

Brain tumours (primary) and brain metastases in adults

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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Overview

This guideline covers diagnosing, monitoring and managing any type of primary brain tumour or brain metastases in people aged 16 or over. It aims to improve diagnosis and care, including standardising the care people have, how information and support are provided, and palliative care.

Who is it for?

- Healthcare professionals involved in the multidisciplinary care of people with primary brain tumours or brain metastases
- Commissioners and providers of brain tumour services
- People using services for the diagnosis, management and care of a primary brain tumour or brain metastases, and their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 *Investigation of suspected glioma*

Imaging for suspected glioma

- 1.1.1 Offer standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as the initial diagnostic test for suspected glioma, unless MRI is contraindicated.
- 1.1.2 Refer people with a suspected glioma to a specialist multidisciplinary team at first radiological diagnosis for management of their tumour.
- 1.1.3 Consider advanced MRI techniques, such as MR perfusion and MR spectroscopy, to assess the potential of a high-grade transformation in a tumour appearing to be low grade on standard structural MRI.

To find out why the committee made the recommendations on imaging for suspected glioma and how they might affect practice, see [rationale and impact](#).

Use of molecular markers to determine prognosis or guide treatment for glioma

- 1.1.4 Report all glioma specimens according to the latest version of the [World Health Organization \(WHO\) classification](#). As well as histopathological assessment, include molecular markers such as:
 - IDH1 and IDH2 mutations
 - ATRX mutations to identify IDH mutant astrocytomas and glioblastomas
 - 1p/19q codeletion to identify oligodendrogliomas

- histone H3.3 K27M mutations in midline gliomas
- BRAF fusion and gene mutation to identify pilocytic astrocytoma.

1.1.5 Test all high-grade glioma specimens for MGMT promoter methylation to inform prognosis and guide treatment.

1.1.6 Consider testing IDH-wildtype glioma specimens for TERT promoter mutations to inform prognosis.

To find out why the committee made the recommendations on use of molecular markers to determine prognosis or guide treatment for glioma and how they might affect practice, see [rationale and impact](#).

1.2 *Management of glioma*

Initial surgery for suspected low-grade glioma

1.2.1 The surgical expertise in the multidisciplinary team should include:

- access to awake craniotomy with language and other appropriate functional monitoring and
- expertise in intraoperative neurophysiological monitoring and
- access to neuroradiological support and
- access to intraoperative image guidance.

1.2.2 Consider surgical resection as part of initial management (within 6 months of radiological diagnosis) to:

- obtain a histological and molecular diagnosis and
- remove as much of the tumour as safely possible after discussion of the possible extent of resection at multidisciplinary meeting and with the person with the brain tumour, and their relatives and carers.

1.2.3 If surgical resection is not appropriate, consider biopsy to obtain a histological and molecular diagnosis.

1.2.4 Consider [active monitoring](#) without a histological diagnosis, for lesions with radiological features typical of very low-grade tumours, for example, DNET (dysembryoplastic neuroepithelial tumour) or optic pathway glioma.

1.2.5 If people having active monitoring show radiological or clinical disease progression, discuss this at a multidisciplinary team meeting and consider:

- surgical resection **or**
- biopsy if surgical resection is not possible.

To find out why the committee made the recommendations on initial surgery for suspected low-grade glioma and how they might affect practice, see [rationale and impact](#).

Further management of newly diagnosed low-grade glioma

1.2.6 After surgery, offer radiotherapy followed by up to 6 cycles of PCV chemotherapy (procarbazine, CCNU [lomustine] and vincristine) for people who:

- have a 1p/19q codeleted, IDH-mutated low-grade glioma (oligodendroglioma) **and**
- are aged around 40 or over, or have residual tumour on postoperative MRI.

1.2.7 After surgery, consider radiotherapy followed by up to 6 cycles of PCV chemotherapy for people who:

- have a 1p/19q non-codeleted, IDH-mutated low-grade glioma (astrocytoma) **and**
- are aged around 40 or over, or have residual tumour on postoperative MRI.

1.2.8 Consider [active monitoring](#) for people who are aged around 40 or under with an IDH-mutated low-grade glioma and have no residual tumour on postoperative MRI.

1.2.9 Consider radiotherapy followed by up to 6 cycles of PCV chemotherapy for people with an IDH-mutated low-grade glioma who have not had radiotherapy before if they have:

- progressive disease on radiological follow-up or
- intractable seizures.

1.2.10 When delivering radiotherapy for people with IDH-mutated low-grade glioma, do not use a treatment dose of more than 54 Gy at 1.8 Gy per fraction.

1.2.11 Be aware that the prognosis for people with histologically confirmed IDH-wildtype grade II glioma may be similar to that of people with glioblastoma if other molecular features are consistent with glioblastoma. Take this into account when thinking about management options.

To find out why the committee made the recommendations on further management of newly diagnosed low-grade glioma and how they might affect practice, see [rationale and impact](#).

Management of newly diagnosed grade III glioma following surgery or if surgery is not possible (or has been declined)

1.2.12 For guidance on using temozolomide for treating newly diagnosed grade III glioma, see the NICE technology appraisal guidance on [carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma](#).

1.2.13 After surgery, offer sequential radiotherapy and 4 to 6 cycles of PCV chemotherapy to people who have:

- a Karnofsky performance status of 70 or more and
- a newly diagnosed grade III glioma with 1p/19q codeletion (anaplastic oligodendroglioma).

1.2.14 Agree with the person with the anaplastic oligodendroglioma the order of PCV chemotherapy and radiotherapy after discussing the potential advantages and disadvantages of each option with them (see table 1).

Table 1 Factors to take into account when deciding whether to have PCV or radiotherapy first for management of anaplastic oligodendroglioma

	PCV first	Radiotherapy first
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Overall survival	No clinically important difference.	No clinically important difference.
Progression-free survival	No clinically important difference.	No clinically important difference.
Fertility preservation	Trying to preserve fertility may cause a delay in the start of treatment.	Allows additional time for fertility preservation without delaying treatment.
Planning treatment around important life events	Initially much less contact with the health system, but potentially more fatigue. Harder to give a precise date for when radiotherapy will start, as people's tolerance of chemotherapy is less predictable.	Initially much more contact with the health system: daily visits to radiotherapy department lasting several weeks. Timing of start of chemotherapy much more predictable.

1.2.15 After surgery, offer radiotherapy followed by up to 12 cycles of adjuvant temozolomide to people who have:

- a Karnofsky performance status of 70 or more and
- a newly diagnosed IDH-wildtype or mutated grade III glioma without 1p/19q codeletion (anaplastic astrocytoma).

1.2.16 Do not offer nitrosoureas (for example, CCNU [lomustine]) concurrently with radiotherapy to people with newly diagnosed grade III glioma.

1.2.17 If asked, advise people with an initial diagnosis of grade III glioma (and their relatives and carers, as appropriate) that the available evidence does not support the use of:

- cannabis oil
- immunotherapy
- ketogenic diets
- metformin

- statins
- valganciclovir.

To find out why the committee made the recommendations on management of newly diagnosed grade III glioma after surgery, or if surgery is not possible or the person declines surgery, and how they might affect practice, see [rationale and impact](#).

Management of newly diagnosed grade IV glioma (glioblastoma) following surgery or if surgery is not possible (or has been declined)

The recommendations in this section are also viewable as a [visual summary](#).

- 1.2.18 For guidance on using temozolomide for treating newly diagnosed grade IV glioma (glioblastoma), see the NICE technology appraisal guidance on [carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma](#).
- 1.2.19 Offer radiotherapy using 60 Gy in 30 fractions with concomitant temozolomide, followed by up to 6 cycles of adjuvant temozolomide, for people aged around 70 or under who have:
- a Karnofsky performance status of 70 or more and
 - had maximal safe resection, or biopsy when resection is not possible, for a newly diagnosed grade IV glioma (glioblastoma).
- 1.2.20 Offer radiotherapy using 40 Gy in 15 fractions with concomitant and up to 12 cycles of adjuvant temozolomide for people aged around 70 or over who have:
- a Karnofsky performance status of 70 or more and
 - a newly diagnosed grade IV glioma (glioblastoma) with MGMT methylation.
- 1.2.21 Consider radiotherapy using 40 Gy in 15 fractions with concomitant and up to 12 cycles of adjuvant temozolomide for people aged around 70 or over who have:
- a Karnofsky performance status of 70 or more and

- a newly diagnosed grade IV glioma (glioblastoma) without MGMT methylation or for which methylation status is unavailable.

1.2.22 Consider best supportive care alone for people aged around 70 or over who have:

- a grade IV glioma (glioblastoma) and
- a Karnofsky performance status of under 70.

1.2.23 For people with an initial diagnosis of grade IV glioma (glioblastoma) not covered in recommendations 1.2.19 to 1.2.22, consider the treatment options of:

- radiotherapy using 60 Gy in 30 fractions with concurrent and up to 6 cycles of adjuvant temozolomide
- radiotherapy alone using 60 Gy in 30 fractions
- hypofractionated radiotherapy
- up to 6 cycles of temozolomide alone if the tumour has MGMT methylation and the person is aged around 70 or over
- best supportive care alone.

1.2.24 Assess the person's performance status throughout the postoperative period and review treatment options for grade IV glioma (glioblastoma) if their performance status changes.

1.2.25 Do not offer bevacizumab as part of management of a newly diagnosed grade IV glioma (glioblastoma).

1.2.26 Do not offer tumour-treating fields (TTF) as part of management of a newly diagnosed grade IV glioma (glioblastoma).

1.2.27 If asked, advise people with an initial diagnosis of grade IV glioma (and their relatives and carers, as appropriate) that the available evidence does not support the use of:

- cannabis oil

- immunotherapy
- ketogenic diets
- metformin
- statins
- valganciclovir.

To find out why the committee made the recommendations on management of newly diagnosed grade IV glioma (glioblastoma) following surgery, or if surgery is not possible or the person declines surgery, and how they might affect practice, see [rationale and impact](#).

Management of recurrent high-grade glioma (recurrent grade III and grade IV glioma)

- 1.2.28 When deciding on treatment options for people with recurrent high-grade glioma, take into account:
- Karnofsky performance status
 - the person's preferences
 - time from last treatment
 - tumour molecular markers
 - what their last treatment was.
- 1.2.29 Consider PCV or single agent CCNU (lomustine) as an alternative to temozolomide for people with recurrent high-grade glioma.
- 1.2.30 For guidance on using temozolomide as an option for treating recurrent high-grade glioma, see the NICE technology appraisal guidance on [temozolomide for the treatment of recurrent malignant glioma \(brain cancer\)](#).
- 1.2.31 Consider best supportive care alone for high-grade glioma if other treatments are not likely to be of benefit, or if the person would prefer this. Refer to the

NICE guidance on [improving supportive and palliative care for adults with cancer](#).

1.2.32 For people with focally recurrent high-grade glioma, the multidisciplinary team should also consider the treatment options of:

- further surgery
- further radiotherapy.

1.2.33 Do not offer bevacizumab, erlotinib or cediranib, either alone or in combination with chemotherapy, as part of management of recurrent high-grade glioma.

1.2.34 Do not offer tumour treating fields (TTF) as part of management of recurrent high-grade glioma.

1.2.35 If asked, advise people who have recurrent high-grade glioma (and their relatives and carers, as appropriate) that the available evidence does not support the use of:

- cannabis oil
- immunotherapy
- ketogenic diets
- metformin
- statins
- valganciclovir.

To find out why the committee made the recommendations on management of recurrent grade III and grade IV glioma (recurrent high-grade glioma) and how they might affect practice, see [rationale and impact](#).

Techniques for resection of glioma

1.2.36 If a person has a radiologically enhancing suspected high-grade glioma and the multidisciplinary team thinks that surgical resection of all enhancing tumour is

possible, offer 5-aminolevulinic acid (5-ALA)-guided resection as an adjunct to maximise resection at initial surgery.

- 1.2.37 Consider intraoperative MRI to help achieve surgical resection of both low-grade and high-grade glioma while preserving neurological function, unless MRI is contraindicated.
- 1.2.38 Consider intraoperative ultrasound to help achieve surgical resection of both low-grade and high-grade glioma.
- 1.2.39 Consider diffusion tensor imaging overlays in addition to standard neuronavigation techniques to minimise damage to functionally important fibre tracts during resection of both low-grade and high-grade glioma.
- 1.2.40 Consider awake craniotomy for people with low-grade or high-grade glioma to help preserve neurological function.
- 1.2.41 Discuss awake craniotomy and its potential benefits and risks with the person and their relatives and carers (as appropriate) so that they can make an informed choice about whether to have it. Only consider the procedure if the person is likely not to be significantly distressed by it.
- 1.2.42 Involve other specialists as appropriate, such as neuropsychologists and speech and language therapists, before, during and after awake craniotomy.

To find out why the committee made the recommendations on techniques for resection of glioma and how they might affect practice, see [rationale and impact](#).

1.3 *Follow-up for glioma*

- 1.3.1 Offer [regular clinical review](#) for people with glioma to assess changes in their physical, psychological and cognitive wellbeing.
- 1.3.2 Base decisions on the timing of regular clinical reviews and follow-up imaging for people with glioma on:
- any residual tumour

- life expectancy
- the person's preferences (see table 2 for factors to discuss with them)
- treatments used before
- treatment options available
- tumour subtype.

Table 2 Factors to take into account when deciding on frequency of follow-up for people with glioma

Possible advantages of more frequent follow-up	Possible disadvantages of more frequent follow-up
May identify recurrent disease earlier which may increase treatment options or enable treatment before people become symptomatic.	There is no definitive evidence that identifying recurrent disease early improves outcomes.
May help provide information about the course of the illness and prognosis.	May increase anxiety if changes of uncertain significance are detected on imaging.
Some people can find more frequent imaging and hospital contact reassuring. Provides an opportunity to identify patient or carer needs (such as psychosocial support and late side effects of treatment).	Some people can find more frequent imaging and hospital contact burdensome and disruptive – they feel their life revolves around their latest scan. There may be a financial cost from taking time off work and travelling to appointments.
–	More imaging and follow-up is resource intensive for the NHS.

1.3.3 Consider the follow-up schedule given in table 3 for people with glioma.

1.3.4 Consider standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as part of regular clinical review for people with glioma, to assess for progression or recurrence, unless MRI is contraindicated.

- 1.3.5 Consider advanced MRI techniques, such as MR perfusion, diffusion tensor imaging and MR spectroscopy, if findings from standard imaging are unclear about whether there is recurrence and early identification is potentially clinically useful.
- 1.3.6 For people with glioma having routine imaging:
- explain to them, and their relatives and carers, that imaging can be difficult to interpret and results can be of uncertain significance and
 - be aware that having routine imaging and waiting for the results may cause anxiety.
- 1.3.7 Consider a baseline MRI scan within 72 hours of surgical resection for all types of glioma.
- 1.3.8 Consider a baseline MRI scan 3 months after the completion of radiotherapy for all types of glioma.
- 1.3.9 Arrange a clinical review, including appropriate imaging, for people with glioma who develop new or changing neurological symptoms or signs at any time.

Table 3 Possible regular clinical review schedule for people with glioma depending on grade of tumour

	Years after end of treatment					
	0 to 1	1 to 2	2 to 3	3 to 4	5 to 10	>10 (for the rest of life)
Grade I	Scan at 12 months, then: <ul style="list-style-type: none"> • consider discharge if no tumour visible on imaging unless completely resected pilocytic astrocytoma • consider ongoing imaging at increasing intervals for 15 years for completely resected pilocytic astrocytoma • consider if ongoing imaging is needed at a rate of once every 1 to 3 years for the rest of the person's life if the tumour is visible on imaging. 					

Grade II 1p/19q non-codeleted, IDH mutated	Scan at 3 months, then every 6 months	Annually	Every 1 to 2 years	Consider ongoing imaging every 1 to 2 years
Grade II 1p/19q codeleted				
Grade III 1p/19q codeleted				
Grade II IDH wildtype	Every 3 to 6 months	Every 6 to 12 months	Annually	Consider ongoing imaging every 1 to 2 years
Grade III 1p/19q non-codeleted				
Grade IV (glioblastoma)				

To find out why the committee made the recommendations on follow-up for glioma and how they might affect practice, see [rationale and impact](#).

1.4 Investigation of suspected meningioma

- 1.4.1 Offer standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as the initial diagnostic test for suspected meningioma, unless MRI is contraindicated.
- 1.4.2 Consider CT imaging for meningioma (if not already performed) to assess bone involvement if this is suspected.

To find out why the committee made the recommendations on investigation of suspected meningioma and how they might affect practice, see [rationale and impact](#).

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

- 1.4.3 Base management of meningioma after surgery, or if surgery is not possible or the person declines surgery, on the extent of any surgery and grade of meningioma, as described in table 4.

Table 4 Treatment choices after surgery or if surgery was not possible for different kinds of meningioma

Grade	Extent of surgery			Recurrent
	Completely excised (Simpson 1 to 3)	Incompletely excised (Simpson 4 to 5)	No excision (radiological only diagnosis)	
I	Offer <u>active monitoring</u> .	Consider further surgery (if possible), radiotherapy or active monitoring.	Consider active monitoring or radiotherapy.	Consider further surgery or radiotherapy (if not previously used).
II	Offer a choice between active monitoring and radiotherapy.	Consider further surgery (if possible). Offer radiotherapy if surgery is not possible, including if the person declines surgery, or if the tumour is incompletely excised afterwards.		Consider further surgery and offer radiotherapy (if not previously used).
III	Offer radiotherapy.	Consider further surgery (if possible) and offer radiotherapy.		Consider further surgery and offer radiotherapy (if not previously used).

1.4.4 Before a decision is made on radiotherapy for meningioma, take into account:

- comorbidities
- life expectancy
- neurological function
- oedema

- performance status
- rate of tumour progression
- size and location of tumour
- surgical and radiotherapy morbidity
- the person's preferences (see table 5 for factors to discuss with them)
- treatments used before.

Table 5 Factors to take into account when deciding on radiotherapy as treatment for a surgically treated meningioma

	Radiotherapy	No radiotherapy
Control of tumour	There is evidence that radiotherapy is effective in the local control of a tumour.	Receiving no radiotherapy means the tumour may continue to grow.
Risk of developing subsequent symptoms	Controlling the tumour will reduce the risk of developing symptoms from the tumour in the future.	If the tumour grows, it can cause irreversible symptoms such as loss of vision.
Risk of re-treatment	Less risk of needing second surgery compared with no radiotherapy.	Higher risk of needing second surgery compared with radiotherapy. If the tumour has progressed, then the surgery might be more complex. If the tumour has progressed, then not all radiotherapy techniques may be possible.

Early side effects of treatment	Early side effects from radiotherapy can include: <ul style="list-style-type: none"> • fatigue • hair loss • headache • nausea • seizures • skin irritation. 	No side effects from treatment.
Late side effects of treatment	Late side effects from radiotherapy can include: <ul style="list-style-type: none"> • effect on cognition • risk of stroke • risk of radionecrosis • risk of second tumours • cranial nerve effects • hypopituitarism • cataracts. 	No side effects from treatment.
Management of side effects	Increased use of steroids to manage side effects.	No side effects from treatment.

1.4.5 When deciding on the radiotherapy technique for people with meningioma, take into account:

- the preferences of the person (for example, to minimise the number of appointments or travel distance)
- tumour grade
- tumour location (proximity to optic nerves, optic chiasm and brainstem)

- tumour size.

From the suitable radiotherapy techniques, choose the one which maximises the chances of local tumour control while minimising the radiation dose to normal brain tissue.

- 1.4.6 If the multidisciplinary team thinks that radiotherapy may be appropriate, offer the person the opportunity to discuss the potential benefits and risks with an oncologist.

To find out why the committee made the recommendations on management of confirmed meningioma following surgery, or if surgery is not possible or the person declines surgery, and how they might affect practice, see [rationale and impact](#).

1.5 *Follow-up for meningioma*

- 1.5.1 Offer [regular clinical review](#) for people with meningioma to assess changes in their physical, psychological and cognitive wellbeing.

- 1.5.2 Base decisions on the timing of regular clinical reviews and follow-up imaging for people with meningioma on:

- any residual tumour
- life expectancy
- the person's preferences (see table 6 for factors to discuss with them)
- treatments used before
- treatment options available
- tumour grade.

Table 6 Factors to take into account when deciding on frequency of follow-up for people with meningioma

Possible advantages of more frequent follow-up	Possible disadvantages of more frequent follow-up
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May identify recurrent disease earlier which may increase treatment options or enable treatment before people become symptomatic.	There is no definitive evidence that identifying recurrent disease early improves outcomes.
May help provide information about the course of the illness and prognosis.	May increase anxiety if changes of uncertain significance are detected on imaging.
Some people can find more frequent imaging and hospital contact reassuring. Provides an opportunity to identify patient or carer needs (such as psychosocial support and late side effects of treatment).	Some people can find more frequent imaging and hospital contact burdensome and disruptive – they feel their life revolves around their latest scan. There may be a financial cost from taking time off work and travelling to appointments.
–	More imaging and follow-up is resource intensive for the NHS.

- 1.5.3 Consider the follow-up schedule given in table 7 for people with meningioma.
- 1.5.4 Consider standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as part of regular clinical review for people with meningioma, to assess for progression or recurrence, unless MRI is contraindicated.
- 1.5.5 For people with meningioma having routine imaging, be aware that having routine imaging and waiting for the results may cause anxiety.
- 1.5.6 Arrange a clinical review, including appropriate imaging, for people with meningioma (including incidental meningioma) who develop new or changing neurological symptoms or signs at any time.

Table 7 Possible regular clinical review schedule for people with meningioma depending on grade of tumour

	Years after end of treatment
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	0 to 1	1 to 2	2 to 3	3 to 4	4 to 5	5 to 6	6 to 7	7 to 8	8 to 9	>9 (for the rest of life)
Grade I: no residual tumour*	Scan at 3 months	Annually		Once every 2 years						Consider discharge
Grade I: residual tumour*	Scan at 3 months	Annually				Once every 2 years			Consider discharge	
Grade I: after radiotherapy	Scan 6 months after radiotherapy	Annually		Once every 2 years						Consider discharge
Grade II	Scan at 3 months, then 6 to 12 months later	Annually				Once every 2 years			Consider discharge	
Grade III	Every 3 to 6 months		Every 6 to 12 months		Annually					
Asymptomatic incidental meningioma	Scan at 12 months. If no change consider discharge or scan at 5 years.									
* The presence of any residual tumour can only be established after the first scan at 3 months.										

To find out why the committee made the recommendations on follow-up for meningioma and how they might affect practice, see [rationale and impact](#).

1.6 Investigation of suspected brain metastases

- 1.6.1 Offer standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as the initial diagnostic test for suspected brain metastases, unless MRI is contraindicated.
- 1.6.2 To help establish current disease status, offer extracranial imaging (appropriate to the primary tumour type) to people with any radiologically suspected brain metastases that may be suitable for focal treatment.
- 1.6.3 Perform all intracranial and extracranial diagnostic imaging and, if appropriate, biopsy of extracranial disease, before referral to the neuro-oncology multidisciplinary team.

To find out why the committee made the recommendations on investigation of suspected brain metastases and how they might affect practice, see [rationale and impact](#).

1.7 *Management of confirmed brain metastases*

1.7.1 When choosing management options for brain metastases, take into account:

- extracranial disease
- leptomeningeal disease
- location of metastases
- resection cavity size
- the number and volume of metastases
- the person's preference (based on a discussion of the factors listed in tables 8 and 9)
- their age
- their performance status
- the primary tumour site, type, and molecular profile.

1.7.2 Consider systemic anti-cancer therapy for people who have brain metastases likely to respond effectively, for example, germ cell tumours or small-cell lung cancer.

1.7.3 Consider maximal local therapy with either surgery, stereotactic radiosurgery or stereotactic radiotherapy for people with a single brain metastasis.

1.7.4 Base the choice of treatment for people with a single brain metastasis on:

- comorbidities
- extent of oedema
- location of metastasis
- the person's preference (see table 8)

- tumour size.

Table 8 Factors to take into account when deciding between surgery and stereotactic radiosurgery/ radiotherapy as treatment for a single brain metastasis

	Surgery	Stereotactic radiosurgery / radiotherapy
Overall survival	No clinically important difference.	No clinically important difference.
Risk of needing additional treatment	Risk that stereotactic radiosurgery / radiotherapy may be needed in any case.	Risk that surgery may be needed in any case. However, has higher local control rate than surgery (meaning surgery is less likely after radiotherapy than the other way around).
Key benefit of treatment	Has more rapid control of symptoms. Additionally, surgery allows for obtaining an up-to-date pathological diagnosis which may guide future treatment, making it more effective.	Has a higher local control rate than surgery, meaning more treatment is less likely to be needed. Additionally, is an outpatient treatment and does not need a general anaesthetic.
Key risks of treatment	Surgical procedures carry known risks that vary depending on the person and the tumour. These include infection, stroke, a prolonged hospital stay and death. Surgery is more painful than radiotherapy during recovery.	Radiation carries the risk of delayed effects such as radionecrosis, which might need surgical resection. There is an increased risk of seizures with this technique, although this appears to mostly affect people who have pre-existing epilepsy.
Steroid use	Early reduction in steroid dose.	Likely to need steroids for longer, and at a higher dose. Steroids have significant side effects when used long-term, such as changes in mood, heart problems and changes in body fat.

Planning treatment around important life events	<p>The wound from the surgery may affect the ability to carry out certain activities in the short term, such as air travel and sport.</p> <p>The cosmetic appearance of the wound from surgery may be important to some people, and should be discussed.</p>	<p>Some people find the techniques used in radiotherapy challenging or upsetting, especially the equipment which immobilises the head. This is especially likely to be true for people with claustrophobia.</p>
Other considerations	<p>–</p>	<p>Radiotherapy can reach some areas of the brain that surgery cannot, and might be the only appropriate technique for certain tumour types.</p>

- 1.7.5 Do not offer adjuvant whole-brain radiotherapy to people with a single brain metastasis treated with stereotactic radiosurgery/radiotherapy or surgery.
- 1.7.6 Consider adjuvant stereotactic radiosurgery/radiotherapy to the surgical cavities for people with 1 to 3 brain metastases that have been resected.
- 1.7.7 Consider stereotactic radiosurgery/radiotherapy for people with multiple brain metastases who have controlled or controllable extracranial disease and Karnofsky performance status of 70 or more. Take into account the number and total volume of metastases.
- 1.7.8 Do not offer whole-brain radiotherapy to people with:
- non-small-cell lung cancer and
 - brain metastases that are not suitable for surgery or stereotactic radiosurgery/radiotherapy and
 - a Karnofsky performance status of under 70.
- 1.7.9 For people with multiple brain metastases who have not had stereotactic radiosurgery/radiotherapy or surgery, decide with them whether to use whole-brain radiotherapy after a discussion with them and their relatives and carers (as appropriate) of the potential benefits and risks (see table 9).

Table 9 Potential benefits and harms of whole-brain radiotherapy for multiple metastases

	Whole-brain radiotherapy	No whole-brain radiotherapy
Overall survival	No clinically important difference.	No clinically important difference.
Quality of life	Short-term deterioration in quality of life because of treatment.	No impact on quality of life because of treatment, but deterioration because of the disease progression.
Potential benefits	Can stabilise or reduce the brain metastases.	Brain metastases may continue to grow.
Side effects	Temporary hair loss and fatigue. Potential for accelerated cognitive loss because of radiotherapy.	Potential for cognitive loss because of disease progression.
Time commitment	Requires 5 to 10 hospital visits.	No time commitment.
Other considerations	People with non-small-cell lung cancer will not benefit from treatment if their overall prognosis is poor.	–

- 1.7.10 Do not offer memantine in addition to whole-brain radiotherapy to people with multiple brain metastases, unless as part of a clinical trial.
- 1.7.11 Do not offer concurrent systemic therapy to enhance the efficacy of whole-brain radiotherapy to people with multiple brain metastases, unless as part of a clinical trial.

To find out why the committee made the recommendations on management of confirmed brain metastases and how they might affect practice, see [rationale and impact](#).

1.8 Follow-up for brain metastases

- 1.8.1 Offer [regular clinical review](#) for people with brain metastases to assess changes in their physical, psychological and cognitive wellbeing.

1.8.2 Base decisions on the timing of regular clinical reviews and follow-up imaging for people with brain metastases on:

- extracranial disease status
- life expectancy
- primary cancer
- the person's preferences (see table 10 for factors to discuss with them)
- treatment options available.

Table 10 Factors to take into account when deciding on frequency of follow-up for people with brain metastases

Possible advantages of more frequent follow-up	Possible disadvantages of more frequent follow-up
May identify recurrent disease earlier which may increase treatment options or enable treatment before people become symptomatic.	There is no definitive evidence that identifying recurrent disease early improves outcomes.
May help provide information about the course of the illness and prognosis.	May increase anxiety if changes of uncertain significance are detected on imaging.
Some people can find more frequent imaging and hospital contact reassuring. Provides an opportunity to identify patient or carer needs (such as psychosocial support and late side effects of treatment).	Some people can find more frequent imaging and hospital contact burdensome and disruptive – they feel their life revolves around their latest scan. There may be a financial cost from taking time off work and travelling to appointments.
–	More imaging and follow-up is resource intensive for the NHS.

1.8.3 Consider the follow-up schedule given in table 11 for people with brain metastases.

1.8.4 Consider standard structural MRI (defined as T2 weighted, FLAIR, DWI series and T1 pre- and post-contrast volume) as part of regular clinical review for

people with brain metastases, to assess for progression or recurrence, unless MRI is contraindicated.

- 1.8.5 Consider advanced MRI techniques, such as MR perfusion, diffusion tensor imaging and MR spectroscopy, if findings from standard imaging are unclear about whether there is recurrence and early identification is potentially clinically useful.
- 1.8.6 For people with brain metastases having routine imaging:
- explain to them, and their relatives and carers, that imaging can be difficult to interpret and results can be of uncertain significance and
 - be aware that having routine imaging and waiting for the results may cause anxiety.
- 1.8.7 Arrange a clinical review, including appropriate imaging, for people with brain metastases who develop new or changing neurological symptoms or signs at any time.

Table 11 Possible regular clinical review schedule for people with brain metastases

	Years after end of treatment		
	0 to 1	1 to 2	2 onwards
Brain metastases	Every 3 months	Every 4 to 6 months	Annually

To find out why the committee made the recommendations on follow-up for brain metastases and how they might affect practice, see [rationale and impact](#).

1.9 Care needs of people with brain tumours

- 1.9.1 Be aware that the care needs of people with brain tumours represent a unique challenge, because (in addition to physical disability) the tumour and treatment can have effects on:
- behaviour
 - cognition

- personality.

- 1.9.2 Discuss health and social care support needs with the person with a brain tumour and their relatives and carers (as appropriate). Take into account the complex health and social care support needs people with any type of brain tumour and their relatives and carers may have (for example, psychological, cognitive, physical, spiritual, emotional).
- 1.9.3 Set aside enough time to discuss the impact of the brain tumour on the person and their relatives and carers (as appropriate), and to elicit and discuss their health and social care support needs.
- 1.9.4 Health and social care professionals involved in the care of people with brain tumours should address additional complex needs during or at the end of treatment and throughout follow-up. These include:
- changes to cognitive functioning
 - fatigue
 - loss of personal identity
 - loss of independence
 - maintaining a sense of hope
 - potential for change in personal and sexual relationships
 - the challenges of living with uncertainty
 - the impact of brain tumour-associated epilepsy on wellbeing (see the NICE guideline on [epilepsies: diagnosis and management](#)).
- 1.9.5 Provide a named healthcare professional with responsibility for coordinating health and social care support for people with brain tumours and their relatives and carers, for example, a key worker (often a clinical nurse specialist) as defined in NICE guidance on [improving outcomes for people with brain and other central nervous system tumours](#).
- 1.9.6 Give information to the person with a brain tumour and their relatives and carers (as appropriate):

- in a realistic and empathetic manner
- in suitable formats (written and spoken, with information available to take away), following the principles in the NICE guideline on [patient experience in adult NHS services](#)^[1]
- at appropriate times throughout their care pathway.

- 1.9.7 Explain to the person that they have a legal obligation to notify the Driver and Vehicle Licensing Agency (DVLA) if they have a brain tumour, and that this may have implications for their driving.
- 1.9.8 Provide and explain clinical results, for example, imaging and pathology reports, to the person with a brain tumour and their relatives and carers (as appropriate) as soon as possible.
- 1.9.9 Offer supportive care to people with brain tumours and their relatives and carers (as appropriate) throughout their treatment and care pathway
- 1.9.10 In people aged between 16 and 24 years old, refer to the NICE quality standard on [cancer services for children and young people](#).
- 1.9.11 Discuss the potential preservation of fertility with people with brain tumours where treatment may have an impact on their fertility (see the recommendations on [people with cancer who wish to preserve fertility](#) in NICE's guidance on fertility problems).
- 1.9.12 If the person with a brain tumour is likely to be in their last year of life, refer to the NICE quality standards on [end of life care for adults](#) and, when appropriate, [care of dying adults in the last days of life](#).

To find out why the committee made the recommendations on care needs of people with brain tumours and how they might affect practice, see [rationale and impact](#).

1.10 *Neurorehabilitation needs of people with brain tumours*

- 1.10.1 Consider referring the person with a brain tumour for a neurological rehabilitation assessment of physical, cognitive and emotional function at diagnosis and every stage of follow-up.

1.10.2 Offer people with brain tumours and their relatives and carers (as appropriate) information on accessing neurological rehabilitation, and on what needs it can help address.

1.10.3 Give people with brain tumours and their relatives and carers (as appropriate) information on:

- neurological rehabilitation options in the community, as an outpatient, or an inpatient and
- how to get a neurological rehabilitation assessment.

To find out why the committee made the recommendations on neurorehabilitation needs of people with brain tumours and how they might affect practice, see [rationale and impact](#).

1.11 *Surveillance for the late-onset side effects of treatment*

1.11.1 Be aware that people with brain tumours can develop side effects of treatment months or years after treatment, which can include:

- cataracts
- cavernoma
- cognitive decline
- epilepsy
- hearing loss
- hypopituitarism
- infertility
- neuropathy (for example, nerve damage causing visual loss, numbness, pain or weakness)
- radionecrosis
- secondary tumours

- SMART (stroke-like migraine attacks after radiotherapy)
- stroke.

- 1.11.2 Assess the person's individual risk of developing late effects when they finish treatment. Record these in their written treatment summary and explain them to the person (and their relatives and carers, as appropriate).
- 1.11.3 Encourage people who have had cranial radiotherapy to follow a healthy lifestyle, including exercise, a healthy diet and stopping smoking (if applicable), to decrease their risk of stroke. See the NICE guidelines on [obesity prevention](#), [physical activity](#) and [smoking cessation](#).
- 1.11.4 For people who are at risk of stroke, consider checking their blood pressure, HbA1c level and cholesterol profile regularly.
- 1.11.5 Consider ongoing neuropsychology assessment for people at risk of cognitive decline.
- 1.11.6 If a person has had a radiotherapy dose that might affect pituitary function, consider checking their endocrine function regularly after the end of treatment.
- 1.11.7 Consider referring people who are at risk of visual impairment for an ophthalmological assessment.
- 1.11.8 Consider referring people who are at risk of hearing loss to audiology for a hearing test.
- 1.11.9 Consider referring the person to stroke services if an MRI during [active monitoring](#) identifies asymptomatic ischaemic stroke.

To find out why the committee made the recommendations on surveillance for the late-onset side effects of treatment and how they might affect practice, see [rationale and impact](#).

Terms used in this guideline

Active monitoring

This is regular clinical and radiological review of a person with a brain tumour or brain metastases who are not currently having treatment for their cancer.

Regular clinical review

This is outpatient review of the person with a brain tumour or brain metastases at a planned interval from the previous visit in order to assess symptoms and care needs, to provide support and treatment and to perform imaging when appropriate.

^[1] Also see NHS England's guidance on [Accessible Information Standards](#).

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Managing glioma: management of IDH wildtype grade II glioma

Does the addition of concurrent and adjuvant temozolomide to radiotherapy improve overall survival in patients with IDH wildtype grade II glioma?

Why this is important

The World Health Organization (WHO) 2016 reclassification of brain tumours recognised that the molecular characteristics of glioma are extremely important in helping differentiate between disease entities with very different outcomes. Although evidence exists to guide management recommendations for certain molecular gliomas, such as codeleted and non-codeleted grade III glioma, currently no studies have investigated the best approach for the management of grade II glioma with IDH wildtype. The biological behaviour of these tumours is more like a high-grade glioma with a much shorter prognosis than IDH-mutated grade II glioma.

Because of this, some clinicians have advocated treating such tumours with concurrent chemoradiation recommended for grade IV glioma (glioblastoma multiforme, GBM). However, there is currently no research evidence to support this approach and this regimen is more intensive and people experience increased acute and late side effects compared to radiotherapy alone.

Research is needed to establish whether or not this approach is beneficial in terms of improved survival, and at what cost in terms of toxicity and, potentially, reduced quality of life.

To find out why the committee made the research recommendation on managing glioma, see [rationale and impact](#).

2 Managing glioma: supportive care clinics for low-grade glioma

Does a dedicated supportive care clinic in addition to standard care improve outcomes for people with low-grade gliomas?

Why this is important

People with low-grade gliomas have significant symptoms and complex healthcare needs across multiple physical, cognitive, emotional and social domains. This is often from the initial diagnosis onwards. There are indications from research literature and patient reports that these needs are currently unmet. Helping people with low-grade gliomas maintain their quality of life and function is important, especially as there is currently no cure, because earlier supportive care interventions and care plans may help reduce unplanned or emergency contact with secondary and tertiary providers.

As no research literature exists which establishes the effectiveness of a specific healthcare intervention, uncertainty exists about the most appropriate intervention to address unmet needs and improve patient-reported outcome measures (or to establish whether current healthcare provision can meet these needs). Current uncertainty is likely to have led to variations in service provision across the UK. It is also possible that no specific intervention is available in some areas.

Research is needed to identify whether, in addition to standard care, a specific supportive care intervention can significantly improve patient-reported outcome measures, and if so to establish what this intervention should consist of.

To find out why the committee made the research recommendation on supportive care clinics for low-grade glioma, see [rationale and impact](#).

3 Managing glioma: early referral to palliative care for glioblastoma

Does early referral to palliative care improve outcomes for people with glioblastomas in comparison with standard oncology care?

Why this is important

People with grade IV brain tumours (glioblastomas) have a poor prognosis which has not improved in over a decade. Median overall survival is 14–18 months even with gold-standard chemoradiation following surgery.

From initial diagnosis people experience multiple complex symptoms resulting from neurological impairment. These can significantly impact on their quality of life, function and psychological wellbeing. Their caregivers report high levels of distress and carer burden.

The aim of palliative care is to relieve symptoms and improve people's quality of life and function – not just towards the end of life but throughout the duration of illness. There is some evidence that early palliative care referral significantly improves overall survival, quality of life and mood.

Research in this area is important because this group of people have substantial health needs, which use significant healthcare resources. Supportive care interventions such as early palliative care may improve quality of life and function throughout the duration of illness. It may also help people to manage the distress associated with a reduced life expectancy and participate in advanced care planning.

To find out why the committee made the research recommendation on the early referral to palliative care for glioblastoma, see [rationale and impact](#).

4 Managing glioma: early detection of recurrence after treatment

Does early detection of recurrence after treatment improve overall survival/outcomes in molecularly stratified glioma?

Why this is important

Prognosis for brain tumours is inherently uncertain, and recent advances in treatment mean many people with a brain tumour will live for a long time after the initial diagnosis. For these individuals, follow-up is the longest component of their treatment and it is both expensive for the NHS and (sometimes) a burden for the person. There is no high-quality evidence that follow-up after treatment is beneficial, no high-quality evidence on the optimal frequency of imaging, and clinical uncertainty about whether such follow-up is likely to alter outcomes of importance to people with tumours (such as overall life expectancy or quality of life).

Research is needed to establish at what point the value of identifying recurrence early is outweighed by the harms of increasing burden to patients.

To find out why the committee made the research recommendation on the early detection of recurrence after treatment, see [rationale and impact](#).

5 Managing meningioma: immediate versus deferred radiotherapy for incompletely excised grade I meningioma

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

Why this is 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.

To find out why the committee made the research recommendation on managing meningioma, see [rationale and impact](#).

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice. They link to details of the evidence and a full description of the committee's discussion.

Investigations for suspected glioma: imaging

The discussion below explains how the committee made recommendations [1.1.1–1.1.3](#).

Why the committee made the recommendations

The evidence indicated that standard structural MRI is useful in distinguishing high-grade from low-grade glioma. The committee noted that this knowledge will inform management. Based on their experience, the committee recommended a protocol that they defined as a minimum standard for imaging acquisition.

No evidence was found on more advanced MRI techniques. However, the committee agreed that in their experience such techniques can be useful for assessing malignant features of a tumour – in particular, for ensuring that high-grade tumours are not misdiagnosed as low-grade tumours, which could have serious consequences for people who receive suboptimal management as a result. However the committee explained that a specialist multidisciplinary team would be needed to interpret features of the scan and decide management, even if advanced techniques were used.

How the recommendations might affect practice

Currently, various imaging strategies are used in different centres and depending on the person's circumstances. These recommendations aim to reduce variation in practice, and ensure that images obtained at different sites and using different equipment can be more accurately compared. Some centres may need to change their imaging protocols. This might increase or reduce costs depending on the imaging protocols which are currently in place.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Investigations for suspected glioma: molecular markers

The discussion below explains how the committee made recommendations [1.1.4–1.1.6](#).

Why the committee made the recommendations

Molecular markers are an emerging and important area in the treatment of brain tumours. The committee looked for evidence on these markers but did not find any. However, they noted that there are some molecular markers for which the evidence of benefit if tested is overwhelming, as reported in studies identified in searches for other review questions. This applies in particular for MGMT promoter methylation and TERT promoter mutations in IDH-wildtype glioma, although the committee agreed the evidence was of a higher quality in the first case than the second. The committee agreed that even these markers are not being consistently tested for and that testing should be standardised. Therefore they made recommendations based on their knowledge and experience, highlighting the World Health Organization (WHO) classification, to ensure that all centres follow a consistent process for assessing and interpreting information on molecular markers. This was important, since failure to consistently report molecular markers can mislead clinicians or limit treatment options.

How the recommendations might affect practice

As testing for molecular markers is relatively new, practice can vary widely and this is to be expected. In principle there should not be a major change, although the time taken to implement the new molecular tests will vary significantly between centres.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Management of glioma: initial surgery for low-grade glioma

The discussion below explains how the committee made recommendations [1.2.1–1.2.5](#).

Why the committee made the recommendations

There was evidence that optimal resection of a large percentage of the tumour improved survival for people with low-grade glioma. The committee noted that it is sometimes not appropriate to offer maximal safe resection (for example, if the balance of risks and benefits favours not resecting

all areas) and that a specialist surgical team should look at the value of doing an operation given its safe extent. They agreed that biopsy should be considered in these cases, based on limited evidence showing improved overall survival after biopsy compared with active monitoring. However, the committee also concluded that some tumours were of such limited risk that the risks of surgery outweighed the possible gain of biopsy or resection.

The committee described how there was no evidence for immediate intervention, but that intervention should not be delayed due to the probability that surgical resection would have benefit for the person with the tumour. They therefore recommended intervention within 6 months, to allow for time to discuss treatment options with the person with the tumour. This also allows for the possibility of a second imaging sequence to be done later to look for progression and to assess for symptom change, as the committee also recognised that a proportion of low-grade gliomas have unfavourable gene profiles (for example, IDH wildtype) that make them more like high-grade tumours from a prognostic perspective.

A small number of people might have had initial treatment before it was standard practice to save a tissue sample for biopsy, and these people would currently be actively monitored. Based on their experience the committee agreed that these people may not need further surgery as long as their condition is stable (that is, they are not showing radiological or clinical disease progression).

How the recommendations might affect practice

The recommendations are likely to change practice at some centres, and remove unnecessary variation. There are currently differences between centres in which molecular diagnoses are performed and in treatment of very low-risk, low-grade tumours. This is partly because low-grade gliomas may be managed by non-expert surgical teams.

The recommendation about the management of low-grade gliomas that have been managed but then progress is unlikely to substantially change practice, as management would be largely unchanged.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Management of glioma: further management of low-grade glioma

The discussion below explains how the committee made recommendations [1.2.6–1.2.11](#).

Why the committee made the recommendations

There was evidence that PCV chemotherapy (procarbazine, CCNU [lomustine] and vincristine) after radiotherapy improved overall survival and progression-free survival compared with radiotherapy alone. The committee discussed how the evidence for the exact regime was complex, and used their judgement to recommend possible sequence and dose. In addition, the committee noted that there are some circumstances where radiotherapy and PCV might not be appropriate (particularly for the very lowest-concern and highest-concern low-grade tumours) and made recommendations based on their experience in these cases.

The committee included approximate age cut-offs based on evidence showing that treatment improved survival in people aged around 40 or over with or without residual tumour, and their clinical judgement that treatment would be unlikely to be of benefit for people aged around 40 or under without residual tumour.

The committee found no evidence on the treatment of IDH wildtype grade II glioma. They determined that management of this type of glioma was likely to be different from other low-grade glioma, as IDH wildtype grade II glioma behaves more like a high-grade glioma. The committee therefore made a research recommendation on whether treating this tumour type more like a grade II glioma or grade IV glioma was most beneficial.

How the recommendations might affect practice

These recommendations aim to standardise practice. They will probably result in the same amounts of chemotherapy and radiotherapy being given, but these treatments will be more precisely targeted and it is possible that they will be given earlier. This would result in more people requiring long-term treatment for the side effects of radiation and chemotherapy. More people are likely to have active monitoring alone, which is not likely to create a resource impact.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Management of glioma: grade III glioma following surgery

The discussion below explains how the committee made recommendations [1.2.12–1.2.17](#).

Why the committee made the recommendations

The committee considered evidence for grade III and grade IV glioma separately.

Treatments to be offered

Based on randomised controlled trial evidence, the committee recommended radiotherapy and either PCV or temozolomide chemotherapy, depending on tumour subtype and performance status, for people with grade III glioma.

Treatments that should not be offered

Based on the available evidence, the committee recommended that some treatments should not be offered because they were harmful. They also agreed, based on their experience, that it would be useful for healthcare professionals to tell people with glioma that no evidence had been found to indicate that certain treatments are beneficial.

How the recommendations might affect practice

Adjuvant PCV for treating codeleted grade III glioma is standard practice, but adjuvant temozolomide for non-codeleted grade III gliomas is a change in practice. However, some centres may already have started to adopt this as standard care, since the results of the study supporting this treatment were made publicly available in 2016.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Management of glioma: grade IV glioma following surgery

The discussion below explains how the committee made recommendations [1.2.18–1.2.27](#).

Why the committee made the recommendations

The committee considered evidence for grade III and grade IV glioma separately.

Treatments to be used

The committee saw some evidence demonstrating improved overall survival in some groups of people with grade IV glioma who had radiotherapy with concurrent and adjuvant temozolomide (compared with radiotherapy alone). However, based on their clinical experience they were unsure that these results could be generalised to all people with grade IV glioma, so suggested a range of possible treatments that can be considered for other groups, depending on the exact clinical characteristics of the tumour.

Approximate age cut-offs for people with grade IV glioma were specified by the committee based on evidence that a radiotherapy dose of 40 Gy did not result in lower survival in people aged around 70 or over compared with a 60 Gy dose. Therefore a lower radiotherapy dose is likely to cause fewer side effects without compromising clinical effectiveness for this group.

The committee were aware that the prognosis of people with a grade IV glioma and a low performance status was poor, and recommended palliative care be considered. However the committee did not find any evidence on whether earlier or later palliative care was most beneficial for people who might need it. They therefore made a research recommendation on this topic, with the aim of finding out the point in the treatment pathway when it would be most beneficial for people with this type of glioma to have palliative care.

Treatments that should not be used

Based on the available evidence, the committee recommended that certain treatments should not be offered. This included tumour treating fields (TTF) based on published health economic evidence that they are not an efficient use of NHS resources. They also agreed, based on their clinical experience, that it would be useful for healthcare professionals to tell people with glioma that no evidence had been found to suggest that certain treatments are beneficial.

How the recommendations might affect practice

For younger people with a grade IV glioma and a good performance status, a course of radiotherapy with concurrent and adjuvant temozolomide is standard care. However, for people aged around 70 and over, particularly those with a glioma with methylated MGMT, the use of concurrent and adjuvant temozolomide with 15 fractions of radiotherapy is a change of practice that will probably

result in more people being treated. This is a relatively small group of people, and so the recommendation is unlikely to have a significant resource impact.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Management of glioma: recurrent high-grade glioma

The discussion below explains how the committee made recommendations [1.2.28–1.2.35](#).

Why the committee made the recommendations

Treatments to be offered

Based on the available evidence, the committee recommended that treatment options for people with recurrent glioma should include temozolomide, PCV and single-agent CCNU (lomustine). No evidence was found to indicate which of these 3 options is likely to lead to the best outcomes, and on the basis of their clinical experience the committee concluded that the choice of treatment should take several factors into account, including the individual features of the tumour and the preferences of the person. The committee also highlighted the possibility of considering supportive care alone.

Treatments that should not be offered

Based on the available evidence, the committee recommended that certain treatments should not be offered. This included tumour treating fields (TTF) on the basis of evidence of some clinical benefit but indirect published health economic evidence, in people with newly diagnosed high-grade glioma, that they are not cost effective. They also agreed, based on their clinical experience, that it would be useful for healthcare professionals to tell people with glioma that no evidence had been found to suggest that certain treatments are beneficial.

How the recommendations might affect practice

These recommendations reflect standard treatment for recurrent high-grade glioma, and therefore should not represent a substantial change in practice.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Management of glioma: techniques for resection of glioma

The discussion below explains how the committee made recommendations [1.2.36–1.2.42](#).

Why the committee made the recommendations

There was evidence that 5-aminolevulinic acid (5-ALA), intraoperative MRI and diffusion tensor imaging could improve either the extent or safety of resection (particularly the preservation of neurological function). The committee noted that a combination of techniques might be needed to optimise both the extent and safety of resection for a particular surgical plan. The committee concluded that the evidence for MRI could be generalised to intraoperative ultrasound on the basis of their clinical experience, and therefore that clinicians should be able to choose either technique depending on availability.

The evidence for awake craniotomy was equivocal (non-significant differences compared with surgery under general anaesthesia), therefore from the evidence it was not possible to conclude that awake craniotomy would benefit all people with glioma. This is in line with the committee's clinical experience that some people benefit from the procedure (in terms of preserving language, motor and visual function) but others are harmed – particularly from psychological effects which act as a contraindication to awake craniotomy. The committee described how better preoperative procedures could reduce the number of people distressed by the procedure.

How the recommendations might affect practice

Some techniques recommended by the committee require a very high level of intraoperative skill, and this might have resource implications for hospitals recruiting people with these specialist skills. There is significant variation in the current provision of psychological support for people before and during awake craniotomy, and implementing this could carry a high cost to an individual unit.

If a unit does not have access to intraoperative ultrasound or MRI, the cost of acquiring this equipment could be substantial (MRI is relatively expensive, ultrasound is relatively cheap). However the committee concluded that most units should have access to one or the other already. Therefore the only resource impact would be if a unit currently using intraoperative ultrasound decided that the additional evidence for preservation of neurological function in intraoperative

MRI justified the cost of switching machines. However, the committee thought this was unlikely to happen.

Using 5-ALA is associated with a high cost, and 5-ALA-guided surgery needs a non-standard fluorescence-detecting microscope. Therefore the resource impact of this recommendation is likely to be high in all settings, and very high in settings without access to a fluorescence-detecting microscope. The anticipated resource impact of this recommendation is greater than £1 million per year.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Follow-up for glioma

The discussion below explains how the committee made recommendations [1.3.1–1.3.9](#).

Why the committee made the recommendations

In the absence of evidence, the committee made recommendations based on their clinical experience. They recommended regular clinical review as the only plausible way of identifying and potentially managing recurrence or changing symptoms. They also recommended the review schedule take into account all of the person's relevant characteristics, including grade of tumour. As this is quite difficult to work out, the committee suggested a schedule of clinical reviews that is likely to be beneficial for a 'typical' person, which can be amended as needed to take into account individual variation. The committee did not uncover evidence on who should do the follow-up and so did not make a recommendation on this topic as it would vary according to clinical need, but discussed how it could be – for example – the local oncologist, neuro-oncologist, neurologist, neurosurgeon, clinical nurse specialist or GP.

As regular clinical review should include imaging, based on their experience the committee suggested an MRI sequence which they believed would be suitable to monitor for recurrence. They discussed how advanced MRI techniques might be valuable, but as these techniques are time-consuming and difficult to interpret the committee concluded they should only be recommended under certain circumstances where extra information was likely to substantially alter treatment plans. The committee recommended that any change in neurological signs or symptoms (which would include changes in behavioural, emotional and psychological signs and symptoms) be treated

as a sign of a potential change to the tumour, and therefore recommended clinical review outside the usual schedule in order to investigate this.

The committee believed that a dedicated supportive care clinic could improve outcomes for people with low-grade glioma, but did not find any evidence on this. Therefore they made a research recommendation on improving the long-term outcomes of people with low-grade glioma.

How the recommendations might affect practice

The recommendations are in line with current best practice, and should standardise practice. They are unlikely to cause a significant increase in resource use, but there may be some additional costs or changes in service configuration if practice differs in a particular centre.

The imaging sequences are recommended on the basis of evidence for the appropriate sequences for initial diagnosis, and so might not be the standard sequence for follow-up in all centres. As a result, adopting the recommended sequences might create some additional workload for some centres. However the recommendations for exact schedules are examples based on consensus in the committee, and there is therefore flexibility for centres to adapt these to their own models, limiting resource impact.

Full details of the evidence and the committee's discussion are in [evidence review A: investigation, management and follow-up of glioma](#).

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Investigation of suspected meningioma

The discussion below explains how the committee made recommendations [1.4.1](#) and [1.4.2](#).

Why the committee made the recommendations

Evidence indicated that standard structural MRI is useful in distinguishing high-grade from low-grade glioma, and the committee agreed that it is appropriate to extrapolate from this evidence to a belief that MRI can be used to distinguish meningioma from healthy brain tissue. In the committee's experience, CT scans can be more accurate than MRI for assessing meningioma with bone involvement.

How the recommendations might affect practice

Currently, various imaging strategies are used depending on the centre and the person's circumstances. These recommendations aim to reduce variation in practice, and ensure that images obtained at different sites and using different equipment can be more accurately compared. Some centres may need to change their imaging protocols as a result, but this should not require the purchase of additional equipment.

Full details of the evidence and the committee's discussion are in [evidence review B: investigation, management and follow-up of meningioma](#).

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

The discussion below explains how the committee made recommendations [1.4.3–1.4.6](#).

Why the committee made the recommendations

Based on limited evidence and their clinical experience, the committee concluded that management of this group of meningiomas will depend on the type of meningioma. They noted that evidence for 1 grade of meningioma could not normally be used to suggest best management for another grade. Therefore the committee made recommendations for each grade of meningioma separately, using evidence if this was available and their judgement if it was not. The committee identified that management could be more conservative if the tumour grade was lower and initial resection more complete, and should be more aggressive if the tumour grade was higher or initial resection more partial.

The committee agreed that the 3 management options – further radiotherapy, surgery and active monitoring – had different balances of benefits and harms in different situations. However they also agreed that serious harm could be done to a person with a tumour if they were over- or under-treated given the risk profile of their tumour, and so made recommendations according to this risk. For example, for a low-grade almost completely-resected tumour (grade I, Simpson 2 excision), radiotherapy or further surgery could expose the person to risk of harm for no expected clinical gain.

Based on limited evidence, the committee made recommendations on how to deliver radiotherapy or radiosurgery where this was appropriate. They used their experience to highlight features of the

tumour or preferences of the person that might help select the most appropriate radiotherapy or radiosurgery modality, and explained that the best results would come through minimising the dose of radiation delivered to healthy brain tissue while maximising the chance of local control.

The committee were unable to find evidence comparing different timings of radiotherapy in incompletely excised grade I meningioma. As the disease is slow growing it can be difficult to assess the risks of immediate side effects from treatment compared to the longer-term benefits of tumour control. Therefore the committee made a research recommendation to investigate this topic.

How the recommendations might affect practice

The recommendations reflect standard practice in many centres, and should make treatment more consistent.

An appointment with an oncologist for all people who may have radiotherapy is not currently standard practice. However, for most people this is likely to mean a change in the timing of their first appointment with an oncologist, rather than many more people having oncologist appointments.

Full details of the evidence and the committee's discussion are in [evidence review B: investigation, management and follow-up of meningioma](#).

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Follow-up for meningioma

The discussion below explains how the committee made recommendations [1.5.1–1.5.6](#).

Why the committee made the recommendations

In the absence of evidence, the committee made recommendations based on their clinical experience. They recommended regular clinical review as the only plausible way of identifying and potentially managing recurrence or changing symptoms. They also recommended the review schedule take into account all of the person's relevant characteristics, including grade of tumour. As this is quite difficult to work out, the committee suggested a schedule of clinical reviews that is likely to be beneficial for a 'typical' person, which can be amended as needed to take into account individual variation. The committee did not uncover evidence on who should do the follow-up and so did not make a recommendation on this topic as it would vary according to clinical need, but

discussed how it could be – for example – the local oncologist, neuro-oncologist, neurologist, neurosurgeon, clinical nurse specialist or GP.

As regular clinical review should include imaging, based on their experience the committee suggested an MRI sequence which they believed would be suitable to monitor for recurrence. They discussed how advanced MRI techniques might be valuable, but as these techniques are time-consuming and difficult to interpret the committee concluded they should only be recommended under certain circumstances where extra information was likely to substantially alter treatment plans. The committee recommended that any change in neurological signs or symptoms (which would include changes in behavioural, emotional and psychological signs and symptoms) be treated as a sign of a potential change to the tumour, and therefore recommended clinical review outside the usual schedule in order to investigate this.

How the recommendations might affect practice

The recommendations are in line with current best practice, and should standardise practice. They are unlikely to cause a significant increase in resource use, but there may be some additional costs or changes in service configuration if practice differs in a particular centre.

The imaging sequences are recommended on the basis of evidence for the appropriate sequences for initial diagnosis, and so might not be the standard sequence for follow-up in all centres. As a result, adopting the recommended sequences might create some additional workload for some centres. However the recommendations for exact schedules are examples based on consensus in the committee, and there is therefore flexibility for centres to adapt these to their own models, limiting resource impact.

Full details of the evidence and the committee's discussion are in [evidence review B: investigation, management and follow-up of meningioma](#).

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Investigation of suspected brain metastases

The discussion below explains how the committee made recommendations [1.6.1–1.6.3](#).

Why the committee made the recommendations

In the absence of evidence, the committee recommended standard structural MRI based on their experience, because it is important to establish the exact number of metastases in the brain, which

can guide further treatment. The committee described how failing to establish this could be dangerous. Extracranial imaging, biopsy of the extracranial disease (where indicated) and performing all imaging before multidisciplinary team discussions should ensure that all necessary information is available so that appropriate decisions are made and delays in treatment avoided.

How the recommendations might affect practice

The recommendations reinforce current best practice and should reduce delays to local intracranial treatment.

Full details of the evidence and the committee's discussion are in [evidence review C: investigation, management and follow-up of brain metastases](#).

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Management of confirmed brain metastases

The discussion below explains how the committee made recommendations [1.7.1–1.7.11](#).

Why the committee made the recommendations

The committee made recommendations based on the available evidence and their judgement. They described how features of brain metastases, including the number and volume (which is important for establishing prognosis), should be evaluated before starting treatment, and decisions about treatment made on the basis of these features and the person's preferences.

The committee described how systematic anti-cancer therapies were widely used in the management of other types of metastases, and therefore they might be expected to work for brain tumours. In the absence of evidence, the committee recommended considering systematic anti-cancer therapies on the basis of their clinical experience. Whether or not these therapies should be given depends on the type of metastasis: if it is not likely to respond then the side effects would not justify giving the therapy, whereas if the metastasis was likely to respond then the therapy was likely to be beneficial.

Evidence indicated that surgery, stereotactic radiosurgery and stereotactic radiotherapy are effective for treating a single brain metastasis, but there was no evidence to recommend 1 technique over the other. There was some evidence that irradiation of the cavity site improved local control, so the committee recommended it on the basis that improving local control should improve quality of life.

For people with multiple brain metastases, the committee described how treatment options are more variable, and that resection, stereotactic radiosurgery, stereotactic radiotherapy and whole-brain radiotherapy could all be considered in certain circumstances.

The committee recommended that neither memantine nor concurrent systemic therapy should be offered to enhance the efficacy of whole-brain radiotherapy, on the basis of evidence of no benefit and a potential risk of harm. However, there were biological reasons to think these treatments might be beneficial in some settings, so the committee agreed these therapies could be offered in the context of a clinical trial to investigate this.

How the recommendations might affect practice

Current practice varies greatly between centres. Some of the variation reflects clinically relevant factors such as expertise in a particular technique or the patient population. The recommendations should help to standardise care and prevent some harmful and wasteful practices from continuing. Economic modelling identified that the recommendations will likely increase costs, but the committee believed that this was still an efficient use of NHS resources, as the improvement to quality of life was significant.

Full details of the evidence and the committee's discussion are in [evidence review C: investigation, management and follow-up of brain metastases](#).

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Follow-up for brain metastases

The discussion below explains how the committee made recommendations [1.8.1–1.8.7](#).

Why the committee made the recommendations

In the absence of evidence, the committee made recommendations based on their clinical experience. They recommended regular clinical review as the only plausible way of identifying and potentially managing recurrence or changing symptoms. They also recommended the review schedule take into account all of the person's relevant characteristics, including grade of tumour. As this is quite difficult to work out, the committee suggested a schedule of clinical reviews that is likely to be beneficial for a 'typical' person, which can be amended as needed to take into account individual variation. The committee did not uncover evidence on who should do the follow-up and so did not make a recommendation on this topic as it would vary according to clinical need, but

discussed how it could be – for example – the local oncologist, neuro-oncologist, neurologist, neurosurgeon, clinical nurse specialist or GP.

As regular clinical review should include imaging, based on their experience the committee suggested an MRI sequence which they believed would be suitable to monitor for recurrence. They discussed how advanced MRI techniques might be valuable, but as these techniques are time-consuming and difficult to interpret the committee concluded they should only be recommended under certain circumstances where extra information was likely to substantially alter treatment plans. The committee recommended that any change in neurological signs or symptoms (which would include changes in behavioural, emotional and psychological signs and symptoms) be treated as a sign of a potential change to the tumour, and therefore recommended clinical review outside the usual schedule in order to investigate this.

How the recommendations might affect practice

The recommendations are in line with current best practice, and should standardise practice. They are unlikely to cause a significant increase in resource use, but there may be some additional costs or changes in service configuration if practice differs in a particular centre.

The imaging sequences are recommended on the basis of evidence for the appropriate sequences for initial diagnosis, and so might not be the standard sequence for follow-up in all centres. As a result, adopting the recommended sequences might create some additional workload for some centres. However the recommendations for exact schedules are examples based on consensus in the committee, and there is therefore flexibility for centres to adapt these to their own models, limiting resource impact.

Full details of the evidence and the committee's discussion are in [evidence review C: investigation, management and follow-up of brain metastases](#).

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Care needs of people brain tumours

The discussion below explains how the committee made recommendations [1.9.1–1.9.12](#).

Why the committee made the recommendations

Based on the evidence and their own experience, the committee determined that people with brain tumours have very specific needs that are often not met. In particular, they highlighted ways in

which the care needs of people with brain tumours differ from those of people with other types of cancer, such as the impact on the person's sense of identity and legal requirements related to driving. Losing the ability or legal right to drive can have a profound effect on the patient's independence, employment status and self-esteem. The committee's aim was to improve the support and information offered to people with brain tumours.

The committee described how the care needs of people with brain tumours were often more complex than could be considered in a single guideline. In particular, young people, people wishing to preserve their fertility, and people nearing the end of their life have especially complex needs. In order to address these needs, the committee signposted to existing NICE guidance in the specific area.

How the recommendations might affect practice

The recommendations should improve care for both people living with brain tumours and their relatives and carers. It is likely that there will be a short-term resource impact in some areas, as supportive care for people with brain tumours is currently variable, with very little support available in some areas.

Full details of the evidence and the committee's discussion are in [evidence review D: supporting people living with a brain tumour](#).

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Neurorehabilitation needs of people with brain tumours

The discussion below explains how the committee made recommendations [1.10.1-1.10.3](#).

Why the committee made the recommendations

No evidence was found for this topic. Based on their experience, the committee agreed that neurological rehabilitation is likely to be suitable for many people with brain tumours. Given that neurological rehabilitation is time-consuming (especially if the person with a tumour lives a long way from the rehabilitation centre) and sometimes not appropriate, the committee agreed that assessment should be carried out at every stage of diagnosis and follow-up to identify which, if any, forms of rehabilitation are suitable for the person. The aim of the recommendations is to ensure that neurological rehabilitation is considered at every stage of treatment and follow-up.

How the recommendations might affect practice

There is currently variation in practice in assessing whether people with a brain tumour need neurological rehabilitation. Some of this reflects the availability of neurological rehabilitation services. The recommendations reinforce current best practice, and will mean a change in practice in some areas, including where assessment is 'ad hoc' rather than systematic.

People with a brain tumour make up a small percentage of people referred for neurological rehabilitation, so only a small increase in demand on resources is expected. There should not be any extra training needs because professionals already have the knowledge and skills to provide the services.

Full details of the evidence and the committee's discussion are in [evidence review D: supporting people living with a brain tumour](#).

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Surveillance for the late-onset side effects of treatment

The discussion below explains how the committee made recommendations [1.11.1-1.11.9](#).

Why the committee made the recommendations

No evidence was found for this topic. Some people experience late effects after treatment for a brain tumour. With the possible exception of stroke risk it is unknown if these late effects can be prevented, but the committee agreed that any negative impact can be managed through clinical vigilance and referral into appropriate specialist monitoring pathways. The committee explained that it was important to consider referral for anyone at risk of late effects – not just those at 'high' risk – but that there may be no value in such a referral overall in lower risk groups.

How the recommendations might affect practice

The recommendations should not significantly alter practice, as they reflect common clinical practice.

Full details of the evidence and the committee's discussion are in [evidence review D: supporting people living with a brain tumour](#).

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Context

It is estimated there are around 10,000 new cases of primary brain tumours per year. These tumours come from the brain tissue or its coverings – the meninges. Malignant high-grade gliomas (anaplastic gliomas and glioblastomas) and pre-malignant low-grade gliomas come from the brain tissue glial cells, and make up over 60% of primary brain tumours. Meningiomas make up a further 30%. Although often thought benign, meningiomas can have an acute presentation and are associated with significant long-term neurological morbidity. Because of this, they can behave in a malignant fashion in terms of recurrence and impact.

Over 60% of people with primary brain tumours present at, and are diagnosed by, accident and emergency services rather than from conventional GP or specialist referral. This causes a significant demand on these services. Although primary malignant brain tumours represent only 3% of all cancers, they result in the most life-years lost of any cancer. There is concern that the true incidence of these tumours is rising.

Cancers that have spread to the brain from somewhere else in the body are called secondary brain tumours, or brain metastases. Many different cancer types can spread to the brain, with lung and breast cancers being the most common. More people with systemic cancers are surviving longer and are referred to neuroscience multidisciplinary teams for management of their brain metastases. The number of people needing assessment for cranial treatment is now over 10,000 per year in the UK and rising.

The specialist nature of neuro-imaging and the need for complex diagnostic and reductive surgery emphasises the importance of well-organised service delivery by dedicated units. The singular effects of brain tumours on mental performance (both psychological state and cognitive decline) are a particular challenge to carers and professionals alike, especially in delivering support to people at home. The peak age of presentation of brain cancer is between 65 and 69, and there are concerns that delivery of all services to these older people is suboptimal. There are also concerns that the transition from paediatric to adult units could create a care gap. This would most specifically affect patients who are between 18 and 30 years old.

Survival with malignant brain tumours has remained poor despite some improvements in surgery, radiotherapy and chemotherapy, and a greater understanding of molecular classification. The management of a low-grade glioma that is likely to transform to high grade remains controversial, and presents issues for ongoing care. Follow-up for people with meningiomas after primary treatment is often long term, and there is variation in both follow-up and treatments for recurrence.

Conventional whole-brain irradiation as optimal therapy for brain metastases is being challenged by concerns about its effectiveness and toxicity, as well as the availability and immediacy of surgery and stereotactic radiotherapy.

Finding more information and resources

You can see everything NICE says on brain tumours (primary) and brain metastases in our interactive flowchart on [brain tumours and metastases](#).

To find out what NICE has said on topics related to this guideline, see our web page on [brain cancers](#).

For full details of the evidence and the guideline committee's discussions, see the [evidence reviews](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources](#) to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see [resources to help you put guidance into practice](#).

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