

RANK the questions for the Neuro-Oncology PSP meeting

	Question	One stakeholder's explanation of why the question might be important	Second survey rank	Rank (1-25)
A	Do lifestyle factors (e.g. sleep, stress, diet) in patients with a brain or spinal cord tumour, influence tumour growth?	This question would reflect a useful insight into how lifestyle factors could influence the biological disease process. This would support current Public Health campaigns with recommendations of a balanced lifestyle to promote healthy living.	Overall Top 10 (1st) Patient Top 10 (1st) Relative Top 10 (2nd) Prof Top 10 (10th)	
B	In brain tumour patients, what is the effect of interval scanning to detect tumour recurrence, compared with scanning on symptomatic recurrence, on prognosis?	After a brain tumour is diagnosed and treated, patients will be offered future brain scans as surveillance to monitor how the tumour is behaving - whether it is showing signs of becoming active again and recurring or whether it has remained stable. If the tumour has recurred, it may need some further treatment. We do not currently know for each tumour type what the optimal scanning interval for monitoring brain tumours is and whether or not scans should be done regularly or on an 'as required' basis if patients develop symptoms. It may be that if a recurrence is picked up early, more effective treatments may be available and this could affect the outcome for a patient. However, if the patient is well with no symptoms, immediate treatment may not be appropriate and regular additional scans may cause unnecessary worry.	Overall Top 10 (2nd) Patient Top 10 (3rd) Relative 12th Prof Top 10 (2nd)	
C	Does earlier diagnosis improve outcomes in brain and spinal cord tumour patients, compared to standard diagnosis times?	Brain tumours and spinal cord tumours are rare and so there can be a delay in diagnosis because they are not foremost in patients' and professionals' minds when they are presented with a group of symptoms and signs. We do not currently know if earlier diagnosis, e. g. through screening procedures, has an impact on patient survival and reduction of side-effects from the treatments required to manage the tumour. "Markers" in the blood, or cerebrospinal fluid, of people with brain tumours may pick up molecules (miRNA), using cellular and molecular biology techniques. These markers are unlikely to be present in patients without tumours. They could potentially be used for improved diagnosis, prognosis, and treatment decisions. This area has potential for being helpful in addition to imaging.	Overall Top 10 (3rd) Patient Top 10 (3rd) Relative Top 10 (5th) Prof Top 10 (10th)	
D	In brain tumour patients, what is the effect of short-course steroid use, compared with continuous steroid use, on managing symptoms?	Steroids are given to patients with raised intracranial pressure with headache or with weakness. They are associated with short-term and longer-term side effects. There is some evidence from treatment of inflammatory and auto-immune conditions that intermittent steroid use has fewer chronic side effects, although this has not been tried in brain tumours. For example, intravenous (iv) methylprednisolone may work for 3 weeks. The overall incidence of side effects with intravenous pulse therapy may exceed 50%, but effects, such as Cushingoid facial appearance, are not as severe as with daily steroid therapy. A trial of iv Methylprednisolone 500mg/day for 1 day vs oral dexamethasone (at whatever dose is clinically required) may be feasible.	Overall Top 10 (4th) Patient Top 10 (6th) Relative 12th Prof Top 10 (9th)	

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E	In second relapse glioblastoma, what is the effect of further treatment on survival and quality of life, compared with best supportive care?	In patients with Glioblastoma, the fittest patients get radiation therapy followed by chemotherapy (Temozolomide). The average time till recurrence is 6.9 months. If patients are reasonably fit, they receive a second line chemotherapy (e.g. CCNU and procarbazine). The average time to progression after second line treatment is about 1.8 months. Chemotherapy can be associated with serious complications of infection, bleeding and fatigue, as well as acute toxic symptoms (nausea, vomiting etc) – all of which adversely affect quality of life. The likelihood of a lasting benefit is exceptionally low and the likelihood of getting serious side effects much higher. There is currently clinical balance on whether to suggest it or not.	Overall Top 10 (5th) Patient 12 th Relative 12 th Prof Top 10 (1st)	
F	In patients with a brain tumour, what is the effect of early surgical intervention on prognosis, compared with standard guidelines for surgery?	It is not clear what the standard guidelines for surgery should be. For example whether, in patients with a low-grade glioma, whether there is a benefit in overall prognosis from early surgical intervention compared with surgical intervention at the time of demonstrable growth or progression. There is some evidence that tumours that are completely removed at surgery have a better prognosis than those that are only partially removed and there is supportive evidence that complete removal is more likely to be achieved with smaller tumours. However, previous series have been biased so it is impossible currently to be sure if this is true.	Overall Top 10 (6th) Patient Top 10 (2nd) Relative Top 10 (6th) Prof 20 th	
G	For people with low grade gliomas (LGG) at risk of malignant transformation to high grade gliomas (HGG), what is the optimal MRI monitoring protocol?	Low grade brain tumours can be in what is called 'a pre-malignant state'. At a future point they may become more malignant, or active. This question is about what the best type of MRI scans would be so that any changes in the state of the tumour may be picked up in good time. We do not currently know for each tumour type what the optimal scanning protocol (method) for monitoring brain tumours is and whether or not these should be done regularly or on an 'as required' basis if patients develop symptoms. It may be that if progression is picked up early, more effective treatments may be available and this could affect the outcome for a patient. However, if the patient is well with no symptoms, immediate treatment may not be appropriate and regular additional scans may cause unnecessary worry.	Overall Top 10 (7th) Patient 20 th Relative Top 10 (8th) Prof Top 10 (5th)	
H	In brain tumour patients, what is the effect of cognitive interventions (including memory training) on improving memory after radiotherapy, compared with standard care?	Cognitive functioning (memory and thinking ability) is well-known to be affected by radiation therapy to the brain. We do not know how but it is likely that brain cells vital for memory and thinking are somehow damaged by the radiotherapy. Worsening memory and thinking skills can lower quality of life in many ways and so by finding ways to improve them, quality of life could potentially be improved for the many patients who experience these symptoms. One way to reduce the memory side-effects of radiotherapy is to try to boost brain function by asking the patient to do mental exercises. These can be given in various ways including face-to-face training, self-help booklets, or semi-interactive tools like apps or computer programmes. At the moment we do not know how effective these approaches are for brain tumour patients.	Overall Top 10 (7th) Patient Top 10 (9th) Relative Top 10 (6th) Prof Top 10 (8th)	

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I	In carers of brain tumour patients, what is the effect of interventions to support families on coping with changes that occur in the patient, compared with standard care?	Patients presenting with brain tumours are totally dependent upon their family and carer support working with local services in community and hospitals. This is a major task for those providing care in the family home. A variety of approaches have been developed to support families in such circumstances, no one model has overwhelming support to justify its even/widespread introduction. Trials of models of supportive care with comparative outcome data would lead to a harmonisation of support services with evidence for optimised outcomes thereby assisting with the sustained tasks of justifying health spending on such processes.	Overall Top 10 (9th) Patient Top 10 (10th) Relative Top 10 (3rd) Prof 22 nd	
J	In patients with a low grade or a high grade glioma, what is the effect of extent of resection on neuropsychological function, compared with no resection/biopsy?	In patients with gliomas (primary brain tumours), are there different effects on neuropsychological function (memory, comprehension, ability to process thoughts) in patients having surgical removal versus those just having a biopsy? This is important in helping to determine whether or not surgery has a beneficial role on neuropsychological function as well as on overall survival. This is important as quality of life is as important as quantity of life.	Overall Top 10 (10th) Patient 27 th Relative 18 th Prof Top 10 (2nd)	
K	In brain and spinal cord tumour patients, do new molecular sub-typing techniques improve treatment selection, prediction and prognostication?	A number of distinct molecular genetic alterations have been identified in gliomas over the last two decades. For example, paediatric glioblastoma, Adult Primary GBM and Adult Secondary GBM each have distinct gene changes. Identification of some of these changes might help select patients for different studies based on the expected prognosis. It may also be that some treatments may be best for specific subtypes of tumour. If this were the case, treatment could be targeted to the presence of molecular subtypes. A prospective study of treatment studies based on subtypes may help decide who should be treated early and using which drug.	Overall 11 th Patient 34 th Relative 23 rd Prof Top 10 (5th)	
L	Does chromosomal analysis of low grade gliomas improve prediction of transformation to a higher grade?	The analysis of some markers (mutations, amplifications) can be used to indicate a transformation. To achieve this however, it is necessary to obtain a tumour biopsy and the transformation should always be assessed in the context of the histological appearance. .	Overall 11 th Patient 20 th Relative 18 th Prof Top 10 (7th)	
M	In malignant brain tumour patients, how effective are complementary and alternative medicines, which include supplements and herbal remedies, compared to standard treatment alone, for extending and improving quality of life?	This would be a useful research question as several patients already follow alternative therapies for their health and well-being. This question would allow investigation into any additional benefits to patients' prognosis and quality of life that could be achieved through alternative medicine and therapies alongside current standard conventional medicine and treatment. These could include: naturopathic therapy e.g. homeopathy, nutritional & herbal therapy; biologically based therapies, e.g. dietary & nutritional supplements; mind-body interventions, e.g. meditation & prayer; energy therapies, e.g. therapeutic touch & massage.	Overall 11 th Patient Top 10 (7th) Relative Top 10 (4th) Prof 32 nd	
N	In glioma, what is the effect of extent of resection on survival?	In patients with a primary brain tumour, does the proportion of tumour removed influence overall survival times? It is thought that the more tumour is removed, the better the survival might be, whilst the risks of surgery might increase with more radical surgery. Presently, there is no definitive evidence that extent of tumour resection improves survival, although much research does support this concept. Answering this question will help surgeons and patients make better decisions on surgery in the future.	Overall 14 th Patient 16 th Relative 20 th Prof Top 10 (10th)	

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O	In patients with low grade glioma, can the use of circulatory biomarkers predict an early malignant transformation process?	In patients with low grade glioma, can the use of circulatory biomarkers predict the likelihood of the tumour becoming malignant? Currently circulatory biomarkers are in an experimental phase for most tumours, and even only in a very preliminary stage for brain tumours, and there are currently no circulatory biomarkers that can indicate a progression.	Overall 15 th Patient 27 th Relative 20 th Prof 15 th	
P	What are the long-term physical and cognitive effects of surgery for removing brain and spinal cord tumours, especially for a child or young person?	How does surgery to remove brain and/or spinal cord tumours during early life (up to 24 years) change people subsequently, with respect to intelligence, personality, capacity for movement, employment and consequently their ability to live independently? Performing surgery is a critical step to diagnose and/or remove a tumour. It is possible to relieve symptoms by removing the tumour but also cause additional damage despite the best technique. This question sets out to ask what aspects of surgical approaches threaten subsequent functioning in a young person presenting with a brain or spinal tumour and asks what specifically during surgery poses a risk for subsequent functioning. Once clarified, it would lead to investigation of technical adaptations of surgical timing and approach that can be undertaken to further minimise that surgical risk.	Overall 15 th Patient Top 10 (10th) Relative 20 th Prof 17 th	
Q	In patients with brain and spinal cord tumours, what is the effect of psychological interventions on coping with living with a brain tumour, compared with standard care?	Brain and spinal cord tumour patients have to be able to cope mentally with many sudden and ongoing changes to their lives. Psychological difficulties in adjusting are found in 30-40% of patients. Signs of adjustment difficulties might include denial, anger, tearfulness, withdrawal from daily life, or anxiety. They can be targeted by psychological treatments designed (for example) to improve acceptance of change. Brain and spinal cord tumour patients can also have problem coping practically with respect to day-to-day tasks. Overall, this question is important because it focuses on the day-to-day emotional and practical experiences of patients struggling to cope with living with a brain tumour. Using psychological techniques may improve this; however we do not currently know whether these techniques are effective.	Overall 17 th Patient 12 th Relative 12 th Prof 18 th	
R	In elderly patients with a high grade glioma, what is the most effective treatment? For example, 30Gy dose in 6 fractions for 2weeks with concurrent Temozolomide vs Temozolomide vs Radiotherapy alone?	Age is a factor when thinking about treatments for a high grade glioma, the most aggressive form of brain cancer. The standard of care for people over a certain age is not as clear as it is for younger patients. Sometimes older patients have other conditions that they have to live with so it can be about choosing the best options to meet individual needs. Given the short survival that most elderly patients with GBM have, balancing quality of life with quantity of life has been a major focus for both patients and clinicians. Although elderly patients have not been included in many GBM clinical trials, recent trials have sought to work out how best to manage treatments for a GBM in elderly patients. Based on current evidence, there are several ways to appropriately manage GBM among the elderly, so this question is asking whether it is better to have a short burst of radiotherapy over two weeks with chemotherapy, or whether it is better to have chemotherapy or radiotherapy alone.	Overall 18 th Patient 32 nd Relative 37 th Prof Top 10 (4th)	

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S	In imaging-diagnosed Glioblastoma Multiforme patients, where the benefits of biopsy are uncertain, does biopsy improve survival, compared to no biopsy?	<p>This could be written as: 'In patients with an MRI scan suggesting a Glioblastoma (malignant brain tumour), does biopsy influence treatment and, therefore, impact on survival?' This might be important to know as increasingly many patients are referred now with high-quality MRI scans that are highly accurate in their prediction of glioblastoma and surgical biopsy carries a small risk.</p> <p>Low grade gliomas grow slowly when compared with their high grade glioma counterparts, but undergo malignant transformation to high grade gliomas at a variable and unpredictable point in their natural history. When the pathologist looks at the tumour biopsy, they can test for special chromosomal changes present in some tumour cells (e.g. loss of Chromosome 1p and 19q). Depending on whether the tumour has these changes, or not, is associated with survival. It may be that by testing for these might predict malignant transformation. A prospective study could show this and might help determine a reasonable frequency of scanning, or which types should be treated early depending on whether changes are present or not.</p>	Overall 19 th Patient 27 th Relative 33rd Prof Top 10 (10th)	
T	In patients with brain or spinal cord tumours, does referral to specialist palliative care services at diagnosis improve quality of life?	<p>Palliative care is the holistic care of patients with life-limiting conditions and aims to improve the quality of patients' lives and support those caring for them. Palliative care historically has usually only been given towards the end of the someone's illness; however, in certain studies in patients with other types of tumours, it has been shown that receiving palliative care at the start of one's illness can not only improve patient quality of life throughout their illness but can also prolong their life. Much research in patients with brain and spinal tumours focuses on finding a cure but not on improving their life. The aim of the question is to see whether in patients with brain or spinal cord tumours referral to specialist palliative care services at the start of their disease improves their quality of life.</p>	Overall 20 th Patient 32 nd Relative 23rd Prof Top 10 (10th)	
U	In patients with a brain or spinal cord tumour, how effective is additional clinical nurse specialist support, compared to standard care, in improving quality of life?	<p>The clinical nurse specialist acts as a patient's 'brain tumour buddy', to guide them through the treatment pathway, from discussion in a multidisciplinary team, through surgery, radiotherapy and chemotherapy, and then into survivorship. The clinical nurse specialist is there to support, guide, advise and act as a knowledge resource; they should be easily available to contact via phone or email. They gain a relationship with patients and their families that allows them to advocate on a patient's behalf and assist them at every stage.</p>	Overall 20 th Patient 20 th Relative Top 10 (1st) Prof 16th	
V	In patients with brain or spinal cord tumour, how effective are interventions that provide structured emotional support during diagnosis and primary treatment in reducing psychological distress, compared to care as usual?	<p>The first two months of diagnosis and initial treatment is a particularly stressful time. When patients are unable to cope, the result is psychological distress. 'Distress' can be loosely defined as a general and unpleasant mix of sadness, tension and anxiety, which is not severe and persistent enough to justify a formal psychiatric diagnosis but still affects quality of life. Around 40% of patients report high levels of distress during primary treatment. One way of managing distress is for the treating clinical staff, or in some cases the patient's family, to pragmatically 'troubleshoot' problems as patients disclose them, by listening and advising on the relevant social, practical, emotional and physical questions or difficulties. This is an unstructured approach. It is not currently known whether structured emotional support, such</p>	Overall 22 nd Patient 27th Relative Top 10 (9th) Prof 22nd	

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		as through professional counselling (e.g., by a psychologist or accredited counsellor) or support groups (e.g. via charities), is effective in helping patients come to terms with their diagnosis and treatment.		
W	In brain or spinal cord tumour patients, what is the effect of management of depression on outcome, compared with standard care?	For about 1 in 5 patients, the natural sadness of the diagnosis of brain or spinal cord tumour is sufficiently severe and prolonged for a diagnosis of clinical depression. Depression affects sleep, appetite, self-esteem and quality of life, and even make people feeling suicidal. Yet depression often goes untreated in patients with cancer. Clear evidence that a particular treatment was effective would help improve treatment rates. Although antidepressants and psychotherapy (talking therapy) are well known effective treatments for depression, no study has looked at whether these treatments work in brain tumour patients. In some circumstances antidepressants can cause seizures, tiredness or memory difficulties: whether they do so in brain tumour patients – who are at very high risk of all these things - is unknown. To be effective, psychotherapy needs patients to be able to concentrate and remember what they learn - and brain tumour patients can struggle with these thinking skills. At the moment, we do not know whether either antidepressants or psychotherapy are effective in treating clinical depression in brain tumour patients. Neither do we know whether in some circumstances antidepressants may cause harm.	Overall 22 nd Patient 12 th Relative 33 rd Prof 22 nd	
X	In patients with brain tumours, what is the effect of adopting a healthy diet on progression-free survival?	When weighing up different treatments and lifestyle choices people think about how much longer a person may survive if they try a new treatment (called overall survival or OS), and how long it is before the brain tumour shows progression or recurrence (called progression-free survival or PFS). Progression-free survival is the time from diagnosis to when a tumour recurs, or progresses, which sits within an 'overall survival' timeline. Sometimes treatments only extend life by a very few weeks. Each individual needs to think about what their values are, how they want to be in the time that they have left and think about what is important to them. You may be able to extend life by a few weeks if you have a specific treatment. But then you may spend several weeks travelling to receive the treatment and it may make you feel poorly. It is not currently known whether eating healthily will prolong the time to progression. For example, some people living with a brain tumour try different specific diets, other people give up sugar. It's complex because there are so many choices of diets.	Overall 22 nd Patient Top 10 (5th) Relative 12 th Prof 41 st	
Y	In brain or spinal cord tumour patients, what is the effect of additional strategies for managing fatigue, compared with standard care?	Fatigue is one of the most common symptoms in brain and spinal cord tumour patients. It can be caused by the tumour itself, or tumour treatment. There are currently no guidelines in the UK for cancer-related fatigue and the standard care of cancer treatment for patients with fatigue often does not include fatigue management. There is evidence to suggest aerobic exercise and fatigue-specific psychosocial interventions may help cancer-related fatigue, but this is not specific to brain and spinal cord tumour patients. More research is needed to determine whether any additional strategies (e.g. education on activity, pacing, talking therapy, relaxation therapy) can help to improve patients' symptoms of fatigue.	Overall 25 th Patient Top 10 (8th) Relative 33 rd Prof 32 nd	

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