National Institute for Health and Care Excellence

Final

Brain tumours (primary) and brain metastases in adults

Glossary and abbreviations

NICE guideline NG99

July 2018

Final

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



Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the <u>Welsh Government</u>, <u>Scottish Government</u>, and <u>Northern Ireland Executive</u>. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

© NICE 2018. All rights reserved. Subject to Notice of rights.

ISBN: 978-1-4731-3001-2

Contents

| lossary | 5 |
|---------------|---|
| obreviations2 | 8 |

Glossary

| Term | Definition |
|--------------------------------|--|
| 5-amino-levulinic acid (5-ALA) | A drug given to people with aggressive brain tumours to help the surgeon resect the maximum amount of tumour safely. The drug is dissolved in water and drunk before surgery. 5- ALA causes tumour cells to glow pink under special lighting, allowing the surgeon to distinguish between tumour and normal brain. |
| Abstract | Summary of a study, which may be published alone or as an introduction to a full scientific paper. |
| Active monitoring | This is regular clinical and radiological review of a person with a brain tumour or brain metastases who are not currently having treatment for their cancer.See also 'watch and wait'. |
| Adjuvant | When a second treatment is added after another in order to try and improve the success of the treatment. For example when chemotherapy is given after radiotherapy. See also 'sequential' and 'concomitant'. |
| Anaesthesia | Loss of pain sensation as intentionally induced by drugs or medication. |
| Area under the curve (AUC) | Summary measure of the accuracy of a diagnostic test. |
| Arm (of a clinical study) | Subsection of individuals within a study who receive one particular intervention, for example placebo arm. |
| Association | Statistical relationship between 2 or more events, characteristics or other variables. The relationship may or may not be causal. |
| Astrocytoma | A type of brain tumour that originates from the same cell that also produce the normal brain cells called astrocytes. Astrocytomas bear some similarity a normal brain cells called astrocyte. Astrocytomas can vary from not very concerning (almost benign) pilocytic astrocytoma to highly concerning anaplastic astrocytoma and glioblastoma. |
| ATRX mutations | The ATRX gene provides the cells with instructions for making a protein that is important for cell survival. In some types of brain tumour this gene is mutated and causes continued growth. Knowledge of the mutation is important for the pathologist to make a correct diagnosis and it can be useful to clinicians to know if these mutations are present or not. |
| Attrition bias | Systematic differences between comparison groups for withdrawal or exclusion of participants from a study. |

| Term | Definition |
|---------------------------------------|--|
| Awake craniotomy | Surgery performed on the brain where the person undergoing the surgery is conscious for part of the procedure. This may be recommended when a tumour is close to an important part of the brain, such as areas to do with language. |
| Baseline | The initial set of measurements at the beginning of a study (after run-in period where applicable) with which subsequent results are compared. |
| Benign (for example, 'benign tumour') | All tumours will be either benign or malignant. The main difference between the two types is that benign tumours cannot spread to other places in the body (they are not 'cancerous'). This does not mean that the tumour is 'harmless' - benign tumours can have serious health effects on a person such as oedema or by pressing on a blood vessel. See also 'malignant'. |
| Bias | Influences on a study that can make the results look better or worse than they really are. Bias can occur by chance, deliberately or as a result of systematic errors in the design and execution of a study. It can also occur at different stages in the research process, for example during the collection, analysis, interpretation, publication or review of research data. For examples see Confounding factor, Performance bias, Publication bias Selection bias. |
| Biopsy | Minimally invasive surgery designed only to obtain a sample of tissue for examination to confirm diagnosis (not to treat the underlying condition). This can help understand prognosis and guide treatment. |
| Blinding | The practice of keeping the investigators or subjects of a study ignorant of the group to which a subject has been assigned. For example, a clinical trial in which the participating patients or their doctors are unaware of whether they (the patients) are taking the experimental drug or a placebo (dummy treatment). The purpose of 'blinding' or 'masking' is to protect against bias. See also double-blind study and single-blind study. |
| Case series | Report of a number of cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients. |
| Case-control study | A study to find out the cause(s) of a disease or condition. This is done by comparing a group of patients who have the disease or condition (cases) with a group of people who do not have it (controls) but who are otherwise as similar as possible (in characteristics thought to be unrelated to the causes of the disease or condition). This means the researcher can look |

| Term | Definition |
|-----------------------------------|---|
| | for aspects of their lives that differ to see if they may cause the condition. Such studies are retrospective because they look back in time from the outcome to the possible causes of a disease or condition. |
| Clinical effectiveness | How well a specific test or treatment works when used in the 'real world' (for example when used by a doctor with a patient at home), rather than in a carefully controlled clinical trial. Trials that assess clinical effectiveness are sometimes called management trials. Clinical effectiveness is not the same as efficacy. |
| Clinical efficacy | The extent to which an intervention is active when studied under controlled research conditions. |
| Clinician | A healthcare professional who provides patient care. For example a doctor, nurse or physiotherapist. |
| Cochrane Review | The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of RCTs prepared by the Cochrane Collaboration). |
| Cohort | A group of people sharing some common characteristic (for example, patients with the same disease), followed up in a research study for a specified period of time. |
| Cohort study | A study with 2 or more groups of people – cohorts – with similar characteristics. One group receives a treatment, is exposed to a risk factor or has a particular symptom and the other group does not. The study follows their progress over time and records what happens. |
| Comorbidity | A disease or condition that someone has in addition to the health problem being studied or treated. |
| Comparative group | The group in the study who do not receive the treatment/procedure or who receive the norm treatment. This group is used to measure against the treatment/procedure being investigated. |
| Computerised tomography (CT scan) | A type of scan which uses X-rays to build up an image of the inside of the body. This can be important in some situations where MRI is impossible or otherwise not clinically recommended. |
| Concealment of allocation | The process used to ensure that the person deciding to enter a participant into an RCT does not know the comparison group into which that individual will be allocated. This is distinct from blinding and is aimed at preventing selection bias. Some attempts at concealing allocation are more prone to manipulation than others and the |

| Term | Definition |
|--------------------------|---|
| | method of allocation concealment is used as an assessment of the quality of a trial. |
| Concomitant | When two (or more) treatments are conducted simultaneously in order to try and improve the success of the treatment. For example when chemotherapy is given at the same time as radiotherapy. See also 'sequential' and 'adjuvant'. |
| Confidence interval (CI) | There is always some uncertainty in research. This is because a small group of patients is studied to predict the effects of a treatment on the wider population. The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. The CI is usually stated as '95% CI', which means that the range of values has a 95 in 100 chance of including the 'true' value. For example, a study may state that "based on our sample findings, we are 95% certain that the 'true' population blood pressure is not higher than 150 and not lower than 110". In such a case the 95% CI would be 110 to 150. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment – often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example if a large number of patients have been studied). |
| Confounding factor | Something that influences a study and can result in misleading findings if it is not understood or appropriately dealt with. For example, a study of heart disease may look at a group of people who exercise regularly and a group who do not exercise. If the ages of the people in the 2 groups are different, then any difference in heart disease rates between the 2 groups could be because of age rather than exercise. Therefore age is a confounding factor. |
| Continuous outcome | Data with a potentially infinite number of possible values within a given range. Height, weight and blood pressure are examples of continuous variables. |
| Control group | A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. The aim is to check for any differences. Ideally, the people in the control |

| Term | Definition |
|-----------------------------------|--|
| | group should be as similar as possible to those in the treatment group, to make it as easy as possible to detect any effects due to the treatment. |
| Cost–benefit analysis (CBA) | Cost-benefit analysis is one of the tools used to carry out an economic evaluation. The costs and benefits are measured using the same monetary units (for example UK pounds) to see whether the benefits exceed the costs. |
| Cost–consequence analysis (CCA) | Cost-consequence analysis is one of the tools used to carry out an economic evaluation. This compares the costs (such as treatment and hospital care) with the consequences (such as health outcomes) of a test or treatment with a suitable alternative. Unlike cost-benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (such as the quality adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out. |
| Cost-effectiveness analysis (CEA) | Cost-effectiveness analysis is one of the tools used to carry out an economic evaluation. The benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which life is extended as a result of the intervention). |
| Cost-effectiveness model | An explicit mathematical framework which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes. |
| Cost-minimisation analysis (CMA) | Cost-minimisation analysis is a type of economic evaluation which can be used when the alternatives being compared have equivalent clinical effectiveness. The costs of alternatives are compared in order to determine which is the cheapest. |
| Cost–utility analysis (CUA) | Cost–utility analysis is one of the tools used to carry out an economic evaluation. The benefits are assessed in terms of both quality and duration of life, and expressed as quality adjusted life years (QALYs). See also; Utility |
| Craniotomy | A craniotomy is the surgical removal of part of the skull, almost always to perform some procedure on the brain afterwards. |
| Cross-over study design | A study comparing two or more interventions in which the participants, upon completion of the |

| Term | Definition |
|---|--|
| | course of one treatment, are switched to another. A problem with this study design is that the effects of the first treatment may carry over into the period when the second is given. Therefore a crossover study should include an adequate 'wash-out' period, which means allowing sufficient time between stopping one treatment and starting another so that the first treatment has time to wash out of the patient's system. |
| Cross-sectional study | The observation of a defined set of people at a single point in time or time period – a snapshot. (This type of study contrasts with a longitudinal study, which follows a set of people over a period of time). |
| Decision analysis | An explicit quantitative approach to decision- making under uncertainty, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes. |
| Diagnostic study | A study to assess the effectiveness of a test or measurement in terms of its ability to accurately detect or exclude a specific disease. |
| Dichotomous outcomes | Outcome that can take one of 2 possible values, such as dead/alive, smoker/non-smoker, present/not present (also called binary data). |
| Diffusion tensor imaging (DTI MRI) | A special kind of magnetic resonance imaging which generates pictures of the major nerve connections in the brain, used particularly for the study of 'white-matter' regions. Knowing where these regions are can be important to neurosurgeons. In addition, DTI is able to detect abnormalities in the brain that do not show up on standard MRI scans. |
| Diffusion-weighted magnetic resonance imaging (DWI MRI) | A method of using an MRI scanner to build up a more accurate image of types of tissue in the body. This technique uses the diffusion of water molecules to generate contrast in an MRI image. The way water diffuses through tissue can be used to infer facts about the structure of that tissue. DWI MRI is able to detect abnormalities in the brain that do not show up on standard MRI scans. |
| Discounting | Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present. |

| Term | Definition |
|--|--|
| Dominance | A health economics term. When comparing tests or treatments, an option that is both less effective and costs more is said to be 'dominated' by the alternative. |
| Double-blind study | A study in which neither the subject (patient) nor the observer investigator/ clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias. |
| Drop-out | A participant who withdraws from a trial before the end. |
| Dysembryoplastic neuroepithelial tumour (DNET) | A type of brain tumour usually located in the cortical grey matter which is very unlikely to transform into a high grade tumour. |
| Economic evaluation | An economic evaluation is used to assess the cost effectiveness of healthcare interventions (that is, to compare the costs and benefits of a healthcare intervention to assess whether it is worth doing). The aim of an economic evaluation is to maximise the level of benefits – health effects – relative to the resources available. It should be used to inform and support the decision-making process; it is not supposed to replace the judgement of healthcare professionals. There are several types of economic evaluation: cost–benefit analysis, cost–consequence analysis, cost-effectiveness analysis, cost-minimisation analysis and cost–utility analysis. They use similar methods to define and evaluate costs, but differ in the way they estimate the benefits of a particular drug, programme or intervention. |
| Edema | The American spelling of Oedema. |
| Effect (as in effect measure, treatment effect, estimate of effect, effect size) | A measure that shows the magnitude of the outcome in 1 group compared with that in a control group. For example, if the absolute risk reduction is shown to be 5% and it is the outcome of interest, the effect size is 5%. The effect size is usually tested, using statistics, to find out how likely it is that the effect is a result of the treatment and has not just happened by chance. |
| Effectiveness | How beneficial a test or treatment is under usual or everyday conditions. |
| Effectiveness reviews | Evaluation of how beneficial a test or treatment is under everyday conditions. |
| Efficacy | How beneficial a test, treatment or public health intervention is under ideal conditions (for example in a laboratory). |

| Term | Definition |
|--|--|
| Endometrial biopsy | A procedure in which a sample of the endometrium (tissue lining the inside of the uterus) is removed for microscopic evaluation. |
| Endometrial pathology | Endometrial hyperplasia or carcinoma. |
| Epidemiological study | The study of a disease within a population, defining its incidence and prevalence and examining the roles of external influences (for example infection, diet) and interventions. |
| EQ-5D (EuroQol 5 dimensions) | A standardised instrument used to measure health-related quality of life. It provides a single index value for health status. |
| Evidence | Information on which a decision or guidance is based. Evidence is obtained from a range of sources including RCTs, observational studies, expert opinion (of clinical professionals or patients). |
| Evidence based | The process of systematically finding, appraising and using research findings as the basis for clinical decisions. |
| Evidence table | A table summarising the results of a collection of studies which, taken together, represent the evidence supporting a particular recommendation or series of recommendations in a guideline. |
| Exclusion criteria (clinical study) | Criteria that define who is not eligible to participate in a clinical study. |
| Exclusion criteria (literature review) | Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence. |
| Extended dominance | If Option A is both more clinically effective than Option B and has a lower cost per unit of effect when both are compared with a do-nothing alternative, then Option A is said to have extended dominance over Option B. Option A is therefore more cost effective and should be preferred, other things remaining equal. |
| Extra cranial imaging | Imaging to examine parts of the body outside the brain. This is usually in the context of brain metastases (secondaries) when a CT scan of chest, abdomen and pelvis is used to look for the primary source or to see if there has been progression of disease outside the brain. |
| Extrapolation | An assumption that the results of studies of a specific population will also hold true for another population with similar characteristics. |
| False negative | A diagnostic test result that incorrectly indicates that an individual does not have the disease of interest, when they do actually have it. |
| False positive | A diagnostic test result that incorrectly indicates that an individual has the disease of interest, when they actually do not have it. |
| False positive | interest, when they do actually have it. A diagnostic test result that incorrectly indicates that an individual has the disease of interest, |

| Term | Definition |
|--------------------------------------|---|
| Fixed-effect model | In meta-analysis, a model that calculates a pooled effect estimate using the assumption that all observed variation between studies is caused by random sample variability. Studies are assumed to estimating the same overall effect. |
| Fluid attenuation inversion recovery | A method of using an MRI scanner to build up a more accurate image of types of tissue in the body. This technique is especially useful in images of the brain, as it makes the cerebrospinal fluid in resulting images look less bright, which results in a clearer image. |
| Follow-up | Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables. |
| Forest plot | A graphical representation of the individual results of each study included in a meta-analysis together with the combined meta-analysis result. The plot also allows readers to see the heterogeneity among the results of the studies. The results of individual studies are shown as squares centred on each study's point estimate. A horizontal line runs through each square to show each study's confidence interval. The overall estimate from the meta-analysis and its confidence interval are shown at the bottom, represented as a diamond. The centre of the diamond represents the pooled point estimate, and its horizontal tips represent the confidence interval. |
| Generalisability | The extent to which the results of a study hold true for groups that did not participate in the research. |
| Glioblastoma (GBM) | A type of brain tumour that originates from the same cell that also produce the normal brain cells called astrocytes (glial cells). Glioblastomas are fast-growing, likely to spread and difficult to treat. |
| Glioma | A type of tumour that starts in the brain or the spine, and bears similarity to glial cells of the nervous system. They can grow slowly (pilocytic astrocytoma) or very fast (anaplastic astrocytoma, or glioblastoma). |
| Gold standard | A method, procedure or measurement that is widely accepted as being the best available to test for or treat a disease. |
| GRADE, GRADE profile | A system developed by the GRADE Working Group to address the short-comings of present grading systems in healthcare. The GRADE system uses a common, sensible and transparent approach to grading the quality of evidence. The results of applying the GRADE |

| Term | Definition |
|---|---|
| | system to clinical trial data are displayed in a table known as a GRADE profile. |
| Gray (Gy) | The standard unit used for radiotherapy doses. |
| Harms | Adverse effects of an intervention. |
| Health economics | Study or analysis of the cost of using and distributing healthcare resources. |
| Health-related quality of life (HRQoL) | A measure of the effects of an illness to see how it affects someone's day-to-day life. |
| Heterogeneity | The term is used in meta-analyses and systematic reviews to describe when the results of a test or treatment (or estimates of its effect) differ. |
| High grade transformation | Where a tumours starts as a lower grade slow growing tumour, but over time changes in the cells occur so they start to grow faster and become a high grade tumour. |
| High-grade glioma (sometimes known as HGG) | Gliomas which grow faster - the main types are anaplastic astrocytoma, anaplastic oligodendroglioma and glioblastoma. |
| Histological (diagnosis) | The study of the structure of tissues at high magnification, usually with a microscope, in order to classify and grade them; that is to say, to make a diagnosis. |
| Histopathology | The study of microscopic anatomical changes or structure in diseased tissue. |
| Hypofractionated radiation therapy | A method of delivering radiotherapy where the total dose is divided into fewer, but larger daily (or alternate day) treatments. |
| Hysterectomy | Surgical removal of the uterus. |
| Imprecision | Results are imprecise when studies include relatively few patients and few events and thus have wide confidence intervals around the estimate of effect. |
| Incidence | The incidence of a disease is the rate at which new cases occur in a population during a specified period. |
| Inclusion criteria (clinical study) | Specific criteria that define who is eligible to participate in a clinical study. |
| Inclusion criteria (literature review) | Explicit criteria used to decide which studies should be considered as potential sources of evidence. |
| Incremental cost | The extra cost linked to using one test or treatment rather than another. Or the additional cost of doing a test or providing a treatment more frequently. |
| Incremental cost effectiveness ratio (ICER) | The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for one treatment compared with another. |

| Term | Definition |
|--|--|
| Incremental net benefit (INB) | The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000×QALYs gained) minus incremental cost. |
| Indirectness | The available evidence is different to the review question being addressed, in terms of population, intervention, comparison and outcome (PICO). |
| Intention-to-treat analysis (ITT) | An assessment of the people taking part in a clinical trial, based on the group they were initially (and randomly) allocated to. This is regardless of whether or not they dropped out, fully complied with the treatment or switched to an alternative treatment. Intention-to-treat analyses are often used to assess clinical effectiveness because they mirror actual practice: that is, not everyone complies with treatment and the treatment people receive may be changed according to how they respond to it. |
| Internal validity | How well an experiment is done and if it is clear that the variable being tested is what is causing the measured effect. |
| Intervention | In medical terms this could be a drug treatment, surgical procedure, diagnostic or psychological therapy. Examples of public health interventions could include action to help someone to be physically active or to eat a more healthy diet. |
| Invasive techniques | A technique which is some way 'invades' the body; this can be anything from an injection to surgery. |
| Isocitrate dehydrogenase mutations (IDH mutations) | Isocitrate dehydrogenase is an enzyme which is produced normally in the body. In some types of brain tumours this enzyme shows specific mutations, and therefore it can sometimes be useful to clinicians to know if these mutations are present or not to help them determine what type of brain tumour they are treating. |
| Karnofsky Performance Status (KPS) | A measure of functional impairment, which can be used to identify which of two treatments gives better outcomes and to help identify what care a person with a brain tumour might need. For example someone with moderate functional impairment might have some loss of sight, or loss of movement of a limb. |
| Length of stay | The total number of days a patient stays in hospital. |
| Licence | See Product licence. |

| Term | Definition |
|---|--|
| Life years gained | Mean average years of life gained per person as a result of the intervention compared with an alternative intervention. |
| Likelihood ratio | The likelihood ratio combines information about the sensitivity and specificity. It tells you how much a positive or negative result changes the likelihood that a patient would have the disease. The likelihood ratio of a positive test result (LR+) is sensitivity divided by (1 minus specificity). |
| Local control | Stopping cancer growth at the site of origin. |
| Loss to follow-up | Patients who have withdrawn from the clinical trial at the point of follow-up. |
| Low-grade glioma (sometimes known as LGG) | A type of glioma which typically grows slower and has better outcomes than average. |
| Magnetic Resonance Imaging (MRI) | Medical imaging technique that uses a magnetic field and pulses of radio wave energy to make pictures of organs and structures inside the body. MRI can show larger differences between soft tissue types than CT scanning, and can be used to measure more complex tissue characteristics such as blood flow. |
| Malignancy | An illness that is a cancer. |
| Malignant (for example, 'malignant tumour') | All tumours will be either benign or malignant. The main difference between the two types is that malignant tumours cannot spread to other places in the body (they are 'cancerous'). This usually means that treating a malignant tumour quickly is more important than treating a benign tumour quickly. See also 'benign'. |
| Markov model | A method for estimating long-term costs and effects for recurrent or chronic conditions, based on health states and the probability of transition between them within a given time period (cycle). |
| Maximal safe resection | Surgery when as much of a tumour is removed as possible whilst trying to avoid damaging important areas of the brain. Typical reasons a tumour cannot be completely resected will be because it is (entirely or partially) located somewhere which cannot be safely accessed, because of its grade, or because it appears to be performing some functional role in the brain. |
| Mean | An average value, calculated by adding all the observations and dividing by the number of observations. |
| Mean difference | In meta-analysis, a method used to combine measures on continuous scales (such as weight), where the mean, standard deviation and sample size in each group are known. The weight given to the difference in means from each study (for example how much influence each study has on the overall results of the |

| Term | Definition |
|------------------------------------|---|
| | meta-analysis) is determined by the precision of its estimate of effect. |
| Median | The value of the observation that comes half- way when the observations are ranked in order. |
| Meningioma | A type of tumour that starts in the meninges (the layer of cells surrounding the brain and spinal cord). |
| Meta-analysis | A method often used in systematic reviews. Results from several studies of the same test or treatment are combined to estimate the overall effect of the treatment. |
| Metastasis or Metastases | When cancer cells spread around the body they can start to grow in a new location forming a metastases. The source is called the 'primary' and the metastases 'secondaries'. Metastasis is for one tumour, metastases is for many. |
| Methodology | Systematic, theoretical analysis of the methods applied to a field of study. |
| Minimal important difference (MID) | Threshold for clinical importance which represents the minimal important difference for benefit or for harm; for example the threshold at which drug A is less effective than drug B by an amount that is clinically important to patients. |
| Molecular (diagnosis) | The study of the sub-microscopic structure of tissues in order to classify them. |
| Monte Carlo | A technique used to approximate the probability of certain outcomes by running multiple simulations using random variables. |
| MR perfusion | A special type of MRI that uses an injected dye in order to see blood flow through tissues to build up a more accurate image of types of tissue in the body. This is actually a name for a cluster of techniques which look at how blood flows to different tissues in the body (for example distinguishing high grade brain tumours from low grade brain tumours by the amount of blood that flows to them). |
| MR spectroscopy | A method of using an MRI scanner to build up a more accurate image of types of tissue in the body. This is actually a name for a cluster of techniques that attempt to identify biochemical information about tissues in the body without the need for invasive surgery. |
| Multivariate model | A statistical model for analysis of the relationship between 2 or more predictors, (independent) variables and the outcome (dependent) variable. |
| Multi-way sensitivity analysis | Multi-way simple sensitivity analysis (scenario analysis) – 2 or more parameters are varied at the same time and the overall effect on the results is evaluated. |
| Mutation / mutated | A gene mutation is a permanent alteration to a sequence of DNA such that that strand of DNA |

| Term | Definition |
|--|--|
| | is different to what most people have. It is usually used in the context of meaning that the mutation does something bad to a patient. A mutated protein is a protein made from the instructions contained in a mutated gene. A mutated cell is a cell made up from one or more mutated proteins. |
| Net monetary benefit (NMB) | The value (usually in monetary terms) of an intervention net of its cost. The NMB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the NMB is calculated as: (£20,000×QALYs gained) minus cost. |
| Network meta-analysis (NMA) | Meta-analysis in which multiple treatments (that is, 3 or more) are being compared using both direct comparisons of interventions within RCTs and indirect comparisons across trials based on a common comparator. |
| Non-randomised | When subjects of a study are not allocated to a specific treatment/group at random. |
| Number needed to treat (NNT) | The average number of patients who need to be treated to get a positive outcome. For example, if the NNT is 4, then 4 patients would have to be treated to ensure 1 of them gets better. The closer the NNT is to 1, the better the treatment. For example, if you give a stroke prevention drug to 20 people before 1 stroke is prevented, the number needed to treat is 20. |
| O6-methylguanine-DNA methyltransferase (MGMT) | MGMT is a protein which is naturally produced by the cell and has the function to repair the DNA. The MGMT gene, which produces the protein, can become 'methylated' which shuts down its function. This will reduce the repair, which is important to know when trying to kill a cancer cell with agents such as temozolomide. |
| Observational study | Individuals or groups are observed or certain factors are measured. No attempt is made to affect the outcome. For example, an observational study of a disease or treatment would allow 'nature' or usual medical care to take its course. Changes or differences in one characteristic (for example whether or not people received a specific treatment or intervention) are studied without intervening. There is a greater risk of selection bias than in experimental studies. |
| Odds ratio (OR) | Odds are a way to represent how likely it is that something will happen (the probability). An odds ratio compares the probability of something in one group with the probability of the same thing in another. An odds ratio of 1 between 2 groups would show |

| Term | Definition |
|------------------------------|---|
| | that the probability of the event (for example a person developing a disease, or a treatment working) is the same for both. An odds ratio greater than 1 means the event is more likely in the first group. An odds ratio less than 1 means that the event is less likely in the first group. |
| | Sometimes probability can be compared across more than 2 groups – in this case, one of the groups is chosen as the 'reference category' and the odds ratio is calculated for each group compared with the reference category. For example, to compare the risk of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. Odds ratios would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. |
| | |
| Oedema | Swelling around a brain tumour caused by the blood vessels becoming leaky. Oedema in the brain can cause that area of the brain to function less well. |
| Oligodendrogliomas | A type of brain tumour that originates from cells that also give rise to the normal brain cells called oligodendrocytes. Oligodendrocytes are involved in making a special fatty substance in the brain called myelin. This is important as it help the nerve cells (neurons) conduct signals efficiently. Oligodendrogliomas grow diffusely into the brain (they put down 'roots') and specific molecular markers such as 1p\19q can make a significant difference to treatment effectiveness. |
| One-way sensitivity analysis | One-way simple sensitivity analysis (univariate analysis) – each parameter is varied individually in order to isolate the consequences of each parameter on the results of the study. |
| Oophorectomy | Surgical removal of one or both ovaries. |
| Opportunity cost | The loss of other healthcare programmes displaced by investment in or introduction of another intervention. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention. |
| Optic pathway glioma | The type of brain tumour that is located in the nerves that connect the eyes with the brain (optic nerve). Although it is growing slowly, it is located in a position that makes treatment extremely difficult and can cause visual loss. |
| Outcome | The impact that a test, treatment, policy, programme or other intervention has on a person, group or population. Outcomes from |

| Term | Definition |
|-------------------|---|
| | interventions to improve the public's health could include changes in knowledge and behaviour related to health, societal changes (for example a reduction in crime rates) and a change in people's health and wellbeing or health status. In clinical terms, outcomes could include the number of patients who fully recover from an illness or the number of hospital admissions, and an improvement or deterioration in someone's health, functional ability, symptoms or situation. Researchers should decide what outcomes to measure before a study begins. |
| p value | The p value is a statistical measure that indicates whether or not an effect is statistically significant. For example, if a study comparing 2 treatments found that one seems more effective than the other, the p value is the probability of obtaining these results by chance. By convention, if the p value is below 0.05 (that is, there is less than a 5% probability that the results occurred by chance) it is considered that there probably is a real difference between treatments. If the p value is 0.001 or less (less than a 1% probability that the results occurred by chance), the result is seen as highly significant. If the p value shows that there is likely to be a difference between treatments, the confidence interval describes how big the difference in effect might be. |
| Pairwise analysis | A process of comparing entities in pairs to judge which of each entity is preferred, or has a greater amount of some quantitative property. |
| PCV chemotherapy | A combination of three chemotherapy drugs - procarbazine, CCNU and vincristine (CCNU is also known as lomustine). |
| Performance bias | Systematic differences between intervention groups in care provided apart from the intervention being evaluated. Blinding of study participants (both the recipients and providers of care) is used to protect against performance bias. |
| Placebo | A fake (or dummy) treatment given to participants in the control group of a clinical trial. It is indistinguishable from the actual treatment (which is given to participants in the experimental group). The aim is to determine what effect the experimental treatment has had over and above any placebo effect caused because someone has received (or thinks they have received) care or attention. |
| Placebo effect | A beneficial (or adverse) effect produced by a placebo and not due to any property of the placebo itself. |

| Term | Definition |
|------------------------------------|---|
| Post-hoc analysis | Statistical analyses that are not specified in the trial protocol and are generally suggested by the data. |
| Power (statistical) | The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed. |
| Prevalence | The prevalence of a disease is the proportion of a population that are cases at a point in time. |
| Primary care | Healthcare delivered outside hospitals. It includes a range of services provided by GPs, nurses, health visitors, midwives and other healthcare professionals and allied health professionals such as dentists, pharmacists and opticians. |
| Primary outcome | The outcome of greatest importance, usually the one in a study that the power calculation is based on. |
| Probabilistic sensitivity analysis | Probabilistic sensitivity analysis – probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (for example Monte Carlo simulation). |
| Product licence | An authorisation from the Medicines and Healthcare Products Regulatory Agency (MHRA) to market a medicinal product. |
| Prognosis | A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes. |
| Progression | When a tumour begins to grow. This usually means more aggressive treatment will be suggested by the clinician. |
| Prospective study | A research study in which the health or other characteristic of participants is monitored (or 'followed up') for a period of time, with events recorded as they happen. This contrasts with retrospective studies. |
| Protocol (review) | A document written prior to commencing a review that details exactly how evidence to answer a review question will be obtained and synthesised. It defines in detail the population of interest, the interventions, the comparators/controls and the outcomes of interest (PICO). |
| Publication bias | Publication bias occurs when researchers publish the results of studies showing that a treatment works well and don't publish those |

| Term | Definition |
|-----------------------------------|--|
| | showing it did not have any effect. If this happens, analysis of the published results will not give an accurate idea of how well the treatment works. This type of bias can be assessed by a funnel plot. |
| Quality adjusted life year (QALY) | A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality-of-life. One QALY is equal to 1 year of life in perfect health. QALYS are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality-of-life score (on a scale of 0 to 1). It is often measured in terms of the person's ability to perform the activities of daily life, and freedom from pain and mental disturbance. |
| Quality of life | See Health-related quality of life. |
| Radiotherapy | Radiotherapy uses high-energy X-ray beams to treat malignant and benign tumours. |
| Random effect model | In meta-analysis, a model that calculates a pooled effect estimate using the assumption that each study is estimating a different true treatment effect due to real differences between studies. Observed variation in effects are therefore caused by a combination of random sample variability (within-study variation) and heterogeneity between studies (between-study variation). The overall effects is an average of the estimated true study effects. |
| Randomisation | Assigning participants in a research study to different groups without taking any similarities or differences between them into account. For example, it could involve using a random numbers table or a computer-generated random sequence. It means that each individual (or each group in the case of cluster randomisation) has the same chance of receiving each intervention. |
| Randomised controlled trial (RCT) | A study in which a number of similar people are randomly assigned to 2 (or more) groups to test a specific drug or treatment. One group (the experimental group) receives the treatment being tested, the other (the comparison or control group) receives an alternative treatment, a dummy treatment (placebo) or no treatment at all. The groups are followed up to see how effective the experimental treatment was. Outcomes are measured at specific times and any difference in response between the groups is assessed statistically. This method is also used to reduce bias. |
| Recruitment bias | When proper randomisation is not achieved when recruiting individuals, meaning that the |

| Term | Definition |
|-------------------------|---|
| | sample obtained may not be representative of the population intended to be analysed. |
| Recurrence | When a tumour which has been treated (or otherwise seems to have disappeared) begins to show up on scans again. |
| Reference standard | The test that is considered to be the best available method to establish the presence or absence of the outcome – this may not be the one that is routinely used in practice. |
| Regular clinical review | This is outpatient review of the person with a brain tumour or brain metastases at a planned interval from the previous visit in order to assess symptoms and care needs, to provide support and treatment and to perform imaging when appropriate. |
| Relative risk (RR) | The ratio of the risk of disease or death among those exposed to certain conditions compared with the risk for those who are not exposed to the same conditions (for example the risk of people who smoke getting lung cancer compared with the risk for people who do not smoke). If both groups face the same level of risk, the relative risk is 1. If the first group had a relative risk of 2, subjects in that group would be twice as likely to have the event happen. A relative risk of less than 1 means the outcome is less likely in the first group. Relative risk is sometimes referred to as risk ratio. |
| Reporting bias | See Publication bias. |
| Resource implication | The likely impact in terms of finance, workforce or other NHS resources. |
| Retrospective study | A research study that focuses on the past and present. The study examines past exposure to suspected risk factors for the disease or condition. Unlike prospective studies, it does not cover events that occur after the study group is selected. |
| Review question | The plan or set of steps to be followed in a study. A protocol for a systematic review describes the rationale for the review, the objectives and the methods that will be used to locate, select and critically appraise studies, and to collect and analyse data from the included studies. |
| Scenario analysis | See multi-way sensitivity analysis. |
| Secondary care | Care provided in hospitals. |
| Secondary outcome | An outcome used to evaluate additional effects of the intervention deemed a priori as being less important than the primary outcomes. |
| Selection bias | Selection bias occurs if: the characteristics of the people selected for a study differ from the wider population from which they have been |

| Term | Definition |
|----------------------------|--|
| | drawn; or there are differences between groups of participants in a study in terms of how likely they are to get better. |
| Sensitivity | How well a test detects the thing it is testing for. If a diagnostic test for a disease has high sensitivity, it is likely to pick up all cases of the disease in people who have it (that is, give a 'true positive' result). But if a test is too sensitive it will sometimes also give a positive result in people who don't have the disease (that is, give a 'false positive'). For example, if a test were developed to detect if a woman is 6 months pregnant, a very sensitive test would detect everyone who was 6 months pregnant but would probably also include those who are 5 and 7 months pregnant. If the same test were more specific (sometimes referred to as having higher specificity), it would detect only those who are 6 months pregnant and someone who was 5 months pregnant would get a negative result (a 'true negative'). But it would probably also miss some people who were 6 months pregnant (that is, give a 'false negative'). |
| | The number of women who are recalled for a second breast screening test is relatively high because the test is very sensitive. If it were made more specific, people who don't have the disease would be less likely to be called back for a second test but more women who have the disease would be missed. |
| Sensitivity analysis | A means of representing uncertainty in the results of an analysis. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. See one-way sensitivity analysis, multi-way sensitivity analysis, threshold sensitivity analysis and probabilistic sensitivity analysis for more details. |
| Sequential | Where one treatment is given after another treatment has been completed, such as radiotherapy followed by chemotherapy. See also 'adjuvant' and 'concomitant'. |
| SF-12 | A 12-question questionnaire to measure Health- Related Quality of life. |
| SF-36 | A 36-question questionnaire to measure Health- Related Quality of life. |
| Significance (statistical) | A result is deemed statistically significant if the probability of the result occurring by chance is less than 1 in 20 (p<0.05). |

| Term | Definition |
|---------------------------------|--|
| Single blind study | A study in which either the subject (patient/participant) or the observer (clinician/investigator) is not aware of which treatment or intervention the subject is receiving. |
| Specificity | The proportion of true negatives that are correctly identified as such. For example, in diagnostic testing the specificity is the proportion of non-cases correctly diagnosed as non-cases. In terms of literature searching a highly specific search is generally narrow and aimed at picking up the key papers in a field and avoiding a wide range of papers. See also Sensitivity |
| Stakeholder | An organisation with an interest in a topic on which NICE is developing a clinical guideline or piece of public health guidance. Organisations that register as stakeholders can comment on the draft scope and the draft guidance. Stakeholders may be: • manufacturers of drugs or equipment • national patient and carer organisations • NHS organisations • organisations representing healthcare professionals. |
| Standard deviation (SD) | A measure of the spread or dispersion of a set of observations, calculated as the average difference from the mean value in the sample. |
| Stereotactic radiosurgery | A method of delivering a high dose of radiotherapy to small tumours (usually under 3cm) while minimising the volume of normal brain treated with radiation. Despite the name, it is a treatment not a kind of surgery. |
| Stereotactic radiotherapy | A method of precisely and accurately giving radiotherapy to small tumours. |
| Subgroup analysis | An analysis in which the intervention effect is evaluated in a defined subset of the participants in a trial, or in complementary subsets. |
| Supportive care | Care given to improve the quality of life of people with life-limiting diseases, especially related to management of side-effects of treatment and psychological support. Sometimes called 'palliative care'. |
| Systematic review | A review in which evidence from scientific studies has been identified, appraised and synthesised in a methodical way according to predetermined criteria. It may include a meta- analysis. |
| T1 sequence (in context of MRI) | A method of using an MRI scanner to build up a more accurate image of structures in the body. T1 refers to the speed that the protons in a tissue return to their resting alignment after stimulation. This is a component of what is |

| Term | Definition |
|---|--|
| | sometimes called a 'standard MRI' and is useful for differentiating between fat, water, and other tissues. |
| T2 sequence (in context of MRI) | A method of using an MRI scanner to build up a more accurate image of structures in the body. T2 refers to the interactions between protons themselves. This is a component of what is sometimes called a 'standard MRI' and is useful for identifying water in the body. |
| Telomerase reverse transcriptase (TERT) | TERT is an enzyme which is naturally produced by the cells and it is important in controlling cell growth. If a control element of the TERT enzyme (the so-called promoter) is mutated this will support cancerous cells to grow. It can be useful for pathologists to know about this mutation as it can help making the diagnosis more precise. As a result is can also be useful to clinicians to know if these mutations are present or not. |
| Threshold sensitivity analysis | Threshold sensitivity analysis – the critical value of parameters above or below which the conclusions of the study will change are identified. |
| Time horizon | The time span over which costs and health outcomes are considered in a decision analysis or economic evaluation. |
| Treatment allocation | Assigning a participant to a particular arm of a trial. |
| True negative | A diagnostic test result that correctly indicates that an individual does not have the disease of interest when they actually do not have it. |
| True positive | A diagnostic test result that correctly indicates that an individual has the disease of interest when they do actually have it. |
| Ultrasound scan | Procedure that uses high-frequency sound waves to create an image of part of the inside of the body. |
| Univariate | Analysis which separately explores each variable in a data set. |
| Univariate analysis | See one-way sensitivity analysis. |
| Utility | In health economics, a utility is the measure of the preference or value that an individual or society places upon a particular health state. It is generally a number between 0 (representing death) and 1 (perfect health). The most widely used measure of benefit in cost-utility analysis is the quality-adjusted life year, but other measures include disability-adjusted life years (DALYs) and healthy year equivalents (HYEs). |
| Watch and wait | A management strategy where no active treatment is given after diagnosis. This is usually because the side effects of treatment are worse than the risks of leaving the disease to behave |

| Term | Definition |
|-----------------------|---|
| | naturally. People recommended a strategy of watchful waiting will still be offered support and monitoring. See also 'active monitoring'. |
| White matter | Pathways important for connecting different parts of the brain to each other. |
| WHO Performance Score | A measure of functional impairment, which can be used to identify which of two treatments gives better outcomes and to help identify what care a person with a brain tumour might need. For example someone with moderate functional impairment might have some loss of sight, or loss of movement of a limb. |

Abbreviations

| Abbreviation | Meaning |
|--------------|--|
| 3D CRT | 3d conformal radiotherapy |
| 5-ALA | 5-amino-levulinic acid |
| | |
| ACNU-CDDP | Chemotherapy with nimustine – ciplastin |
| ADC | Apparent diffusion coefficient |
| ASL | Arterial spin labelling |
| AUC | Area under the concentration-time curve |
| BRAF | Proto-oncogene b-raf / v-raf murine sarcoma viral oncogene homolog b |
| BSC | Best supportive care |
| Bx | Biopsy |
| сGy | Centi-gray (unit of radiation) |
| Cho/NAA | Cho/n-acetylaspartate |
| CI | Confidence interval |
| cMRI | Conventional mri |
| CNS | Central nervous system |
| СРТ | Cisplatin |
| СТ | Computerised tomography |
| CTCAE | Common terminology criteria for adverse events |
| DCE | Dynamic contrast-enhancement |
| DD | Dose dense |
| DNET | Dysembryoplastic neuroepithelial tumour |
| DSC | Dynamic susceptibility contrast |
| DTI | Diffusion tensor imaging |
| EBRT | External beam radiotherapy |
| EGFR | Epidermal growth factor receptor gene |
| EQ-5D | EuroQol 5 dimensions |
| FACT-Br | Functional assessment of cancer therapy-brain |
| FDG | 2-deoxy-2-(18)fluoro-d-glucose |
| FET | (18)f-fluoro-ethyl-l-tyrosine |
| FLAIR | Fluid Attenuation Inversion Recovery |
| FSRT | Fractionated stereotactic radiotherapy |
| GBM | Glioblastoma |
| GFT | Gefitinib |
| GLCM | Gray level co-occurrence matrix |
| GTR | Gross total resection |
| Gy | Gray (unit of radiation) |
| hFSRT | Hypo-fractionated stereotactic radiotherapy |
| HGG | High-grade glioma |
| HR | Hazard ratio |
| HRQoL | Health-related quality of life |
| | |

| Abbreviation | Meaning |
|------------------------------|---|
| ICER | Incremental cost effectiveness ratio |
| IDH (IDH1 or IDH2) mutations | Isocitrate dehydrogenase mutations |
| IMRT | Intensity modulated radiotherapy |
| INB | Incremental net benefit |
| ITT | Intention-to-treat analysis |
| KPS | Karnofsky performance status |
| LASA (QOL) | Linear analog scale assessment of quality of life |
| LGG | Low-grade glioma |
| MDT | Multidisciplinary team |
| MET | (11)c-methionine |
| MGMT | O6-methylguanine-dna-methyltransferase |
| MID | Minimal important difference |
| MRI | Magnetic resonance imaging |
| MV | Mega volt |
| NAA/Cho | n-acetylaspartate/choline ratio |
| NIH | National Institute for Health |
| NMA | Network meta-analysis |
| NMB | Net monetary benefit |
| NNT | Number needed to treat |
| NOS | Not otherwise specified |
| NR | Not reported |
| OR | Odds ratio |
| OS | Overall survival |
| PaR | Partial resection |
| PCV | Procarbazine lomustine vincristine |
| PET-CT | Positron emission tomography - computed tomography |
| PET-MRI | Positron emission tomography - magnetic resonance imaging |
| PFS | Progression free survival |
| QALY | Quality-adjusted life year |
| QoL | Quality of life |
| rCBV | Relative cerebral blood volume |
| RCT | Randomised controlled trial |
| rSTR | Radical subtotal resection |
| RT | Radiotherapy |
| RTOG | Radiation therapy oncology group |
| SD | Standard deviation |
| SRS | Stereotactic radiosurgery |
| SRT | Stereotactic radiotherapy |
| STR | Subtotal resection |
| TERT | Telomerase reverse transcriptase |
| TMZ | Temozolomide |
| TTF | Tumour treating fields |

| Abbreviation | Meaning |
|--------------|----------------------------------|
| TTP | Time to progression |
| VMAT | Volumetric modulated arc therapy |
| WBRT | Whole brain radiation therapy |
| WHO | World Health Organization |