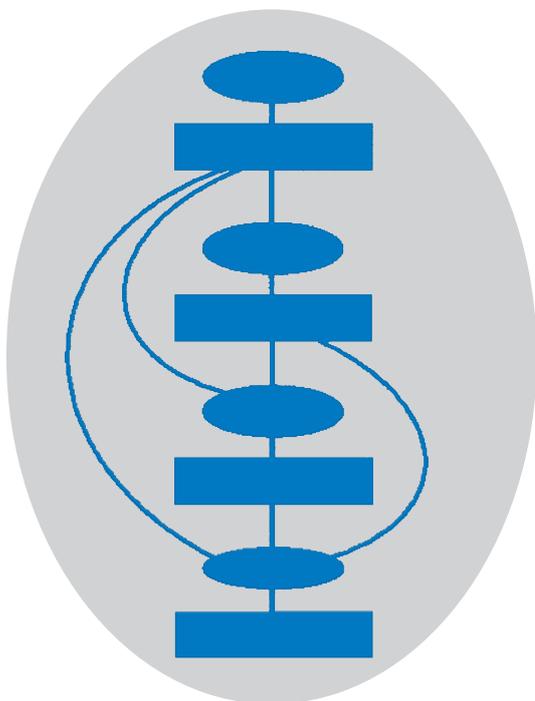


Guidance on Cancer Services

Improving Outcomes for People with Brain and Other CNS Tumours

The Manual



June 2006

Developed by the National Collaborating Centre for Cancer

Improving Outcomes for People with Brain and Other CNS Tumours

Cancer service guidance supports the implementation of *The NHS Cancer Plan* for England,¹ and the NHS Plan for Wales *Improving Health in Wales*.² The service guidance programme was initiated in 1995 to follow on from the Calman–Hine Report, *A Policy Framework for Commissioning Cancer Services*.³ The focus of the cancer service guidance is to guide the commissioning of services and is therefore different from clinical practice guidelines. Health services in England and Wales have organisational arrangements in place for securing improvements in cancer services and those responsible for their operation should take this guidance into account when planning, commissioning and organising services for cancer patients. The recommendations in the guidance concentrate on aspects of services that are likely to have significant impact on health outcomes. Both the objectives and resource implications of implementing the recommendations are considered. This guidance can be used to identify gaps in local provision and to check the appropriateness of existing services.

References

1. Department of Health (2001) *The NHS Cancer Plan*. Available from: www.dh.gov.uk
2. National Assembly for Wales (2001) *Improving Health in Wales: A Plan for the NHS and its Partners*. Available from: www.wales.gov.uk/healthplanonline/health_plan/content/nhsplan-e.pdf
3. *A Policy Framework for Commissioning Cancer Services: A Report by the Expert Advisory Group on Cancer to the Chief Medical Officers of England and Wales* (1995). Available from: www.dh.gov.uk

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This is the latest guidance document in the *Improving outcomes in cancer* series and gives advice on the service arrangements for patients with brain and other central nervous system (CNS) tumours. The great majority of patients whose care is covered by this guidance have brain tumours, and some of the most important recommended changes largely apply to them. This is a group of patients whose care can be fragmented and uncoordinated, and who may face a lengthy period of physical and cognitive decline following their initial treatment, often without access to appropriate support and rehabilitation. I hope that the recommendations in the guidance will be seen as a constructive way of trying to improve this situation.

In addition, there is guidance on the management of patients with the less common tumours of the CNS. Some of these patients require access to highly specialised services, and many would benefit from more consistent care across the UK. The guidance has some very specific recommendations in this area.

I am very grateful to all the members of the Guidance Development Group, especially the chair, Dr Penny Bridger, and the lead clinician, Dr Sean Elyan, who gave so much of their time to the development of the guidance. I hope that all their hard work will be rewarded by significant improvements in the way that care is organised and delivered and, eventually, in clinical outcomes for these patients.

Dr Fergus Macbeth

Note: The title of the guidance uses the term ‘brain and other CNS tumours’. This term is used once in each chapter but thereafter, for the sake of brevity, the term ‘CNS tumours’ is used, unless a specific group of patients is being referred to (for example those with ‘pituitary tumours’ or ‘base of skull tumours’).

- The care of all patients with brain and other central nervous system (CNS) tumours should be coordinated through a specific model of multidisciplinary assessment and care:
 - a designated lead in every acute trust (see Table 6)
 - a neuroscience brain and other CNS tumours multidisciplinary team (MDT), usually based at a neuroscience centre (see Tables 7 and 8)
 - a cancer network brain and other CNS tumours MDT (see Tables 9 and 10)
 - a key worker.
- Cancer networks should set up robust local mechanisms to ensure that every patient with imaging that suggests a diagnosis of CNS tumour is discussed by the neuroscience brain and other CNS tumours MDT without delay. This is to ensure that radiological diagnosis is confirmed and advice on further management can be given, regardless of the source of the initial referral or possible need for specialist treatment (see Chapter 3).
- Neuropathology and neuroradiology services should be provided to a level that ensures practitioners in these specialties can deliver appropriate diagnostic investigations in a timely and efficient manner, complying with national cancer waiting times targets, and such that they can be involved in preoperative and postoperative management decisions and intraoperative diagnosis. Neuropathologists should be able to report to the standards defined by the Royal College of Pathologists.¹ Neuroradiologists should be able to report and review examinations to the standards defined by the Royal College of Radiologists.²

¹ The Royal College of Pathologists (2004) *Minimum dataset for the histopathological reporting of tumours of the central nervous system*. London: Royal College of Pathologists. Available from: www.rcpath.org

² Board of the Faculty of Clinical Radiology and Royal College of Radiologists (2005) *Cancer Multidisciplinary team meeting – standards for clinical radiologists*. London: Royal College of Radiologists. Available from: www.rcr.ac.uk

- There should be ready access to a neurosurgical biopsy or resection service, including image localisation and stereotactic techniques. Preoperative discussions should take place at the neuroscience brain and other CNS tumours MDT to determine the optimum approach to surgery and the processing of tissue specimens, including intraoperative histological evaluation.
- Healthcare professionals should have face-to-face communication with patients, their relatives and carers at critical points in the care pathway to discuss diagnosis, prognosis, treatment options (including no treatment), recurrence and end-of-life care. Clear, high-quality and relevant written information material should be made available to support patients, their relatives, carers and professionals in this process.
- Clinical nurse specialists should be core members of the neuroscience brain and other CNS tumours MDT and the cancer network brain and other CNS tumours MDT, and may need to work across several geographical sites. They are likely to take on the role of key worker for many patients, especially during the early stages of their clinical care, providing supportive care, information and continuity of care with other healthcare professionals. There should be ready access to specialist neuropsychology and neuropsychiatry services for assessment and management of complex cognitive, emotional and behavioural problems. There should also be access to specialist healthcare professionals as appropriate for any other problems patients may experience, such as epilepsy, headaches, and functional loss, for example speech, language or visual problems.
- Palliative care specialists should be included as members of the neuroscience brain and other CNS tumours MDT and the cancer network brain and other CNS tumours MDT. They should provide advice on palliative and supportive care, the management of symptoms, and contribute to the patient's management plan.
- There should be rapid access to allied health professional assessment and rehabilitation services, including specialist neurorehabilitation when appropriate, as a patient's condition changes. There should be immediate access to specialist equipment as necessary.
- Data collection systems should be in place that allow entry of information on all patients with a radiologically or histopathologically confirmed CNS tumour. Consideration should be given to a web-based information system that will allow easy data sharing between healthcare professionals across services.

- The National Cancer Research Institute Clinical Studies Group on brain tumours is encouraged to develop an extended portfolio of trials. Cancer networks should be able to demonstrate how they intend to ensure that trials are supported. Patient entry into these studies should be actively monitored.
- National tumour groups for rare CNS tumours should be established to coordinate the approach to care; this should include developing protocols for the investigation, management, registration and clinical research into rare tumours. They should also maintain a national register of all these cases.

Scope of the document

The purpose of this guidance is to describe key aspects of services required to achieve the best outcomes for adult patients with tumours of the brain and central nervous system (CNS). The document predominantly deals with primary tumours although metastases from other primary sites that need complex neurological or neurosurgical interventions are also included. Spinal cord compression as a result of metastatic tumours is not included (see scope in appendix 1); this is the subject of a separate National Institute for Health and Clinical Excellence (NICE) clinical guideline 'Diagnosis and management of patients with metastatic spinal cord compression', expected publication in 2008.

This guidance covers all aspects of care for adult patients with CNS tumours from diagnosis onwards. The interface between services for adolescents and adults is covered in the recently published NICE guidance 'Improving outcomes in children and young people with cancer'. [1]

This cancer service guidance manual is intended to inform the commissioning and provision of services for people with CNS tumours. It will not offer the level of detail required to inform decision-making about specific treatments for individual patients.

This background section is intended to inform non-specialist readers about this group of diseases and their management.

CNS tumours: nature

Primary CNS tumours are uncommon. The most numerous are brain tumours, which are said to account for only 1.6% of cancers in England and Wales. [2] The variety of pathological tumour types is large. In addition, the following four important characteristics of tumours in the CNS determine why the terms 'malignant tumour' (often equated with 'cancer') and 'benign tumour' lack validity when applied to this clinical setting.

- The cranium (skull), which surrounds the brain, is a rigid box, so that even a small, slowly growing tumour can cause severe symptoms and detrimental (even fatal) effects when it raises intracranial pressure.
- Slowly growing tumours in the brain can infiltrate extensively into adjacent normal tissue, which makes excision impossible.
- The vital functions of the brain, in which these tumours arise, pose a particular challenge for surgical excision.
- A slowly growing tumour may undergo transformation to an aggressive tumour.

Therefore, the terms ‘high-grade tumour’ and ‘low-grade tumour’ are preferred to define, respectively, a tumour that grows rapidly and is aggressive and a tumour that grows slowly, but which may or may not be successfully treated. These terms will be used in this guidance document. However, as national official registrations are compiled with the terms ‘benign’ and ‘malignant’, there is reference to these terms in this background chapter. High-grade tumours are grades 3 and 4 and low-grade tumours are grades 1 and 2 in the World Health Organization (WHO) classification (see appendix 2). The grade of CNS tumour correlates with prognosis (1 – best; 4 – worst). At present the cancer waiting time standards only apply to CNS tumours with a ‘malignant’ diagnosis, and those with a ‘benign’ diagnosis are not reported in the same manner. For the reasons stated above, it is the opinion of the Guidance Development Group (GDG) that all intrinsic CNS tumours (grade 1–4) should be reported under the cancer waiting time standards. This will enable quicker access to appropriate treatments for patients with these tumours in order to improve outcomes.

In general, CNS tumours have a poor prognosis. Both their anatomical position and pathology play an important role in prognosis and decisions about appropriate investigation and treatment. Sometimes, the risks of obtaining tissue for histopathological assessment are considered clinically unacceptable, and the patient is managed on the basis of a diagnosis made on neuroradiological features.

The anatomical location influences symptoms that include physical, cognitive and psychological components. For this reason, adults with CNS tumours pose a unique challenge to healthcare professionals; the patient may not be the best person to explain his or her symptoms, and cognitive dysfunction may greatly increase the need for psychological/psychiatric, social and physical support. In view of the poor survival of many patients, even with optimal treatment, an important aspect of improving outcome is maximising quality of life.

Incidence, prevalence, mortality, and survival rates and trends

Background

1

Approximately 6500 primary tumours of the CNS in those aged 15 years and over were registered annually in England and Wales between 1995 and 2000, of which 58% were classed as ‘malignant’ (Table 1). There is, however, evidence of significant under-registration of intracranial tumours in the UK, particularly low-grade tumours. It has been suggested that almost half of intracranial tumours are not recorded by cancer registries. [3,4]

The incidence of these tumours rises throughout adulthood (after a peak in childhood) to reach its highest among the 75–79-year age group at 37 registrations per 100,000 population per year over the above mentioned 6-year period (Figure 1). In the 10 years from 1991 to 2000 the rate of tumour registration increased by 17%. The rise was particularly marked in older age groups and registrations for these tumours more than doubled among very elderly people in that decade (Table 2). The reasons for this are unclear, but the increase may be due to more intensive investigation of neurological deficit in older patients in recent years. As the number of tumours registered in England and Wales has risen, hospital admissions recorded for this group of patients have also increased (Figure 2).

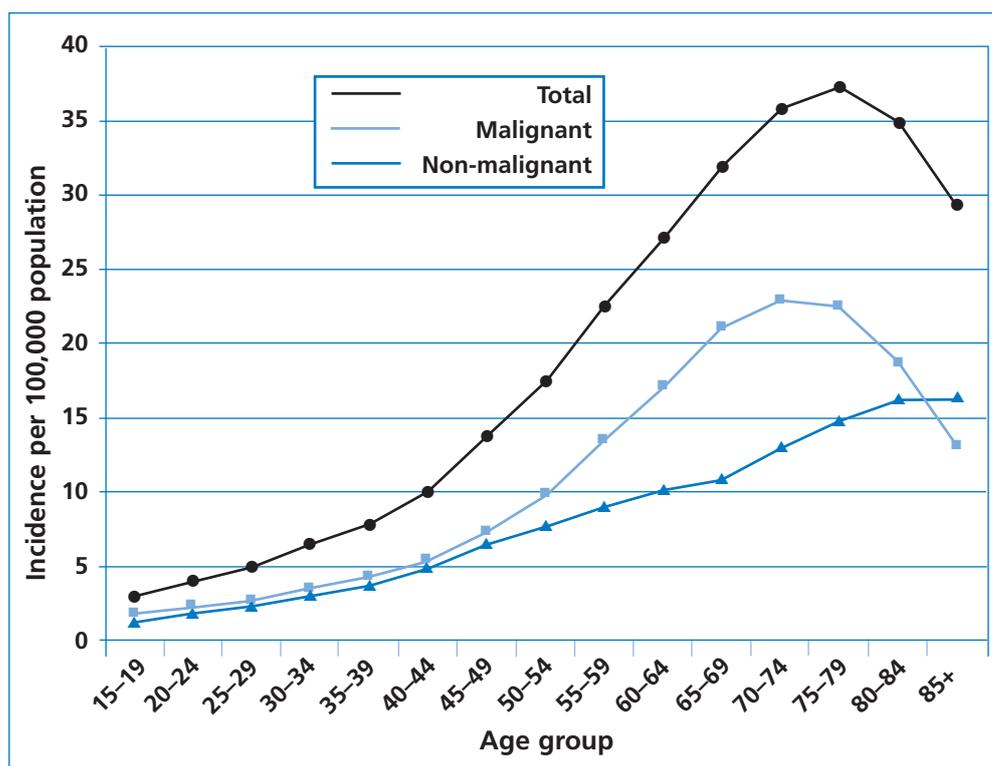
Table 1. Registrations and mortality from primary brain and central nervous system tumours in England and Wales, 1995–2000, people aged 15 and over

| | Registrations | | | Mortality | |
|--|------------------|-----------------------------|---------------------------|------------------|-----------------------------|
| | Number per annum | Crude rate per 100,000 ≥ 15 | Male:female ratio (rates) | Number per annum | Crude rate per million ≥ 15 |
| Brain tumours | | | | | |
| Malignant | 3550 | 8.54 | 1.44 | 2691.2 | 64.74 |
| Benign/uncertain behaviour | 520 | 1.25 | 1.04 | 699.2 | 16.82 |
| Intracranial meningiomas | | | | | |
| Malignant | 54 | 0.13 | 0.85 | 18.0 | 0.43 |
| Benign/uncertain behaviour | 758 | 1.82 | 0.46 | 226.5 | 5.45 |
| Spinal cord tumours | | | | | |
| Malignant | 69 | 0.17 | 1.38 | 21.5 | 0.52 |
| Benign/uncertain behaviour | 56 | 0.13 | 1.12 | 0.8 | 0.02 |
| Spinal meningiomas | | | | | |
| Malignant | 5 | 0.01 | 0.65 | 0.5 | 0.01 |
| Benign/uncertain behaviour | 60 | 0.14 | 0.27 | 1.2 | 0.03 |
| Pituitary tumours* | | | | | |
| Malignant | 29 | 0.07 | 0.99 | 7.8 | 0.19 |
| Benign/uncertain behaviour | 661 | 1.59 | 1.13 | 31.0 | 0.75 |
| Cranial nerve tumours | | | | | |
| Malignant | 17 | 0.04 | 1.27 | 2.8 | 0.07 |
| Benign/uncertain behaviour | 412 | 0.99 | 1.02 | 17.8 | 0.43 |
| Pineal tumours | | | | | |
| Malignant | 19 | 0.05 | 4.29 | 5.0 | 0.12 |
| Benign/uncertain behaviour | 13 | 0.03 | 0.66 | 1.7 | 0.04 |
| Other registered as CNS tumours | | | | | |
| Malignant | 24 | 0.06 | 0.75 | 9.7 | 0.23 |
| Benign/uncertain behaviour | 215 | 0.52 | 0.58 | 0.5 | 0.01 |
| Total malignant | 3767 | 9.06 | 1.42 | 2748.8 | 66.13 |
| Total benign/uncertain | 2695 | 6.48 | 0.79 | 986.3 | 23.73 |
| Total | 6462 | 15.54 | 1.11 | 3735.2 | 89.86 |

Data supplied by the National Cancer Intelligence Centre of the Office for National Statistics and the Wales Cancer Intelligence and Surveillance Unit. As these data use the International Classification of Diseases (ICD) coding, CNS lymphomas are not distinguished as a separate group. Registrations (ICD-10) and mortality (ICD-9) codes may not match exactly.

*Including craniopharyngeal tumours.

Figure 1. Age-related rates per 100,000 population for total primary tumours, subdivided as 'malignant'/non 'malignant', 1995–2000



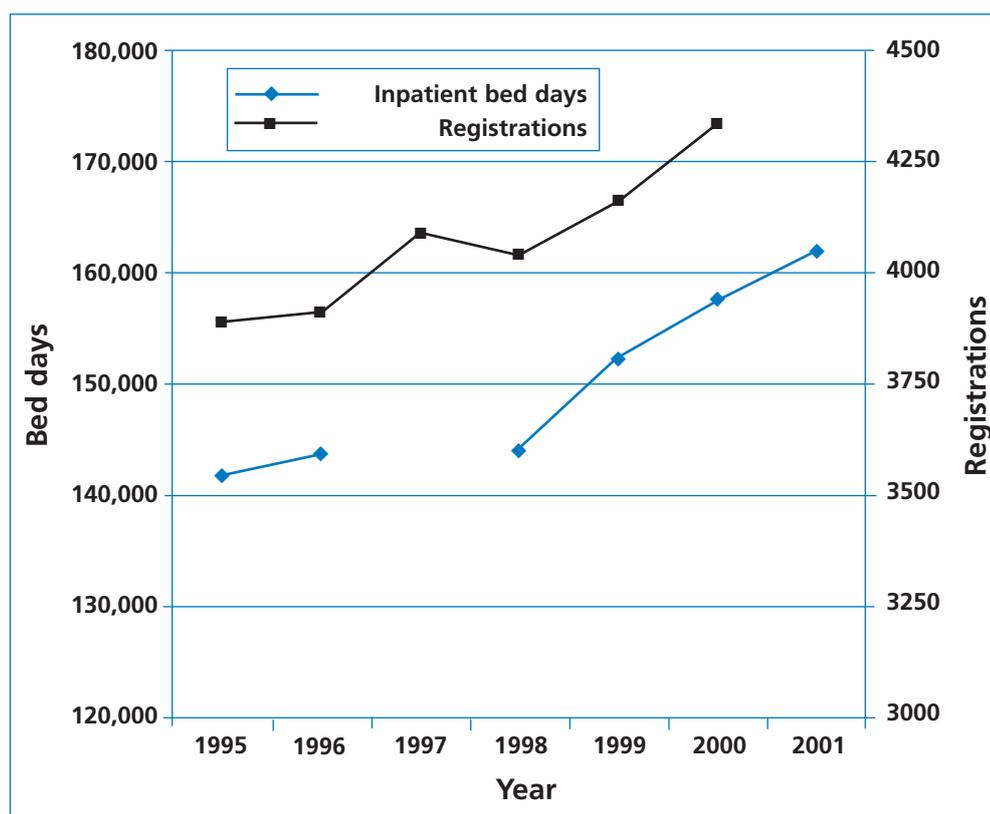
Data supplied by the National Cancer Intelligence Centre of the Office for National Statistics and the Wales Cancer Intelligence and Surveillance Unit

Table 2. Age-specific registration rates for primary brain/central nervous system tumours per 100,000 population per year among those aged 15 years and older; selected ages x year (1991–2000)

| | 15–19 | 30–34 | 40–49 | 55–59 | 65–69 | 75–79 | 85+ | All ages |
|------|-------|-------|-------|-------|-------|-------|------|----------|
| 1991 | 2.7 | 6.4 | 14.0 | 23.1 | 27.7 | 31.1 | 18.4 | 13.7 |
| 1992 | 3.5 | 6.9 | 14.7 | 22.5 | 33.1 | 31.6 | 20.0 | 15.1 |
| 1993 | 3.0 | 7.4 | 13.6 | 22.9 | 32.2 | 30.1 | 20.7 | 14.7 |
| 1994 | 3.4 | 6.7 | 13.1 | 20.9 | 30.3 | 35.9 | 22.6 | 14.7 |
| 1995 | 2.7 | 6.9 | 13.1 | 23.3 | 29.7 | 34.9 | 23.7 | 15.2 |
| 1996 | 2.5 | 6.2 | 13.6 | 22.5 | 32.1 | 34.3 | 25.6 | 15.3 |
| 1997 | 2.8 | 6.8 | 14.7 | 23.9 | 34.6 | 37.7 | 27.9 | 15.8 |
| 1998 | 2.8 | 6.1 | 13.8 | 20.7 | 30.8 | 35.5 | 28.9 | 15.4 |
| 1999 | 3.5 | 5.9 | 13.2 | 22.9 | 32.7 | 39.0 | 31.4 | 15.6 |
| 2000 | 3.2 | 6.8 | 13.8 | 21.3 | 31.4 | 41.5 | 37.3 | 16.1 |

Double line indicates transition from ICD-9 to ICD-10; definitions of tumour groups included do not match exactly across this transition. 'All ages' refers to crude rate in those aged 15 and over. Data supplied by the National Cancer Intelligence Centre of the Office for National Statistics and the Wales Cancer Intelligence and Surveillance Unit. ICD, International Classification of Diseases.

Figure 2. Inpatient bed days and registrations for patients with brain tumours ('benign', 'malignant' and 'uncertain') 1995–2001



Hospital activity data represent any admission for patients with a known diagnosis of this tumour type. Data supplied by the National Cancer Services Analysis Team (Hospital Episodes Statistics/Patient Episode Database in Wales data; year refers to commencement of financial year (incomplete data available for financial year 1997–98), National Cancer Intelligence Centre of the Office for National Statistics and the Wales Cancer Intelligence and Surveillance Unit.

It is not known how many primary lymphomas of the CNS are registered in England and Wales each year, as the coding system used ('International classification of diseases', 10th edition [ICD-10]) does not readily distinguish these from primary lymphomas occurring in other sites. They are, however, rare, accounting for approximately 2–3% of biopsied CNS tumours. [5] At a national level a substantial number of CNS tumours do not have specific morphology recorded,³ and so reliable data are not available for tumour subtypes defined by their morphology (for example oligodendroglioma).

For approximately 3700 deaths per year in England and Wales among those aged 15 years and over, primary tumours of the CNS are given as the underlying cause. The majority of these are due to brain tumours. As with registrations, mortality among very elderly people

³ Of brain tumours registered for England for 1995–2000, 37% had non-specific morphology codes (20% 'neoplasm' malignant/benign/uncertain whether benign or malignant; 17% 'glioma, malignant'). Data supplied by the National Cancer Intelligence Centre of the Office for National Statistics.

(those aged over 85 years) attributed to tumours of the CNS has increased substantially in the decade between 1991 (13 per 100,000) and 2000 (26 per 100,000). As with incidence, this may be related to increased investigation (in particular computed tomography [CT] and magnetic resonance imaging [MRI] scans) among this age group. Details of the recorded incidence and mortality of CNS tumours for England and Wales are shown in Table 1.

Survival of those with brain tumours classed as ‘malignant’ (ICD-10 C71) is poor, and is shown in Table 3. Relative survival has decreased in the past 20 years. The increased incidence in elderly people does not explain the decrease in relative survival, but an increased tendency to investigate severe disability in elderly people and hence diagnose tumours with poor prognosis may be a contributing factor. The European cancer registries study on cancer patients’ survival and care (EUROCORE-3),[6] with participating registries from both England and Wales, showed that the 5-year age-standardised relative survival rates were similar to those among other participating registries of other countries of Europe, although both England and Wales were among the lower range for 1-year survival (Table 3).

Table 3. Age-standardised 1-year and 5-year relative survival (95% confidence intervals) for adults diagnosed (1990–94) with ‘malignant’ brain tumour (ICD-9 191), participating registers for EUROCORE study, England, Wales and Europe

| | Men | | Women | |
|----------------|------------------------|------------------------|------------------------|------------------------|
| | 1-year | 5-year | 1-year | 5-year |
| England | 31.7 (30.7 to 32.8) | 15.7 (14.9 to 16.7) | 34.2 (32.9 to 35.4) | 17.9 (16.8 to 19) |
| Wales | 33.8 (30.2 to 37.8) | 17.5 (14.3 to 21.4) | 33.6 (29.9 to 37.8) | 19.7 (16.1 to 24.1) |
| Europe | 37 (35.6 to 38.5) | 16.4 (15.2 to 17.6) | 39 (37.4 to 40.7) | 18.5 (17.1 to 20) |

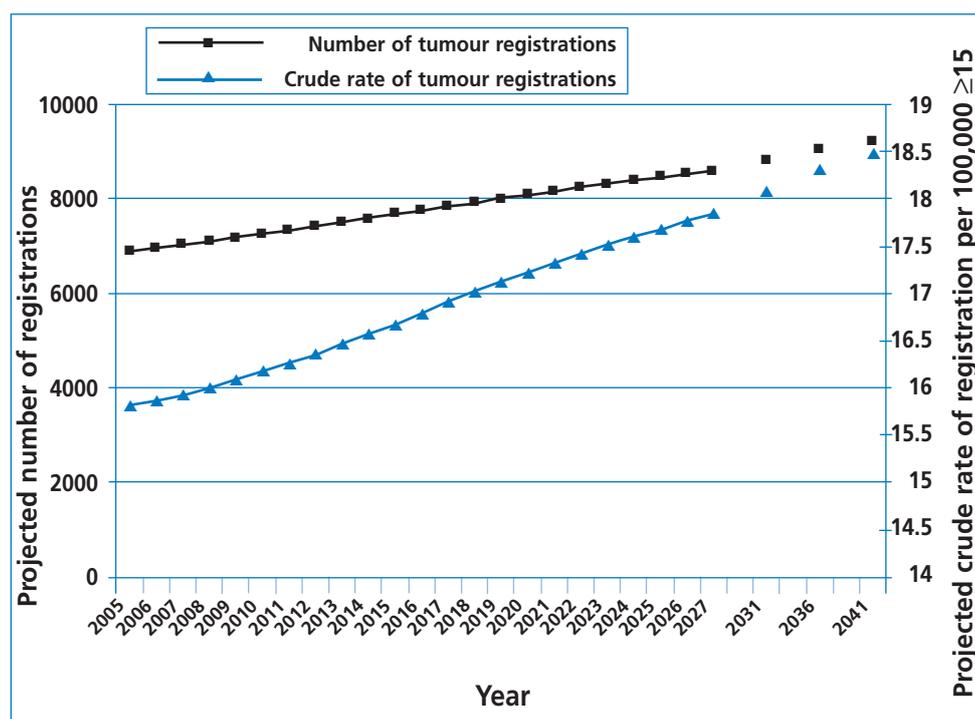
Table 4. Age-standardised 1-year and 5-year relative survival (95% confidence intervals) for men and women aged 15–99 diagnosed with ‘malignant’ brain tumours (ICD-10 C71) in 1991–95 and 1996–99, England and Wales

| | Patients diagnosed 1991–1995 | | Patients diagnosed 1996–1999 | | Difference* | |
|--------------|------------------------------|------------------------|------------------------------|------------------------|-------------|--------|
| | 1-year | 5-year | 1-year | 5-year | 1-year | 5-year |
| Men | 30.8 (30.0 to 31.7) | 13 (12.4 to 13.7) | 32.2 (31.3 to 33.2) | 12.5 (11.6 to 13.4) | 1.4 | –0.5 |
| Women | 32.2 (31.2 to 33.2) | 15.4 (14.5 to 16.2) | 32.1 (31.0 to 33.3) | 15.3 (14.2 to 16.4) | –0.1 | –0.1 |

* The difference (in percentage points) between the relative survival rates for patients diagnosed in 1991–95 and in 1996–99. [7]

As the proportion of elderly people in the population increases, the incidence of CNS tumours is expected to rise. Based on the Government Actuary’s Department figures [8] and the average number of registrations for CNS tumours between 1995 and 2000, Figure 3 shows the predicted registrations of tumours of the CNS up to 2041. The growth in registrations may be greater than predicted if the trend of increased incidence of CNS tumours among elderly people continues.

Figure 3. Predicted numbers and crude rates of brain and central nervous system tumour registrations based on age- and sex-specific rates, 1995–2000; age ≥ 15 years



Classification of CNS tumours

The classification of CNS tumours is complex, and various classifications have been developed since that of Bailey and Cushing in the 1920s. [9] The WHO produced a classification in 1993, most recently updated in 1999. [10] The use of this classification is now endorsed by professional bodies (Royal College of Pathologists [11]) and the European Network of Cancer Registries. [12] It is also used as part of the United Kingdom National External Quality Assessment Service [13] for laboratory and diagnostic neuropathology. In this classification CNS tumours are divided into the basic types of tumours of neuroepithelial tissue (including what are often described as gliomas), tumours of the peripheral nerves, tumours of the meninges, lymphomas and haematopoietic neoplasms, tumours of the sellar region, and metastatic tumours. Each type has further subdivisions.

The usefulness of this WHO classification in epidemiological terms is limited by the fact that tissue from tumours of the CNS is not always available for analysis. Also, the system used to collect statistics on pathology of CNS tumour registrations at a national level does not conform to this WHO classification.

For simplicity and ease of understanding, this guidance classifies tumours into the categories of brain tumours and rarer CNS tumours, in particular, intradural spinal cord tumours, skull base tumours, pituitary tumours, optic tract gliomas, primary CNS lymphomas, medulloblastomas and pineal tumours.

Aetiology and risk factors

The aetiology of tumours of the CNS is largely unknown. The only unequivocally identified causative factors are inherited cancer syndromes and, in rare cases, ionising radiation. [14] Unlike a number of other cancers, currently there is no evidence that brain tumours can be prevented by lifestyle changes. Immunosuppression, for example as a result of AIDS, is a well-recognised cause of cerebral lymphoma. [10]

The risk of developing CNS tumours is dependent on age and gender (see above), and also shows an inverse social gradient; tumours of the brain are more common among more affluent groups, [2] and this is also true for mortality. The reverse trend is evident for brain metastases. [4]

Geographical variation in CNS tumours is less than for most human neoplasms. Less developed countries have a lower incidence than more developed countries. There is also evidence that in multicultural communities those of African or Asian descent have a lower incidence than those of Caucasian descent. Japan is a developed country with a particularly low level of reported tumours although it is not clear if this is related to inadequate registration. [14] There is no consistent regional variation within England and Wales. [2]

Familial syndromes with an increased risk of tumours of the CNS

A number of familial syndromes give rise to an increased risk of tumours of the CNS. These syndromes are shown in Table 5. These are, in general, autosomal dominant conditions, [10] and many have distinctive skin features (phakomatoses). Neurofibromatosis type 1 is the most common of these syndromes with a prevalence of 1 in 3000. [15] Neurofibromatosis type 2 has an incidence of about 1 in 40,000. [16] Multiple endocrine neoplasia type I, associated with pituitary tumours, is sometimes included in this group. [5]

Table 5. Inheritable syndromes carrying an increased risk for central nervous system neoplasms

| Syndrome | Gene | Chromosome | Nervous system |
|---|-----------------------|----------------------|---|
| Neurofibromatosis type 1 | NF1 | 17q11 | Neurofibromas, malignant nerve sheet tumour, optic nerve gliomas, astrocytoma |
| Neurofibromatosis type 2 | NF2 | 22q12 | Bilateral acoustic schwannomas, multiple meningiomas, astrocytomas, glial hamartomata |
| von Hippel–Lindau Syndrome | VHL | 3p25 | Haemangioblastomas |
| Tuberous sclerosis | TSC1 TSC 2 | 9q34 16p13 | Subependymal giant cell astrocytoma, cortical tubers |
| Li–Fraumeni | p53 | 17p13 | Astrocytomas/primitive neuroectodermal tumour |
| Cowden’s disease | PTEN | 10q23 | Dysplastic gangliocytoma of the cerebellum |
| Turcot’s syndrome | APC HMLH1 HPSM2 | 5q21 3p21 7p22 | Medulloblastoma Glioblastoma |
| Naevoid basal cell carcinoma syndrome (Gorlin syndrome) | PTCH | 9q22 | Medulloblastoma |

Source: adapted from references [5,10] and [17].

Symptoms, diagnosis and treatment

CNS tumours can result in a wide range of physical, cognitive and psychological symptoms. The list of differential diagnoses is considerable, and the incidence of many of these alternatives is usually far greater than that of brain tumours, such that these may be exhaustively explored before the diagnosis of a CNS tumour is considered. Consequently, for some patients and families there is a long delay from first symptoms to reaching a diagnosis, causing considerable stress and anxiety. [18]

Brain tumours

Brain tumours account for the majority of CNS tumours. In this document they are taken to include all primary intracranial tumours apart from rare and unusual tumours considered separately. In particular this group includes tumours of the brain substance itself, many of which arise from the glial or support cells of the brain, for example, glioblastoma multiforme. Glial tumours (gliomas) may be considered low grade (grades I and II, less aggressive) or high grade (grades III and IV, more aggressive) in accordance with the WHO classification of tumours of the nervous system (see appendix 2). This group also includes tumours that arise from the tissues around the brain, such as tumours of the meninges and metastases from other primary sites that require complex neurological or neurosurgical interventions.

In spite of the variety of brain tumour pathologies, presentation tends to be related to:

- headache with cognitive or behavioural symptoms
- epilepsy
- progressive focal neurological deficits

or

- headache with raised intracranial pressure.

Headache accompanied by cognitive, memory or behavioural symptoms is a common presentation. Adult-onset epilepsy is a common feature of brain tumours, and may present as either focal or generalised seizures. It usually presents without other neurological symptoms or signs.

Focal neurological deficits may result in a large variety of symptoms depending on the part of the neurological system affected. Gradual-onset weakness or sensory loss on one side of the body is common, as is difficulty with speech or understanding. Occasionally patients present with unilateral visual field loss.

Raised intracranial pressure typically causes headaches, which may be worse in the morning, nausea and vomiting or visual deterioration. More severe raised intracranial pressure may be associated with altered levels of consciousness, and this may be in the form of lethargy or somnolence in the early stages. Swelling of the optic disc (papilloedema) is a sign that may be present when there is raised intracranial pressure.

The diagnosis of a possible brain tumour is first indicated following imaging of the brain with CT or MRI. The diagnosis is confirmed by surgical biopsy, which allows histopathological classification, although in a few cases biopsy is either not feasible or clinically inappropriate.

Management of these tumours depends on their anatomical position and their pathological type. Tumours within the skull, but outside the brain, such as meningiomas, can often be completely excised with a very good prognosis. Tumours within the brain, such as gliomas, can rarely be completely removed because of their relation to critical structures and the infiltrating nature of the tumour. Depending on the type of tumour (for example, high-grade glioma) there may be benefits associated with treatment by resection, radiotherapy, chemotherapy or a combination. Steroids are often used to reduce intracranial pressure or to try to improve focal signs, for example weakness on one side. Most patients will also require input from a variety of healthcare professionals, including allied health professionals, and those providing psychological help and support for patients, their relatives and carers.

Rarer CNS tumours

In this document, rarer CNS tumours are those considered to be sufficiently uncommon to warrant specialist input beyond that required for those brain tumours included above.

Spinal tumours

Primary tumours of the spinal cord are rare. Patients with these tumours are likely to present with focal neurological symptoms relating to compression or invasion of nerve roots or the spinal cord itself. Pain along a nerve root is a common initial symptom.

Tumours around the spinal cord, such as meningiomas, and nerve sheath tumours, often schwannomas, are more likely to grow slowly. Complete excision may lead to a good prognosis, although their location may pose technical difficulties. This guidance includes services for nerve sheath tumours that cause compression of the spinal cord and chordomas (an uncommon tumour that may occur in the sacral or cervical region); it does not cover services for spinal cord compression due to metastatic tumours.

Skull base tumours

The term 'skull base tumour' does not appear in formal classifications of CNS tumours and does not specify the pathological type. The term refers to multiple tumour types that occur at this anatomical location, for example, acoustic schwannoma (a cranial nerve tumour), some meningiomas and invasive tumours from adjacent sites, such as nasal tumours. These tumours may cause specific symptoms because of damage to structures in the region, such as cranial nerves, resulting in palsies, difficulty with balance or hearing. Patients with acoustic schwannoma often present with hearing loss on one side (90%), and many experience tinnitus (70%). [19] The progress of symptoms is highly variable depending on tumour type.

Pituitary tumours

Pituitary tumours may be functional and secrete hormones, or non-functional. Larger tumours (> 1 cm) are usually non-functional. [20] Symptoms may be the result of either hormone secretion or pressure effects. Pressure on the pituitary gland/hypothalamus may result in hormonal imbalance (for example, hypopituitarism) and pressure on the optic chiasma/optic nerves in visual disturbance. Craniopharyngiomas, more common in children, also arise in the sellar region, and are grouped with pituitary tumours in this guidance.

Diagnosis of these tumours is primarily by imaging, although hormonal measurements are also important. Apart from any hormonal or medical treatment that may be required, the management of these tumours involves surgical resection, which may be undertaken by either the trans-sphenoidal or the standard craniotomy approaches. [21]

Other rarer CNS tumours

Some tumour groupings are rare. For example, in England and Wales there are 0.08 registrations of pineal tumours per 100,000 population per year (that is, 32 registrations). Some rarer tumours have been given particular attention in the guidance because of their specific needs. These include primary CNS lymphomas, which have been increasing in incidence globally as a result of the AIDS epidemic. [10] Immunocompetent patients show treatment response rates of 85%, with 2- and 5-year survival of 40–70% and 25–45%, respectively. Outlook is much poorer for patients with AIDS, in whom the median survival is 2–6 months. [10]

Medulloblastoma requires particular attention because of its biological behaviour, in particular its tendency to spread through the neuraxis. Pineal tumours, and in particular germ cell tumours, may be curable with appropriate management. Optic pathway gliomas, which usually present with visual disturbance, may be associated with neurofibromatosis type I, which usually occurs in children, and the uncertainties surrounding their treatment requires specialist input.

NHS services for patients with CNS tumours

Services for patients with tumours of the CNS are provided in all healthcare sectors. Primary healthcare teams and local acute hospitals often provide essential services for these patients; however, as these tumours are rare, the role of specialised services is particularly important.

The route of care for patients may be complex because catchment areas for neuroscience centres and oncology/radiotherapy centres often do not coincide and may not match well with the boundaries of cancer networks or strategic health authorities. An analysis was undertaken of the catchment areas of the 27 neuroscience centres, as mapped by the National Cancer Services Analysis Team (NATCANSAT) for this guidance, and the 37 cancer networks covering England and Wales. Only 11 of the neuroscience centres cover areas contained within one network, 15 of the other neuroscience centre catchment areas cover more than one network area⁴ (see appendix H in the needs assessment, which is available on the CD-ROM that accompanies this guidance and on the NICE website [www.nice.org.uk/csgbraincns]). As a result of this incongruity, it has been necessary in this guidance to distinguish functions that occur at a cancer network level from those that occur at the neuroscience/neurosurgical unit level.

⁴ For one of the London units the relation was unclear from the analysis.

Patients may present to general practitioners (GPs), accident and emergency departments or other acute medical services before being referred on to specialist services. The average GP would see approximately one new patient with a primary brain tumour every 7 years and one new patient with any other primary CNS tumour every 12 years.

The following description of services is based on a survey of neuroscience centres (with the assistance of the Society of British Neurological Surgeons) and oncology/radiotherapy units, which was undertaken in England and Wales during early 2004, to inform this guidance.

Neurosurgical services

Neuroscience centres are often the first specialist service to which patients with tumours of the CNS are referred. There are 27 units providing neurosurgical services to adults in England and Wales. Most are based within a university hospital (78%), and their self-estimated population ranges from 1 million to 3.5 million (average 2.2 million). Obtaining information on the total number of new patients with CNS tumours seen by a unit per year is difficult because of the variation in the way data are (or are not) collected by the units; the estimates given varied widely from 63 to 700 new patients (median 190).

For CNS tumours as a whole there is little evidence of specialisation among neurosurgeons; in virtually all units in England and Wales all neurosurgeons perform surgery on CNS tumours. However, for some subtypes of tumours, in particular pituitary and acoustic nerve/skull base tumours, there is a high level of specialisation with only one or two surgeons performing procedures in most units. Most neuroscience centres have clinical nurse specialists in neuro-oncology (80%) although the role varies from unit to unit. Often a key function of clinical nurse specialists in neuro-oncology is the coordination of services for patients.

Increasingly, multidisciplinary teams (MDTs) are being established for CNS tumours. In the report by the Commission for Health Improvement on NHS cancer care in England and Wales, [22] based on visits during 2000/2001, about a third of acute trusts providing services for CNS tumours had defined MDTs. In the survey undertaken for this guidance, 2003/04, 80% of neuroscience centres reported that they had established MDTs. Almost half of units have specific MDTs for pituitary tumours, and many have MDTs for skull base tumours and other specific types of CNS tumours.

Specialist clinics for patients with CNS tumours were described in 40% of units. These may be joint clinics with oncologists (22% of units), endocrinologists (19% of units) or otolaryngologists (15% of units). In some cases there were nurse-led tumour clinics, and an epilepsy nurse was also present.

The survey showed that allied health professionals were available on-site in all the neuro-oncology units, but in a third of units no palliative care consultant or palliative care nurse was available on-site.

Oncology and radiotherapy services

The survey of the 52 radiotherapy units in England and Wales (92% response rate) found that almost all of these units (94%) undertake CNS tumour work. Although a number are standalone, approximately 40% are located in university/teaching hospitals and 40% in district general hospitals. These units each see between 17 and 350 neuro-oncology patients a year.

Oncology/radiotherapy units may provide treatments such as inpatient and outpatient chemotherapy and radical or palliative radiotherapy. There appears to be variation among units not only in the types of treatment provided, [23] but also in the access to these services. Mean waiting times quoted for a patient with a CNS tumour to start radical radiotherapy varied from less than 1 week to 8–12 weeks.

All but one unit reported having some degree of specialisation among oncologists for CNS tumours. More than half the units (56%) have clinical nurse specialists in neuro-oncology.

Around three quarters of units have access to an MDT, either on-site or at another site, for their patients. Multiple-site MDTs exist, where either several units communicate by videoconference or conclusions are passed on to treating clinicians who may not attend the meetings. In some cases a local expert team is available to provide support in a smaller unit without an MDT.

Many allied health professionals are available on-site in all or almost all units. Just under half of units have on-site access to neuropsychological/neuropsychiatric services, and two thirds of units have on-site access to a neurologist with an interest in epilepsy.

Specialist neurorehabilitation units

Almost all neuroscience centres in England and Wales (96%) reported having access to a specialist neurorehabilitation unit. Access to specialist neurorehabilitation units was much lower for oncology/radiotherapy units (60%).

Stereotactic radiosurgery

Stereotactic radiosurgery is a specialised technique designed to focus high doses of ionising radiation on a tumour in a single fraction while sparing normal tissue. Much of the stereotactic radiosurgery is undertaken at the national centre in Sheffield. However, there are eight centres in total in England and Wales to which patients are referred for stereotactic radiosurgery by neuroscience centres.

References

1. National Institute for Health and Clinical Excellence (2005) Improving outcomes in children and young people with cancer. *NICE cancer service guidance*. London: National Institute of Health and Clinical Excellence. Available from: www.nice.org.uk/CSGCYP
2. Quinn M, Babb P, Brock A et al. (2001) *Brain. Cancer trends in England and Wales 1950–1999: studies on medical and population subjects No. 66*. London: The Stationery Office, p34–9.
3. Pobereskin LH, Chaddock JB (2000) Incidence of brain tumours in two English counties: a population based study. *Journal of Neurosurgical Psychiatry* 69: 464–71.
4. Counsell CE, Collie DA, Grant R (1996) Incidence of intracranial tumours in the Lothian region in Scotland: 1989–90. *Journal of Neurology, Neurosurgery, and Psychiatry* 61: 143–50.
5. Ellison D, Chimelli L, Harding B et al. (2004) *Neuropathology* 2nd edition. London: Mosby.
6. EURO CARE. ‘The EURO CARE-3 results’ [online]. Available from: www.eurocare.it [accessed 12 January 2004].

7. Office for National Statistics (2004) 'Cancer survival: England and Wales, 1991–2001, twenty major cancers by age group' [online]. Available from: www.statistics.gov.uk/statbase/ssdataset.asp?vlnk=7899 [accessed 24 October 2004].
8. Government Actuary's Department. <http://www.gad.gov.uk/Population/2002/engwal/wew025y.xls> [accessed 2 March 2004].
9. Davis FG, Preston-Martin S (1998) Epidemiology. In: Bigner DD, McLendon RE, Bruner JM, editors *Russell and Rubenstein's pathology of tumours of the nervous system* 6th edition. Volume 1. New York: Arnold.
10. Kleihues P, Cavenee WK (2000) *Pathology and genetics of tumours of the nervous system*. Lyon: IARC Press.
11. Royal College of Pathologists (2003) 'Standards and minimum datasets for recording common cancers: minimum dataset for the histopathological reporting of tumours of the central nervous system' [online]. London: Royal College of Pathologists. Available at: www.rcpath.org/resources/pdf/CNSminimumDatasetFINAL04.pdf [accessed 13 October 2004].
12. European Network of Cancer Registries (1998) *Recommendations for coding tumours of the brain and central nervous system*. Lyon: ENCR. Available from: www.encl.com.fr/ [accessed 13 October 2004].
13. United Kingdom National External Quality Assessment Service (2003) 'Neuropathology' [online]. Available from: www.ukneqas.org.uk/Directory/HIST/neurpath.htm [accessed 13 October 2004].
14. International Agency for Research on Cancer (2003) Tumours of the Nervous System. In: Stewart BW, Kleihues P, editors *World cancer report*. Lyon: IARC Press.
15. Friedman JM (1999) Epidemiology of neurofibromatosis type I. *American Journal of Medical Genetics* 89: 1–6.
16. Evans DGR, Sainio M, Baser ME (2000) Neurofibromatosis type 2. *Journal of Medical Genetics* 37: 897–904.
17. Pan E, Uyehara-Lock JH, Nicholas MK (2002) Familial brain tumour syndromes. In: Steele GD, Phillips TL, Chabner BA, editors *American Cancer Society Atlas of Clinical Oncology: Brain Cancer*. London: BC Decker, Inc.

18. Grant R (2004) Overview: Brain tumour diagnosis and management/Royal College of Physicians guidelines. *Journal of Neurology, Neurosurgery, and Psychiatry* 75 (Suppl. 2): ii18–ii23.
19. British Association of Otorhinolaryngologists – Head and Neck Surgeons (2002) *Clinical effectiveness guidelines: acoustic neuroma (vestibular schwannoma) BAO-HNS Document 5*. London: Royal College of Surgeons of England. Available from: www.sbns.org.uk/members/society_reports/ceg_acousticneuroma.pdf [accessed 22 October 2004].
20. Chin CT, Dillon WP (2002) Magnetic resonance imaging of central nervous system tumours. In: Steele GD, Phillips TL, Chabner BA, editors *American Cancer Society Atlas of Clinical Oncology: Brain Cancer*. London: BC Decker, Inc.
21. Thorner MO (1996) Anterior pituitary disorders. In: Weatherall DG, Ledingham JGG, Warrell DA, editors *Oxford textbook of medicine* 3rd edition. Volume 3. Oxford: Oxford University Press.
22. Commission for Health Improvement (2001) NHS cancer care in England and Wales, supporting data 5, multidisciplinary team working. In: *National Service Framework Assessments No. 1 NHS Cancer Care in England and Wales*. London: The Stationery Office. Available from: www.chi.nhs.uk/cancer/data/sd5.pdf [accessed 24 May 2004]. (The Commission for Health Improvement was replaced by the Healthcare Commission on 1 April 2004. The link is now at www.healthcarecommission.org.uk/assetRoot/04/00/00/18/04000018.pdf.)
23. Gerrard GE, Prestwich RJ, Franks KN et al. (2003) Neuro-oncology practice in the UK. *Clinical Oncology* 15: 478–84.

Multidisciplinary teams

Patients with brain and other central nervous system (CNS) tumours have very particular clinical needs which means that the arrangements for their care need to be structured quite differently from those for people with the more common cancers.

Their healthcare needs are complex for a number of reasons:

- Many patients are severely disabled by their disease.
- Many patients have a poor prognosis.
- The patients present through a variety of specialties.
- There are significant differences in the care needs of patients with tumours of different histological types and arising in different parts of the CNS.
- Many tumour subtypes are extremely rare.
- Many patients experience long-term progressive cognitive, physical and emotional problems.

Because of this, care often has to be provided at different locations.

This chapter describes the organisation of care for the majority of patients, that is those with brain gliomas, meningiomas or metastatic tumours. Specific specialist care is required for those with spinal cord and other less common tumours and this is described in more detail Chapter 6.

Patients present in a variety of ways. Patients are referred by their general practitioner (GP) to one of a number of specialties including neurology, acute services (such as acute medicine), ophthalmology, endocrinology, radiology or orthopaedics. First-line investigations, including imaging, are usually carried out at the local hospital. Radiological imaging (computed tomography [CT] or magnetic resonance imaging [MRI], see Chapter 4) is essential in the diagnosis of CNS tumours, and it is the first point at which a suspected diagnosis of a CNS tumour is made that prompts entry into the multidisciplinary team (MDT).

The initial treatment options for these patients can vary greatly, so the definition and measurement of key time points for the monitoring of ‘cancer waiting times’ may need careful consideration and general agreement. It is important that a consistent approach is adopted within and across MDTs. The MDT is pivotal in the management of patients with CNS tumours and attendance of healthcare professionals at the multidisciplinary meetings is essential. The meetings should form part of the timetabled activities of core members. All patients, including those who have had emergency surgery, need to have their clinical history and images reviewed by a specialist neuroscience brain and other CNS tumours MDT, whether or not they go on to have further active treatment.

Once the initial treatment (surgery, radiotherapy, chemotherapy or a combination) is completed, many patients will have a prolonged period of follow-up, with input from a variety of support services, either to monitor the effects of treatment or to manage gradual physical or neuropsychological decline. Many of the continuing rehabilitation, supportive and palliative care needs are met by allied health professionals (AHPs), and these services need to be provided as near to the patient’s home as possible. During this time all aspects of the patient’s care should be properly assessed and addressed, and immediate access provided to the appropriate services.

This guidance, together with the ‘Manual for cancer services’,⁵ is explicit in describing the role of core members of the MDT. The Society of British Neurosurgeons, currently implementing new manpower and training needs under the process of Modernising Medical Careers,⁶ has recognised that training and service demands will need to develop to achieve the supply of neurosurgeons specialising in CNS tumours.

As the management of patients with CNS tumours is often provided in different care settings, it is important that their care is, at all stages, adequately coordinated. This may be best achieved by ensuring that every patient has a clearly identified key worker.⁵ The key worker is the identified point of contact for patients, their relatives and carers; is responsible for ensuring that the supportive care needs of the patients, their relatives and carers are met; and is responsible for coordinating care across the patient pathway. The role of the key worker is outlined in the NICE guidance ‘Improving supportive and palliative care for adults with cancer’⁷ (Chapter 1 – coordination of care and recommendation 1.29).

⁵ Department of Health (2004) *Manual for cancer services*. London: Department of Health. Available from: www.dh.gov.uk

⁶ More information is available from the Society of British Neurosurgeons website <http://www.sbns.org.uk/site/1092/default.aspx> and the NHS Modernising Medical Careers website <http://www.mmc.nhs.uk/pages/home>

⁷ National Institute for Clinical Excellence (2004) *Improving supportive and palliative care for adults with cancer. NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

The clinical nurse specialist role is well established in oncology and clinical neuroscience. The emphasis of the role is to provide continuity throughout the patient pathway. As members of the MDT, neuro-oncology clinical nurse specialists provide a variety of services: advice, information and supportive care to patients, their relatives and carers; assessment of needs of patients, relatives and carers; and facilitation of appropriate referrals to AHPs, palliative care and community services. The role also involves the coordination of services, provision of consultative advice to hospital and community teams and education to healthcare professionals working with this group of patients.

Some neuro-oncology clinical nurse specialist posts are peripatetic and will cover both the neuroscience centre and the oncology/radiotherapy centre. Other services cover a large geographical area, and in these instances there may be clinical nurse specialists at the neuroscience centre and the oncology/radiotherapy centre. While a patient's care is being managed at either the neuroscience centre or the oncology/radiotherapy centre it is likely that the clinical nurse specialist will take on the role of key worker.

Patients with CNS tumours need a multidisciplinary approach to their care throughout their illness and follow-up, with continuing input from a variety of rehabilitation and support services. The patient pathway must be structured to ensure that access to appropriate services is always safe, easy and equitable. At all stages of the patient pathway, there may be a need to involve AHPs and supportive and palliative care services to address the patient's problems.

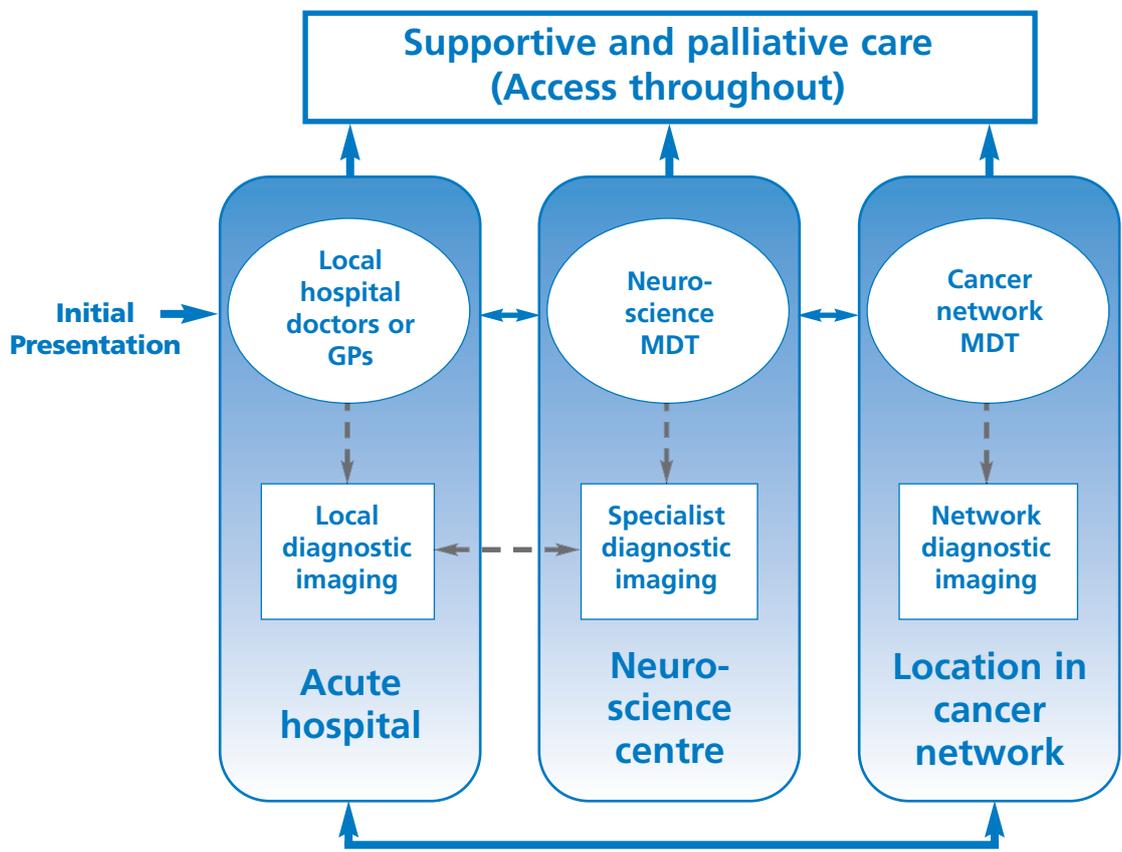
Appropriate clinical assessments are essential at three specific times:

- When the diagnosis of a CNS tumour is initially suggested by radiological investigations and appropriate onward referral is arranged.
- When the diagnosis of a CNS tumour is reviewed, usually in conjunction with further radiological and pathological diagnostic tests, and when the initial management plan (as defined in responsibilities of MDTs, page 35), which may or may not include neurosurgery and/or adjuvant therapy, is determined.
- When any indicated adjuvant therapy is instigated, and when further clinical review and initial and continuing access to rehabilitation, supportive and palliative care services are arranged.

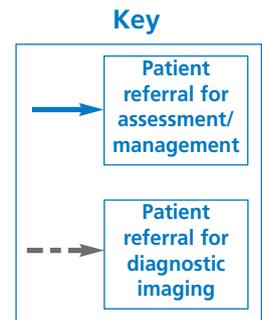
It is possible that some patients may have all their care coordinated and delivered in one location. But, as is clear from Chapter 1, the populations served by neuroscience centres and cancer networks are different in many parts of the country. Where they coincide it should be easier to coordinate the necessary care, but where they differ, clear arrangements for referral and continuing management are essential to ensure that patients get the most appropriate care.

Fundamental to ensuring efficient clinical care when patients are managed by different teams on different sites is good communication. Figure 4 summarises the flow of information through the patient pathway.

Figure 4. Brain and other central nervous system (CNS) tumours patient pathway



MDT, multidisciplinary team; GP, general practitioner.



A. Recommendations

The care of all patients with CNS tumours should be coordinated through a specific model of multidisciplinary assessment and care:

- A designated lead in every acute trust (see Table 6).
- A neuroscience brain and other CNS tumours MDT, usually based at a neuroscience centre (see Tables 7 and 8).
- A cancer network brain and other CNS tumours MDT (see Tables 9 and 10).
- A key worker.

Where the population served by the neuroscience centre and the cancer network are the same, the neuroscience MDT and cancer network MDT may involve many of the same healthcare professionals, but their responsibilities should be distinct (see below). In these circumstances it may be possible for the neuroscience and cancer network MDT meetings to occur at the same time. However, in many places separate MDTs with close working relationships should be in place (see Chapter 1).

All bodies that commission services for adults with CNS tumours within each cancer network should work together to ensure that these services function in a coordinated way. As many neuroscience units cover more than one cancer network area, it is important that networks collaborate and pool resources to deliver a full range of services. The establishment of teleconferencing facilities should be considered if geography makes it difficult for core team members to attend MDT meetings in person.

Neuroscience brain and other CNS tumours MDTs and cancer network brain and other CNS tumours MDTs should define their patient pathways.

Designated lead

In every acute hospital there should be clearly defined mechanisms, coordinated by a designated lead for the trust (see Table 6), for referring all patients with suspected primary CNS tumours to the neuroscience MDT. These should ensure that clinical summaries for discussion and imaging scans of all patients with suspected primary CNS tumours are sent as soon as possible for review.

Table 6. Designated lead

The designated lead should coordinate care at a trust level for all the hospitals within that trust. It is likely to be the role of the trust cancer lead clinician at the hospital or delegated to an appropriate consultant colleague. He or she is NOT clinically responsible for the individual patients, but should ensure that mechanisms are in place for the following:

- Receipt and management/processing of general practitioner referrals of patients with suspected CNS tumours
- Direct referral of patients to the neuroscience, spinal cord, pituitary or skull base MDTs as appropriate
- Availability of imaging scans and reports concerning suspected CNS tumours to the neuroscience MDT from radiology departments
- Timely communication between hospital clinicians, the neuroscience MDT and the cancer network MDT where these exist as separate teams
- Implementing actions within the trust arising from audits relevant to this component of the patient pathway

Multidisciplinary teams

Designated coordinator

Each neuroscience MDT should have a designated coordinator whose responsibilities include obtaining the imaging scans of patients with CNS tumours from radiology departments in their catchment area. In addition, the designated coordinator should obtain clinical summaries requested by the neuroscience MDT lead clinician (see Table 11).

MDT lead clinician

The neuroscience MDT lead clinician should ensure that processes are in place for obtaining information about patients with CNS tumours directly from the clinician who arranged the imaging, if this is not forthcoming.

Neuroscience brain and other CNS tumours MDT

The responsibilities and membership of the neuroscience MDT should be as defined in Tables 7 and 8, respectively.

All specialist neurosurgeons treating patients with CNS tumours should be core members of the neuroscience brain and other CNS tumours MDT (see Table 8).

The neuroscience MDT (see Tables 7 and 8) should review the case history and images and suggest a management plan which should be communicated back to the appropriate consultant. This plan might suggest referral of the patient for neurosurgical or oncological management or continuing care locally.

The neuroscience MDT should meet at weekly intervals to review all new patients and advise on the initial management of their disease in accordance with national cancer waiting times standards. If emergency intervention is necessary on clinical grounds, particularly out of hours, this should proceed according to agreed protocols prior to discussion by the neuroscience MDT. The operating surgeon should present these patients to the next available neuroscience MDT for discussion and referral, if necessary, to an appropriate core member. Patients reviewed and discussed previously should be referred back to the neuroscience MDT by the cancer network MDT for advice on further surgery or specialist interventions on relapse, according to agreed protocols.

The neuroscience MDT, in collaboration with the cancer network MDT, should develop, regularly review and audit evidence-based protocols for the management of patients with CNS tumours.

Following surgery or a decision by the neuroscience MDT that surgery would be inappropriate, continuing management and specialist supportive care should be provided according to protocol under the supervision of the cancer network MDT.

There may be some frail patients in whom active medical intervention is not considered appropriate. After review of the imaging scans and clinical summary at the neuroscience MDT, these patients should not be seen at the neuroscience centre but referred to the cancer network MDT to arrange appropriate assessment locally by a member of the MDT.

Clinical nurse specialist

Clinical nurse specialists should be core members of the neuroscience brain and other CNS tumours MDT and the cancer network brain and other CNS tumours MDT, and may need to work across several geographical sites. They are likely to take on the role of key worker for many patients, especially during the early stages of their clinical care, providing supportive care, information and continuity of care with other healthcare professionals.

Key worker

All patients should have a clearly identified key worker⁸ as nominated by the neuroscience or cancer network MDT.

The key worker should promote continuity of care and manage transitions of care. This is achieved by assessing patients' needs, ensuring care plans have been agreed with patients and that findings from assessments and care plans are communicated to others involved in a patient's care. Coordination of care across the patient pathway should also include ensuring referral of patients to the appropriate multidisciplinary services at any time.

The key worker should ensure that patients, their relatives and carers know whom to contact when help and advice is needed. The key worker is likely to be the clinical nurse specialist or AHP most closely involved with a patient's care.

The key worker role should be transferred to the most appropriate healthcare professional, for example a neurosurgeon, neurologist, GP, community nurse, AHP or palliative care team member, as the patient's needs change, or at transitional points in the patient pathway, for example a neuroscience centre, oncology/radiotherapy centre or community.

The patient, their relatives and carers, should be informed of who their key worker is and how their key worker may be contacted.

Cancer network brain and other CNS tumours MDT

The responsibilities and membership of the cancer network MDT should be as defined in Tables 9 and 10, respectively.

The cancer network MDT (see Tables 9 and 10) should meet at least monthly to coordinate care for 5–15 new patients and to monitor the ongoing care of approximately 50–100 patients on follow-up.

⁸ Department of Health (2004) *Manual for cancer services. Topic 2A The generic multidisciplinary team*. London: Department of Health. Available from: www.dh.gov.uk

Table 7. Neuroscience brain and other CNS tumours MDT – responsibilities

The neuroscience MDT is the team responsible for the diagnosis and initial management (both surgical and non-surgical aspects of care) of most adult patients with CNS tumours. Membership of this team is summarised in Table 8, and its responsibilities include the following:

- Establish a diagnosis for the optimal clinical management of the patient
- Develop management plans for patients with CNS tumours at first presentation, to include initial supportive care needs, diagnostic and surgical interventions, non-surgical oncology interventions, treatment of symptoms and follow-up
- Nominate and record a key worker to act as point of contact for patients, their relatives and carers. This should be agreed with the patient, their relatives and carers
- Agree who is responsible for implementing the next stage of the management plan
- Inform the diagnostic clinician/team at the local referring hospital and GP of the management plan (see communication below)
- Inform the cancer network MDT of the management plan (usually via a representative who is a member of the neuroscience MDT and also in writing)
- Review and advise on patients referred back from the cancer network MDT on disease progression or relapse
- Develop MDT protocols, in collaboration with the cancer network MDT, to define appropriate follow-up imaging requirements for patients with CNS tumours
- Implement the national management protocols for CNS lymphoma, medulloblastoma, pineal tumours and optic gliomas (see Chapter 7)

Table 7. Continued

- Act as an educational resource for local service providers
- Develop and maintain evidence-based local management protocols covering all aspects of the patient pathway
- Participate in regular site-specific group meetings to review care pathways and protocols
- Introduce and maintain systems for data entry across the area of service provision including links to cancer registries
- Audit practice against this guidance and other national guidelines as they are published
- Facilitate the entry of patients into appropriate National Cancer Research Network (NCRN) and local clinical trials
- Liaise with the cancer network MDT

Lead clinician responsibilities

- Ensure that processes are in place for obtaining information about patients directly from the clinician who arranged the imaging, if this is not forthcoming
- Refer onwards patients with spinal cord, pituitary or skull base tumours if inappropriately referred to this MDT

Table 8. Core membership of the neuroscience brain and other CNS tumours MDT*

| MDT member | Description |
|---|---|
| Neurosurgeon(s) | A specialist neurosurgeon who spends at least 50% of his or her clinical programmed activities in neuro-oncological surgery and is regularly involved in dedicated specialty clinics caring for these patients |
| Neuroradiologist(s) | A consultant radiologist in a substantive post with at least 50% of clinical programmed activities spent in the practice of neuroradiology |
| Neuropathologist(s) | An accredited pathologist who is registered as a neuropathologist or histopathologist, has specialist expertise in neuro-oncology, and takes part in the national External Quality Assurance scheme for neuropathology organised by the British Neuropathological Society |
| Neurologist(s) | A consultant neurologist with expertise in neuro-oncology, epilepsy or neuro-rehabilitation |
| Oncologist(s) | A clinical oncologist with a special interest in tumours of the CNS |
| Clinical nurse specialist(s) | A nurse with specialist knowledge of CNS tumours and skills in communication as defined by the 'Manual for cancer services' ⁹ |
| Palliative care | A healthcare professional (normally a member of the specialist palliative care team) with experience and expertise in the provision of palliative care services for patients with CNS tumours |
| Neuropsychologist(s) | A clinical neuropsychologist with a special interest in tumours of the CNS |
| Specialist AHP(s) | Representative(s) of the allied health professions, including occupational therapy, physiotherapy, speech and language therapy, dietetics and others as appropriate, who have knowledge and experience of dealing with this patient group, with responsibility for education and liaison with other local specialist AHPs |
| Coordinator(s) | An administrative post responsible for coordinating patient registration with the neuroscience MDT and data collection |
| Others as required (extended MDT members) | For example, representatives from ward nursing, community palliative nursing, psychology/psychiatry, neuropsychiatry and epilepsy nurse specialists |

*Appropriate cross-cover should be available for all MDT members.
AHP, allied health professional.

⁹ Department of Health (2004) *Manual for cancer services. Topic 2A The generic multidisciplinary team 2A-122 to 2A-127*. London: Department of Health. Available from: www.dh.gov.uk

**Table 9. The cancer network brain and other CNS tumours
MDT – responsibilities**

The cancer network MDT is the coordinating team for the non-surgical management of most adult patients with CNS tumours. Membership of this team is summarised in Table 10, and its responsibilities include the following:

- Implement the non-surgical aspects of the management plan produced by the neuroscience MDT
- Nominate and record a key worker to act as point of contact for patients, their relatives and carers. This should be agreed with the patient, their relatives and carers
- Agree who is responsible for implementing the next stage of the management plan
- Ensure that there are systems in place for the continuous assessment of the needs of patients, their relatives and carers, and provide or ensure provision of appropriate support
- Re-refer patients to the neuroscience MDT where appropriate, as defined in local protocols
- Inform the local referring hospital and general practitioner of the current management plans
- Involve the local referring hospital or community services in continuing, palliative and supportive care where appropriate, and provide specialist advice to local healthcare professionals when needed
- Develop MDT protocols, in collaboration with the neuroscience MDT, to define appropriate follow-up imaging requirements for patients with CNS tumours
- Act as an educational resource for local service providers
- Develop and maintain evidence-based local management protocols covering all aspects of the patient pathway
- Participate in regular site-specific group meetings to review pathways of care and protocols
- Maintain data entry across the area of service provision
- Audit practice against this guidance and other national guidelines as they are published
- Facilitate entry of patients into appropriate NCRN and local clinical trials
- Liaise with the neuroscience MDT

Table 10. Core membership of the cancer network brain and other CNS tumours MDT*

| MDT member | Description |
|---|---|
| Neurologist(s) | A consultant neurologist with expertise in neuro-oncology, epilepsy or neuro-rehabilitation |
| Radiologist(s) | A radiologist with a specialist interest in CNS imaging |
| Radiographer(s) | A therapy radiographer with a special interest in patients with CNS tumours who has dedicated time allocated to participate in the local MDT |
| Oncologist(s) | A clinical oncologist with a special interest in tumours of the CNS and who is the designated neuro-oncologist for the cancer network |
| Clinical nurse specialist(s) | A nurse with specialist knowledge of CNS tumours and skills in communication as defined by the 'Manual for cancer services' ¹⁰ |
| Palliative care | A healthcare professional (usually a member of the specialist palliative care team) with experience and expertise in the provision of palliative care services for CNS tumour patients |
| Specialist AHP(s) | Representative(s) of the allied health professions, including occupational therapy, physiotherapy, speech and language therapy, dietetics and others as appropriate who have knowledge and experience of dealing with this patient group, with responsibility for education and liaison with other local specialist AHPs, who participate in MDT meetings |
| Coordinator(s) | An administrative post coordinating the MDT meeting and collecting/collating and recording appropriate information through clinicians, radiology and the neuroscience and cancer network MDTs |
| Others as required (extended MDT members) | For example, epilepsy nurse specialists, and representatives from ward nursing, community palliative nursing, epilepsy nurse specialist, psychology/psychiatry, neuropsychology/neuropsychiatry |

*Appropriate cross-cover should be available for all MDT members.
AHP, allied health professional.

¹⁰ Department of Health (2004) *Manual for cancer services. Topic 2A The generic multidisciplinary team 2A-122 to 2A-127*. London: Department of Health. Available from: www.dh.gov.uk

Communication between MDTs

Good communication is essential for the smooth and effective provision of services and should be a standard of care.

Communication episodes and expected timescales are summarised in Table 11.

Table 11. Communication framework

| Communication episode | Expected timescale |
|--|---|
| Logging of patients with a possible diagnosis of CNS tumour onto neuroscience MDT data base | Within 1 week of imaging report date |
| Clinical summary from the diagnosing clinician received by the neuroscience MDT | Within 2 working days of the imaging report |
| Written summary of the proposed management plan produced by the neuroscience MDT sent back to the referring clinician, cancer network MDT and GP | Within 1 working day of the MDT |
| Informing the patient, their relatives or carers of diagnosis and management plan | Within 1 working day of MDT for inpatients Within 5 working days for outpatients |
| Referral to the rehabilitation and supportive care services and palliative care team where appropriate | Within 1 working day of the decision |
| Referral to the cancer network MDT for further management | Within 2 working days of discharge from neurosurgical care |
| Discussion of key worker appointment and their role with patient, their relatives and carers | Within 1 working day of MDT for inpatients Within 5 working days for outpatients |
| Referral back to the neuroscience MDT for further management | Within 1 working day of decision |

CNS, central nervous system; GP, general practitioner; MDT, multidisciplinary team.

B. Anticipated benefits

The establishment of neuroscience MDTs, the appointment of a designated lead clinician at each trust and the development of clear mechanisms for review of imaging and referral of patients will increase the speed of referral and ensure that all patients are discussed at a specialist MDT, whether or not they need specialist intervention.

A fully staffed neuroscience MDT that meets regularly and discusses all relevant patients will improve diagnostic accuracy, as well as the speed and quality of management decisions.

A fully staffed cancer network MDT will ensure that the ongoing treatment, care and support for patients are properly coordinated and that the patients' needs are regularly assessed.

C. Evidence

The management of patients with CNS tumours requires a range of disciplines (see Chapters 2–9) and the survey carried out to inform the guidance revealed that many neuroscience centres have established MDTs. Evidence for the optimal configuration of the MDT for CNS tumours, however, is limited to expert opinion and consensus-based guidelines.

There is limited evidence to support MDTs for the management of patients with other types of cancer; in a review conducted for the NHS Executive 'Improving outcomes in breast cancer', multidisciplinary breast cancer teams were more likely to provide appropriate diagnosis and treatment.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance.

D. Measurement

Structure

- designated lead clinician
- neuroscience and cancer network MDTs established
- support staff in place for every MDT
- rapid and effective communication systems between local hospitals and the neuroscience MDT to the time standards identified (see above)
- establishment of Internet-based database for central data collection

Process

- numbers of neurosurgeons, neuropathologists, pituitary surgeons and neuroradiologists
- referral patterns for CNS tumours
- current information and audit of diagnosis and treatment
- protocols in place and whether they are agreed across the pathway
- relationship between different specialties involved in diagnosis and/or management of patients with CNS tumours, for example, ophthalmology
- staffing and configuration of existing MDTs
- evidence that every patient with a diagnosis of CNS tumour is registered with the neuroscience MDT
- evidence that a clinical summary is sent to the neuroscience MDT for all patients with a radiological diagnosis of CNS tumour
- audit agreed and reviewed over whole network

Outcome

- all patients with a presumptive diagnosis of CNS tumour are reviewed by the neuroscience MDT
- evidence that MDTs audit treatment interventions against MDT decisions
- record of each member's attendance at MDT meetings
- record of business carried out (including patients discussed and decisions made) at MDT meetings
- logging of patients with imaging suspicious of brain tumour

E. Resource implications

Neuroscience MDTs

The estimated annual employment costs per neuroscience centre for full attendance at weekly neuroscience MDT meetings is between £140,660 for a 2-hour meeting and £188,084 for a 3-hour meeting. This estimate is based on the employment cost for all core members plus preparation time for members including lead clinicians, key workers and MDT coordinators. However, with the exception of the MDT coordinator (who attends 100% of the MDT meetings), if other MDT members attend only the minimum of 50% of the MDT meetings the annual employment cost would be between £73,320 and £97,370 for a 2-hour and 3-hour meeting, respectively.

It is anticipated that for those networks without a neuroscience MDT in place, there will be an additional annual opportunity cost of between £73,320 for minimum attendance at weekly 2-hour neuroscience MDT meetings and £188,084 for full attendance at weekly 3-hour MDT meetings. For those neuroscience centre MDTs that currently meet fortnightly, moving to weekly MDT meetings will have an estimated annual opportunity cost of between £70,330 and £94,042 for a 2-hour and 3-hour meeting, respectively. For those networks that currently meet monthly, moving to weekly MDT meetings will have an estimated annual opportunity cost of between £108,200 and £144,680 for a 2-hour and 3-hour meeting, respectively.

Not all MDTs have the full complement of consultants, AHPs, nurse specialists and palliative care specialists attending regular meetings. The opportunity cost implications for those centres with these additional staff attending neuroscience MDT meetings where required would vary from £4160 (palliative care specialist) to £16,224 (consultant), depending on the duration of the meeting and the specialty required.

Additional staffing required to support the guidance, together with minimum staffing for neuroscience centres, is discussed in the resource implications of Chapter 5 and in more detail in section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance.

Cancer network MDTs

The estimated annual employment cost for each cancer network MDT, for full attendance at monthly MDT meetings, is between £13,332 for a 1-hour meeting and £18,336 for a 2-hour meeting. This estimate is for all core members plus preparation time for members including lead clinicians, key workers and MDT coordinators. However, with the exception of the MDT coordinator (who attends 100% of the MDT

meetings), if other MDT members attend only the minimum of 50% of the MDT meetings the annual employment cost would be between £7266 and £9858 for a 1-hour and 2-hour meeting, respectively.

It is assumed that there are no cancer network MDTs at present, therefore this represents an additional opportunity cost of between £7266 per year for minimum attendance at monthly 1-hour MDT meetings and £18,336 per year for full attendance at monthly 2-hour MDT meetings for each cancer network. In practice, some networks may choose to combine MDT provision across networks, for example where neuro-oncology patients are referred into a neighbouring cancer network for treatment. Where neuroscience and cancer network MDT co-locate and membership overlaps, the costs will be significantly less.

MDT coordinators

It is estimated that each neuroscience MDT will require one full-time MDT coordinator and each cancer network MDT will require a 0.5 full-time equivalent (FTE) MDT coordinator. The employment cost of a full-time MDT coordinator is estimated to be £22,582 per annum (Agenda for Change point 16, 2005/06 payscale).

The total number of additional MDT coordinator posts required are uncertain. If each of the 37 cancer networks in England and Wales required 0.5 FTE post for a cancer network MDT, the maximum additional annual employment cost for MDT coordinators is estimated to be £417,767. In practice, some networks may choose to work together and combine services, for example where neuro-oncology patients are referred into a neighbouring network, so the actual costs of additional MDT coordinator posts for cancer network MDTs is likely to be less than this estimate.

There will be uncertainty in our estimates reflecting variation in staffing levels and actual salaries paid to individuals. Local commissioners will need to consider this further according to their existing patterns of work.

Key worker

The resource implications of each patient having a designated key worker have been included in the cost estimate for minimum core staffing levels at neuroscience centres to provide a safe and sustainable service. Further details are discussed in section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Presentation and referral

This chapter primarily refers to the services for patients with primary brain tumours. This is partly because these patients constitute the largest proportion of patients with central nervous system (CNS) tumours, and partly because aspects of services for those with other CNS tumours are dealt with in specific chapters later on in the guidance. However, the organisational arrangements that are recommended will also be relevant to many patients with other CNS tumours.

The symptoms associated with brain tumours include headaches, seizures, changes of mental, psychological or mood states, unilateral deafness and progressive neurological deficit. All of these symptoms are common in general practice. On average, a general practitioner (GP) may expect to see one adult with a primary brain tumour in 7 years (data from needs assessment conducted for this guidance).¹¹

The aim of the referral process is to ensure early access to imaging for people most likely to have brain tumours. The more disabled a patient with a brain tumour is at presentation, the worse the prognosis, so early diagnosis is important. However, this does pose a dilemma in that diagnostic services are limited and referrals need to be prioritised. The combination of new neurological symptoms with new neurological signs is more suggestive of pathology than symptoms alone. The combination of new neurological symptoms in any patient with a past history of cancer is suggestive of metastatic disease and needs to be referred back as a priority to the original team treating the patient.

The National Institute for Health and Clinical Excellence (NICE) 'Referral guidelines for suspected cancer'¹² make specific recommendations for the referral of patients with suspected brain or other CNS tumours. Implementation of these guidelines should help professionals and agencies providing first contact care to identify

¹¹ Humphreys C (2005) *Health needs assessment: adults with tumours of the brain and central nervous system in England and Wales*. National Public Health Service for Wales, Gwasanaeth Iechyd Cyhoeddus Cenedlaethol Cymru. Available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

¹² National Institute for Health and Clinical Excellence (2005) Referral guidelines for suspected cancer. *NICE clinical guideline* no. 27. Available from: www.nice.org.uk/CG027

those adult patients more likely to have a high-grade tumour. Such professionals and agencies include GPs, nurse practitioners, ophthalmic practitioners, out-of-hours services, NHS Direct and clinicians in accident and emergency departments. The advice for managing children and young people with these conditions has been addressed separately in the NICE guidance 'Improving outcomes in children and young people with cancer'.¹³

It is important that there are explicit local arrangements whereby GPs can access appropriate advice or diagnostic tests.

Many patients who are eventually diagnosed with a primary brain tumour will have been referred for investigation of problems not initially thought to be tumour related or be admitted as an emergency with an acute neurological problem such as epilepsy and stroke. Hospital staff who care for these patients need to be aware of how they access the appropriate advice.

A. Recommendations

Primary care trusts/local health boards should ensure appropriate training is provided for implementation of the NICE clinical guidelines on 'Referral guidelines for suspected cancer'¹⁴ as they apply to CNS tumours. This provision should include the new forms of primary care contact such as NHS Direct, walk-in centres, nurse practitioners and health visitors, and the use of relevant information technology (IT) links. The contents of the guidelines should be incorporated into electronic decision support systems/algorithms used in such settings.

Cancer networks should ensure that the trust lead clinician has set up clear and well-publicised mechanisms for the receipt and management/processing of GP referrals of patients with suspected primary brain tumours. There should be similar mechanisms for the management of internal referrals.

Where a brain tumour is identified on imaging requested by the GP, the trust lead clinician should ensure that processes are in place for the GP to be informed quickly, allowing early referral through local arrangements.

¹³ National Institute for Health and Clinical Excellence (2005). Improving outcomes in children and young people with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsyp

¹⁴ National Institute for Health and Clinical Excellence (2005) Referral guidelines for suspected cancer. *NICE clinical guideline* no. 27. Available from: www.nice.org.uk/CG027

Cancer networks should set up robust local mechanisms to ensure that every patient with imaging that suggests a diagnosis of CNS tumour is discussed by the neuroscience MDT without delay (see Table 11). This is to ensure that radiological diagnosis is confirmed and advice on further management can be given, regardless of the source of the initial referral or possible need for specialist treatment.

Radiological images sent to the neuroscience MDT should be supplemented by clinical information provided either by the consultant responsible for the patient's care or by a member of the MDT who has seen the patient. There should be prior review of all images by the participating neuroradiologist(s) who should have sufficient time to provide an unhurried professional opinion for the MDT meeting. The opinion given should be annotated on the MDT list and retained for future reference.¹⁵

B. Anticipated benefits

Prompt identification of patients whose symptoms are likely to be due to a primary CNS tumour and subsequent rapid referral to a neurologist or appropriate imaging services will minimise delays in diagnosis. This will reduce the level of anxiety for patients, their relatives and carers.

Explicit systems for managing patients with radiological imaging showing a possible primary CNS tumour should reduce the time taken to review by the neuroscience MDT and to the start of appropriate management. Overall diagnostic accuracy will also be increased.

C. Evidence

A review of the evidence on factors influencing delays in referral and diagnosis in the NICE guidelines 'Referral guidelines for suspected cancer'¹⁶ showed that there was insufficient evidence to make statements on the reasons for delay between the onset of symptoms and referral from primary to secondary care.

Evidence from observational and qualitative studies identified both patient/carer and physician factors that contribute to diagnostic delays.

¹⁵ Board of the Faculty of Clinical Radiology and Royal College of Radiologists (2005) *Cancer multidisciplinary team meeting – standards for clinical radiologists*. London: Royal College of Radiologists. Available from: www.rcr.ac.uk

¹⁶ National Institute for Health and Clinical Excellence (2005) *Referral guidelines for suspected cancer*. NICE clinical guideline no. 27. Available from: www.nice.org.uk/CG027

The evidence confirms that early symptoms of CNS tumours mimic common and self-limiting conditions in adults.

There is a low volume of observational study evidence on the effect of delays in diagnosis on outcomes such as survival. One retrospective, population-based study from a UK cancer registry observed that in patients with CNS tumours, planning radical treatment in patients with good prognosis took longer than planning palliative treatment in patients with poor prognosis. In patients with high-grade glioma, survival was significantly shorter for patients treated within a month of referral, which was attributed to the observation that patients with more urgent symptoms and poorer prognosis necessitated urgent referral and treatment.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurements

The following should be subject to regular audit.

Structure

- evidence of a designated lead clinician in every acute trust
- evidence that fully staffed MDTs are established in appropriate neurosciences centres and in each cancer network
- local protocols for referring patients to the neuroscience and cancer network MDT, and for image and information transfer

Process

- staff attendance at MDT meetings
- time between first presentation to the GP with possible symptoms of primary CNS tumour and referral by the GP to secondary care or to the neuroradiologist for imaging (GP delay)
- time between GP referral and first image suggestive of a CNS tumour (hospital plus imaging delay)
- for brain imaging, time between request and imaging procedure (by source of request) (imaging delay)

- time between imaging and referral to the neuroscience MDT (MDT referral delay)
- time between imaging and pathological diagnosis (surgical delay)
- time between GP referral and first surgical treatment (that is, first treatment, for example steroids + biopsy or steroids + resection) (Cancer Audit Standard A [surgical])
- time between neuroscience MDT and appropriate feedback to referrers and to the GP (neuroscience MDT communication delay)
- time between surgery (pathological diagnosis) to start of radiotherapy (radiotherapy delay)
- time between GP referral and first radiotherapy treatment (Cancer Audit Standard B [radiotherapy])
- audit of all communication targets in Table 11

E. Resource implications

No resource implications were identified as a result of these recommendations.

Diagnosis: radiology and pathology

The establishment of an accurate diagnosis to inform management decisions is a key element in the care pathway for patients with brain and other central nervous system (CNS) tumours. This usually involves neuroradiological imaging and histopathological evaluation following biopsy or tumour resection. Other laboratory tests, such as for germ cell tumour markers, occasionally have a role in specific situations. Molecular analysis will increasingly be used alongside histopathological evaluation to characterise CNS tumours, providing information about prognosis and therapeutic response, and thereby facilitating patient stratification.

Timely access to the neuroscience brain and other CNS tumours multidisciplinary team (MDT), defined in Chapter 2, is needed to discuss potential diagnoses and to ensure that patients are actively considered for the full range of investigations and treatments.

Neuroradiological imaging is central to the diagnostic process because this is when the diagnosis of a tumour is raised or confirmed. Radiology departments are in a unique position to identify the majority of patients with potential CNS tumours. Delays may occur because of competing demands on imaging services. Despite an increase in equipment during the past few years there is still unmet need, partly because of difficulties in funding and recruiting staff. Even if these are resolved, there will continue to be a significant number of patients who present with advanced disease as an emergency.

Magnetic resonance imaging (MRI) may remain a limited resource. Therefore, many patients will have computed tomography (CT) as their primary investigation. A CT scan read by a neuroradiologist, or radiologist experienced in CNS imaging, should reliably exclude a tumour in the majority of cases. However, CT may miss early tumours, for example in the temporal lobes. Some patients will have an MRI scan – as an initial investigation or in addition to CT – at the local hospital before referral to the neuroscience MDT. The neuroscience MDT may require an additional MRI to obtain a more definitive diagnosis, discriminate between areas of infarction and tumour, and assist in planning for surgery and radiotherapy.

Many other imaging techniques, including MR spectroscopy, diffusion and perfusion imaging, single photon emission computed tomography (SPECT) and positron emission tomography (PET) may help to identify foci of high-grade tumour prior to surgery, thereby improving the accuracy of histopathological evaluation. Diffusion tensor analysis and MR spectroscopy may be able to distinguish between primary and secondary tumours, and they may also show that the lesion is more extensive than was defined on conventional MRI.

These newer techniques also have the potential to identify specific biopsy sites, aid the planning of surgery, and provide additional information that will inform preoperative discussions between the surgeon and patient about prognosis. However, they cannot replace neurosurgical biopsy and histopathological assessment in making the definitive diagnosis. Currently, neuroradiological imaging has a high sensitivity for identifying a brain tumour, but not for determining the type or grade of tumour, and it may be difficult to distinguish tumour from ischaemic or inflammatory lesions. Thus, histopathological classification of a CNS tumour is regarded as a prerequisite to effective patient management. Occasionally, a diagnosis can be achieved by cytological examination of the cerebrospinal fluid (CSF).

Tissue for histopathology can be obtained either by biopsy or by tumour resection. The decision about which surgical procedure to undertake is based on a presumptive diagnosis made on the neuroradiological imaging features. Potential procedures include stereotactically guided biopsy, neuroradiologically guided needle biopsy, neuroradiologically guided open biopsy (usually in the form of an operation to remove the tumour), endoscopic biopsy and electrophysiologically guided resection.

There should be preoperative discussion between the neurosurgeon, neuropathologist and neuroradiologist regarding the optimum approach to surgery and the processing of tissue specimens, including intraoperative histopathological evaluation.

Intraoperative histopathological evaluation by a specialist pathologist is particularly valuable during needle biopsy and helps to ensure that sufficient and appropriate tissue is obtained for diagnostic purposes. It can also provide information that will influence the course of the operation.

The neuroscience MDT meeting (see Chapter 2) provides a setting in which the histopathological findings are compared with clinical disease features and the results of neuroimaging. The participating neuropathologist might be in a position to issue a definitive diagnosis before the meeting, or to use information provided at this time to direct further tests or to inform a definitive (final) report. The final neuropathology report is regarded as the definitive distillation of information from the histopathological evaluation process informed by discussions held at the neuroscience MDT meeting. Patient management decisions should be made on the basis of the final report which should form part of the patient's record. The process for disseminating the final report should be agreed locally.

Recent translational research on high-grade gliomas has begun to define novel molecular diagnostic tests with clinicopathological utility, such as the association between a profile of loss on chromosomes 1p and 19q and chemosensitivity among anaplastic oligodendrogliomas. Further developments in the use of molecular tests alongside histopathological assessment are to be expected in future.

Even with the benefit of modern histopathological techniques, precise classification of a CNS tumour is not always feasible. In such cases, management decisions are helped by discussion of the clinical, radiological and histopathological disease features at the neuroscience MDT meeting. When a histopathological diagnosis is difficult to make, a system should be in place to facilitate either referral for a second opinion to a CPA-accredited department or double reporting, if appropriate.

A. Recommendations

All acute trusts should have adequate CT and MRI facilities so that investigations of patients with suspected CNS tumours meet cancer waiting time national targets.^{17,18}

An electronic image transfer system should be in place to ensure timely image transfer between the local hospital and neuroscience MDT (see Chapter 3). A function of the MDT meeting should be to determine whether or not further imaging is necessary prior to surgery.

When initial CT imaging is not diagnostic there should be rapid access to adequate MRI resources.

¹⁷ Department of Health (2000) *The NHS plan*. London: Department of Health. Available from: www.dh.gov.uk

¹⁸ Welsh Assembly Government (2005) *Monthly data collection of cancer waiting times to start of definitive treatment*. Welsh health circular 2005 (027). Cardiff: Welsh Assembly Government. Available from: www.wales.nhs.uk

Neuropathology and neuroradiology services should be provided to a level that ensures practitioners in these specialties can deliver appropriate diagnostic investigations in a timely and efficient manner, complying with national cancer waiting times targets, and such that they can be involved in preoperative and postoperative management decisions and intraoperative diagnosis. Neuropathologists should be able to report to the standards detailed in the document 'Minimum dataset for the histopathological reporting of tumours of the central nervous system' (Royal College of Pathologists).¹⁹ Neuroradiologists should be able to report and review examinations to the standards detailed in the document 'Cancer multidisciplinary team meeting – standards for clinical radiologists' (Royal College of Radiologists).²⁰

There should be ready access to a neurosurgical biopsy or resection service, including image localisation and stereotactic techniques. Preoperative discussions should take place at the neuroscience MDT to determine the optimum approach to surgery and the processing of tissue specimens, including intraoperative histological evaluation.

Molecular diagnostic tests will become increasingly important as supplementary investigations to the neuropathological assessment of CNS tumours, informing diagnosis, prognosis and therapeutic decisions. The evaluation, development and implementation of these tests should be supported.

There is a need for improved biological research into CNS tumours; tumour biopsy material, when processed optimally at the time of operation, should be stored for future scientific research, with appropriate consent, as well as for diagnostic purposes.

B. Anticipated benefits

Better access to modern diagnostic radiological, neuropathological and neurosurgical services for CNS tumour patients will improve the speed and accuracy of diagnosis.

Improvements in the nature and scope of radiological, neuropathological and molecular diagnostic tests will result in better-informed clinical management decisions and the ability to offer patients, their relatives and carers, clearer information about the specific diagnosis and prognosis.

¹⁹ The Royal College of Pathologists (2004) *Minimum dataset for the histopathological reporting of tumours of the central nervous system*. London: The Royal College of Pathologists. Available from: www.rcpath.org

²⁰ Board of the Faculty of Clinical Radiology and Royal College of Radiologists (2005) *Cancer multidisciplinary team meeting – standards for clinical radiologists*. London: Royal College of Radiologists. Available from: www.rcr.ac.uk

C. Evidence

There is consistent evidence that MRI is more sensitive than CT in the detection of CNS tumours and gives better definition of tumour extent. Observational studies suggest the specificity of MRI for tumour histology is not sufficient to allow it to replace biopsy.

Individual case series highlight the potential usefulness of new diagnostic imaging technologies, such as MR spectroscopy, diffusion and perfusion imaging, SPECT and PET, in the management of CNS tumours. However, meta-analysis of such studies is problematic because of small sample sizes, non-standardised techniques and differences in study populations.

Two evidence-based technology appraisals of MR spectroscopy for the evaluation of brain tumours reported that there was insufficient high-quality evidence to conclude that MR spectroscopy could replace biopsy in the diagnosis of brain tumours.

There is consensus supporting the usefulness of PET in distinguishing between brain tumour and radiation necrosis. An evidence-based technology appraisal estimated the sensitivity of PET in this context as between 76% and 83%, with specificity between 50% and 62%. The review also estimated the sensitivity of PET for distinguishing high-grade from low-grade gliomas as ranging from 69% to 100%, with specificity from 57% to 100%. However, in the absence of studies directly comparing the accuracy of PET with that of conventional MRI for distinguishing low-grade and high-grade gliomas, it is difficult to estimate whether the addition of PET would improve the preoperative evaluation of tumour grade.

There is a lack of prospective research designed to compare biopsy techniques, with evidence limited to case series describing the morbidity and mortality associated with biopsy. These studies suggest that the risk for additional permanent morbidity from stereotactic or image-directed biopsy is about 4%, with a less than 0.4% risk of death. However, these figures relate to centres carrying out large numbers of biopsies, where more difficult cases may be referred.

Two systematic reviews have compared the outcomes of adults with high-grade gliomas following surgical resection or biopsy. Both were unable to draw firm conclusions, as only one small randomised controlled trial was identified. Observational case series report improved median survival in patients undergoing resection; but these studies are prone to selection bias as patients with better prognosis are more likely to undergo resection.

Consistent evidence supports the usefulness of intraoperative neuropathology to confirm the adequacy of biopsy specimens. A UK-based case series described how the diagnostic rate for stereotactic CT-guided biopsy of intracranial lesions was improved from 87% to 94% by the introduction of intraoperative cytopathology. Two UK audits both showed increased diagnostic yield following stereotactic biopsy if an intraoperative histological procedure was done to confirm that sufficient tissue had been obtained for diagnostic purposes.

Four observational studies examined the accuracy of the intraoperative histopathological and cytopathological diagnosis of CNS tumours. Agreement between intraoperative diagnosis based on frozen sections and the definitive diagnosis was seen in between 87% and 90% of cases. When intraoperative diagnosis was based on both histopathological and cytopathological techniques, accuracy was slightly higher, with 91–94% concordance.

Observational studies suggest that characteristic cytogenetic changes in anaplastic oligodendrogliomas are predictive of chemosensitivity and prognosis, and useful in differential diagnosis. A recent trial identified a potential role for molecular diagnostic testing in predicting the response of patients with glioblastoma to temozolomide.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- access to appropriate imaging equipment (both radiological and pathological) for neuroscience MDTs
- sessional time for neuroradiologists/neuropathologists to attend neuroscience MDT meetings
- provision of adequate resources and staff or demonstrable contingency plans to cope with the estimated demand for biopsy and resectional surgery to reduce the risk of cancellation and waiting times for diagnostic/therapeutic surgery to recommended levels

Process

Audit of:

- waiting times for neuroimaging and biopsy/resection
- proportion of patients with potential CNS tumours identified to the MDT meeting via a referral from the responsible clinician
- percentage of patients being identified to the MDT meeting by review of the imaging reports that identify a potential tumour
- frequency of obtaining a definitive histopathological diagnosis
- turnaround times for neuropathology reports
- number of patients with advanced disease presenting as emergencies.

Outcome

- morbidity and mortality associated with biopsy procedures
- patients', their relatives' and carers' satisfaction with the diagnostic process

E. Resource implications

Government initiatives are underway to improve access to CT and MRI facilities. However, not all of the existing facilities have sufficient staff to keep them fully operational. Based on staffing levels for a dedicated brain and CNS patient scanner, it is estimated that each MRI scanner requires minimum staffing provision of 1.3 full-time equivalent (FTE) consultant neuroradiologists, 3.0 FTE neuroradiographers and additional administrative support. The annual employment costs for this level of staffing per MRI scanner are estimated to be £267,071. There may be some overlap between this estimate and that for the minimum staffing discussed in the resource implications in Chapter 5 (and section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website [www.nice.org.uk/cs/braincns]). Local commissioners will need to investigate current staffing levels and increase staffing where necessary.

Systems to enhance electronic data transfer are being implemented in England and Wales as a result of the National Programme for Information Technology in England and Informing Healthcare in Wales. This will take some time to be fully implemented. Cost estimates for electronic transfer of data have been included for those networks with inadequate provision. The estimated costs for high-quality electronic transfer of data and images, including videoconferencing capability, are around £15,000 (£18,000 inclusive of value-added tax [VAT] and delivery) per centre inclusive of installation, software and a 3-year maintenance contract.

Molecular diagnosis is a fast-developing area of clinical practice, and cancer networks will need to plan for expansion in the next 10–20 years. At present, existing services for molecular diagnosis are adequate for the numbers of patients who require testing. However, if a specific molecular diagnostic test such as the O⁶-methylguanine-DNA methyltransferase (MGMT) assay is introduced, then it is anticipated that an additional biomedical scientist per testing laboratory would be needed. The current annual employment cost of a grade 2 biomedical scientist is around £26,103. The total number of extra staff across the UK would probably be 30 at maximum. There would be an additional cost of around £500,000 for consumables for the estimated 2500 tests that would be expected to be required across England and Wales. The total additional annual cost for 2500 MGMT tests including consumables for the tests and staffing to carry out the tests is estimated at £1,283,090.

Cancer networks will need to monitor the situation and if two more similar molecular tests were to be adopted for CNS tumours over a period of 10 years, then the total costs might double. However, it is not possible to predict the implications of this recommendation; it will be for cancer networks to consider in line with local requirements.

It has been estimated that an additional 15 FTE neuropathologists will be needed across England and Wales with an estimated annual employment cost of around £1,474,208. This is discussed in more detail in the resource implications of Chapter 5 and section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Treatment and follow-up: brain tumours

This chapter covers healthcare services for the more common brain tumours:

- low-grade gliomas
- high-grade gliomas
- meningiomas
- metastases.

5

Treatment

A wide variety of treatments is available for these tumours. Choice between the various options crucially depends on the diagnosis made, either by histopathological evaluation of specimens from biopsy or resection, or by review of the radiological imaging.

Low-grade glioma (WHO grades I and 2)

The natural history of low-grade glioma (LGG) and neuronally based tumours is variable, and the histopathological characteristics of the tumour are the most important determinant of outcome. Imaging is not reliable for determining the grade of a glioma and up to 40% of LGGs diagnosed on imaging are found to have features of high-grade tumour on histopathological evaluation of biopsy material. All patients need to have a confirmed histopathological diagnosis unless the neuroscience brain and other central nervous system (CNS) tumours multidisciplinary team (MDT) decides that performing a biopsy would be too high a risk for the patient or is otherwise inappropriate.

Local protocols agreed by the neuroscience and cancer network brain and other CNS tumours MDTs are required to define those patients managed by watchful waiting or early surgical intervention. The European Organisation for Research and Treatment of Cancer (EORTC) criteria (appendix 3) will help identify those at increased risk of rapid deterioration who may benefit from early intervention. Similarly, local protocols that define those patients requiring radiotherapy should be in place.

The exact role of chemotherapy is uncertain; the research evidence is not strong and the results of recent trials are awaited.

The requirements for follow-up imaging should be decided by the neuroscience MDT in collaboration with the cancer network MDT and defined by the MDT protocol.

High-grade glioma (WHO grades 3 and 4)

High-grade glioma (HGG) includes glioblastoma, anaplastic astrocytomas, anaplastic oligodendrogliomas and anaplastic ependymomas (see Chapter 7 on rare tumours). These are usually associated with a poor prognosis, although some patients with anaplastic oligodendrogliomas and anaplastic astrocytomas have a better outcome than others. Among the important prognostic factors are age, performance status, comorbidity, tumour type and grade, and presence or absence of seizures.

Initial treatment

The main aims of treatment and follow-up are to increase survival while maximising a patient's functional capability and quality of life, and to ensure ready and timely access to appropriate supportive care for patients, their relatives and carers.

The first management decision is to identify whether the patient:

- needs urgent surgical intervention (for example, emergency decompression or shunt insertion for hydrocephalus)
- needs elective surgery to decide the management plan within protocols and guidelines agreed by the MDT
- is fit for any intervention.

The current cancer waiting time targets (in both Wales and England) from general practitioner (GP) referral to first definitive treatment is 2 months, and from diagnosis ('the decision to treat date') to first definitive treatment is 1 month.^{21,22} It is important to emphasise that these targets also apply to patients with CNS tumours, although there may be some patients with rapidly growing tumours and/or worsening symptoms who will need treatment much more quickly.

Some patients in whom tumour growth is very rapid may deteriorate quickly with or without surgical intervention.

Radical radiotherapy may be considered following confirmed histopathological diagnosis. In exceptional circumstances where the neuroscience MDT considers that any surgical intervention would put the patient at an unacceptable risk, radical radiotherapy may be given in the absence of histology.

Adjuvant chemotherapy has been shown to have a small but significant survival advantage and may be considered in some patients after careful discussion according to local protocol.

The use of carmustine implants in combination with surgical resection and of adjuvant postoperative temozolomide in combination with radiotherapy in patients with newly diagnosed HGG is the subject of an ongoing National Institute for Health and Clinical Excellence (NICE) technology appraisal, due for publication in August 2006.²³ Implementation of these and other appraisal recommendations will be considered and used appropriately with the approval of the neuroscience MDT. They will inform the development of a management plan for each patient.

HGGs encompass the brain tumours for which novel molecular diagnostic tests have clinicopathological utility. The development of molecular tests for these and future biological markers that can be used alongside histopathological evaluation has resource implications.

New service developments would require additional resources.

²¹ Department of Health (2000) *The NHS plan*. London: Department of Health. Available from: www.dh.gov.uk

²² Welsh Assembly Government (2005) *Monthly data collection of cancer waiting times to start of definitive treatment*. Welsh health circular 2005 (027). Cardiff: Welsh Assembly Government. Available from: www.wales.nhs.uk

²³ See www.nice.org.uk/appraisals.inprogress

Treatment at relapse

Treatment with chemotherapy may be considered in some patients with HGG. NICE guidance²⁴ recommends that nitrosourea-based chemotherapy be considered following first relapse of HGG in patients who have had surgery and radiotherapy. Temozolomide may then be considered following failure of nitrosourea-based chemotherapy. This technology appraisal guidance on the use of temozolomide for recurrent malignant HGG is scheduled for update in 2006 with publication expected in November 2007.²⁵

Implantable intra-tumoural chemotherapy (carmustine implants) may be useful in some patients at relapse. This is the subject of a NICE health technology appraisal in 2006 with publication expected in November 2007.²⁵ The implementation of these and subsequent recommendations in formulating a management plan for patients with recurrent tumours is the responsibility of the neurosciences MDT.

The use of new approved treatments for patients with CNS tumours may result in increased patient survival and hence an increased demand for supportive care resources, drug monitoring (for example temozolomide) and pharmacy costs (for example carmustine implants). Survival is very poor in elderly, frail patients with comorbidities. Such patients tolerate active intervention poorly and are often best managed with corticosteroids and supportive care only. The role of newer chemotherapies remains uncertain and needs to be the subject of clinical trials.

Meningioma

Meningiomas are tumours arising from the meninges. They most commonly arise in the skull vault and are usually low grade (WHO grade 1) with an indolent course. The commonest presenting symptom is with focal or generalised epilepsy. The wider use of CNS imaging has led to an increase in the incidental discovery of meningiomas.

Management depends on signs, symptoms, the patient's fitness and the site and size of the tumour. Small, incidental meningiomas can be safely managed conservatively, although there is a lack of consensus regarding the optimum follow-up periods. Skull base meningiomas are considered in Chapter 6.

²⁴ National Institute for Clinical Excellence (2001) Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer). *NICE technology appraisal guidance* no. 23. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

²⁵ See www.nice.org.uk/appraisals.inprogress

Resection may be appropriate for patients with skull vault meningiomas. It can prevent further disease progression and the associated deterioration in neurological function although recurrence may occur. Radiotherapy may be considered following histopathological confirmation of the diagnosis in patients with the following features:

- a WHO histopathological grade 2/3 tumour
- invasion by tumour of adjacent brain or extensive invasion of other tissues
- a second or subsequent relapse
- a contraindication to surgery.

Stereotactic radiotherapy and radiosurgery may be useful in selected patients although the value of these approaches is still uncertain. There is no clearly established role for chemotherapy, hormonal therapy and radiolabelled treatments in the management of these patients.

Metastases

Metastases in the brain occur in 20–40% of patients with other primary cancers. Brain metastases are usually associated with a poor prognosis. Most of these patients require appropriate palliative management which may include radiotherapy, chemotherapy or hormone therapy depending on the site of the primary tumour. However, there is a small group of patients needing consideration by a specialist neuro-oncology team:

- Patients presenting with cerebral metastases as the first sign of malignant disease where surgery is required to clarify the diagnosis.
- Patients in whom imaging findings are in doubt following neuroradiological assessment.
- Patients presenting with solitary metastases, who are otherwise fit, with a prognosis that warrants considering neurosurgical intervention.

Complete surgical excision should be considered in patients with single metastases where the risk of unacceptable complications is low. Postoperative radiotherapy following the resection of solitary metastases may reduce the likelihood of intracranial relapse in appropriately selected patients.

Stereotactic radiotherapy can be considered as an alternative to surgery in small lesions (< 3 cm) when the histopathological diagnosis is known. Occasionally it may be considered in patients with more than one lesion. The role of further treatment with radiotherapy to the brain following stereotactic radiotherapy is uncertain, although it may prevent intracranial relapse.

Follow-up

There are difficulties in defining the most appropriate methods and frequency of follow-up in patients with brain tumours. The follow-up required varies between tumour types and will involve a combined approach to symptom management and disease surveillance. The main reasons for clinical assessment and imaging follow-up are to:

- manage any continuing problems, such as epilepsy, resulting from the disease or initial treatment
- diagnose recurrence when symptoms change and refer for appropriate management
- provide access to appropriate information, support and rehabilitation
- provide symptomatic and palliative care
- provide information to patients on new treatments and opportunities to participate in research studies.

Imaging is an integral part of follow-up for patients with brain tumours. There is uncertainty about the value and frequency of follow-up imaging. Ideally it should be reserved for patients in whom the result of the scan is going to alter management. The frequency of scans should then be determined by the MDT. The role of the newer imaging techniques such as positron emission tomography (PET) and single photon emission computed tomography (SPECT) is uncertain.

With regard to patients with LGGs and benign meningiomas, locally agreed protocols for follow-up need to be in place. It is important to identify a key worker (see Chapter 2) who is the main point of contact for the GP, patients, their relatives and carers.

A. Recommendations

The neuroscience MDT should ensure that there are explicit and widely known mechanisms for the urgent management of patients developing acute problems that might require neurosurgical intervention.

The neuroscience MDT (Tables 7 and 8) should be adequately resourced to ensure that all patients start their definitive treatment without delay.

Members of the neuroscience MDT should be responsible for implementing the surgical aspects of the management plan and adjuvant therapy based on neuropathological diagnosis. All other care including chemotherapy, radiotherapy and coordination of supportive care should be the responsibility of the cancer network MDT (Tables 9 and 10).

The neuroscience MDT should be responsible for assessing new treatments and relevant NICE technology appraisals and updates. The patient's management plan defined by the neuroscience MDT should take these into consideration. The final recommendations for treatment should apply the relevant patient factors such as comorbidity when considering these treatments.

The cancer network MDT and the neuroscience MDT should develop locally agreed guidelines for follow-up. There should be robust mechanisms in place to ensure that GPs and community palliative care teams are able to communicate efficiently with the specialist teams as the need arises. Patients, their relatives and carers should be given clear information on whom to contact and how if they are concerned about their condition.

After initial treatment, patients should have follow-up as close to home as possible, with a member of either the neuroscience MDT or the cancer network MDT in a multidisciplinary outpatient clinic setting.

There should be ready access to specialist neuropsychology and neuropsychiatry services for assessment and management of complex cognitive, emotional and behavioural problems. There should also be access to specialist healthcare professionals as appropriate for any other problems patients may experience, such as epilepsy, headaches and functional loss, for example speech, language or visual problems.

The neuroscience MDT should advise on the management of patients presenting with metastases in the brain in whom:

- biopsy is required to clarify the diagnosis

- there is doubt about the imaging findings following neuroradiological assessment
- neurosurgical intervention is considered appropriate.

Stereotactic radiotherapy should be available as an alternative to surgery in patients with a single, small (< 3 cm) metastasis in the brain, or occasionally two small metastases, when the histopathological diagnosis is known.

Novel treatments currently under evaluation should not generally be used outside the context of a clinical trial/research setting.

B. Anticipated benefits

Patients will have faster access to the most appropriate specialist care, whatever the diagnosis. They will also have better access to trained health professionals for support, rehabilitation and management of specific problems such as epilepsy.

Follow-up will be provided in the most appropriate place, balancing the needs for geographical convenience and specialist expertise.

C. Evidence

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Low-grade gliomas

The data supporting the recommendations for surgery are lacking and constitute expert opinion based on retrospective studies. However, there is an association between extent of resection (where this can be done safely) and prolonged survival. There is observational evidence that radiotherapy improves survival in LGG. There is a single randomised controlled trial (RCT) indicating that early radiotherapy delays local relapse compared with radiotherapy at clinical or radiological progression, but does not extend survival. Early radiotherapy is associated with a higher risk of late radiation damage compared with delayed radiotherapy.

High-grade gliomas

One rigorous systematic review concluded that there is insufficient evidence to conclude whether better outcomes arise for patients with HGG following surgical resection compared with stereotactic biopsy, as only one underpowered RCT was identified. Evidence from observational studies is suggestive of an association between extent of resection (where this can be done safely) and prolonged survival.

Radiotherapy has been shown to prolong survival in patients with HGG in four RCTs and one well-conducted systematic review.

In radiotherapy for patients with HGG, evidence to support the use of a localised treatment to spare as much normal brain tissue as possible is provided by one RCT. This study compared whole-brain radiotherapy (WBRT) with low-dose brain radiotherapy plus a boost local to the tumour and found no significant survival difference between the groups.

Dose escalation beyond 60 Gy has not been shown to be beneficial and neither brachytherapy nor stereotactic boost have been shown to confer benefit. A well-conducted systematic review found that seven of eight randomised studies of hyperfractionated versus conventionally fractionated radiotherapy demonstrated no significant survival benefit of hyperfractionated radiotherapy.

Chemotherapy in an adjuvant setting has been the subject of a recent, high-quality meta-analysis. The meta-analysis included 12 RCTs, representing numerous chemotherapy regimens and demonstrated a 2-month median survival advantage for chemotherapy plus radiotherapy compared with radiotherapy alone (hazard ratio [HR] 0.85; 95% confidence interval [CI] 0.78 to 0.91; $p = 0.00004$) and a 5% increase in 2-year survival.

Single-agent versus multiple-agent chemotherapy in patients with high-grade astrocytoma was studied in a meta-analysis of nine RCTs. The meta-analysis found no significant difference in the odds of survival at 1 year between patients treated with radiotherapy plus single-drug chemotherapy and patients treated with radiotherapy plus combination chemotherapy (odds ratio [OR] 1.22; 95% CI 0.99 to 1.36).

A recent, well-conducted RCT demonstrated benefit from concurrent and adjuvant chemotherapy with temozolomide and radiotherapy, compared with radiotherapy alone, in improving median survival by 2.5 months (HR 0.63; 95% CI 0.52 to 0.75; $p < 0.001$) and a 16% increase in patients surviving at 2 years.

Three double-blinded RCTs demonstrated improved survival following the use of surgically implanted carmustine wafers compared with placebo wafers in patients with HGG. One RCT included 222 patients with recurrent HGG requiring re-operation. Median survival of patients in the carmustine group was 31 weeks compared with 23 weeks for the placebo group with a 33% reduction in risk of death in the carmustine group during the study period (HR 0.67, 95% CI 0.51 to 0.90, $p = 0.006$). In a second RCT of 32 patients undergoing primary surgical resection, median overall survival was 58.1 weeks for the carmustine group compared to 39.9 weeks for the placebo group ($p = 0.012$). In a third RCT of 240 patients undergoing primary surgical resection, median survival was 13.9 months in the carmustine group and 11.6 months in the placebo group ($p = 0.03$), with a 29% reduction in risk of death in the carmustine group during the study period (HR 0.71, 95% CI 0.52 to 0.96).

The effect of temozolomide on recurrent malignant HGG was the subject of *NICE technology appraisal guidance* no. 23 published in 2001.²⁶ This guidance will be updated in 2006/7. The effect of both carmustine implants and temozolomide treatment on patients with newly diagnosed HGG is the subject of an ongoing NICE health technology appraisal due for publication in August 2006.²⁷

There are numerous case reports of palliative chemotherapy although the optimum regimen has not yet been established.

Anaplastic oligodendrogliomas are more frequently responsive to chemotherapy than astrocytomas. Observational study evidence suggests that in patients with oligodendroglioma, demonstration of chromosome 1p/19q loss of heterozygosity not only predicts response to chemotherapy but also survival.

Meningiomas

No RCTs to guide the management of these tumours were identified. Evidence from case series describes the population, and can be used to suggest a safe population for watch and wait and to indicate the safety of surgery.

The role of radiotherapy has been explored in a number of case series but none had sufficient follow-up for conclusions to be drawn.

²⁶ National Institute for Clinical Excellence (2001) Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer). *NICE technology appraisal guidance* no. 23. London: National Institute for Clinical Excellence. Available from: www.nice.org.uk

²⁷ See www.nice.org.uk/appraisals.inprogress

Metastases

A systematic review and an evidence-based guideline each compared surgical resection and WBRT with WBRT alone in selected patients with a single brain metastasis. No significant difference in overall survival was noted in a meta-analysis of three RCTs. Improved functionally independent survival was seen in patients receiving surgical resection and WBRT in the single RCT that included this outcome.

One of the reviews considered the issue of stereotactic biopsy of presumed solitary brain metastases before initiation of treatment and identified two primary studies. In one study of patients with a known systemic malignancy and a CT scan reported as being consistent with a single brain metastasis, 11% of patients were diagnosed as having either primary brain tumours or non-neoplastic lesions following biopsy. The authors concluded that all patients should undergo biopsy. However, a second study reported the rate of MRI misdiagnosis in patients undergoing surgical resection of presumed solitary brain metastases as 2%.

An RCT comparing WBRT plus stereotactic radiosurgery boost with WBRT alone in patients with one to three brain metastases found no significant difference in the median overall survival or performance status of the two treatment groups. However, in patients with a single metastasis a stereotactic radiosurgery boost was associated with improved median overall survival on univariate analysis, and this benefit approached significance on multivariate analysis.

Evidence comparing surgical resection with stereotactic radiosurgery for patients with a solitary brain metastasis was limited to a retrospective case series. The study did not observe an overall survival difference between the treatment groups, but noted improved local control in patients treated using stereotactic radiosurgery.

It remains uncertain whether WBRT is really necessary after resection of a single brain metastasis. Although WBRT may reduce likelihood of further brain metastases, it may also be associated with radiation-related CNS toxicity.

An evidence-based guideline comparing WBRT with supportive care alone in patients with multiple brain metastases identified a single RCT. Median survival was 14 weeks in the WBRT compared with 10 weeks in the supportive care group (p value not stated) with similar improvements in performance status seen in both groups. Patients in both groups received oral corticosteroids.

Hospital case volume and patient outcome

Consistent observational evidence suggests a positive relationship between hospital case volume and perioperative outcome following neurosurgery. A large population-based American study noted postoperative mortality following craniotomy for CNS tumour resection was significantly lower in hospitals with high case volumes, and for surgeons with high case volumes. Similar findings were reported in a study of mortality in patients undergoing craniotomy for tumour in 33 American acute care hospitals and in a population-based study of craniotomy for the resection of metastatic brain tumours. A positive association between case volume and patient outcome was reported in a study of mortality and morbidity following surgical removal of primary brain tumours in Russia, although case mix adjustment was not made in this study. Two American studies reported that perioperative mortality after surgery for cerebral aneurysm was significantly lower in higher-volume hospitals and for higher-volume surgeons.

Evidence reviewed, for example in the NICE guideline 'Improving outcomes in colorectal cancer', suggests that for complex or high-risk cancer surgery outcomes are better in higher-volume hospitals.

Place of care

A report by Northern and Yorkshire Cancer Registry compared the survival of patients with CNS tumours (HGG, LGG or meningioma) treated at three specialist neuroscience centres with those managed elsewhere, in the period 1986–94. Although in a simple comparison survival was better for those treated in neuroscience centres, patients with very poor prognosis tended not to be referred for neurosurgery. When patient age and treatment factors were adjusted for, there was no significant difference in survival between those referred to the neuroscience centres and those treated elsewhere.

The Glioma Outcomes Project examined patterns of care and survival in 565 American patients with HGG. In a case-mix-adjusted analysis, patients treated in academic institutions did not have improved survival compared with those treated elsewhere. In a univariate comparison, survival was better for those treated in academic centres. The authors concluded that the survival difference reflected the increased use of chemotherapy and radiotherapy at academic centres, and the younger age of patients referred to such institutions.

Subspecialisation in neurosurgery

A Scottish observational study compared the survival of a series of 168 patients with HGG treated by a specialist surgical neuro-oncologist with 68 patients treated by non-specialist neurosurgeons. No survival difference was seen in a case-mix-adjusted comparison.

A small retrospective audit of surgery for intracranial aneurysm in a UK neurosurgery department noted that there was less morbidity and mortality and better patient performance status after neurovascular subspecialisation was established in the unit.

An American observational study analysed the correlation between neurosurgical subspecialisation and outcome using data from three clinical trials which included 485 children with medulloblastomas/primitive neuro-ectodermal tumours (PNET) and 247 children with HGGs. Paediatric neurosurgeons were more likely than general neurosurgeons to resect more than 90% of the tumour. No difference was observed in the rates of complications of the paediatric and general neurosurgeons, and survival data were not reported. Evidence for neurosurgical subspecialisation in the treatment of pituitary and skull base tumours is presented in the Chapter 6.

D. Measurement

Structure

- evidence for the establishment of adequately resourced MDTs
- provision of staff and resources to provide an adequate neurosurgical service, including emergency procedures
- access to stereotactic radiotherapy equipment

Process

- time intervals from diagnosis to start of definitive treatment (31 days), especially for HGG patients, in whom the total time from GP referral to definitive treatment should be well within the 62-day target
- number of operations carried out per annum by specialist neurosurgeons and number of new referrals for treatment by clinical oncologists
- the proportions of patients having surgery, radiotherapy and chemotherapy
- entry of patients into clinical trials
- delays to start of radiotherapy
- follow-up imaging

Outcome

- neurosurgical complication rates
- 1-year and 5-year survival rates
- quality of life for patients
- patients', their relatives' and carers' satisfaction

E. Resource implications

The resource implications of the neuroscience MDT and cancer network MDT are presented in Chapter 2. Additional costs will be incurred in some neuroscience centres where the recommended minimum staffing levels to provide a safe and sustainable service are not met.

Core staffing components for brain and other CNS tumour patients at neuroscience centres

To estimate the costs of providing a safe and sustainable service for the care and treatment of patients with CNS tumours, minimum staffing levels have been estimated. The costs represent opportunity costs because the staff involved in the treatment centres are already contracted to the NHS.

The annual employment costs of the core medical, nursing and other staff caring for 100 new patients per year is estimated to be around £1,744,006 (± 25% range, £1,308,005 to £2,180,008). The cost calculations are for the core components of the staff who will be caring for patients with CNS tumours, but it is not inclusive of all staff who would be involved with the patients' care.

There is likely to be an additional requirement for some healthcare professionals, in particular, neuropathologists, clinical nurse specialists, specialist allied health professionals (AHPs), neuropsychologists and palliative care specialists. Additional administrative staff are also required to support the functions of the MDT.

There will be uncertainty in these estimates reflecting variation in staffing levels and actual salaries paid to individuals. Local commissioners will need to consider this further according to their existing patterns of work. Staffing is discussed in more detail in section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Neuropathologists

The increase in MDT working would increase the workload of neuropathologists. A report for the Royal College of Pathologists from the British Neuropathological Society has recommended that there should be one full-time equivalent (FTE) neuropathologist per 1,000,000 population. To achieve this level, a further 15 FTE posts are required across England and Wales with an estimated employment cost of around £1,474,208. There are currently seven single-handed neuropathologists in England and Wales, and these would need to be supported to ensure continual cover of the adult neuro-oncology service in these centres.

Clinical nurse specialists

Based on evidence from the needs assessment²⁸ conducted for this guidance, it has been estimated that an additional 50 clinical nurse specialists will be required across England and Wales with an estimated annual employment cost of around £1,932,346.

Allied health professionals and speech therapists

It has been estimated by members of the Guidance Development Group (GDG) that it is likely an additional 0.5–1 FTE speech and language therapist, occupational therapist and physiotherapist may be needed at each neuroscience centre as a result of the guidance. The employment cost estimate for the three additional AHPs is between £48,726 (1.5 FTE) and £97,453 (3 FTE) per centre. This estimate is uncertain, as it may be that some centres would recruit additional junior staff to enable more experienced staff to concentrate on specialist work.

²⁸ Humphreys C (2005) *Health needs assessment: adults with tumours of the brain and central nervous system in England and Wales*. National Public Health Service for Wales, Gwasanaeth Iechyd Cyhoeddus Cenedlaethol Cymru. Available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Palliative care specialists

The needs assessment²⁹ conducted to inform the guidance development indicated that additional palliative care staff were required at neurosurgical units. To ensure that there are a minimum of 0.4 FTE palliative care specialists available at all neuroscience centres additional staff will need to be recruited. The estimated costs for the neurosurgical centres without palliative care support is estimated to be around £223,848. The employment cost estimate is based on a 40/60 split between palliative care consultants and palliative care nurses. Further investigation will be required at a local level to establish whether palliative care consultants, nurse specialists or a mixture of both professionals are required. In addition, those centres that stated that palliative care was available may require additional funding to increase their current level of staffing.

²⁹ Humphreys C (2005) *Health needs assessment: adults with tumours of the brain and central nervous system in England and Wales*. National Public Health Service for Wales, Gwasanaeth Iechyd Cyhoeddus Cenedlaethol Cymru. Available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbrains).

Treatment and follow-up: pituitary, spinal cord and skull base tumours

This chapter covers the care of those patients with brain and other central nervous system (CNS) tumours who would benefit from the advice and management of specialist multidisciplinary teams (MDTs) (different from the neurosciences brain and other CNS tumours MDT as defined in Chapter 2). These include pituitary, spinal cord and skull base tumours. These MDTs are defined by the specialist expertise required to manage the patients and will be detailed in the individual sections that follow.

Patients with tumours of the pituitary, spinal cord or skull base present in a variety of ways and, as with other CNS tumour patients, the diagnosis will normally first be indicated by imaging. The designated lead in every trust (see Table 6) will be responsible for ensuring clear pathways are in place to refer such patients directly to the appropriate specialist MDT.

Currently, controversy exists regarding the manpower requirements for many pituitary tumours. The Society of British Neurological Surgeons is considering manpower planning for specialist services for the next 10 years. The service configuration will depend on local circumstances and in some cases there will be overlap in the membership between the pituitary MDT and the neurosciences MDT. However, all patients should benefit from assessment by the specialist membership of the pituitary MDT.

For spinal cord and skull base tumours the specialist teams are likely to relate to more than one neuroscience centre. This will be determined by the access to specialist healthcare professionals and services. There will need to be clear pathways of referral to these very specialist teams. The general responsibilities of these specialist MDTs are described in Table 12.

Table 12. Pituitary, spinal cord and skull base MDTs – responsibilities

*Treatment and follow-up:
pituitary, spinal cord and
skull base tumours*

The pituitary, spinal cord and skull base MDTs are responsible for the diagnosis and initial management plan (both surgical and non-surgical aspects of care) of most adult patients with these tumours. Membership of these is summarised in Tables 13–15 and responsibilities include the following:

- Establish as complete a diagnosis as possible for the optimal clinical management of the patient
- Develop management plans at first presentation, to include initial supportive care needs, diagnostic and surgical interventions, non-surgical oncology interventions, treatment of symptoms and follow-up
- Inform the diagnostic clinician/team at the local referring hospital of the management plan
- Inform the cancer network MDT of the management plan
- Review of and advise on patients referred back for disease progression or relapse
- Develop MDT protocols, in collaboration with the neuroscience MDT and the cancer network MDTs, to define appropriate follow-up imaging requirements for patients
- Act as an educational resource for local service providers
- Organise regular site-specific group meetings to review pathways of care and protocols
- Nominate and record a key worker to act as a point of contact for patients, their relatives and carers. This should be agreed with the patient, their relatives and carers
- Develop and maintain evidence-based local management protocols covering all aspects of the patient pathway
- Introduce and maintain systems for data entry across the area of service provision including links to cancer registries
- Audit practice at local, cancer network and supra network levels against national standards of care
- Facilitate the entry of patients into appropriate National Cancer Research Network (NCRN) and local clinical trials
- Liaise with the cancer network MDT.

Table 13. Core membership of the pituitary MDT*

| MDT member | Description |
|---|--|
| Specialist pituitary surgeon | A neurosurgeon or ear, nose and throat (ENT) surgeon with appropriate training who works in close association with the specialist endocrinologist, including specialist pituitary clinics and has specialist pituitary surgical responsibility |
| Specialist endocrinologist | An endocrinologist with a special interest in tumours of the pituitary gland and appropriate expertise in the diagnosis and management of pituitary dysfunction who runs a specialist pituitary clinic |
| Neuroradiologist(s) | A consultant radiologist in a substantive post with at least 50% of clinical programmed activity spent in the practice of neuroradiology |
| Neuropathologist(s) | An accredited pathologist who is registered as a neuropathologist or histopathologist, has specialist expertise in the pathology of tumours in the region of the pituitary gland, and takes part in the national External Quality Assurance (EQA) scheme for neuropathology organised by the British Neuropathological Society or an equivalent EQA scheme for endocrine pathology |
| Clinical oncologist | A consultant clinical oncologist with specialist expertise in the management and irradiation of tumours of the sellar region |
| Clinical nurse specialist | A nurse with expertise and experience in neurology/neurosurgery and/or endocrinology working in close association with the specialist endocrinologist and skills in communication as defined by the 'Manual for cancer services' ³⁰ |
| Coordinator(s) | An administrative post responsible for coordinating patient registration with the neuroscience MDT and data collection |
| Others as required (extended MDT members) | A consultant ophthalmologist with expertise in the management of patients with visual disturbance associated with a central nervous system tumour. Representative(s) of the allied health professions, including prosthetics, speech and language therapy, dietetics and others as appropriate, who have knowledge and experience of dealing with this patient group |

*Appropriate cross-cover should be available for all MDT members. AHP, allied health professional.

³⁰ Department of Health (2004) *Manual for cancer services. Topic 2A The generic multidisciplinary team 2A-122 to 2A-127*. London: Department of Health. Available from: www.dh.gov.uk

Table 14. Core membership of the spinal cord MDT*

| MDT member | Description |
|---|---|
| Spinal surgeons(s) | A specialised spinal surgeon (neurosurgical/ orthopaedic) who spends at least 50% of clinical programmed activities in neuro-oncological spinal surgery/spinal surgery and is appropriately trained and participates in a specialist clinic |
| Neuroradiologist(s) | A consultant radiologist in a substantive post with at least 50% of clinical programmed activities spent in the practice of neuroradiology |
| Neuropathologist(s) | An accredited pathologist who is registered as a neuropathologist or histopathologist, has specialist expertise in neuro-oncology, and takes part in the national External Quality Assurance scheme for neuropathology organised by the British Neuropathological Society |
| Clinical nurse specialist(s) | A nurse with specialist knowledge of central nervous system tumours and skills in communication as defined by the 'Manual for cancer services' ³¹ |
| Specialist AHP(s) | Representative(s) of the allied health professions, including occupational therapy, physiotherapy, dietetics and others as appropriate, who have knowledge and experience of dealing with this patient group |
| Coordinator(s) | An administrative post responsible for coordinating patient registration with the neuroscience MDT and data collection |
| Others as required (extended MDT members) | <ul style="list-style-type: none"> • A named clinical oncologist • Palliative care specialist |

*Appropriate cross-cover should be available for all MDT members.
AHP, allied health professional.

³¹ Department of Health (2004) *Manual for cancer services. Topic 2A The generic multidisciplinary team 2A-122 to 2A-127*. London: Department of Health. Available from: www.dh.gov.uk

Table 15. Core membership of the skull base MDT*

| MDT member | Description |
|---|---|
| Surgeons | Neurosurgical, ear, nose and throat (ENT), maxillofacial, ophthalmic or plastic surgeons. The skull base team should include or have access to surgeons proficient in reconstruction, including microvascular techniques. Each surgeon should be expected to dedicate a defined contractual element of their time to skull base cancer and participate in specialist skull base clinics |
| Neuroradiologist(s) | A consultant radiologist in a substantive post with at least 50% of clinical programmed activities spent in the practice of neuroradiology |
| Neuropathologist(s) | An accredited pathologist who is registered as a neuropathologist or histopathologist, has specialist expertise in neuro-oncology, and takes part in the national External Quality Assurance scheme for neuropathology organised by the British Neuropathological Society |
| Oncologist(s) | A clinical oncologist with a special interest in tumours of the skull base |
| Clinical nurse specialist(s) | A nurse with specialist knowledge of brain and other CNS tumours and skills in communication as defined by the 'Manual for cancer standards' ³² |
| Specialist AHP(s) | Representative(s) of the allied health professions, including prosthetics, speech and language therapy, dietetics and others as appropriate, who have knowledge and experience of dealing with this patient group |
| Coordinator(s) | An administrative post responsible for coordinating patient registration with the neuroscience MDT and data collection |
| Others as required (extended MDT members) | Palliative care specialist |

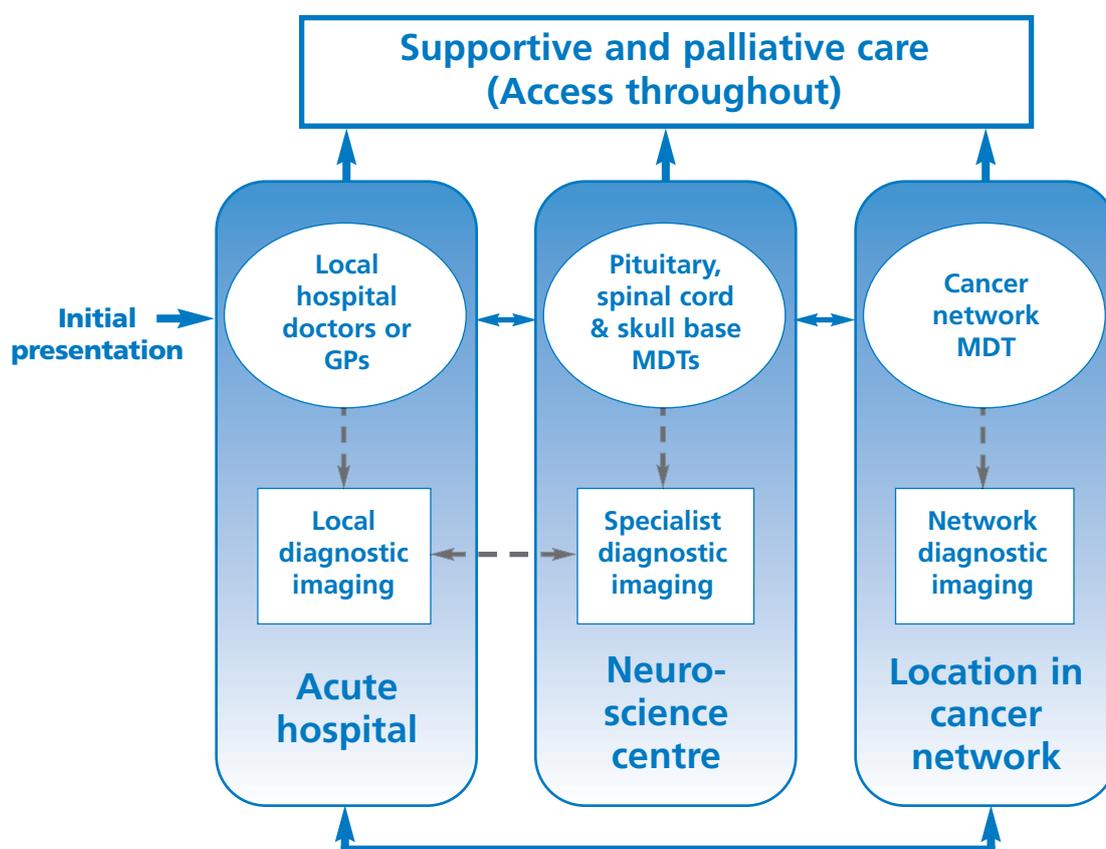
*Appropriate cross-cover should be available for all MDT members.
AHP, allied health professional.

³² Department of Health (2004) *Manual for cancer services. Topic 2A The generic multidisciplinary team 2A-122 to 2A-127*. London: Department of Health. Available from: www.dh.gov.uk

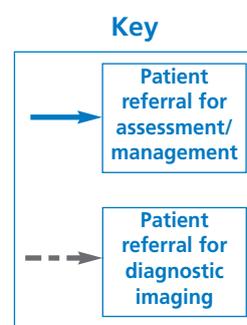
For all patients with pituitary, spinal cord and skull base tumours the cancer network MDT will be the focus of non-surgical treatment and follow-up unless there are particular treatments and techniques that require a specialist referral. These pathways will need to be defined by protocol determined by the specialist MDT.

Fundamental to ensuring efficient clinical care when patients are managed by different teams on different sites is good communication. Figure 5 summarises the flow of information through the patient pathway.

Figure 5. Pituitary, spinal cord and skull base tumours patient pathway



MDT, multidisciplinary team; GP, general practitioner.



A. Recommendations – general

Patients with pituitary, spinal cord or skull base tumours should have their management plan decided by a dedicated specialist MDT.

The relationship between these specialist MDTs and the neuroscience MDT should be clearly defined by local protocols.

All patients should have specialist follow-up as defined by the relevant MDT.

Pituitary and pituitary-related tumours

The majority of pituitary tumours (95%) are adenomas. The remainder include craniopharyngiomas, Rathke's cleft cysts and meningiomas as these involve similar clinical problems, surgical management and personnel.

The initial diagnosis may be suspected or confirmed by neurologists, physicians, ophthalmologists or gynaecologists who then have no further involvement in the patient's management. Patients usually present with headache, visual disturbance or endocrine dysfunction; patients who are asymptomatic may be incidentally identified on a computed tomography (CT) scan.

The following principles of care apply.

- Patients with pituitary tumours may require prolonged periods in the care of an endocrinologist who specialises in pituitary dysfunction.
- All patients will benefit at presentation from specialist MDT (Table 13) discussion to formulate a management plan.
- Magnetic resonance imaging (MRI) is the preferred investigation for patients with potential pituitary or parasellar tumours. In patients with Cushing's syndrome, specialist interventional radiology experience may be needed.
- The majority of patients require surgery. This is usually carried out by either an ear, nose and throat (ENT) surgeon or neurosurgeon.
- The surgical workload for these tumours will decrease in the next few years as new endocrinological treatments become available.

- Histopathological assessment of these tumours requires particular expertise and access to electron microscopy and possibly a second opinion from specialists nationwide.
- Postoperative radiotherapy may be required.
- Radiosurgery techniques may help in the management of patients with residual tumours. Otherwise, radiosurgery should be the subject of research studies.
- Follow-up of patients who have been treated for pituitary tumours may require the following:
 - regular assessment by an endocrinologist
 - regular assessment of the visual fields by perimetry with access to a neuro-ophthalmologist as clinically indicated
 - MRI.
- Most patients with pituitary tumours will not need palliative and supportive care, although there should be ready access to these services when needed.

A. Recommendations – pituitary and pituitary-related tumours

Patients should be followed up by a member of the specialist pituitary MDT at a multidisciplinary clinic. More local follow-up based on protocols may be arranged in conjunction with the specialist pituitary MDT or the cancer network MDT and the relevant endocrinology team.

Specialist histopathological assessment should be available, as should mechanisms for ready access to a second opinion.

Intradural spinal cord tumours

There is a wide variety of primary spinal column tumours and all are relatively rare. Intradural tumours may be within the spinal cord (intramedullary; 5% of spinal column tumours) or outside the cord (extramedullary; 15% of spinal column tumours) or occasionally both. The majority of spinal intradural lesions are slow growing and clinical presentation may be protracted. Rapid deterioration may occasionally occur in patients with glial tumours. The prognosis for high-grade tumour types is nearly always poor with an average life expectancy of between 6 and 12 months.

The following principles of care apply:

- All patients will benefit at presentation from specialist MDT (Table 14) discussion to formulate a management plan.
- Imaging with MRI is used to investigate these tumours. Spinal angiography may be necessary for a few patients.
- In patients with low-grade tumours the main aim of treatment, usually surgical, is to prevent further neurological deterioration.
- Patients need to be managed by teams treating other spinal disease that may require surgical management (for example disc prolapse), including emergency services for patients with suspected spinal cord compression.
- There needs to be a single point of referral to the on-call spinal team for both imaging and specialist referral.
- The majority of intradural tumours can be completely excised. The excision of intramedullary glial tumours risks further damage to the spinal cord, and survival is not improved if the lesion is high-grade. The intraoperative pathological evaluation of biopsy material is therefore essential to ensure that a high-grade lesion, for example an invasive anaplastic astrocytoma, is not further excised.
- Intraoperative neurophysiological recording helps to identify and thereby preserve normal spinal cord and should be available.
- Certain groups of patients, for example those with neurofibromatosis types 1 and 2, are at particular risk of developing intradural spinal tumours. They require monitoring and early resection if lesions enlarge or cause symptoms.
- Radiotherapy is appropriate treatment for some patients.
- Regular follow-up requires MRI scanning and clinical examination to identify and treat postoperative complications or tumour recurrence.

A. Recommendations – intradural spinal cord tumours

Intradural spinal cord tumours should be managed by teams that deal with other spinal disease that may require surgical management (for example disc prolapse), including emergency services for patients with suspected cord compression.

There should be a single point of referral into the on-call spinal team for both imaging and specialist referral including urgent MRI scans, CT myelography, spinal angiogram and specialist management.

There should be access to intraoperative histopathological evaluation and intraoperative neurophysiological recording with appropriate neurophysiologist and technical support.

There should be access to appropriate rehabilitation services.

Skull base tumours

There is a wide variety of tumours of the base of the skull, ranging from slow growing to very aggressive, but they are usually associated with progressive morbidity as the tumour grows and invades. Most are diagnosed following the investigation of sino-nasal, balance, or hearing problems. Symptoms may include seizures, headache, nerve palsies, facial pain, hearing loss and balance disorders.

The commonest tumour at this site is the schwannoma, a low-grade, generally slow-growing tumour that arises from the acoustic nerve. The following principles of care apply.

- All patients will benefit at presentation from specialist MDT (Table 15) discussion to formulate a management plan.
- A combination of MRI and high-resolution CT is used to assess the tumour before surgery. MR angiography, CT angiography, conventional angiography or a combination of these techniques may be needed to assess vascular involvement.
- Endoscopic or CT-guided needle biopsy is usually required depending on the site involved. Occasionally, open intracranial biopsy is necessary.

- Patients with skull base tumours also may require the following assessments before treatment:
 - neuro-otological evaluation
 - audiological testing
 - specialist pathological assessment
 - auditory-evoked brain stem responses testing
 - vestibular testing
 - prosthetic assessment to establish the need for ocular, aural or skull bone replacement
 - speech and language therapy assessment and explanation to the patient of likely postoperative impairment
 - dietetic assessment of neurological status and the need for postoperative nutritional support (for example, nasogastric or percutaneous endoscopic gastrostomy feeding).
- Surgery is often the treatment of choice but complete excision is not always possible because of involvement of surrounding structures. Ventricular shunting or draining may be required for large tumours.
- Because of the nature and location of these tumours the expertise of a variety of surgical specialists (ENT surgeon, maxillofacial surgeon, specialist neurosurgeon or reconstructive surgeon) may be required.
- Specialised techniques, such as embolisation of highly vascular tumours, may be required.
- Radiotherapy may be considered where complete excision is not possible, or for consolidation. The use of external beam conformal radiotherapy is well established and there is increasing evidence for the role of stereotactic techniques. Patients with small acoustic schwannomas can be offered the choice of surgery or stereotactic radiosurgery.
- Follow-up may include imaging with CT, MRI, positron emission tomography (PET) and bone scan and audiology.

A. Recommendations – skull base tumours

There should be ready access to MRI, high-resolution CT, MR angiography, CT angiography and conventional angiography. There should be ready access to pre-operative neurophysiological assessment.

An appropriate mix of surgical skills is required for these patients. This will necessitate that those surgeons forming the core or extended surgical team should have sufficient flexibility in their timetable to accommodate joint operating when necessary. There should be access to stereotactic radiotherapy/radiosurgery.

The following sections (B, C, D and E) apply to all tumour types described above.

B. Anticipated benefits

Management by specialist MDTs will improve the access to and appropriateness of treatment, as well as continuity of care and rehabilitation.

Early diagnosis and appropriate treatment that preserves neurological function will:

- improve survival
- reduce treatment-related morbidity
- improve the patient's quality of life.

There will be improved extent of resection and functional and cosmetic outcome from the use of multiexpertise surgical teams.

C. Evidence

Pituitary tumours

Consensus-based UK clinical guidelines recommend the referral of patients with pituitary tumours to specialist centres where management plans may be agreed jointly by endocrinologists, pituitary surgeons and radiotherapists.

Consistent evidence supports the recommendation for specialist pituitary neurosurgery. A population-based American study reported lower perioperative mortality and complication rates for those hospitals and surgeons with a high case volume of trans-sphenoidal pituitary surgery. A UK institutional audit reported better cure rates when responsibility for pituitary surgery was transferred from a group of neurosurgeons to a single dedicated pituitary surgeon. In a large survey of American neurosurgeons, more experienced surgeons reported fewer complications of trans-sphenoidal pituitary surgery.

Spinal cord tumours

No studies comparing different service models for the management of patients with spinal cord tumours were identified.

A UK case series describing 13 children with primary spinal cord tumours highlighted the problem of diagnostic delay as a result of poor referral pathways. The delay between the onset of symptoms and diagnosis was several years for two patients and averaged approximately 10 months in the remainder of cases. The importance of prompt diagnosis and treatment is supported by case series describing the prognosis of patients with intramedullary spinal cord tumours. These studies identify tumour histology, neurological status before surgery and complete removal of the tumour as prognostic factors for outcome after surgery.

During surgery, neurophysiological monitoring may be used to predict postoperative outcome or to avoid neurological complications. Somatosensory-evoked potentials, which assess the integrity of sensory pathways leading from peripheral nerve to the sensory cortex, and motor-evoked potentials, which assess the functional integrity of descending motor pathways in the spinal cord, may both be monitored. By comparing intraoperative values with presurgical baseline readings, the surgeon may be directed towards an approach that balances tumour removal with the preservation of postoperative motor and sensory function.

Skull base tumours

Treatment options such as surgery, radiosurgery and radiotherapy have been evaluated. Evaluations have been conducted using a diversity of study designs and study objectives, giving rise to a diversity of results. Generally, some prolonged rates of disease-free survival and increase in overall survival rates have been reported for specific treatments. Complications exist for each treatment evaluated and include effects on emotion control, physical function and performance, and neurological deficit status. Further details about these studies and results are described in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Although no direct evidence relating to skull base MDTs was identified, other studies suggest that the concentration of expertise within dedicated teams could improve patient outcomes. Two population-based American studies, one nationwide and one limited to California, reported that outcomes for patients with acoustic neuroma were better if their surgery was performed at higher-volume hospitals or by higher-volume surgeons. Evidence-based clinical guidelines note that patients with acoustic neuroma require multidisciplinary care, and recommend that such patients should be managed by centres treating large numbers of cases.

D. Measurement

Structure

- evidence that fully staffed and functional MDTs for pituitary, spinal cord and skull base tumours have been established
- clear protocols for referral and management of such patients

Process

- staff attendance at MDT meetings
- times from presentation and diagnosis to first definitive treatment

Outcome

- survival
- treatment-related morbidity
- quality of life
- patients', their relatives' and carers' satisfaction

E. Resource implications

The estimated annual employment cost for each pituitary MDT, for full attendance at monthly MDT meetings, is between £10,788 for a 1-hour meeting and £15,768 for a 2-hour meeting. This estimate is for all core members plus preparation time for members including lead clinicians, key workers and MDT coordinators. However, with the exception of the MDT coordinator (who attends 100% of the MDT meetings), if other MDT members attend only the minimum of 50% of the MDT meetings the annual employment cost would be between £5994 and £8574 for a 1-hour and 2-hour meeting, respectively.

The estimated annual employment cost for each spinal cord MDT, for full attendance, is £9144 for a 1-hour meeting and £12,924 for a 2-hour meeting. This estimate is for all core members plus preparation time for members including lead clinicians, key workers and MDT coordinators. However, with the exception of the MDT coordinator (who attends 100% of the MDT meetings), if other MDT members attend only the minimum of 50% of the MDT meetings the annual employment cost would be between £5172 and £7152 for a 1-hour and 2-hour meeting, respectively.

The estimated annual employment cost for each skull base MDT, for full attendance, is £12,888 for a 1-hour meeting and £18,912 for a 2-hour meeting. This estimate is for all core members plus preparation time for members including lead clinicians, key workers and MDT coordinators. However, with the exception of the MDT coordinator (who attends 100% of the MDT meetings), if other MDT members attend only the minimum of 50% of the MDT meetings the annual employment cost would be between £7044 and £10,146 for a 1-hour and 2-hour meeting, respectively.

Further details of the estimated employment costs for core members of pituitary, spinal cord and skull base tumour MDTs are in section 3.5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Treatment and follow-up: primary CNS lymphoma, medulloblastoma, pineal tumours and optic gliomas

Tumours of the brain and central nervous system (CNS) in adults with an incidence of less than 1–2 per million per year include primary CNS lymphoma, medulloblastoma, pineal tumours and optic gliomas and other rare CNS tumours, for example ependymoma. As described in Chapter 1, reliable data on the incidence of some of these CNS tumours are not available.

The majority of these patients will be managed initially by the neuroscience brain and other CNS tumours multidisciplinary team (MDT) through the pathways described in Chapter 2. As with other CNS tumours, the diagnosis will often be suspected on imaging before surgery or biopsy confirmation. Some rare tumours of the brain in adults are relatively more common in children. In appropriate clinical situations involving such tumours, the neuroscience MDT might benefit from a paediatric oncology opinion or a review of current paediatric therapeutic strategies.

Few centres and clinicians will gain wide experience in managing patients with these tumours because of their rarity, which means that these patients present particular problems in management and service coordination. These problems are quite similar to those experienced in the management of tumours in children. The national coordination of treatment protocols through the UK Childrens' Cancer Study Group (UKCCSG) provides an excellent model for standardisation of care for adults with rarer tumours.

It is proposed that national tumour groups should be established and funded to standardise care for these patients, for example through the British Neuro-Oncology Society. The neuroscience MDT would normally act as the conduit through which these national treatment protocols would be applied. It will be a responsibility of these MDTs to audit the adherence to these treatment protocols. The principle is demonstrated with reference to the four tumours listed above but could be extended to include other CNS tumours with a similarly low incidence.

A. Recommendations – general

National tumour groups for rare CNS tumours should be established to coordinate the approach to care; this should include developing protocols for the investigation, management, registration and clinical research into rare tumours. They should also maintain a national register of all these cases.

All patients with rare CNS tumours should be managed within the context of an MDT – usually the neuroscience MDT but, where appropriate, in collaboration with the cancer network MDT.

Primary central nervous system lymphoma

Primary central nervous system lymphoma (PCNSL) accounts for about 2% of all primary CNS tumours. A disease of middle and older age, it may be associated with immunosuppression (particularly HIV infection) and so all patients need to be investigated for evidence of immune suppression, including HIV infection.

Patients with PCNSL present in the same way as patients with other primary CNS tumours. Although the diagnosis may be suspected from CNS imaging, a biopsy is essential to diagnose and classify the lymphoma. Intraoperative histopathological evaluation of the biopsy specimen is necessary to establish the diagnosis and avoid further surgery. The prognosis is usually very poor and the disease may be associated with serious neuropsychological problems, the most severe of which is dementia. There is no benefit from surgical resection.

Management policies appear to vary around the country and there is little good research evidence on which to base management decisions. Steroids help to reduce symptoms and most patients who are fit enough are treated with chemotherapy. Regimens with high CNS penetration are required and the expertise to safely administer and monitor these treatments is essential in the MDT managing the patients.

Post-chemotherapy radiotherapy may help to control the disease but its usefulness may be outweighed by the increased risk of dementia or other neuropsychological problems. Therefore early neuropsychological input and advice as part of the MDT approach is essential. Patients who are frail, elderly or immunosuppressed may only tolerate less intensive treatment.

Following treatment most patients with PCNSL relapse and many of those who do not relapse or who relapse late have neurological problems. Follow-up arrangements are required that provide supportive care for patients during remission and consider further palliative treatment at relapse. There is no consensus about what this should be and no evidence that early detection and intervention is beneficial.

A. Recommendations – primary central nervous system lymphoma

A national PCNSL tumour group should be established to unify management approaches, develop national standardised guidelines and treatment protocols, and determine research programmes. A multidisciplinary approach to the management and care of patients with PCNSL should be provided by the neuroscience MDT, and the cancer network MDT as described in Chapter 2. It is important that a haemato-oncologist, or medical or clinical oncologist with a special interest, should be involved in the management of lymphomas. Where the neuroscience MDT does not have appropriate expertise in the core membership, there should be a named representative of the lymphoma MDT to act in this capacity.

Facilities for neurosurgery should include stereotactic biopsy, image-guided surgery and an on-site neuropathology service for intraoperative histopathological evaluation. The on-site neuropathology service should have access to specialist lymphoreticular pathology services to distinguish lymphoma from other lymphoid pathologies and to grade and classify the lymphoma.

Chemotherapy services must meet the national guidance on the safe administration of intrathecal chemotherapy³³ and the corresponding measures are given in the ‘Manual for cancer services’.³⁴

³³ Department of Health (2003) Updated national guidance on the safe administration of intrathecal chemotherapy. *Health service circular* 2003/010. London: Department of Health. Available from: www.dh.gov.uk

³⁴ Department of Health (2004) *Manual for cancer services*. London: Department of Health. Available from: www.dh.gov.uk

There should be ready access to ophthalmic services as PCNSL often involves the visual pathways, and ophthalmic review is required to complete disease staging.

All patients with HIV-related lymphoma should also be under the care of the local HIV service.

Medulloblastoma

Medulloblastoma is a very rare tumour in adults and probably fewer than 50 patients present annually in England and Wales. It usually occurs in the posterior fossa and is associated with cerebellar symptoms and raised intracranial pressure. It commonly spreads through the craniospinal axis.

Patients need to have a magnetic resonance imaging (MRI) scan of the brain and whole spine before surgery. Standard treatment would be surgery to remove as much tumour as possible, followed by radiotherapy to the whole neuraxis. The role of chemotherapy following surgery and radiotherapy in the management of adults is not established.

A. Recommendations – medulloblastoma

A national adult medulloblastoma tumour group should be established to unify management approaches, develop national standardised guidelines and treatment protocols, and determine research programmes.

Patients with medulloblastoma should be reviewed by the neuroscience MDT and receive further investigations and treatment according to nationally agreed protocols.

All adult patients with medulloblastoma should receive their neuraxis radiotherapy in radiotherapy centres that also treat paediatric medulloblastoma, to utilise their experience and expertise in planning for these tumours.

Pineal tumours

Tumours involving the pineal gland or body are very unusual in adults. There are three main histological types: germ cell tumours (GCTs), astrocytomas and pineal parenchymal tumours, which include pineocytomas and pineoblastomas.

Pineal tumours most commonly present with symptoms and signs of raised intracranial pressure. Because they are rare their clinical course and prognosis are not well described, but many GCTs and pineal parenchymal tumours are curable with appropriate management. GCTs occurring elsewhere in the CNS are managed according to principles similar to those for tumours in the pineal region.

Diagnosis of GCTs may be confirmed in some cases by the measurement of hormonal markers. When positive, no biopsy is needed. In patients who are negative for markers, biopsy is needed.

Treatment varies according to the tumour type, the level of marker, and cerebrospinal fluid (CSF) cytology status. The treatment needs to be part of the management plan developed and agreed by the neuroscience MDT. Surgery is often the treatment of choice and may require stereotactic or endoscopic biopsy, cerebrospinal fluid diversion or surgical resection of the tumour.

Radiotherapy may be needed, especially for GCTs, but only once the diagnosis has been confirmed from the histopathological evaluation of biopsy material. Craniospinal axis irradiation may be required for the treatment of patients with pineoblastoma and metastatic germ cell tumours. Stereotactic radiotherapy may be appropriate for low-grade pineocytomas.

Chemotherapy can be used in the management of GCTs but has no proved role in the management of other pineal tumours.

A. Recommendations – pineal tumours

A national pineal tumour group should be established to unify management approaches, develop national standardised guidelines and treatment protocols, and determine research programmes.

Facilities for the neurosurgical management of patients with pineal lesions should include access to surgical teams with practice in complex pineal approaches and should provide the following procedures:

- ventricular endoscopy (including third ventriculostomy)
- stereotactic techniques.

There should be access to on-site neuropathology services to provide intraoperative histopathological evaluation.

Patients with low-grade pineocytomas should have access to stereotactic radiotherapy services.

Optic pathway glioma

Gliomas of the optic nerve and tract account for approximately 2% of cerebral gliomas. They are slow growing and predominately occur in children with approximately 60% occurring in children younger than 10 years of age. Optic pathway gliomas are classified by location and by their association or lack of association with neurofibromatosis type 1.

The signs and symptoms of optic gliomas usually develop over the course of 6–9 months and depend on the location of the tumour. Diagnosis is best made by MRI, but computed tomography (CT) is superior for bony detail and detection of intra-tumoural calcifications, which suggest low-grade histology.

These tumours vary in their growth, impact on vision and effect on local structures and need careful specialist management. In adults the tumours tend to grow quickly and result in rapid visual loss. Management is controversial and treatment decisions need to take into account the patient's age, association with neurofibromatosis 1 and location of the tumour. Radiotherapy and chemotherapy should be considered in situations where surgery is not appropriate, for example irradiation of tumours of the optic chiasm.

These patients often have long-term problems with vision, endocrine dysfunction and cognitive impairment.

A. Recommendations – optic pathway glioma

A national optic glioma tumour group should be established to unify management approaches, develop national standardised guidelines and treatment protocols, and determine research programmes.

A multidisciplinary approach to the management and care of patients with optic gliomas should be provided by the neuroscience MDT and the cancer network MDT, as described in Chapter 2.

There should be access to ophthalmic services with regular ophthalmic review.

Endocrine support should be available where required.

There should be access to conformal stereotactic procedures.

Lifelong follow-up and support should be provided for patients with optical pathway glioma.

The following sections (B, C, D and E) apply to all tumour types described above.

B. Anticipated benefits

Establishment of national groups to advise on the management of these rare tumours will ensure that:

- treatment policies are standardised across the NHS in England and Wales
- clinical research is encouraged and facilitated
- national audits can take place.

Having local protocols, based on national guidance, will ensure that the MDTs involve other non-core MDT members (for example, haematologists for PCNSL) and that treatment is more efficient and more standardised.

C. Evidence

Authors agree that high-dose methotrexate is the chemotherapy of choice for PCNSL, although the dose is yet to be optimised. It appears to be no more effective when combined with other drugs than when given alone, prior to radiotherapy and/or cytarabine. As whole-brain radiotherapy is associated with toxicity in older patients, it has been suggested that it be withheld in cases where a patient responds well to chemotherapy or is reserved for treatment of relapse. The effective dose of whole-brain radiotherapy is yet to be determined and in elderly patients may represent a trade-off between the risk of relapse and the strong probability of disabling delayed neurotoxicity.

Very little evidence was identified to inform the configuration of services for adult patients with medulloblastoma, pineal region tumours or optic nerve glioma. Most studies have been conducted in children in whom these tumours are more common. Evidence in adult populations is limited to institutional case series describing clinical presentation, diagnosis and treatment. Indirect evidence in support of specialist care comes from American observational studies of children with medulloblastoma. One of the studies observed that paediatric neurosurgeons were more likely than general neurosurgeons to resect more than 90% of a tumour. Another study noted that the overall survival of children treated in cancer centres was better than those treated elsewhere.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- establishment of national groups to advise on the management of rare CNS tumours
- local protocols for the management of rare tumours and for involvement of non-core MDT members in MDT meetings when needed

Process

- times from presentation and diagnosis to first definitive treatment
- number of patients treated each year per surgeon and per oncologist
- non-core member involvement in MDT meetings

Outcome

- postoperative mortality
- survival
- quality of life
- patients', their relatives' and carers' satisfaction

E. Resource implications

Treatment and follow-up for this group of patients has not been included in the resource implications. However, it is not considered to be a major resource implication of the guidance.

Genetic predispositions

Approximately 1–5% of brain tumours are due to genetic syndromes that confer an increased risk of developing tumours of the CNS. Patients with these genetic diseases provide an important insight into our understanding of the molecular mechanisms involved in cancer development. In addition, these patients need special care in terms of the management of their high-risk status for the development of future tumours. Some of these tumours are associated with neurofibromatosis and several other inherited syndromes.

- **Cowden's disease**

Cowden's disease is characterised by multiple hamartomatous lesions and an increased risk of early-onset breast and thyroid cancer and dysplastic gangliocytoma of the cerebellum.

- **Gorlin syndrome**

Gorlin syndrome is synonymous with naevoid basal cell cancer syndrome and is associated with an increased risk of medulloblastoma in children.

- **Li–Fraumeni syndrome**

Li–Fraumeni syndrome is primarily characterised by soft tissue and bone sarcomas and breast cancer. Other tumours that may occur are gliomas, leukaemia and adrenocortical cancer.

- **Neurofibromatosis**

Tumours of the CNS are seen with increased frequency in both type 1 and type 2 neurofibromatosis. These include acoustic nerve schwannomas, paraspinal neurofibromas, meningiomas and gliomas. Neurofibromas may undergo malignant transformation. The astrocytic gliomas are usually low grade and have a predilection for the optic pathways, hypothalamus and cerebellum.

- **Tuberous sclerosis**

Tuberous sclerosis is an inherited neurocutaneous disorder that is associated with the subependymal giant cell astrocytoma and benign cysts of kidney, liver and lung.

- **Turcot's syndrome**

Turcot's syndrome is occasionally associated with medulloblastomas and high-grade gliomas.

- **Von Hippel–Lindau syndrome**

The von Hippel–Lindau syndrome is associated with benign vascular tumours, especially of the eye and cerebellum (haemangioblastoma). Renal, pancreatic and epididymal cysts are also common.

A. Recommendations

Patients with genetic syndromes that confer an increased risk of developing tumours of the CNS require management within the context of a multidisciplinary team, which should incorporate advice from clinical geneticists on diagnosis and screening.

Coordinated follow-up and interval imaging/investigation of patients with neurocutaneous syndromes should be performed, where possible, in combined specialised neurogenetic clinics where there is access to a neurologist and geneticist.

Cases of people with familial predilection to cancer (for example, Li–Fraumeni and Turcot’s syndrome) should be coordinated, where possible, via cancer genetic clinics or by clinicians with the most appropriate clinical skills (for example, Turcot’s – gastroenterology; Gorlin – dermatology).

B. Anticipated benefits

Clearly established and well-known mechanisms for the identification and follow-up of these patients will lead to earlier diagnosis and management of brain and other CNS tumours.

C. Evidence

The National Institute for Health and Clinical Excellence (NICE) guidance ‘Improving outcomes for people with sarcoma’³⁵ has considered the management of patients with neurofibromatosis and those with Li–Fraumeni syndrome, and the guidance on ‘Improving outcomes in people with skin tumours including melanoma’³⁶ considered the management of patients with Gorlin syndrome. These documents recommend that the MDT with the most appropriate clinical expertise should coordinate the care of these patients (for example the specialist skin MDT for those with Gorlin syndrome). They also both recommend that patients with evidence of such a genetic predisposition, and their families, should be offered referral to clinical genetics services.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- provision of specialised clinics for these patients

Outcome

- patients’, their relatives’ and carers’ satisfaction

E. Resource implications

It is recommended that patients are referred to cancer genetic services where appropriate. The capacity within existing cancer genetic services will need further investigation by local commissioners.

³⁵ National Institute for Health and Clinical Excellence (2005) Improving outcomes for people with sarcoma. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsarcoma

³⁶ National Institute for Health and Clinical Excellence (2005) Improving outcomes for people with skin tumours including melanoma. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgstim

Supportive care

Supportive care is an umbrella term encompassing the work of a broad range of healthcare professionals to address the changing needs of patients, and their relatives and carers throughout the patient journey. The supportive care issues for patients with cancer have been extensively described in the NICE guidance 'Improving supportive and palliative care for adults with cancer'.³⁷ The supportive care needs for patients with long-term conditions is described in the Department of Health document 'National service framework for long term conditions'.³⁸

The needs of patients with brain and other central nervous system (CNS) tumours are diverse and the supportive care services offered should not be dependent on diagnosis, but on need. The needs of a patient with a slow-growing CNS tumour may be as great as those of one with a more aggressive tumour.

Patients with CNS tumours who require specialist supportive care can access this through the neuroscience brain and other CNS tumours multidisciplinary team (MDT) or the cancer network brain and other CNS tumours MDT. At all levels of care, referral criteria need to reflect the specific needs of this group of patients and be sufficiently flexible to ensure rapid and timely access to the necessary supportive care services.

All professionals involved in the provision of supportive care need to be aware of the full range of specialised services in the area, the local referral criteria and care pathways. Healthcare professionals offering supportive care may consider running joint clinics to facilitate the assessment of patients and their referral to support services.

³⁷ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

³⁸ Department of Health (2005) National Service Framework for long term conditions. London: Department of Health. Available from: www.dh.gov.uk

Communication

Good, rapid communication between healthcare professionals is particularly important for patients with CNS tumours whose care pathway is often complex. This will ensure that members of the different MDTs caring for the patient have timely, accurate knowledge and understanding of the patient's current situation thereby reducing the possibility of conflicting information being provided to the patient, their relatives and carers.

Another aim of good communication is to ensure that the patients, their relatives and carers have the opportunity to be involved in the decision-making process about management and care. For this patients need sufficient information about prognosis to understand the advantages and disadvantages of treatment options. However, the ability to communicate and be involved in the decision-making process may be compromised in patients with CNS tumours, as many have significant cognitive deficit either at presentation or during the course of their illness. In such cases, relatives and carers may need to be more involved in decision-making than the patient.

A. Recommendations

Communication skills training, sensitive to the particular needs of patients with CNS tumours, should be provided for healthcare professionals caring for patients with CNS tumours.

Healthcare professionals should have face-to-face communication with patients, their relatives and carers at critical points in the care pathway to discuss diagnosis, prognosis, treatment options (including no treatment), recurrence and end-of-life care.

8

B. Anticipated benefits

Formal training in communication skills will improve clinical care, particularly for CNS tumour patients, among whom cognitive and communication impairments are common.

Good communication will improve the experience for patients, their relatives and carers, and healthcare professionals throughout the patient pathway and ensure that, whenever possible, patients have the opportunity to participate in the decision-making process.

C. Evidence

A comprehensive literature review considered the issue of communication between healthcare workers and patients with high-grade glioma. Evidence from three observational studies suggested that just over half the patients were aware of their prognosis. The relatives of patients tended to be more informed. There was only indirect and inconsistent evidence about how much patients wanted to know about their prognosis. No studies comparing ways of disclosing diagnosis or prognosis to patients with CNS tumours were identified.

In a recent UK observational study 25% of patients with brain tumours expressed concerns about the way in which doctors or nurses communicated with them.

Evidence from a systematic review, considered in the NICE guidance 'Improving supportive and palliative care for adults with cancer',³⁹ supports the use of communication skills training for healthcare professionals.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- provision of training in communication skills for all healthcare professionals involved in the care of patients with CNS tumours
- availability of key professionals with advanced communication skills for communicating complex medical information and potentially distressing information, such as about prognosis and end-of-life issues
- development of guidelines for face-to-face communications at key points in the patient pathway

³⁹ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Process

- attendance at advanced courses on communications skills by senior clinicians and key professionals treating patients with CNS tumours
- evidence of the provision of clear, written records of significant communications and consultations at all points in the patient pathway and their outcome
- evidence of clear, timely communication of information and policies for informing relevant clinical teams in other settings (primary, secondary and tertiary care)
- audit of interprofessional communication

Outcome

- patients', their relatives' and carers' and healthcare professionals' satisfaction with communication process
- patients' awareness of their diagnosis and prognosis before treatment is started, with the opportunity to be involved in decision-making

E. Resource implications

The recommendation concerning training in communication skills has not been formally costed as it is likely to be part of existing continuing professional development arrangements.

8

Patient information

The patient information issues for patients with cancer have been extensively described in the NICE guidance 'Improving supportive and palliative care for adults with cancer' (topic 4, page 64).⁴⁰

⁴⁰ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Patients with CNS tumours have specific information needs, particularly when there is some degree of cognitive impairment. There are many specialist organisations that can help with the provision of suitable information for specific groups of patients. Information can be provided in different formats such as spoken, written and audio-visual. Different patient groups and their relatives and carers will have different needs and the provision of access to appropriate information is important.

Healthcare professionals should discuss the use of complementary therapies with patients, their relatives and carers and help identify possible side effects or interactions with conventional treatment.

A. Recommendations

There should be a nominated CNS tumours information lead at cancer network MDT level. These CNS tumours information leads should consider ways to develop a regularly updated central register of information for patients.

Cancer networks should ensure that patient and carer groups have the opportunity to ask questions of specialist healthcare professionals. Cancer networks should determine the most effective way to facilitate this via their patient and public involvement arrangements.

Information on CNS tumour services should use existing high-quality sources.

Information on CNS tumours should include local and national societies, appropriate websites and other relevant publications.

Information materials containing clear, accurate and relevant information about each CNS tumour type should be made available to patients, their relatives and carers by all healthcare professionals. This material should explain what patients can expect to happen to them at each stage of their disease journey, and when and where each event will occur, with an explanation of the terminology. This should include information concerning any relevant clinical trials and research on a particular treatment.

Information on local specialist palliative care services should be available for professionals, patients, their relatives and carers at each stage of the patient pathway.

B. Anticipated benefits

The provision of clear, accurate information throughout the patient pathway will benefit patients, their relatives, carers and healthcare professionals.

Timely communication with the GP and primary healthcare team about the information materials given to the patient at various stages of the pathway will minimise the risk of patients receiving conflicting information.

A lead for CNS tumours patient information will enable members of the MDT and healthcare professionals involved with patients in other settings to increase their knowledge, and the level of support and coordination of services for the patient.

Through the information lead, information centre and group information sessions, patients, their relatives and carers can be directed to additional sources of information, self-help and support in their area, particularly voluntary organisations that have relevant helpline and information services.

C. Evidence

A systematic literature review considered the provision of information for adults with high-grade cerebral glioma. In one UK observational study approximately a third of patients and relatives said that the information they received lacked coherence. In two observational studies patients reported having had to seek out information themselves. No studies comparing different methods of providing information were identified. Qualitative data about consultations confirmed that information about diagnosis and prognosis should be tailored to the individual coping of patients and relatives but there was insufficient evidence to suggest a standard approach to disclosure.

An observational study of outpatients at a London cancer centre observed that 38% of the 60 patients with brain tumours complained of a lack of information about their illness and treatment. Problems with concentration or memory were reported by 83% of patients with brain tumours, suggesting that the method of delivery of information is an important consideration for this group of people.

The development and distribution of information for patients, their relatives and carers is considered in the NICE guidance 'Improving supportive and palliative care for adults with cancer'.⁴¹ A systematic review confirms that patients with cancer obtain benefit from accurate and relevant information.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- evidence that patient pathway information is available that is specific to the service provided
- high-quality patient information material available for each CNS tumour type in appropriate formats
- a nominated lead for patient information on CNS tumours at the cancer network MDT
- provision of appropriate information materials

Process

- survey of experience of MDT members of the quality of information and support on CNS tumours provided by the cancer network lead

Outcome

- patients', their relatives' and carers' satisfaction with information giving

⁴¹ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

E. Resource implications

The total costs in England and Wales to charities in producing information leaflets for patients with CNS tumours are estimated to be around £14,620 for the first year and £10,400 for subsequent years (this estimate does not include any overheads). The estimate includes three generic leaflets on different types of CNS tumours and one neuroscience centre-specific leaflet. This calculation assumes that the centre-specific leaflets are designed and produced collaboratively to avoid unnecessary duplication.

Booklets produced by CancerBACUP are free to individual patients with cancer and at a charge of £1.95 each to professionals.

Cancer networks need to be aware that there will be an additional funding requirement for the information to be available in audio and visual format, the costs of which are not yet available.

Further information can be found in the resource implication section of the NICE guidance 'Improving supportive and palliative care for adults with cancer'.⁴²

Psychological support services including neuropsychology and neuropsychiatry

The psychological support service issues for patients with cancer have been extensively described in the NICE guidance 'Improving supportive and palliative care for adults with cancer' (topic 5, page 74).⁴²

Patients with CNS tumours may experience psychological difficulties in adjusting to a serious, life-threatening condition in the same way as other patients with cancer. In addition, patients with CNS tumours frequently have cognitive and psychological problems and undergo personality changes.

Therefore clinical neuropsychologists, with specialist training and expertise in the assessment and management of cognitive impairment and personality change, and neuropsychiatrists, with specialist training and expertise in the management of patients with severe mental health problems in the context of organic brain disease, have a key contribution to the care of patients with CNS tumours.

⁴² National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Regular assessment of the psychological needs of patients and monitoring of their cognitive and personality changes are an important part of their continuing care. Such assessment includes joint working with a range of relevant healthcare professionals.

A. Recommendations

Psychological assessment and support should be an integral part of the MDT management of patients with brain and other CNS tumours.

Neuropsychology and neuropsychiatry services should be adequately resourced to enable referral of patients who require specialist intervention for cognitive, emotional or behavioural problems.

One member of the cancer network MDT should be nominated to maintain links with specialist psychology services.

Ongoing training should be provided for all staff providing psychological support to patients with CNS tumours, their relatives and carers.

The psychological and social well-being of the patient, their relatives and carers should be considered throughout the course of the illness.

B. Anticipated benefits

A coordinated cancer network will be more capable of delivering consistent, efficient and effective psychological/psychiatric support to CNS tumour patients within the network.

There will be a reduction in psychological distress and improvement in health-related quality of life and some other functional outcomes.

C. Evidence

There is observational evidence that neuropsychological assessment consistently reveals cognitive deficits in patients with CNS tumours, both at the time of diagnosis and in long-term survivors. Observational studies in patients with CNS tumours undergoing radiotherapy and surgery support the use of neuropsychological testing to evaluate the effects of treatment. There is limited evidence to suggest that neuropsychological assessment during follow-up may reveal tumour recurrence although the effect of follow-up neuropsychological testing on patient outcomes has not yet been established.

There is limited research on the changes in mood and personality associated with CNS tumours; there is some evidence that such changes are some of the hardest symptoms for relatives and carers to understand and cope with.

Observational studies evaluating the neurorehabilitation of patients with primary malignant CNS tumour indicate the effectiveness of such work. One such study reported on a series of patients with primary or metastatic tumours of the CNS who underwent rehabilitation at a UK neurological rehabilitation unit. The study demonstrated a general improvement, measured using two scales of physical and cognitive functioning; the majority of patients were discharged.

Research on the effectiveness of neuropsychological rehabilitation has so far mainly involved patients with other pathologies, such as survivors of stroke or traumatic brain injury, who have comparable if distinct disabilities. However, three systematic reviews of the effectiveness of cognitive rehabilitation following stroke and two evidence-based technology appraisals of cognitive rehabilitation following traumatic brain injury were unable to draw firm conclusions because of variability in the methods and patient populations of the primary studies.

The need for neuropsychiatry services is supported by observational evidence that psychiatric states of depression and anxiety are relatively common in patients with CNS tumours, both before and after treatment, with a prevalence of between 17% and 30%. However, expert opinion held that many patients who would benefit from neuropsychiatry services were not being referred. The complementary role of neuropsychology in this area is supported by consistent evidence from systematic reviews of therapeutic psychological interventions for depression and anxiety in people with cancer (NICE guidance 'Improving supportive and palliative care for adults with cancer'⁴³).

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

⁴³ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

D. Measurement

Structure

- evidence of specific referral criteria to appropriate specialists, including neuropsychologists and neuropsychiatrists
- a designated MDT member with responsibility for coordination and communication with specialist services
- provision of resources to enable staff to undergo the necessary training and continuing professional development
- a documented organisational map of local specialist clinical services

Process

- evidence of MDT engagement in audit programmes
- annual record of number/proportion of patients referred on for specialist assessment and intervention
- user surveys and questionnaires on psychological support needs and experiences
- delays in the provision of psychology/psychiatric services

Outcome

- patients', their relatives' and carers' satisfaction
- quality of life

E. Resource implications

The resource implications of minimum staffing to provide psychological support services including neuropsychology and neuropsychiatry are presented in Chapter 5 and in more detail in section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns). Additional costs will be incurred in some neuroscience centres where the recommended staffing levels are not met. Local commissioners will need to investigate further to establish numbers.

Rehabilitation services

The rehabilitation needs for patients with cancer have been extensively described in the NICE guidance 'Improving supportive and palliative care for adults with cancer' (topic 10, page 134).⁴⁴ The rehabilitation needs for patients with long-term conditions is described in the 'National service framework for long term conditions'.⁴⁵

Patients with CNS tumours experience complex physical, cognitive and psychological problems. The ensuing functional impairment, loss of independence and potentially severe disabilities are distressing for patients, their relatives and carers. Patients with a poor prognosis require urgent access to rehabilitation services to optimise function and maximise the quality of their remaining life. Some tumours carry a good long-term prognosis, yet a patient's ability to live and function independently may be compromised and they may require ongoing rehabilitation services for a prolonged period of time.

Patients who are unable to continue to live independently need to be in an appropriate environment where their individual needs can be identified and met by a range of healthcare and social care professionals.

Rehabilitation services are provided by a range of allied health professionals (AHPs) including:

- physiotherapists
- occupational therapists
- speech and language therapists
- dieticians.

The following may also have a role in the provision of rehabilitation services for patients with CNS tumours:

- nurses
- primary healthcare team
- neuropsychology, neuropsychiatry and psychological therapy
- social services care manager/continuing care manager

⁴⁴ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

⁴⁵ Department of Health (2005) National Service Framework for long term conditions. London: Department of Health. Available from: www.dh.gov.uk

- orthotists/appliance officers
- wheelchair and other equipment services
- chaplaincy services.

The NICE guidance ‘Improving supportive and palliative care for adults with cancer’⁴⁵ describes a four-level model of rehabilitation, assessment and support services with the range of healthcare professionals involved at each level.

Throughout their disease journey, patients with CNS tumours may require input from healthcare professionals depending on their individual needs and problems. Multidisciplinary rehabilitation teams provide services for stroke patients and patients with head injury, but it is not always possible for patients with CNS tumours to obtain treatment from these teams. There are several reasons for this.

- Strict referral criteria may exclude patients with CNS tumours.
- A large workload may mean that it is not possible for the team to respond quickly enough to a patient with rapidly changing needs.
- Healthcare professionals working in a rehabilitation team may feel inadequately trained to help patients with CNS tumours and require education, advice and support from more experienced specialist colleagues.

8

A. Recommendations

Commissioners should ensure that implementation of the recommendations in the NICE guidance ‘Improving supportive and palliative care for adults with cancer’⁴⁶ includes services for patients with CNS tumours.

There should be rapid access to AHP assessment and rehabilitation services, including specialist neurorehabilitation when appropriate, as a patient’s condition changes.

There should be immediate access to specialist equipment, as necessary.

⁴⁶ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Cancer networks should nominate a lead AHP in neuro-oncology who has overall responsibility for coordinating the provision of rehabilitation services, education, training and research throughout the network.

In addition, cancer networks should ensure that specialist AHPs, working at level 4, are available throughout the network and that patients have access to them as and when appropriate.

Multidisciplinary rehabilitation teams should be available for the continued management of patients with CNS tumours at home or in the community.

Where it is not feasible for patients with CNS tumours to be cared for by the existing neurorehabilitation team(s), commissioners should ensure that an equivalent service is provided by a cancer network neuro-oncology rehabilitation team.

Commissioners should work with local social services to ensure that age-appropriate long-term placements can be found for those patients with CNS tumours requiring such facilities.

Patients with spinal cord tumours should have the opportunity to undergo intensive rehabilitation in a specially adapted unit such as a spinal injuries unit, in order for them to achieve their maximum functional potential. Commissioners should ensure that patients with spinal tumours can be admitted to such units and that the treatment programme is appropriate to their needs.

B. Anticipated benefits

Effective and timely provision of rehabilitation services will help to optimise function and maximise quality of life for patients, their relatives and carers.

A cancer network approach to service provision, including education and training for rehabilitation professionals, will ensure equitable access to services.

C. Evidence

Evidence for specialist motor and cognitive rehabilitation in patients with CNS tumours is of low quality, but several observational studies report on patients who undergo rehabilitation at specialist units.

These observational studies suggest that patients with primary or metastatic CNS tumours may benefit from rehabilitation. However, the studies were non-comparative so it is impossible to say how much of the improvement was due to the rehabilitation. Studies measuring cognitive and motor functioning during rehabilitation found greater relative improvement in motor functioning than in cognitive functioning

The levels of functional improvement observed in these observational studies are reported as similar to those seen in patients with traumatic brain injury.

It is unclear whether greater functional improvement is seen in patients who undergo concurrent radiotherapy than in those who do not, although expert review evidence suggests that rehabilitation need not be excluded where aggressive therapy is taking place.

Studies report that a high proportion of patients with CNS tumours are discharged following rehabilitation, although readmission to acute hospitals is also common.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- lead AHP in neuro-oncology in cancer network
- availability of cancer-network-wide access to appropriate rehabilitation specialists and services
- evidence of referral criteria to neurorehabilitation teams
- provision of rehabilitation facilities – inpatient, outpatient, domiciliary services, hydrotherapy, specialist neurorehabilitation services, specialist palliative care services
- provision of cancer-network-wide training/support/education programmes for all healthcare professionals involved in the care of patients with CNS tumours

Process

- audit of delays in the provision of rehabilitation services and equipment
- audit of numbers of specialist AHPs coordinating rehabilitation
- audit of delays in the provision of long-term placements in age-appropriate facilities, where appropriate

Outcome

- patients', their relatives' and carers' satisfaction
- quality of life
- functional status with rehabilitation

E. Resource implications

The resource implications for multidisciplinary rehabilitation services for patients with brain and CNS tumours have not been analysed as a separate service. Resource implications associated with allied healthcare professionals who provide rehabilitation services are presented in Chapter 5. Additional costs will be incurred in some neuroscience centres where the recommended minimum staffing levels described in the resource implications for Chapter 5 are not met. Further details are provided in section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Further information can also be found in the resource implication section of the NICE guidance 'Improving supportive and palliative care for adults with cancer'.⁴⁷

General palliative care

The general palliative care issues for patients with cancer have been extensively described in the NICE guidance 'Improving supportive and palliative care for adults with cancer' (topic 8, page 105).⁴⁷

⁴⁷ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Although palliative care is particularly important for patients with CNS tumours in the later stages of their illness, a palliative approach is needed for many from the time of diagnosis.

As CNS tumours are relatively rare, most generalist health and social care professionals (members of the primary care team, community nurses, care home staff, hospital doctors and nurses, AHPs, social workers, self-help and support groups) will have little experience of the particular care needs of these patients. However, they will be the ones who deliver the majority of care in most settings, including those where little or no specialist service is available. Palliative care may be only a small part of the normal workload of these professionals and so they should know when and how to seek advice from, or refer to, specialist palliative care services.

A number of important measures can help them to provide a high-quality service for patients with CNS tumours. These include access to education and training in palliative care, and being involved in regular assessment of the patients' needs.

Regular needs assessments will increase communication and cooperation between services providing care, and improve delivery of a service shaped to the individual needs of patients. To aid best practice in the community, a GP practice-based managed plan of care for patients at home, such as the gold standards framework 'A programme for community palliative care',⁴⁸ could be used.

Patients with brain tumours may undergo progressive cognitive impairment, personality change and other neurological deterioration and it may not be feasible for them to determine their preferred place of care or death. An increased burden therefore may fall on their relatives and other carers, who will in turn need appropriate support. However, it is important that the patient's preferred place of death is noted and measures taken to comply when possible.

A. Recommendations

Palliative care education and training for healthcare professionals should include when and how to seek advice from, or refer to, specialist palliative care services.

⁴⁸ Royal College of General Practitioners and NHS End of Life Care Programme (2005) Gold standards framework. *A programme for community palliative care*. London: Royal College of General Practitioners Available from: www.goldstandardsframework.nhs.uk

Patients with CNS tumours should have the opportunity for regular systematic needs assessment by healthcare professionals with training in general palliative care, and discussion with the local specialist palliative care service about further involvement as needed.

The preferred place of care and place of death should be discussed with patients with CNS tumours and their relatives and carers, and their wishes should be observed where possible.

B. Anticipated benefits

Implementation of the NICE guidance 'Improving supportive and palliative care for adults with cancer',⁴⁹ with its emphasis on regular needs assessment, will increase communication and cooperation between the services providing care and with patients, their relatives and carers. This will lead to the delivery of a service better shaped to the patient's needs and increase the chances of the patient's preference for place of death being met.

Providing training and education for generalists will also aid the appropriate involvement of specialist palliative care throughout the course of the patient's illness.

C. Evidence

Most of the evidence presented in support of the recommendations for general palliative care was originally reviewed in the NICE guidance 'Improving supportive and palliative care for adults with cancer'.⁴⁹

Evidence from surveys suggests shortcomings in the assessment of the palliative care needs of patients with advanced cancer in general healthcare settings.

A recent literature review noted additional difficulties in the assessment of symptoms and concerns in patients with cognitive impairments as a result of a brain tumour.

⁴⁹ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Surveys of healthcare professionals have identified a need for education and training in the management of patients with advanced-stage illness. Evidence from randomised controlled trials supports the use of such training programmes in helping to change clinical practice. There is limited evidence that the use of guidelines can help coordinate referral from general to specialist palliative care services.

A UK survey into trends over a 10-year period showed that although many people wanted to die at home, only around 25% of people with cancer did so, the remainder dying in hospital, hospice or care home. Reasons for the change in place of death included lack of out-of-hours nursing care, medication or equipment as well as a change of mind by the patient.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- availability of criteria/pathway for referral to specialist palliative care, including contact information and service provided
- availability of a preferred place of care plan for patients with CNS tumours

Process

- development of palliative care training/education for generalists and audit of staff involved in direct patient care who have attended such sessions
- audit of patients with CNS tumours achieving/maintaining their preferred place of care and death

Outcome

- survey of MDT members' experience of access to specialist palliative care for patient needs
- surveys on satisfaction of CNS tumour patients, their relatives and carers with palliative care access and provision, and the outcome of the preferred place of care plan.

E. Resource implications

The resource implications of the recommendations for general palliative care for patients with CNS tumours and their relatives and carers have not been included in the resource implications. It may be helpful for commissioners to refer to the economic analysis for the NICE guidance on 'Improving supportive and palliative care for adults with cancer'.⁵⁰

Social support and continuing care

The social support needs of the patient will vary according to the level of disability, progression of disease, patient preference, level of relatives/carer support and informal services. The provision of care should meet the needs of patients allowing for age, gender and cultural differences.

Continuing care (or long-term care) is a general term that describes the care that people need over an extended period of time, as a result of disability, accident or illness, to address both physical and mental needs. The care can be provided in different settings: NHS hospital, nursing home, residential home or in the patient's home. Patients with an intermediate prognosis but with a high level of care need joint assessment by NHS and local council in accordance with 'Continuing care: NHS and local councils' responsibilities'.⁵¹ There is a 'duty of partnership' between health authorities and councils. Collaborative working across these boundaries is necessary.

A. Recommendations

The provision of long-term care arrangements should be in accordance with 'Continuing care: NHS and local councils' responsibilities'.⁵¹

Younger patients with continuing care needs should also be carefully considered. Procedures should be in place to ensure the continuing care needs of younger patients with CNS tumours are appropriately met.

Needs for social support should be elicited as an integral component of routine assessment, ideally undertaken with or by a social care professional.

⁵⁰ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

⁵¹ Department of Health (2001) *Continuing care – NHS and local councils' responsibilities*. London: Department of Health. Available from: www.dh.gov.uk

Specialist palliative care

Specialist palliative care services help patients with cancer and other life-threatening illnesses that are no longer responsive to curative treatment. Specialist palliative care teams manage complex symptom problems and also provide spiritual and emotional support for patients, their relatives and carers. They may also be a resource for the education and support for healthcare professionals. These services are provided by statutory and voluntary organisations and cover the spectrum of community, hospice and hospital settings. The National Institute for Clinical Excellence (NICE) guidance 'Improving supportive and palliative care for adults with cancer', published in March 2004, provides detailed information and makes recommendations about specialist palliative care that complement and inform this site-specific guidance (topic 9, page 122).⁵²

Patients with brain and other CNS tumours, in particular, have palliative care service needs. They may often experience progressive neurological, cognitive and personality changes over the course of their illness and there may sometimes be rapid changes in their symptoms especially when disease is advanced. More of these patients could benefit from specialist palliative care around or soon after the time of diagnosis, depending on assessed need, but for many this does not happen until much later in their illness when they are considered to have reached the terminal phase.

Closer integration between specialist palliative care and neuro-oncology services throughout the patient's illness can help a smooth transition from more active treatment to palliative care, ensuring access to specialist palliative care services at the right point in the patient pathway.⁵² This will necessitate opportunities for sharing patient care, such as joint clinics and joint ward rounds, as well as ensuring that palliative care specialists are included at MDT meetings.

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⁵² National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

A. Recommendations

Palliative care specialists should be included as members of the neuroscience brain and other CNS tumours multidisciplinary team (MDT) and the cancer network brain and other CNS tumours MDT. They should provide advice on palliative and supportive care and the management of symptoms, and contribute to the patient's management plan, including advice on onward referral to local services as appropriate.

Cancer networks should ensure that healthcare professionals in neuro-oncology services and specialist palliative care services work closely together throughout the patient's illness to ensure an appropriate balance between active treatment and palliative care.

Cancer networks should ensure that there are clear mechanisms in place for referral to and from specialist palliative care services for patients with CNS tumours, with referral at the time of diagnosis, when appropriate.

Information on local specialist palliative care services should be available for healthcare professionals, patients, their relatives and carers at each stage of the patient pathway.

B. Anticipated benefits

Closer integration between services and involvement of specialist palliative care earlier in the patient pathway will improve communication and ensure that services are more responsive to patients' needs. This will lead to increased levels of satisfaction for patients, their relatives and carers.

Closer working relationships between healthcare professionals will aid the timely transfer of patients from services and treatments that maximise survival to those that emphasise optimising symptom control, function, emotional support and quality of life.

Improved continuity of care between services and settings could help more patients to continue to remain in their preferred place of care both as their illness progresses and when they are dying.

C. Evidence

There is consistent evidence, reviewed in the NICE guidance 'Improving supportive and palliative care for adults with cancer',⁵³ to show that specialist palliative care teams in hospital, hospice and community settings are effective for the control of pain and symptoms of people with cancer. Patients cared for by such teams were also more satisfied than those cared for elsewhere. It follows that involvement of specialist palliative care, as soon as is appropriate, should benefit patients with CNS tumours. The importance of early involvement of specialist palliative care teams for the specific, and often severe, symptoms experienced by people presenting with CNS cancer is supported by a recent literature review. A 2003 observational study of outpatients attending a London cancer centre, including 60 patients with brain tumours, identified a high level of unmet need for specialist palliative care, especially among those with lung cancer or brain tumours.

It seems likely that clear referral criteria and a closer working relationship between neuro-oncology and specialist palliative care services will improve communication, support and coordination of care. However, there is insufficient evidence at present to specify the best mix of roles and links between services to ensure that the palliative care needs of patients with CNS tumours are met. The NICE guidance 'Improving supportive and palliative care for adults with cancer'⁵³ considered the coordination of palliative care. Evidence from two randomised controlled trials suggests that a nurse coordinator, acting as the link between patient and health services, reduced the number of days spent in hospital by the patients and the number of home visits by the community care team, and helped enable patients to die at home.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbrains).

D. Measurement

Structure

- evidence that palliative care specialists are included as members of MDT meetings
- availability of referral criteria/pathway to and from specialist palliative care services

⁵³ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

- evidence of integration of patient care between neuro-oncology services and specialist palliative care
- provision of information on specialist palliative care services

*Improving Outcomes for
People with Brain and
Other CNS Tumours*

Specialist palliative care

Process

- audit of referrals to specialist palliative care according to referral criteria/pathway
- audit of shared decision-making, communication and information on patient care
- audit of provision of specialist palliative care interventions such as symptom control

Outcome

- patients', their relatives' and carers' and professionals' satisfaction with experience of service/care

E. Resource implications

The resource implications of providing specialist palliative care for patients with CNS tumours are presented in Chapter 5. Additional estimated annual employment costs of £24,872 will be incurred in some neuroscience centres where the recommended minimum staffing levels to provide a safe and sustainable service are not met. Further details are included in section 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

It may be helpful for commissioners to refer to the economic analysis for the NICE guidance on 'Improving supportive and palliative care for adults with cancer',⁵⁴



⁵⁴ National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

Information management

The information available on the management of patients with brain and other central nervous system (CNS) tumours in England and Wales is limited. Two UK-based regional studies have shown that the registration of patients with primary brain tumours is very incomplete. There is also little reliable information on the national incidence of some of the rarer tumour subtypes, for example brain and CNS lymphoma.

Good-quality data are required to:

- establish a baseline for future comparisons
- provide commissioners with information about appropriate service provision
- monitor performance against standards
- show improvements in outcome.

Collecting data on this group of tumours is particularly difficult for the following reasons.

- These tumours present via a diverse variety of routes.
- They have a complex classification system subject to change between revisions to the 'International Classification of Diseases 10th edition (ICD-10)', which often do not conform to the World Health Organization (WHO) classification of CNS tumours.⁵⁵
- Their management is often complex, involving different teams and services that may not be part of the same cancer network.
- Some are diagnosed on the basis of imaging only, without histopathological confirmation.

It is therefore important that, as a minimum, information is recorded for clinical audit purposes on:

- all patients with a radiological diagnosis of CNS tumours

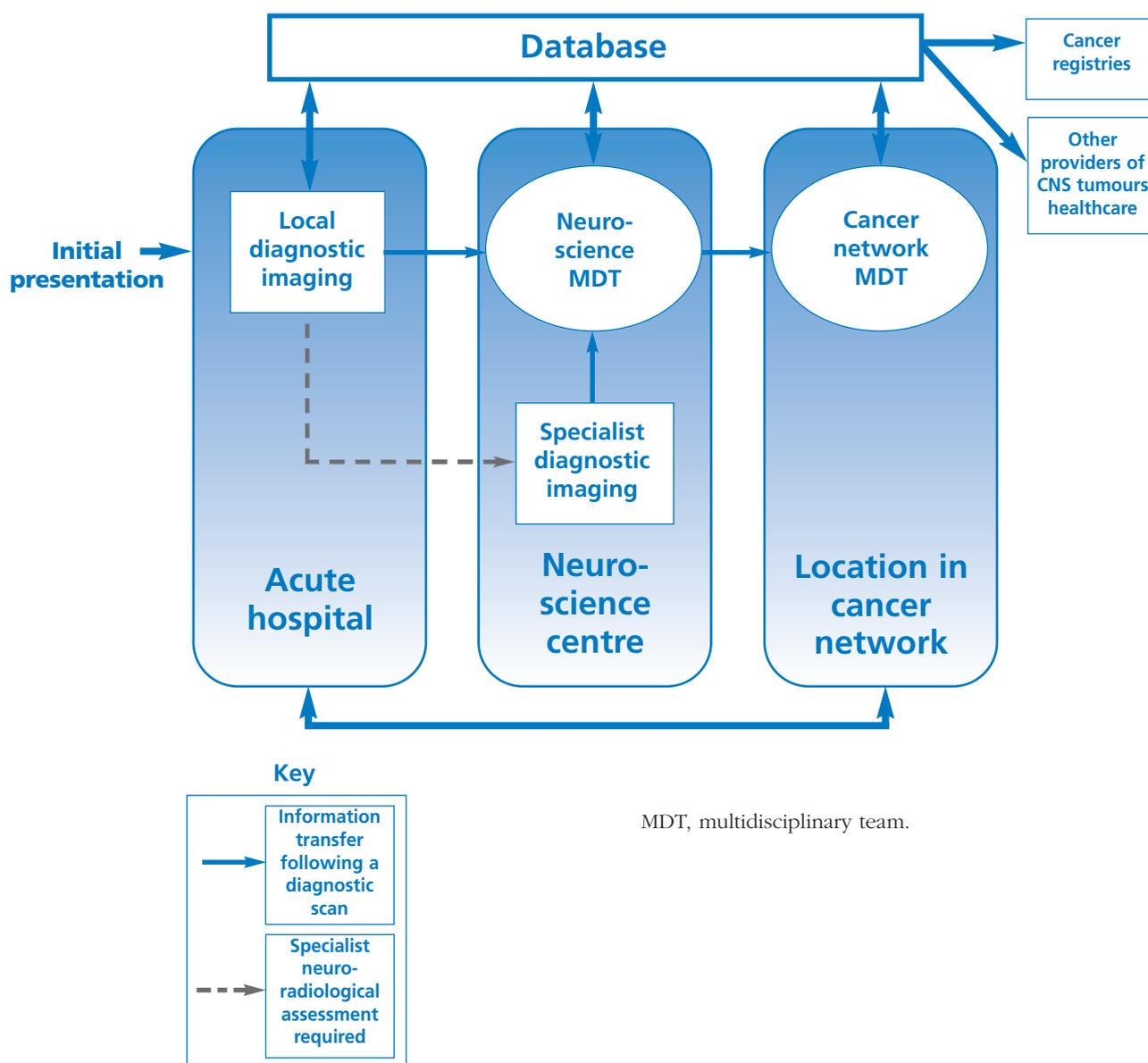
⁵⁵ Kleihues P, Cavenee WK (2000) *Pathology and genetics of tumours of the nervous system*. Lyon: IARC Press.

- any further investigations and the confirmed diagnosis (with the cancer registry notified)
- the management plan agreed by the specialist multidisciplinary team (MDT)
- the initial treatment provided
- outcomes, both short- and long-term.

Complex pathways of care, however, also mean that additional information has to be easily available to support MDT decision-making and clinical management.

A schematic representation of the information management pathway is shown in Figure 6.

Figure 6. Information management pathway for brain and other central nervous system (CNS) tumours



A. Recommendations

Data collection systems should be in place that allow entry of information on all patients with a radiological or histopathologically confirmed CNS tumour. Consideration should be given to a web-based information system that will allow easy data sharing between healthcare professionals across services, and complies with data protection legislation.

A local retrieval system that identifies all radiology reports that mention CNS tumours should be developed and maintained until digital, coded reporting systems are universal.

The lead clinician of the neuroscience MDT and the lead clinician of the cancer network MDT should assume overall responsibility for ensuring that complete data are collected, verified and recorded on all patients reviewed by the teams. Strong links with the local cancer registry should be developed to ensure complete and accurate registration of all patients.

The data collection responsibilities of the various MDT members should be clearly defined in local protocols.

Adequate clerical support should be provided for the MDTs to facilitate data collection.

The national minimum datasets for CNS tumours should be adopted in both England and Wales when they become available.

B. Anticipated benefits

A web-based database and data collection system will enable members of the MDT to enter and review information on patients at all stages of the patient pathway regardless of where treatment or care is delivered. In addition it will provide a versatile mechanism that will facilitate data entry, regardless of the exact structure of service provision at a local level.

Such a system will:

- ensure that all patients with CNS tumours are recorded
- improve registration
- enable management of patients through an appropriate MDT structure

- enhance management of patients to agreed protocols
- allow better monitoring of the access of patients to palliative and supportive care and to advice and support from allied health professionals (AHPs)
- make regular clinical audit of the processes (access, appropriate investigation and treatment, waiting) and outcomes of care easier
- improve communication between clinical teams
- improve recruitment into trials.

C. Evidence

A comprehensive review of primary and secondary brain tumour incidence studies published between 1966 and 1995 provides indirect evidence of the incompleteness of existing data sources. Studies using a single source (such as a cancer registry or hospital database) to identify patients reported incidence rates that were 30% lower than studies using two to four sources, and 50% lower than studies that used more than four sources.

A 2001 study of primary brain tumour registration between 1992 and 1996 compared a clinical database with official figures from the Devon and Cornwall regional cancer intelligence unit. Only 52% of potential cases identified from the clinical database were entered in the official registry, suggesting that figures from registries could significantly underestimate the incidence of primary brain tumours. The study also reported that patients in the registry were not a representative sample of the clinical population with brain tumours. Factors increasing the likelihood of a patient being registered were: having had an operation, being older than 60 years and requirement for radiotherapy. Survival calculated using registry data could therefore be underestimated, since patients with poorer prognosis were more likely to be registered.

A study of the incidence of primary and secondary brain tumours from 1989 to 1990 in the Lothian region of Scotland used multiple methods of case ascertainment to identify 442 patients. Only 34% of the patients were entered in the Scottish Cancer Registry.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- compatible local, regional and, eventually, national electronic information systems that comply with Data Protection legislation

Process

- evidence that information on all patients is available at MDT meetings
- evidence of network, supra-network and national audits of treatment and care

Outcome

- short-, medium- and long-term survival of patients undergoing treatment for brain tumours that includes information on cancer stage, comorbidity, age and other features of case mix
- complication rates after surgery, radiotherapy and chemotherapy
- quality of life and short- and long-term adverse effects of treatment

E. Resource implications

Full recording of the national minimum datasets for CNS tumours in England and Wales when it becomes available will have resource implications that have not been possible to include in this review. The resource implication section of Chapter 2 includes employment costs for MDT coordinators in the neuroscience and cancer network MDTs. Clerical support costs are included in the resource implication section of Chapter 5 in the cost estimates for minimum staffing levels at neuroscience centres to provide a safe and sustainable service. This will ensure that clerical staff are available for full recording of information. In view of the low incidence and the increasing automation of cancer registries, it is unlikely that any additional costs will be incurred at the registries. Further details are discussed in sections 3 and 5 of the economic analysis, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

The research evidence on which the care of patients with brain and other central nervous system (CNS) tumours is at present based is incomplete and often inadequate. There are several reasons for this.

- CNS tumours are uncommon, and there are many histological tumour types, some of which are extremely rare.
- Only a small proportion of patients with CNS tumours are recruited into clinical trials.
- Comparison between trials is often difficult because of varied entry criteria.
- Clinical trials have mainly investigated treatment and largely ignored other important issues such as diagnosis and supportive care.
- There is no coordinated approach across UK neuropathology departments with regard to the collection and storage of adult CNS tumour samples for scientific research.

New technologies with proved usefulness in other areas of cancer care require specific validation before being brought into general use for patients with CNS tumours.

Currently, clinical neuro-oncology research in this field in the UK is haphazard and uncoordinated and dependent on the enthusiasm and interest of individual clinicians and departments. This situation is unlikely to improve where the critical mass of clinical researchers is both small and dwindling from lack of support. Although a considerable proportion of laboratory research is funded by charitable bodies, improvements in the treatment of these rarer tumours is unlikely to match that of more prevalent cancers until funding for research is at least equivalent. This should be directed at strengthening the manpower and infrastructure of clinical research units through, for example, the UK Clinical Research Collaboration (UKCRC) network initiative. Such support would enable well-supported units to compete equally for the appropriate nationally funded grant monies. Further integration of basic laboratory and translational research through such

organisations as the British Neuro-Oncology Society, Society of British Neurological Surgeons and the National Cancer Research Network (NCRN) and the established National Cancer Research Institute (NCRI) Clinical Studies Group on brain tumours should be supported. The development of the NCRI/NCRN/Clinical Trials Advisory and Awards Committee (CTAAC) trials framework together with these initiatives offers a unique opportunity to develop effective CNS tumour research with a strategic, coordinated approach, active leadership, careful management and administrative support to advance the field and ensure that NHS money is spent appropriately.

Some specific clinical/therapeutic issues are important and need to be considered in the development of a clinical research programme.

- Many trials of the management of patients with high-grade gliomas have been selective in patient entry and future trials need to include patients who represent the spectrum of disease to reduce selection bias.
- The most effective method for the management of patients with low-grade glioma is unclear.
- There is no robust research on patients with either high- or low-grade gliomas comparing the effects of resection and biopsy on survival and quality of life.
- Several new radiotherapy techniques, new chemotherapy agents and methods of drug delivery are being introduced into clinical practice, but they still need proper evaluation.
- The effects of treatment following first and subsequent relapse on survival and quality of life are uncertain.
- There is little evidence that the use of newer imaging techniques for surveillance alters clinical outcomes for patients.
- There is currently no nationally coordinated programme of translational research for adult CNS tumours, which could usefully interact with such organisations as the European Organisation for the Research and Treatment of Cancer (EORTC).

A particular issue for patients with CNS tumours is the effect that the disease itself and the treatment may have on cognitive function. Neuropsychological assessment, in conjunction with other performance measures, has been shown to give a better indication of adverse effects of treatments and it may also have a role in the early detection of recurrence of low-grade gliomas. Further research is needed to explore these issues.

Communication may be or may become a problem for patients with CNS tumours when they develop cognitive problems, and there is clearly a need for further research into the most effective ways of communicating information about diagnosis, prognosis and progression of disease and how this may affect quality of life.

There is also scope for health services research into various aspects of care in particular into the most appropriate use of the healthcare professionals involved in supportive care and rehabilitation, and into the links between services to ensure that patients' needs are met most effectively and efficiently.

A. Recommendations

NHS R&D, all relevant research charities, NCRN and senior researchers in this field should collaborate and jointly plan a programme of clinical and translational CNS tumour research, including its funding and the fostering of an appropriate research structure in collaboration with the UKCRC.

The development of new diagnostic tests for CNS tumours should be facilitated by supporting the inclusion of biological studies alongside clinical trials, the retention and storage of appropriate tumour samples for these studies, and translational research aimed at taking molecular markers from the research to the health service environment.

The NCRI Clinical Studies Group on brain tumours should be encouraged to develop an extended portfolio of trials. All neuroscience brain and other CNS tumours multidisciplinary teams (MDTs) should have an active and up-to-date NCRN portfolio of clinical trials to offer to patients.

Cancer networks should be able to demonstrate how they intend to ensure that trials are supported. Patient entry into these studies should be actively monitored.

A national approach should be developed for the storage and retention of tumour samples, with appropriate consent, and for a coordinated programme of basic science and translational research to complement the clinical research programme.

B. Anticipated benefits

A greater number of patients with CNS tumours will have access to clinical trials.

There should be further improvements in outcomes with increased research.

C. Evidence

A recent study estimated years of life lost using data from the East Anglian Cancer Registry to represent the population burden from 17 cancers. Although patients with tumours of the CNS had the highest average years of life lost per patient, this tumour group attracted only 1.5% of NCRI research spending (using 2002 figures).

There is some evidence to suggest low enrolment rates of patients with CNS tumours in clinical trials. The Glioma Outcomes Project reported in 2005 that only 15.1% of its group of 788 American patients with high-grade glioma were enrolled in clinical trials.

The incompleteness of the evidence base for the management of CNS tumours is reflected in the number of systematic reviews unable to draw useful conclusions because of lack of high-quality research. A recent review of randomised clinical trials in low-grade glioma, for example, identified only three completed randomised controlled trials of radiotherapy and one of chemotherapy which was terminated prematurely. In the absence of high-quality randomised controlled trials reviewers must rely on evidence from studies with diverse protocols which are often low powered. It is reasonable to assume that collaboration between research centres should improve the quality of the evidence base both by increasing trial accrual and through the use of agreed protocols.

Full details of the references appraised and evidence tables are available in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

D. Measurement

Structure

- adequate provision of resources including research staff for the entry of patients into clinical trials
- evidence that local research arrangements, particularly within the MDTs, are promoting the participation in national clinical trials

Process

- surveys of the number of eligible patients who are offered entry to an appropriate clinical trial

Outcome

- outcomes of patients treated within a clinical trial or research protocol

E. Resource implications

The resource implications of the research recommendations have not been formally costed. Priorities for allocating research funds are made by national, government and charitable medical research funding agencies.

Appendix 1

Scope of the guidance

A1

1. Guidance title

Guidance on Cancer Services: Improving Outcomes for People with Tumours of the Brain and Central Nervous System (CNS).

1.1 Short title

Brain and CNS tumours

2. Background

- a) The National Institute for Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Cancer to develop service guidance on tumours of the brain and central nervous system for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health and Welsh Assembly Government (see page 139). The guidance will provide recommendations for service provision that are based on the best available evidence.
- b) The Institute's service guidance will support the implementation of the National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The guidance will support current national initiatives outlined in the *NHS Cancer Plan*, the Calman Hine report, the Cameron report, the *Manual for Cancer Service Standards for England* and the *All Wales Minimum Standards for Cancer Services*.

The guidance will also refer to other NICE service guidance documents currently under development, including Referral guidelines for suspected cancer, Supportive and palliative care for people with cancer, Improving outcomes in child and adolescent cancer, Improving outcomes in head and neck cancers and Improving outcomes in haemato-oncology.

Cross-reference will be made to these and other documents as appropriate.

3. Clinical need for the guidance

- a) There were approximately 4000 new cases of primary brain and other CNS tumours in adults registered in the UK during 1999 (Cancer Research UK). These cancers can occur at any age but are more common in adults over 40 years of age. In 2001 around 3300 adults died from brain and other CNS tumours (Cancer Research UK). These figures are now widely thought to be an underestimate and this issue needs investigation as part of the Guidance development.⁵⁶
- b) Although relatively uncommon tumours, at around 2% of all registered cancers, the treatment of brain and CNS tumours is complex requiring the input of many different health care professionals. A proportion of patients are significantly disabled physically, cognitively and psychologically by their illness and the consequences of treatment. This adds considerably to the overall burden of care for both family and health care professionals.

4. The guidance

- a) The guideline development process is described in detail in three booklets that are available from the NICE website (see 'Further information'). *The Guideline Development Process – Information for Stakeholders* describes how organisations can become involved.
- b) This document is the scope. It defines exactly what this piece of service guidance will (and will not) examine, and what the developers will consider. The scope is based on the referral from the Department of Health and Welsh Assembly Government (see page 139).
- c) The areas that will be addressed by the guidance are described in the following sections.

⁵⁶ Pobereskin LH; Chaddock JH (2000) Incidence of brain tumours in two English counties: a population based study. *Journal of Neurology, Neurosurgery, and Psychiatry* 69: 464–71.

4.1 Population

4.1.1 Groups that will be covered

- a) Adults with tumours of the brain (including primary CNS lymphomas and teratomas), meninges and other sites in the central nervous system.
- b) Adults with cranial nerve tumours and primary base of skull tumours.
- c) Adults with pituitary tumours.
- d) Adults with brain metastases from tumours at other primary sites in whom complex neurological or neurosurgical intervention is required.
- e) Adults with syndromes where there is a recognised increased lifelong risk of CNS tumour formation.
- f) Adults with nerve root tumours compressing the spinal cord.

4.1.2 Groups that will not be covered

- a) Children and adolescents with brain and CNS tumours whose care will be covered by the Child and Adolescent guidance.
- b) Adults and children with tumours of peripheral nerves.
- c) Adults and children with other space occupying brain lesions (for example, arteriovenous malformation).

4.2 Healthcare setting and services

- a) Primary care, including diagnosis, treatment and follow up.
- b) Secondary care, including the role of cancer networks and multidisciplinary teams.
- c) Tertiary care in cancer centres and neuroscience centres.
- d) Specialist rehabilitation centres.
- e) Quaternary care in specialist centres for particular indications (for example, stereotactic radiosurgery).

4.3 Key areas of clinical management

The following key areas of clinical management will be included, because they have direct implications for service delivery.

- a) Services for diagnosis and staging (excluding those being addressed as part of the updated referral guidelines) including:
- primary care
 - acute services in secondary care
 - neurology departments
 - neurosurgical departments
 - pathology departments
 - diagnostic radiology departments
 - psychiatric services
 - endocrinology departments

In addition, the guidance will address the important issue of data collection and registration of brain and CNS tumours.

- b) Treatment services, to include treatment in the following settings:
- neurology departments
 - neurosurgical departments
 - cancer centres
 - cancer units
 - endocrinology departments.
 - specialist centres providing stereotactic radiosurgery.
- c) Follow up.
- d) Rehabilitation and supportive care of patients with physical and neuropsychological/neuropsychiatric disability.

- e) Specific elements of supportive and palliative care that meet the particular needs of patients with brain and CNS tumours, and of their families and carers.
- f) Communication and information resources for patients, carers, family members and health care professionals.
- g) Health service research and clinical trials on service delivery.

4.4 Audit support within the guidance

The guidance will include key criteria for audit, which will enable objective measurements to be made of the extent and nature of local implementation of this guidance, particularly its impact upon practice and outcomes for adults with brain and CNS tumours.

4.5 Status

4.5.1 Scope

This is the final version of the scope.

4.5.2 Guidance

The development of the service guidance recommendations will begin in January 2004.

5. Further information

Information on the guideline development process is provided in:

- *The Guideline Development Process – Information for the Public and the NHS*
- *The Guideline Development Process – Information for Stakeholders*
- *The Guideline Development Process – Information for National Collaborating Centres and Guideline Development Groups.*

These booklets are available as PDF files from the NICE website (www.nice.org.uk). Information of the progress of the guideline will also be available from the website.

Appendix – Referral from the Department of Health and Welsh Assembly Government

*Improving Outcomes for
People with Brain and
Other CNS Tumours*

Appendix 1

The Department of Health and Welsh Assembly Government asked the Institute:

‘To prepare service guidance for the NHS in England and Wales for tumours of the brain and central nervous system. This would form part of the *Improving cancer outcomes* series with NICE expected, as previously, to involve the Department of Health and Welsh Assembly Government closely in the development of the guidance. In particular, the Department of Health and Welsh Assembly Government should be alerted at an early stage to any issues in the developing guidance, which are likely to lead to significant changes in the current service provision.’

A1

Appendix 2

List of low-grade glioma (LGG) and high-grade glioma (HGG) tumour classification

A2

Based on World Health Organization classification of tumours. Kleihues P, Cavenee WK (2000) *Pathology and Genetics of Tumours of the Nervous System*. Lyon: IARC Press.

Table A1. Classification of gliomas

| Gliomas | WHO grade | grouping |
|-------------------------------------|-----------|----------|
| Astrocytic tumours | | |
| Diffuse astrocytoma | 2 | LGG |
| Anaplastic astrocytoma | 3 | HGG |
| Glioblastoma | 4 | HGG |
| Pilocytic astrocytoma | 1 | LGG |
| Pleomorphic xanthoastrocytoma | 2 | LGG |
| Subependymal giant cell astrocytoma | 1 | LGG |
| Oligodendroglial tumours | | |
| Oligodendroglioma | 2 | LGG |
| Anaplastic oligodendroglioma | 3 | HGG |
| Mixed gliomas | | |
| Oligoastrocytoma | 2 | LGG |
| Anaplastic oligoastrocytoma | 3 | HGG |

| Gliomas | WHO grade | grouping |
|---------------------------|------------------|-----------------|
| Ependymal tumours* | | |
| Ependymoma | 2 | n/a* |
| Anaplastic ependymoma | 3 | n/a* |
| Myxopapillary ependymoma | 1 | n/a* |
| Subependymoma | 1 | n/a* |

* Although classified as gliomas, ependymomas are uncommon idiosyncratic circumscribed tumours that are regarded clinically and therapeutically as distinct from gliomas of astrocytic or oligodendroglial lineage. There is also uncertainty about the clinicopathological value of distinguishing between classic (WHO grade 2) and anaplastic (WHO grade 3) ependymomas.

Appendix 3

Prognostic factors for survival in adult patients with cerebral low-grade glioma (EORTC criteria)

A3

Factors associated with poor prognosis for survival in adult patients with cerebral LGG are:

- age \geq 40 years
- largest diameter of the tumour \geq 6 cm
- tumour crossing the midline
- astrocytoma histology (compared with oligodendroglioma/mixed histology)
- presence of neurological deficit.

Pignatti F, van den Bent M, Curran D et al. (2002) European Organization for Research and Treatment of Cancer (EORTC) Data Centre. Prognostic factors for survival in adult patients with cerebral low-grade glioma. *Journal of Clinical Oncology* 20: 2076–84.

Economic implications of the guidance

Executive summary

The economic consequences of the recommendations of the 'Guidance on Cancer Services: Improving Outcomes in Brain and Other CNS Tumours' in England and Wales are set out in this document. The analysis focuses on those aspects of the key recommendations that are likely to be of greatest consequence in terms of costs.

The summary of economic implications is outlined in Table A2.

There is uncertainty concerning the estimates presented and there will be variation at the neuroscience centre and cancer network level. Sensitivity analyses were conducted where appropriate in the estimated costs. Further assessments will be needed at cancer network level and/or NHS trust level to determine the exact cost implications. The calculations for employment costs are based on pay levels at 2005/06, any future pay awards will also need to be taken into consideration. Work is currently being carried out in the NHS in England, in connection with 'Payment by Results', to develop a better understanding of costs of treatment and care. This may help these assessments in the future.

A4

Table A2. Summary of estimated annual economic implications

| | Costs per year (£) | |
|--|--|-------------|
| | Lower range | Upper range |
| Staffing costs of weekly neuroscience MDT meetings (per centre) | 73,320 | 188,084 |
| Staffing costs of monthly cancer network MDT meetings (per network) | 7,266 | 18,336 |
| Site-specific MDTs ^a | | |
| Staffing costs of monthly pituitary MDT meetings (per MDT) | 5,994 | 15,768 |
| Staffing costs of monthly spinal cord MDT meetings (per MDT) | 5,172 | 12,924 |
| Staffing costs of monthly skull base MDT meetings (per MDT) | 7,044 | 18,912 |
| Staffing costs for each MRI scanner ^b | 267,071 | |
| Molecular pathology costs (staffing and test costs for MGMT assay) | 1,283,090 | |
| Core employment costs of neuroscience centre | 1,308,005 | 2,180,008 |
| Total employment costs of additional clinical nurse specialists | 1,932,346 | |
| Total employment costs of additional neuropathologists | 1,474,208 | |
| Employment costs per centre of additional allied health professionals | 48,726 | 97,453 |
| Total employment costs of additional palliative care specialists | 223,848 | |
| Cost of producing information leaflets (for all patients with brain and other central nervous system tumours in England and Wales) | 14,620 (year 1) 10,400 (subsequent years) | |

^a It is uncertain how many site-specific multidisciplinary teams (MDTs) will be required.

^b There is overlap between these figures for employment cost of radiologist and radiographer. MGMT, O6-methylguanine-DNA methyltransferase.

The guidance recommends that attendance at multidisciplinary team (MDT) meetings should form part of the timetabled activities for core MDT members. It is assumed that extra resources will need to be made available to enable staff to attend MDT meetings. Meeting costs are derived by estimating the time spent attending meetings by different staff, multiplied by their hourly rate (salary and on-costs), in addition to preparation time.

It is anticipated that for those cancer networks with no neuroscience brain and other CNS tumours MDT in place, there will be an annual opportunity cost of between £73,320 for minimum attendance of a weekly 2-hour neuroscience MDT and up to £188,084 for full attendance at weekly 3-hour neuroscience MDT meetings.

All cancer networks will have an additional opportunity cost for establishing a cancer network brain and other CNS tumours MDT. This is estimated to be between £7266 per year for minimum attendance at monthly 1-hour MDT meetings and £18,336 for full attendance at monthly 2-hour MDT meetings.

Site-specific MDTs

For each pituitary MDT in place, there will be annual opportunity costs of between £5994 for minimum attendance at monthly 1-hour MDT meetings and £15,768 for full attendance at monthly 2-hour MDT meetings.

For each spinal cord MDT in place, there will be annual opportunity costs of between £5172 for minimum attendance at monthly 1-hour MDT meetings and £12,924 for full attendance at monthly 2-hour MDT meetings.

For each skull base MDT in place, there will be annual opportunity costs of between £7044 for minimum attendance at monthly 1-hour MDT meetings and £18,912 for full attendance at monthly 2-hour MDT meetings.

Diagnosis – radiology

Government initiatives are under way to improve access to computed tomography (CT) and magnetic resonance imaging (MRI) facilities. There is a need for imaging facilities to have dedicated time available for patients with brain and CNS tumours. Existing scanners need to be adequately staffed to ensure that they are able to operate throughout the working day. It has been estimated that the staffing

level needed to run an MRI scanner during normal working hours would be 1.3 full-time equivalent (FTE) consultant neuroradiologists, 3.0 FTE neuroradiographers plus additional administrative support. The annual cost of this level of staffing is £267,071 per MRI scanner.

Diagnosis – pathology

Molecular diagnosis is a fast developing area of clinical practice, and cancer networks will need to plan for expansion over the next 10–20 years. At present, existing services for molecular diagnosis are adequate for the numbers of patients who require testing. If a specific molecular diagnostic test such as the MGMT assay becomes available, then it is anticipated that an additional 30 biomedical scientists would be required in England and Wales. The total additional annual cost for the anticipated 2500 MGMT tests in England and Wales, including consumables, and staffing to perform them is estimated to be £1,283,090. If two more similar molecular tests were to be adopted for brain and other CNS tumours over a period of 10 years, then the total costs might double.

Minimum staffing costs at neuroscience centres

The annual employment costs of the core staffing components of a neuroscience centre treating 100 new patients per year is estimated to be around £1,744,006 (\pm 25% range, £1,308,005–2,180,008). There will be economies of scale for neuroscience centres that have all facilities on site. As a result of uncertainty in this estimate a sensitivity analysis of \pm 25% has been applied. It needs to be emphasised that the costs represent opportunity costs, as most of the staff involved in the treatment centres will already be contracted to the NHS.

Clinical nurse specialists

The needs assessment⁵⁷ conducted to inform the guidance development indicated that there was a variation in the numbers of clinical nurse specialists for neuro-oncology across England and Wales. Although 3 (of 27) neurosurgical units and 4 (of 45) oncology/radiotherapy units had more than the recommended minimum staffing for clinical nurse specialists in neuro-oncology, the remainder had less. To ensure that there are a minimum of 1.5 specialist nurses at each unit, a further 39.2 FTE would need to be recruited at oncology/radiotherapy units and a further 11.5 FTE at neurosurgical units. Therefore, an additional 50.7 FTE clinical nurse specialists are required in England and Wales at an estimated annual employment cost of £1,932,346.

⁵⁷ Humphreys C (2005) *Health needs assessment: adults with tumours of the brain and central nervous system in England and Wales*. National Public Health Service for Wales, Gwasanaeth Iechyd Cyhoeddus Cenedlaethol Cymru. Available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns).

Neuropathologists

A report for the Royal College of Pathologists from the British Neuropathological Society has recommended that there should be 1 FTE neuropathologist per 1,000,000 patients. To achieve this level, a further 15 FTE posts are required across England and Wales with an estimated employment cost of around £1,474,208. There are currently seven single-handed neuropathologists in England and Wales, and these would need to be supported to ensure continual cover of the adult neuro-oncology service in these centres.

Allied health professionals

It has been estimated by the members of the Guidance Development Group (GDG) that it is likely that an additional 0.5–1 FTE speech and language therapist, occupational therapist and physiotherapist may be required at each neuroscience centre as a result of the guidance. The employment cost estimate for the three additional allied health professionals (AHPs) is between £48,726 (1.5 FTE) and £97,453 (3 FTE) per centre. This estimate is uncertain, as it may be that some centres would recruit additional junior staff to enable more experienced staff to concentrate on specialist work.

Palliative care specialists

To ensure that there are a minimum of 0.4 FTE palliative care specialists available at all neuroscience centres additional staff will need to be recruited. The estimated additional cost for the nine neurosurgical centres without palliative care support is estimated to be around £223,848. This estimate is based on a split between palliative care specialist nurses and consultants (60/40). Further investigation will be required at a local level to establish whether palliative care consultants, nurse specialists or a mixture of both are required. In addition, those centres that stated that palliative care was available may need additional funding to increase current level of staffing. As with the other staff discussed in this section, it is possible that the staffing situation has improved since this survey was conducted.

Patient information

The guidance suggests that patients with brain and other CNS tumours have specific information needs, particularly when there is some degree of cognitive impairment, and require information to be provided in different formats such as spoken, written and audio-visual. The total cost of producing and distributing generic and centre-specific information leaflets would be £14,620 in the first year for all patients with brain and other CNS tumours in England and Wales. In subsequent years the costs would be £10,400.

A wide range of high-quality information is available from a variety of sources on the internet. These mainly include charitable foundation web pages. Set-up costs of having information available are therefore unlikely to be significant.



How this guidance manual was produced

This service guidance is intended to guide health organisations (strategic health authorities, primary care trusts, local health boards, cancer networks and trusts), their managers and lead clinicians in improving the effectiveness and efficiency of services for people with brain and other central nervous system (CNS) tumours. The information and recommendations in the manual are based on reviews of the best available evidence on diagnosis, treatment and service delivery. This evidence was retrieved by information specialists and assessed by researchers at the National Collaborating Centre for Cancer (NCC-C) and the recommendations are the product of extensive discussion with the Guidance Development Group (GDG). A brief overview of the development process to produce the guidance is provided below.

The first stage in the development of the guidance was the production of a scope (appendix 1) which defined in detail the patient population, the healthcare settings and services and key areas of clinical management that the guidance should cover. This was then subject to a 4-week consultation with registered stakeholders in line with National Institute for Health and Clinical Excellence (NICE) methodology. Following this a multidisciplinary GDG was formed comprising clinicians representing the main stakeholder organisations and representatives from relevant patient organisations and charities (appendix 5.2). The GDG was convened by the NCC-C and chaired by Dr Penny Bridger in close association with the Clinical Lead, Dr Sean Elyan. All GDG members made and updated any declarations of interest. The Group met on a monthly basis during development of the guidance and NCC-C staff provided methodological support and leadership for the development.

During the development phase of the guidance the GDG identified areas where there was a requirement for expert input on particular specialist topic areas. These topics were addressed by the production of a position paper by a recognised expert who had been identified via the relevant registered stakeholder organisation. All relevant expert positions papers are presented in appendix D of the evidence review (available on the CD-ROM that accompanies this guidance and on the NICE website [www.nice.org.uk/csgbraincns]).

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The identification and retrieval of evidence to support the recommendations in the guidance manual is described in detail in the evidence review, which is available on the CD-ROM that accompanies this guidance and on the NICE website (www.nice.org.uk/csgbraincns). Briefly, there were three stages to this process:

- *Clinical question development.* Members of the GDG were asked to submit clinical questions to the NCC-C on issues covered by the project scope.
- *Literature searching.* All clinical questions were prioritised and were subject to either a systematic or 'high-level' search.
- *Critical appraisal.* Finally all full papers relevant to each clinical question were appraised using the methodology described in the 'The guidelines manual' (2006 edition).

It should be noted that most of the published research on cancer topics focuses on clinical evaluations of treatment; little direct research has been carried out on the organisation and delivery of services.

To gain insight into the current cancer services provision for patients with brain and other CNS tumours, a needs assessment was commissioned by the GDG and NCC-C. This study was carried out by Dr Ciaran Humphreys at the National Public Health Service Wales. The full results are published separately on the NICE website (www.nice.org.uk/csgbraincns) and are also available on the CD-ROM that accompanies this guidance.

All the evidence reviews used to inform the manual are summarised in the document 'Improving Outcomes in Brain and Other CNS Tumours: the Research Evidence' and include details of all the studies appraised. This document is published separately on the NICE website (www.nice.org.uk/csgbraincns) and is also available on the CD-ROM that accompanies this guidance.

Additional complementary research, designed to quantify the potential cost of major changes in services, was carried out by the Centre for the Economics of Health, Institute of Medical and Social Care Research (IMSCAR) at the University of Bangor. This work involves literature searching, interviews with clinicians and managers, and analyses of costs. The economic analysis document is published separately on the NICE website (www.nice.org.uk/csgbraincns) and is also available on the CD-ROM that accompanies this guidance.

The writing of the guidance manual was coordinated by the Chair and Clinical Lead of the GDG in accordance with all members of the GDG, assisted by staff at the NCC-C.

*Improving Outcomes for
People with Brain and
Other CNS Tumours*

Appendix 5

The production of this guidance was funded by NICE, and has been subject to the full NICE consultation process.

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Appendix 6

People and organisations involved in the production of this guidance

- 6.1 Members of the Guidance Development Group**
- 6.2 Organisations invited to comment on guidance development**
- 6.3 Researchers carrying out literature reviews and complementary work**
- 6.4 Expert advisers to the Guidance Development Group**
- 6.5 Members of the Guideline Review Panel**

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| Professor Phil Heywood | Professor of Primary Care Development, University of Leeds |
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All Wales Senior Nurses Advisory Group (Mental Health)

Amersham Health

Anglesey Local Health Board

Association for Palliative Medicine of Great Britain and Ireland

Association of British Neurologists

Association of Hospice and Specialist Palliative Care Social Workers

Association of Neuro-oncology Nurses (ANON)

Association of Professional Music Therapists

Association of Surgeons of Great Britain and Ireland

Association of the British Pharmaceuticals Industry (ABPI)

Aventis Pharma

Bard Limited

Barking, Havering & Redbridge NHS Trust

Barts & The London NHS Trust

BASIC (Brain and Spinal Injury Charity)

Bath and North East Somerset PCT

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Bayer PLC

Bedfordshire & Hertfordshire NHS Strategic Health Authority

Boehringer Ingelheim Ltd

Boston Scientific Limited

Brain and Spine Foundation

British Association for Counselling and Psychotherapy

British Association of Neuroscience Nurses

British Association of Oral and Maxillofacial Surgeons

British Dietetic Association

British National Formulary (BNF)

British Nuclear Medicine Society

British Oncology Pharmacy Association

British Orthoptic Society

British Paediatric Neurology Association

British Psychological Society

British Psychosocial Oncology Society

British Society of Neuroradiologists

British Society of Paediatric Radiology

British Society of Rehabilitation Medicine

BUPA

Cancer and Leukaemia in Childhood (UK)

CancerBACUP

Cancer Research UK

Cancer Services Collaborative 'Improvement Partnership' (CSCIP)

Cancer Services Coordinating Group

Cancer Voices

Chartered Society of Physiotherapy

Children's and Adolescent Cancer Partnership (CACP)

Clatterbridge Centre for Oncology NHS Trust

Clinovia Ltd

College of Occupational Therapists

Conwy and Denbighshire NHS Trust

Cornwall Partnership Trust

Department of Health

Derbyshire Mental Health Services NHS Trust

Eisai Limited

Elan Pharmaceuticals Ltd

Eli Lilly and Company Ltd

Faculty of Public Health

GE Health Care

Gloucestershire Hospitals NHS Trust

Gorlin Syndrome Group

Great Ormond Street Hospital for Children NHS Trust

Guerbet Laboratories Ltd

Hammersmith Hospitals NHS Trust

Hampshire & Isle of Wight Strategic Health Authority

Headway – The Brain Injury Association

Healthcare Commission

Help Adolescents with Cancer

Help the Hospices

Hertfordshire Partnership NHS Trust

Institute of Biomedical Science

International Brain Tumour Alliance

Joint Committee on Palliative Medicine

Link Pharmaceuticals

Macmillan Cancer Relief

Marie Curie Cancer Care

Medeus Pharma Ltd

Medical Research Council Clinical Trials Unit

Medicines and Healthcare Products Regulatory Agency (MHRA)

Medway NHS Trust

Merck Pharmaceuticals

National Alliance of Childhood Cancer Parent Organisations

National Cancer Alliance

National Cancer Network Clinical Directors Group

National Cancer Research Institute (NCRI) Clinical Studies Group and
National Cancer Research Network (NCRN)

National Patient Safety Agency

National Public Health Service – Wales

Neurological Alliance

NHS Direct

NHS Health and Social Care Information Centre

NHS Modernisation Agency

NHS Quality Improvement Scotland

Novartis Pharmaceuticals UK Ltd

Pfizer Limited

Plymouth Hospitals NHS Trust

Princess Alexandra Hospital NHS Trust

Richmond & Twickenham PCT

Royal College of Anaesthetists

Royal College of General Practitioners

Royal College of General Practitioners Wales

Royal College of Nursing (RCN)

Royal College of Paediatrics and Child Health

Royal College of Pathologists

Royal College of Physicians of London

Royal College of Psychiatrists

Royal College of Radiologists

Royal College of Speech and Language Therapists

Royal College of Surgeons of England

Royal College Patient Liaison Groups

Royal Liverpool Children's NHS Trust

Royal Pharmaceutical Society of Great Britain

Royal Society of Medicine

Royal West Sussex Trust

Samantha Dickson Research Trust

Schering-Plough

Scottish Intercollegiate Guidelines Network (SIGN)

Sheffield Children's NHS Trust

Sheffield South West Primary Care Trust

Sheffield Teaching Hospitals NHS Trust

Society and College of Radiographers

Society for Endocrinology

Society of British Neurological Surgeons

Southampton University Hospitals NHS Trust

South West Peninsula Strategic Health Authority

Stroke Association

Teenage Cancer Trust

Thames Valley Strategic Health Authority

UK Children's Cancer Study Group

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Appendix 6.5

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Glossary of terms

Adenoma

Adenomas are benign epithelial tumours of glandular tissue.

Adjuvant chemotherapy

Chemotherapy treatment that is given in addition to the main cancer treatment.

Adjuvant therapy

Additional treatment that is added to increase the effectiveness of the main treatment.

Aetiology

The cause or origin of disease.

Allied health professional (AHP)

One of the following group of healthcare workers: physiotherapists, occupational therapists, art therapists, chiropodists/podiatrists, dietitians, drama therapists, music therapists, orthoptists, paramedics, prosthetists/orthotists, diagnostic radiographers, therapeutic radiographers, speech and language therapists.

Anaplastic

Cells in 'anaplastic' tumours show marked variation in size and shape (cytological pleomorphism) and signs of rapid proliferation. Anaplastic tumours may also contain areas of dead (necrotic) tissue and formation of new blood vessels (angiogenesis).

Angiography

The X-ray visualisation of the internal anatomy of the heart and blood vessels after injection of a radio-opaque (shows up on X-rays) contrast material.

Asymptomatic

Without obvious signs or symptoms of disease. In early stages, cancer may develop and grow without producing symptoms.

Audiology

The study of hearing.

Audit

A review and evaluation of healthcare procedures.

Autosomal

Refers to a chromosome that is not involved in determining sex. If a disorder is autosomal it affects both males and females equally.

Base of skull

The sloping floor of the cranial cavity.

Benign

Not cancerous; not malignant.

Biopsy

Removal of a sample of tissue or cells from the body to assist in diagnosis of a disease.

Brachytherapy

Radiotherapy delivered by a temporary or permanent implant of radioactive material into a tissue or organ.

Brain tumour

A tumour found in the intracranial portion of the central nervous system.

Cancer

Growth of altered body cells that keep on growing and is able to spread from where it started to another part of the body.

Cancer networks

The organisational model for cancer services to implement the NHS Cancer Plan, bringing together health service commissioners and providers, the voluntary sector and local authorities. There are currently 34 cancer networks in England and three in Wales, covering a population of between 600,000 and 3 million (two thirds serve a population of between 1 and 2 million people).

Cancer registry

An organisation that systematically collects information about cancer incidence and mortality within its resident population.

Carcinoma

Cancer of the epithelial tissue that covers all the body organs and lines all the body cavities. Most cancers are carcinomas.

Central nervous system

The portion of the nervous system comprising the brain and spinal cord.

Cerebrospinal fluid

The fluid that flows around the brain and the spinal cord.

Chemosensitivity

The specific sensitivity of an individual to chemotherapy drugs.

Chemotherapy

The use of drugs that kill cancer cells, or prevent or slow their growth.

Clinical nurse specialist

A nurse with specialist knowledge of central nervous system tumours and skills in communication as defined by the Manual for Cancer Services.

Clinical oncologist

A doctor who specialises in the treatment of cancer patients, particularly through the use of radiotherapy, but who may also use chemotherapy.

Clinical oncology

The specialist treatment of cancer patients, particularly through the use of radiotherapy, but that may also use chemotherapy.

Clinical trial

A research study with patients, usually to evaluate a new treatment or drug.

Cognitive

Relating to the mental processes of comprehension, judgement, memory and reasoning.

Cohort studies

Research studies in which groups of patients with a particular condition or specific characteristic are compared with matched groups who do not have it.

Community nurse

A nurse who provides care to individuals in the community and outside of hospital.

Computed tomography (CT)

An X-ray technique that produces cross-sectional images.

Concordance

A new way of defining the process of successful prescribing and taking medicines, based on a partnership between doctors and patients (see www.medicines-partnership.org).



Cranial nerves

The 12 pairs of nerves that emerge from the cranial cavity through openings in the skull.

Craniotomy

A surgical incision or opening into the skull.

Curative

Aiming to cure a disease.

Cytogenetics

The study of chromosomes and chromosomal abnormalities.

Cytological examination

The examination of cells on a microscope, especially for diagnosis, performed by a specialist in pathology.

Cytopathology

The study of disease changes within individual cells or cell types.

Diagnostic imaging

Visualising body structures to help identify a disease or condition, by using X-ray, ultrasound, radioisotopes or magnetic resonance.

Diagnostic investigations

Tests undertaken to establish the nature of disease.

Diagnostic radiographer

A health professional trained in the technique of obtaining images of various parts of the body, working closely with a radiologist.

Dietitian

The healthcare professional responsible for the planning and managing of the patient's diet in hospital and providing dietary advice for a wide range of medical conditions.

Ear, nose and throat (ENT)

Diagnosis and treatment of diseases of the ear, nose and throat.

Endocrine

Having to do with glandular tissues that secrete hormones directly into the bloodstream.

Endocrinologist

A doctor who specialises in treating diseases of the endocrine system.

Endoscopy

The visual inspection of any cavity of the body using a special instrument.



Epidemiology

The study of populations in order to determine the frequency and distribution of disease and measure risks.

Epilepsy

A group of neurological disorders characterised by recurrent episodes of either convulsive seizures, sensory disturbances, abnormal behaviour or loss of consciousness.

Excise/excision

Removal by surgery.

Fractionation

Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days.

Germ cell

The reproductive cells of the body: in men, the testicular cell that divides to produce the immature sperm cells; in women, the ovarian cell that divides to form the egg.

Glial

Specialised cells that surround neurones and provide physical support and insulation.

Glioma

A cancer of the brain that begins in glial cells (cells that surround and support nerve cells). A 'high-grade' glioma is one that grows rapidly and has an aggressive behaviour. High-grade tumours are grades 3 and 4 in the WHO classification. The grade of CNS tumour correlates with prognosis (1 – best; 4 – worst)

Gorlin syndrome

An inherited condition that can increase an individual's chance of developing basal cell carcinoma. Also called basal cell naevus syndrome.

Gynaecologist

A doctor who specialises in the diagnosis and treatment of disorders affecting the female reproductive organs.

Haematologist

A doctor who specialises in disorders of the blood and blood-forming tissues.

Haematopoietic

The process by which blood cells are produced in the bone marrow.

Histological

Relating to the study of cells and tissue at a microscopic level.

Histology

The study of body tissue and cells by examination under a microscope.

Histopathologist

A clinical doctor who specialises in examining abnormal tissue samples microscopically in order to make a diagnosis and ensure tumour excision is complete.

Histopathology

The study of microscopic changes in diseased tissues.

Holistic

Looking at the whole system rather than just concentrating on individual components.

Imaging

The production of a clinical image using radiology, for example an X-ray or ultrasound.

Immunosuppression

Suppression of the body's immune system and its ability to fight infections or disease. Immunosuppression may be deliberately induced with drugs. It may also result from certain diseases such as lymphoma or from anticancer drugs.

Intracranial pressure

Pressure that occurs within the cranium (skull).

Intraoperative

Relating to the period during a surgical procedure.

Intrathecal

Into the fluid around the spine.

Ionising radiation

High-energy electromagnetic waves (for example, X-rays) and particles (for example, electrons) used for radiotherapy treatment.

Irradiation

The use of high-energy radiation from X-rays, gamma rays, neutrons and other sources to kill cancer cells and shrink tumours.

Key worker

Person who, with the patient's consent and agreement, takes a key role in coordinating the patient's care and promoting continuity, ensuring the patient knows whom to access for information and advice.

Lesion

An area of abnormal tissue.

Leukaemia

Cancer of the blood-forming system in the bone marrow, usually characterised by the production of abnormal white blood cells, which may be present in the bone marrow and blood.

Li–Fraumeni syndrome

An inherited family trait carrying an increased risk of cancer during childhood and early adulthood.

Local health board

Statutory bodies in Wales responsible for commissioning and providing health services on behalf of the local population.

Low-grade glioma

A CNS tumour that grows slowly, but which may or may not be successfully treated. Low-grade tumours are grades 1 and 2 in the WHO classification. The grade of CNS tumour correlates with prognosis (1 – best; 4 –worst).

Lymphoma

Cancer of the lymphatic system. There are two main types of lymphoma – Hodgkin's disease and non-Hodgkin's lymphoma.

Magnetic resonance imaging (MRI)

A non-invasive method of imaging that allows the form and metabolism of tissues and organs to be visualised (also known as nuclear magnetic resonance).

Malignant

Cancerous. Malignant tumours can invade and destroy nearby tissue and spread to other parts of the body.

Margin

The edge or border of the tissue removed in cancer surgery.

Maxillofacial

The specialty that combines full surgical training with dental expertise for the treatment of diseases, injuries, tumours and deformities of the face and jaws.

Medical oncologist

A doctor who treats cancer patients through the use of chemotherapy, and for some tumours immunotherapy.

Medical oncology

The specialist treatment of cancer patients through the use of chemotherapy, and for some tumours immunotherapy.

Medulloblastoma

A malignant brain tumour that begins in the lower part of the brain and that can spread to the spine or other parts of the body.

Meninges

The three membranes surrounding the brain and spinal cord.

Meta-analysis

The statistical analysis of the results of a collection of individual research studies in order to add the findings together.

Metastases

Cancerous tumours in any part of the body as a result of spread from the original (primary) origin.

Minimum dataset

A widely agreed-upon and generally accepted set of terms and definitions making up a core of data acquired for medical records and used for developing statistics for different types of analyses and users.

Molecular genetics

The branch of genetics that focuses on the chemical structure and the functions, replication and mutations of the molecules involved in the transmission of genetic information, namely DNA and RNA.

Molecular pathology

New techniques for identifying molecular abnormalities in the DNA of cells.

Morbidity

Either (1) the state of being diseased; or (2) the morbidity rate, which reflects the number of cases of disease per unit of population in any specific region, age group, disease or other classification, usually expressed as cases per 1000, 10,000 or 100,000.

Morphology

The science of the forms and structures of organisms.

Mortality

Either (1) the condition of being subject to death; or (2) the death rate, which reflects the number of deaths per unit of population in any specific region, age group, disease or other classification, usually expressed as deaths per 1000, 10,000 or 100,000.

Nasogastric feeding

Feeding via a tube that is passed through the nose and into the stomach.

Needle biopsy

The removal of tissue or fluid through a needle for examination of cells under a microscope.

Neoplasm

An abnormal mass of tissue that results from excessive cell division.

Neurofibromatosis

A genetic condition in which people develop multiple, benign tumours of nerve tissue.

Neuroimaging

Production of images of the brain by non-invasive techniques, for example computed tomography, magnetic resonance imaging or positron emission tomography.

Neurological

Having to do with the nervous system.

Neurologist

A doctor who diagnoses and treats disorders of the central nervous system.

Neuro-oncology

The branch of medical science dealing with tumours of the nervous system.

Neuropathology

The study of disease processes in the nervous system.

Neuropsychiatry

The branch of psychiatry relating to disorders of the central nervous system.

Neuropsychology

A discipline combining neurology and psychology to study the relationship between the functioning of the brain and cognitive processes or behaviour, using psychological testing and assessment to assay central nervous system function and diagnose specific behavioural or cognitive deficits or disorders.

Neuroradiologist

A doctor trained in radiology specialising in creating and interpreting pictures of the nervous system.

Neuroradiology

The branch of radiology that deals with the nervous system.

Neurorehabilitation

Rehabilitation that concentrates on improving physical and cognitive or understanding impairment resulting from damage to the nervous system.

Neurosurgeon

A doctor who specialises in surgery on the brain, spine and other parts of the nervous system.

Neurosurgery

Surgery on any part of the nervous system.

Observational study

A non-randomised study that observes the characteristics and outcomes over time of subjects who do and do not take a particular therapy.

Occupational therapist

A specialist who is concerned with a person's ability to participate in meaningful occupations and the impact of their environment on this; they will work with a person to design a programme of intervention based on the individual's unique lifestyle, environment and preferences.

Oncologist

A doctor who is trained to treat patients with chemotherapy (medical oncologist), radiotherapy or both (clinical oncologist).

Oncology

The study of the biology and physical and chemical features of cancers. Also the study of the causes and treatment of cancers.

Ophthalmology

The area of medicine dealing with the eye.

Optic disc

The small blind spot on the surface of the retina.

Optic glioma

A slow-growing tumour on the optic nerve.

Oral

Having to do with the mouth.

Orthopaedics

A branch of surgery that specialises in the study and treatment of the skeletal system, its joints, muscles and associated structures.

Orthotist

A skilled professional who fabricates orthotic devices that are prescribed by a physician.

Otolaryngologist

A doctor who specialises in treating diseases of the ear, nose and throat.

Palliative

Anything that serves to alleviate symptoms caused by the underlying cancer but is not expected to cure it.

Palliative care

Active, holistic care of patients with advanced, progressive illness that may no longer be curable. The aim is to achieve the best quality of life for patients and their families. Many aspects of palliative care are also applicable in earlier stages of the cancer journey in association with other treatments.

Papilloedema

Swelling of the optic disc.

Pathologist

A doctor who examines cells and identifies them. The pathologist can tell where a cell comes from in the body and whether it is normal or a cancer cell. If it is a cancer cell, the pathologist can tell what type of body cell the cancer developed from. In the hospital, practically all the diagnostic tests performed with material removed from the body are evaluated or performed by a pathologist.

Pathology

A branch of medicine concerned with disease, especially its functional effects on the body.

Patient pathway

A term used to denote the phases patients who are living with the consequences of cancer pass through, from the time they first suspect something might be wrong to beyond the end of treatment. It is dynamic and can be somewhat unpredictable. For some, the pathway will also include the time when cancer recurs and that leading up to their death.

Physiotherapist

A specialist trained in using exercise and physical activities to condition muscles and improve level of activity.

Pineal tumour

A tumour of the pineal body.

Pituitary tumour

A tumour of the pituitary gland.

Plastic surgeon

A doctor who specialises in surgery to correct damage to the skin, for example reducing the amount of scarring or disfigurement that may happen because of surgery to treat a skin tumour.

Positron emission tomography (PET)

A highly specialised imaging technique using a radioactive tracer to produce a computerised image of body tissues to find any abnormalities. PET scans are sometimes used to help diagnose cancer and investigate a tumour's response to treatment.

Prognosis

A prediction of the likely outcome or course of a disease; the chance of recovery or recurrence.

Prognostic factor

Patient or disease characteristics, for example age or comorbidity, which influence the course of the disease under study.

Protocol

An agreed policy that defines appropriate action.

Psychological

Adjective of psychology, which is the scientific study of behaviour and its related mental processes. Psychology is concerned with such matters as memory, rational and irrational thought, intelligence, learning, personality, perceptions and emotions and their relationship to behaviour.

Psychologist

A specialist who can talk with patients and their families about emotional, cognitive and personal matters, and can help them make decisions.

Radiographer

A person who assists the radiologist in imaging (diagnostic radiographer) or the radiotherapist in treatment (therapeutic radiographer).

Radiologist

A doctor who specialises in creating and interpreting pictures of areas inside the body using X-rays and other specialised imaging techniques. An interventional radiologist specialises in the use of imaging techniques to assist treatment, for example catheter insertion for abscess drainage.

Radiology

The use of radiation (such as X-rays) or other imaging technologies (such as ultrasound and magnetic resonance imaging) to diagnose or treat disease.

Radiosurgery

A radiation therapy technique that delivers radiation directly to the tumour while sparing the healthy tissue.

Radiotherapy (radiation treatment)

The use of radiation, usually X-rays or gamma rays, to kill cancer cells and treat tumours.

Randomised controlled trial (RCT)

A type of experiment that is used to compare the effectiveness of different treatments. The crucial feature of this form of trial is that patients are assigned at random to groups that receive the interventions being assessed or control treatments. RCTs offer the most reliable (that is least biased) form of evidence of effectiveness.

Reconstructive surgery

Surgery that is done to reshape or rebuild (reconstruct) a part of the body changed by previous surgery.

Resection

To remove tissue from the body by surgery.

Retrospective study

A study which searches for a relationship between one (usually current) condition and another that occurred in the past.

Single photon emission computed tomography (SPECT)

A variation of computed tomography (CT).

Specialist palliative care

Services in all sectors that specialise in palliative care and that include consultants in palliative medicine, clinical nurse specialists in palliative care and a range of other specialist expertise.

Speech and language therapist

A specialist trained in the assessment and management of communication and swallowing difficulties.

Stereotactic

The precise three-dimensional positioning of a surgical instrument or radiotherapy machine.

Supportive care

Care that helps the patient and their family and carers to cope with cancer and its treatment throughout the cancer journey, and in the case of the family and carers, into bereavement. It aims to help the patient maximise the benefits of treatment and provide the best possible quality of life.

Systematic review

A systematic review of the literature carried out in order to address a defined question and using quantitative methods to summarise the results.

Tertiary

Third level. Relating to medical treatment provided at a specialist institution.

Therapeutic radiographer

Therapeutic radiographers are responsible for providing radiotherapy treatment.

Toxicity

Refers to the undesirable and harmful side effects of a drug.

Trans-sphenoidal

Performed through the sphenoid bone, part of the base of the skull below the brain.

Tumour

A mass of excess tissue that results from abnormal cell division. Tumours perform no useful body function.

Unresectable

A tumour or mass that cannot be removed by surgery.

X-ray

A photographic or digital image of the internal organs or bones produced by the use of ionising radiation.

Abbreviations

| | |
|-----------------|--|
| AHP | allied health professional |
| AIDS | acquired immune deficiency syndrome |
| CI | confidence interval |
| CNS | central nervous system |
| CPA | clinical pathology accreditation |
| CSF | cerebrospinal fluid |
| CT | computed tomography |
| CTAAC | Clinical Trials Advisory and Awards Committee |
| DH | Department of Health |
| DNA | deoxyribonucleic acid |
| ENT | ear, nose and throat |
| EORTC | European Organisation for Research and Treatment of Cancer |
| EQA | external quality assurance |
| EUROCARE | European cancer registries study on cancer patients' survival and care |
| FTE | full-time equivalent |
| GCTs | germ cell tumours |
| GDG | Guidance Development Group |
| GP | general practitioner |
| HGG | high-grade glioma |
| HIV | human immunodeficiency virus |
| HR | hazard ratio |
| ICD | International Classification of Diseases |
| IT | information technology |
| LGG | low-grade glioma |
| MDT | multidisciplinary team |
| MGMT | O6-methylguanine-DNA methyltransferase |
| MR | magnetic resonance |
| MRI | magnetic resonance imaging |

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|------------------|--|
| NATCANSAT | National Cancer Services Analysis Team |
| NCC-C | National Collaborating Centre for Cancer |
| NCRI | National Cancer Research Institute |
| NCRN | National Cancer Research Network |
| NHS | National Health Service |
| NICE | National Institute for Health and Clinical Excellence |
| OR | odds ratio |
| PCNSL | primary central nervous system lymphoma |
| PCT | primary care trust |
| PET | positron emission tomography |
| PNET | primitive neuroectodermal tumor |
| R&D | research and development |
| RCT | randomised controlled trial |
| SPECT | single photon emission computed tomography |
| UK | United Kingdom |
| UKCCSG | United Kingdom Children's Cancer Study Group |
| UKCRC | United Kingdom Cancer Research Campaign |
| WBRT | whole brain radiotherapy |
| WHO | World Health Organization |

