immediate or deferred radiotherapy better for incompletely excised grade I meningioma?

Why is this important?

There are no randomised studies on the use of radiotherapy/radiosurgery in the treatment of grade I meningioma. Though case series have shown that people with inoperable and incompletely excised grade I meningioma treated with radiotherapy have high rates of control of their tumour, treatment risks significant side effects. The side effects include: neuropathy, radionecrosis, significant oedema, neuro-cognitive effects, increased risk of stroke and secondary tumours. Therefore the timing of treatment is a balance between control of tumour and side effects. It is not known if early treatment has a greater or lesser chance of long-term tumour control or risk of tumour complications, or if this just risks complications of treatment earlier.

People with grade I meningioma have traditionally been overlooked as a priority area for research. This is likely because of the slow nature of the disease resulting in need for long-term follow up and the difficulty to obtain funding for radiotherapy-only studies. However, this lack of research is inequitable, hence the reason for its prioritisation by the committee.

A study on this topic would provide clear information to guide clinicians and people with meningiomas, hopefully leading to overall improvement in quality of life. Because of the slow-growing characteristics of grade I meningioma, treatment decisions made early in the management pathway will have long-term effects on the person with the meningioma's overall quality of life outcomes, and potentially overall survival.Table 38: Research recommendation rationale

Research question	Is immediate or deferred radiotherapy better for incompletely excised grade I meningioma?
Importance to 'patients' or the population	Currently treatment recommendations are based on case series only. For people with meningioma treatment of the condition is a balance between side effects of treatment, complications of tumour growth and rate of control of the tumour. From the case series it is unclear if it is better to treat meningioma immediately or only on progression of the tumour/tumour symptoms.
Relevance to NICE guidance	High Priority: Recommendations are extremely complex but based on clinical consensus. It may be that a strong trial in this area could simplify recommendations across subgroups.
Relevance to NHS	Ensuring the people with meningioma receive the best treatment to result in optimal outcomes is important to the NHS, especially as there is large variation in different areas.
National priorities	This research is supportive of NHS England's Cancer Strategy Implementation

Research question	Is immediate or deferred radiotherapy better for incompletely excised grade I meningioma?
	Plan, since it supports the development of a modern radiotherapy service.
Current evidence base	There is some evidence where cohorts have had either immediate radiotherapy or deferred radiotherapy, which could in principle be synthesised to produce low-quality evidence on this research question, but there is no direct evidence on this topic of high importance. The EORTC trial attempted to answer a question similar to this, but could not recruit due to lack of equipoise. However radiotherapy techniques have improved significantly since then, and so the committee believed that a trial would be possible now.
Equality	N/A

Table 39: Research recommendation PICO

Population	Adults (18 years onwards) with an incompletely excised or inoperable grade I meningioma
Intervention	Immediate radiotherapy, understood to usually mean sterotactic radiotherapy/radiosurgery to the residual depending on clinical characteristics
Comparison	Deferred radiotherapy (given on clinical or radiological progression), understood to usually mean sterotactic radiotherapy/radiosurgery to the residual depending on clinical characteristics
Outcomes	• Quality of life • Neurocognitive decline • Overall survival • Progression-free survival • Local control • Radiation Therapy Oncology Group toxicity
Study design	Randomised controlled trial
Timeframe	10-year follow up