



Neuro-Oncology Group
a JLA priority setting partnership



**James
Lind
Alliance**

Priority Setting Partnerships

Top 10 priorities for clinical research in primary brain and spinal cord tumours

Final report of the James Lind Alliance
Priority Setting Partnership in Neuro-Oncology

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on behalf of the Neuro-Oncology Group**
www.neuro-oncology.org

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This report is dedicated to all the people whose lives have been touched by a brain or spinal cord tumour.

Contents

Executive summary	2
Background	6
Preparation	8
People	10
Process	16
a. Stage 1: Gathering questions	16
b. Stage 2: Collating and formatting questions	17
c. Stage 3: Prioritising questions	19
d. Stage 4: Agreeing the Top 10	21
Priorities	23
Next steps	24

Executive summary

After a very successful and productive collaboration between brain and spinal cord tumour patients, carers, major brain and spinal cord tumour charities and multidisciplinary professional organisations, we present the Top 10 UK clinical research uncertainties in brain and spinal cord tumours.

Top 10 Priorities*

- 1 Do **lifestyle factors** (e.g. sleep, stress, diet) influence tumour growth in people with a brain or spinal cord tumour?
- 2 What is the effect on prognosis of **interval scanning** to detect tumour recurrence, compared with scanning on symptomatic recurrence, in people with a brain tumour?
- 3 Does **earlier diagnosis** improve outcomes, compared to standard diagnosis times, in people with a brain or spinal cord tumour?
- 4 In **second recurrence glioblastoma**, what is the effect of further treatment on survival and quality of life, compared with best supportive care?
- 5 Does **earlier referral to specialist palliative care** services at diagnosis improve quality of life and survival in people with a brain or spinal cord tumour?
- 6 Do **molecular subtyping** techniques improve treatment selection, prediction and prognostication in people with a brain or spinal cord tumour?
- 7 What are the **long-term effects** (physical and cognitive) of surgery and/or radiotherapy when treating people with a brain or spinal cord tumour?
- 8 What is the effect of interventions to help **carers** cope with changes that occur in people with a brain or spinal cord tumour, compared with standard care?
- 9 What is the effect of additional strategies for managing **fatigue**, compared with standard care, in people with a brain or spinal cord tumour?
- 10 What is the effect of **extent of resection** on survival in people with a suspected glioma of the brain or spinal cord?

*relate to any age

Background

Brain and spinal cord tumours are rare conditions that can be devastating for those affected and their families. The UK government has expressed commitment to improving the lives of those with rare diseases by 2020. The UK Strategy for Rare Diseases recommends commissioning of high quality research and recognises the value of involving patients at every stage of the research journey. This positive approach to treating rare diseases is also now evident beyond the UK where other countries are developing rare disease plans to better serve patients and improve outcomes.

One important way of involving patients in research has been developed by The James Lind Alliance (JLA; <http://www.lindalliance.org/>), which was established in 2004 and is co-ordinated by the National Institute for Health Research (NIHR). The JLA brings patients, carers and clinicians together in a 'Priority Setting Partnership' (PSP) to ensure that researchers, and those who fund health research, are aware of what matters to those most directly affected by a disease.

Preparation

In July 2013, Dr Robin Grant, Consultant Neurologist at the Edinburgh Centre for Neuro-Oncology, gathered support for embarking upon a brain and spinal cord tumour PSP. The Neuro-Oncology Group was initiated and thus began an 18-month process aimed at identifying the clinical research questions of greatest importance to people living with brain and spinal cord tumours, those who care for them and those involved in their diagnosis and treatment. The Neuro-Oncology JLA PSP is giving patients, carers and clinicians the opportunity to influence the research agenda and to ensure the time and money available for research is directed to the issues that matter most.

At the first Neuro-Oncology JLA PSP Steering Group meeting, the scope of the project was agreed as being clinical uncertainties of interventions for primary brain or spinal cord tumours, any age, from diagnosis to terminal stages. The following project objectives were agreed:

- to work with patients, carers and clinicians to identify uncertainties about the effects of neuro-oncology interventions
- to agree by consensus a prioritised list of those uncertainties
- to translate these prioritised uncertainties into research questions which are amenable to hypothesis testing
- to raise public awareness of why research into brain and spinal cord tumours is necessary
- to improve the prevention, diagnosis, treatment and care of patients and their families, both during and after active treatment
- to publicise the results of the Neuro-Oncology PSP
- to take the results to research commissioning bodies to be considered for funding

Several months were spent planning, producing a protocol, engaging with the JLA team in Southampton, inviting major brain and spinal cord charities to become partners, involving patients, sourcing funding and producing project documentation. We developed a website (<http://www.neuro-oncology.org.uk/>) for the purpose of promoting the collaborative venture to seek unanswered clinical questions around brain and spinal cord tumours.

Process

In March 2014, the Neuro-Oncology Group invited questions from members of the public who had experience or interest in brain and spinal cord tumours, and professionals dealing with this group of patients. Following JLA guidelines, we undertook a dynamic collaborative process of continually refining and prioritising questions until we established a 'Top 10' of the clinical uncertainties that exist in the area of brain and spinal cord tumour diagnosis and treatment. There were four main stages in the refinement process:

- 1 Gathering questions** – the main source of questions was from a survey on our website which was publicised widely through the press and relevant charity, health and research organisations. Demographic data was requested but was optional. This was augmented with a small number of questions from a brain tumour charity patient forum and from UK DUETS (UK Database of Uncertainties about the Effects of Treatments).
- 2 Collating and formatting questions** – we merged duplicate questions and rejected out of scope questions and questions that research has already answered. Questions were categorised and were standardised as far as possible into a PICO (**p**articipants, **i**nterventions, **c**omparisons, **o**utcomes) format to ensure we selected questions that could be explored in a clinical trial. Formatted questions were checked by pairs of stakeholders.
- 3 Prioritising questions** – the number of questions was narrowed down by stakeholders working as a whole group then in pairs and then individually. Once we had what we considered a manageable number, we sent out a second survey to patients, carers and health professionals and more widely, with a request that they vote for their Top 10.
- 4 Agreeing the Top 10** – at the final prioritisation workshop in London in November 2014, JLA facilitators used a modified Delphi and nominal group technique to help stakeholders reach consensus on the final Top 10.

Participation

Our first survey generated over 600 initial individual questions from around 200 people. We were able to ascertain that all age groups had contributed, as had both males and females. Most importantly, we received questions from the three key groups: patients, carers (i.e. family members or friends) and health professionals. Submissions were primarily from the UK, with a few from elsewhere (Australia, France, Ireland, Italy, the Netherlands and the USA).

227 people took part in a second public survey in September 2014, to choose which of 44 questions should be prioritised. Although there appeared to be less representation from the youngest age group and spinal cord patients at this stage, we were confident that we had a sufficiently representative response that included relevant questions pertaining to these demographics. Crucially, our three key groups of patients, families and professionals were well represented.

Our stakeholder group comprised 11 men and 18 women, ranging in age from 14 to 76 years. Stakeholders were patients, relatives, charity representatives, doctors from a breadth of specialities, nurses and allied health professionals. Fourteen people were primarily involved to represent the patient perspective and 15 to represent the professional, but many stakeholders wore more than one hat.

Next steps

Working together, we successfully identified and prioritised 10 crucial questions, structured in a form suitable for clinical trials.

To promote these Top 10 priorities, we will engage with governmental organisations such as the National Institute for Health Research (NIHR) and Chief Scientist Office (CSO), Medical Research Council (MRC), The National Institute for Health and Care Excellence (NICE); independent charities such as Wellcome Trust, Cancer Research UK (CRUK), Marie Curie, UK brain tumour charities; and clinical trials support such as through Cochrane, the National Cancer Research Institute (NCRI) and UK Clinical Research Collaboration (CRC) Clinical Trials Units. We will encourage the commissioning of high quality clinical trials run by specially trained research clinicians and supported by the NCRI Clinical Studies Groups run through the UKCRC Clinical Trials Units. It is hoped that the outputs of these trials will inform guidelines and quality performance indicators.

Our ultimate goal is to find answers to these uncertainties in diagnosis, treatment and care, so that people with a brain or spinal cord tumour will receive the best treatment possible, will live longer and will have better quality of life.

For more information about the project, see our website at www.neuro-oncology.org.uk or contact us at jlagroup@exseed.ed.ac.uk

Acknowledgements

The project could not have taken place without the contributions of our funders: *brainstrust*, The Brain Tumour Charity, Brain Tumour Research, Children with Cancer UK, the Cochrane Collaboration, Edinburgh and Lothians Health Foundation and the International Brain Tumour Alliance.

We also gratefully acknowledge the guidance of the James Lind Alliance and practical support of NHS Lothian and the University of Edinburgh.

We appreciated staff who assisted us at our meeting venues: Western General Hospital Teleconference Suite, Edinburgh; Channings Hotel, Edinburgh; The John Lennon Art and Design Building at the British Neuro-Oncology Society conference in Liverpool; and MSE meeting rooms, London.

We would like to sincerely thank the stakeholders and support team listed in this report.

Thank you to each person who contributed to our surveys.

Thank you to everyone who is working to make life longer and better for people with a brain or spinal cord tumour.

Background

Brain and spinal cord tumours are rare diseases, which can make them difficult to diagnose.¹ Treatment is also challenging as there are more than 120 different types of tumour², and treatment will also vary depending on the type, grade and site of the tumour. While some brain tumours types have good survival rates, survival often brings with it neurological and cognitive deficits, caused not just by the tumour but by the interventions provided to treat it. People with low grade primary brain or spinal cord tumours may live for many years, but those having high grade tumours tend to fare less well, with half of those diagnosed dying within a year.³ In the UK brain tumours kill more children than leukaemia, more women under 35 than breast or cervical cancer, more men under 45 than prostate cancer.⁴ Spinal cord tumours are even rarer than brain tumours but have equally varied prognoses depending on the site, type and grade. Due to having a rare disease, people with a brain or spinal cord tumour may experience inaccurate or delayed diagnosis, poor or no information and support in the early stages, limited access to optimal interventions and clinical expertise in the form of multidisciplinary teams, and limited opportunity to become involved in clinical trials.

Nevertheless, the picture is not all bleak. The UK government has now committed to improving the lives of those with rare diseases by 2020 through high quality research. The UK Strategy for Rare Diseases acknowledges that “the main aim of research into rare disease is to improve diagnosis and treatment for patients with a rare disease. To achieve this, support is required for basic, experimental medicine, clinical and health service research.”⁵

One important way to improve clinical and health service research is to involve patients. “Expert clinical teams can offer advice and treatment but the real experts in living with a rare disease are of course the people suffering from the disease and their families.”⁶ A priority setting exercise, to determine what systematic reviews of the literature should be performed, run by the Cochrane Collaboration’s Neuro-Oncology Group in 2012, revealed that the topics rated the most important by consumers were not the same as those identified by clinicians. The Group’s Co-ordinating Editor Dr Robin Grant, Managing Editor Gail Quinn and Consumer Advisers Kathy Oliver (Co-Director of the International Brain Tumour Alliance) and Helen Bulbeck (Director of *brainstrust*) recognised the need to consider whether these discrepancies over priority areas could usefully be explored through the initiation of a process known as a James Lind Alliance ‘Priority Setting Partnership’.

Since 2004, the James Lind Alliance⁷ has brought together patients, carers and clinicians in Priority Setting Partnerships (PSPs) to identify important ‘unanswered questions’ about a particular condition and to prioritise these in a collaborative way in order to determine the most pressing needs for

¹ RARECARE website, <http://www.rarecare.eu/rarecancers/rarecancers.asp> (accessed 12 June 2015)

² Brain Tumour Research website, <http://www.braintumourresearch.org/statistics> (accessed 12 June 2015)

³ Brain Tumour Research website, <http://www.braintumourresearch.org/statistics> (accessed 12 June 2015)

⁴ Brain Tumour Research website, <http://www.braintumourresearch.org/statistics> (accessed 12 June 2015)

⁵ The UK Strategy for Rare Diseases. Department of Health, 22 November 2013. Section 6.16, page 27

⁶ Consultation on the United Kingdom Plan for Rare Diseases, UK Health Departments, 29 February 2012. Page 4

⁷ <http://www.lindalliance.org/> (accessed 12 June 2015)

future clinical research. To date, more than 30 PSPs have been completed including kidney cancer, prostate cancer, mesothelioma, multiple sclerosis, dementia, Parkinson's disease, spinal cord injuries, anaesthesia and perioperative care, intensive care, and palliative and end of life care.

“Patient-centred care requires pro-active engagement with people who are living with a disease. Our James Lind Alliance (JLA) Neuro-Oncology Priority Setting Partnership (PSP) gave us a great opportunity to focus on this type of engagement by including a strong patient voice in our project to determine the Top 10 priorities for brain and spinal cord tumour research. It was an excellent experience to work side-by-side with healthcare professionals. In the process, we all learned a lot from each other as well as helping to shape new research directions that will be truly responsive to patients’ (and caregivers’) needs.”

Kathy Oliver, Co-Director, International Brain Tumour Alliance

Preparation

In July 2013, Dr Robin Grant, Consultant Neurologist, at the Edinburgh Centre for Neuro-Oncology, gathered key leaders in primary central nervous system tumours, each with a wide network of influence in their specialty, to discuss embarking upon a James Lind Alliance 'Priority Setting Partnership' (PSP). There was support for the idea of getting patients, relatives/carers and health care professionals to work together to decide which, of all the unanswered questions about brain and spinal cord tumours, are most important. Thus began an 18-month process of thinking, planning, talking, publicising, distributing, gathering, analysing, debating and selecting.

At the first Steering Group meeting, the parameters of the project were outlined. It was to have a broad scope, covering clinical uncertainties in the management of primary brain or spinal cord tumours, from birth to old age, and from diagnosis to terminal stages. The following project objectives were agreed:

- to work with patients, their families and clinicians to identify uncertainties about the effects of neuro-oncology interventions
- to agree by consensus a prioritised list of those uncertainties
- to translate these prioritised uncertainties into research questions that are amenable to hypothesis testing
- to raise public awareness of why research into brain and spinal cord tumours is necessary
- to improve the diagnosis, treatment and care of patients and their families, both during and after active treatment
- to publicise the results of the Neuro-Oncology PSP
- to take the results to research commissioning bodies to be considered for funding

The period from August 2013 to February 2014 was spent establishing a core team, securing funding, producing a website and devising necessary paperwork. We applied to the James Lind Alliance for 'Readiness for a PSP' approval and sought support from relevant charities and organisations. We received funding from *brainstrust*, Brain Tumour Research, Children with Cancer UK, International Brain Tumour Alliance, The Brain Tumour Charity, the Cochrane Collaboration Neuro-Oncology Group, and Edinburgh and Lothians Health Foundation. A small team of part-time personnel was established to take forward the day-to-day running of the project, which was situated in Western General Hospital, Edinburgh and supported by NHS Lothian and the University of Edinburgh. The initial name and logo were agreed, and a JLA PSP protocol written. An ethics application was submitted and a specific website designed, along with key documents such as participant information sheets, the surveys, videos and press releases and other publicity.⁸

⁸ These are available on our website: www.neuro-oncology.org.uk

“We have been delighted to support the James Lind Alliance Neuro-Oncology Priority Setting Partnership. We believe finding answers to the top 10 uncertainties identified will pave the way for better outcomes for brain tumour patients and their families.”

Sue Farrington Smith, Chief Executive of Brain Tumour Research

People

Several clinicians and leaders of patient-focused charities had been present at the initial steering group meeting, but it was important to broaden representation to include patients and professionals from a variety of health disciplines. We continued to invite people to join us as stakeholders throughout the process, to take part in decision-making and especially in the iterative process of refining and prioritising the questions submitted. Our stakeholder group eventually comprised 11 men and 18 women, ranging in age from 14 to 76 years. Stakeholders were patients, carers, charity representatives, doctors from a breadth of specialities, nurses and allied health professionals. Fourteen people were primarily involved to represent the patient perspective and 15 to represent the professional, but many stakeholders wore more than one hat.

Helen Bulbeck, *brainstrust* Director



Helen is based on the Isle of Wight and runs a national brain cancer charity. She is on the NCRI (National Cancer Research Institute) Brain and CNS (central nervous system) Clinical Studies Group (CSG) and the quality of life subgroup. She is a member of NCIN (National Cancer Intelligence Network) Brain and CNS and CTRad (Clinical and Translational Radiotherapy Research Working Group) executive. Her key drivers are brain tumour patients, carers and healthcare professionals, with whom she interacts daily. She believes that groups solve problems so she invests time developing partnerships that are patient/carer focused and work towards solving the key issues for people living with a brain tumour.

Michael Carbutt, Patient

Michael is a 23 years old and in September 2012 was diagnosed with a pilocytic astrocytoma, which has been treated with radiotherapy. He works in a doctor's surgery as an administrator/receptionist and enjoys watching rugby and doing the odd bit of web coding.

Stuart Farrimond, Patient



Stuart is a trained medical doctor and brain tumour patient. Diagnosed with a malignant glioma in 2008, he was ultimately forced to leave medicine. Retraining as a teacher in further education, he now works full time as a freelance writer, educator and science communicator; and presently contributes to the digital news distribution for the International Brain Tumour Alliance.

Sue Farrington Smith, Brain Tumour Research Chief Executive (deputy for the JLA PSP project) was Crispin Zeeman, Head of Communications)



Sue is Chief Executive of Brain Tumour Research and trustee of Ali's Dream. They have a passion to find a cure for brain tumours, a most devastating disease which took the life of her beloved niece Alison Phelan when she was just seven years old in June 2001, and has claimed the lives of thousands ever since. With her local MP, John Bercow, she established the Brain Tumour All Party Parliamentary Group in 2005. Brain Tumour Research believes in working collaboratively and recognising the contributions of other organisations.

They fund four dedicated brain tumour research centres in the UK and represent the united campaign voice of their member charities and fundraising groups.

Keith Knight, Patient



Keith is married with three children and has spent his entire career working for international banks in London. He enjoys playing golf when he gets the chance, which isn't very often unfortunately. He was diagnosed with a brain tumour in 2006 and had an operation to de-bulk it in 2009 followed by intensive radiotherapy. He has a positive outlook on life and has an awareness that despite living with a brain tumour, there are millions of people around the world who have far greater problems.

Katie Martin, Children with Cancer UK Research Development Manager



Katie has worked for Children with Cancer UK since 2003, contributing to the ongoing evolution of the charity's research grant programme. In 2013 the charity launched the Children with Cancer UK Brain Tumour Initiative in response to concerns about the historic under-funding of this disease area and the continued poor outlook for very many young brain tumour patients. Children with Cancer UK is investing at least £3m over three years in this initiative and hopes that this will help to increase momentum in the field.

Marilyn Monk, Patient



Marilyn is a research scientist with over 50 years' experience in molecular biology, early mammalian development and cancer. Now Emeritus Professor of Molecular Embryology at the Institute of Child Health, University College London, she continues her interest in genetic, epigenetic and lifestyle factors affecting the development of tumours, as well as their management and clinical interventions. She was diagnosed with an intramedullary ependymoma in her thoracic spinal cord in 1997.

Philippa Murray, The Brain Tumour Charity Trustee



Pippa joined The Brain Tumour Charity as a Trustee in 2008, as Chair of the Information and Support Sub-Committee and a member of its Research Sub-Committee. She is also a Non-Executive Director of the Dasic Group, a marine engineering business. She has taken a career break from the Civil Service, where she was a senior policy adviser, since her 15-month-old son, Lawrence, was diagnosed with a brain tumour. She cared for him until he passed away in September 2007 aged 3 years 9 months.

Kathy Oliver, International Brain Tumour Alliance Co-Director



Kathy lives in Surrey and is the Chair and founding Co-Director of the IBTA. She is a consumer representative for the Cochrane Neuro-Oncology Group; Vice-Chair of the European Cancer Organisation's (ECCO) Patient Advisory Committee; a member of the European Society for Medical Oncology (ESMO) Patient Advocacy Working Group, serves on the NCRI Brain CNS Palliative Care and Quality of Life subgroup and is a member of the British Neuro-Oncology Society (BNOS) Council. She is also active in a wide range of European initiatives, and – with an advocacy colleague from the CML community – represents rare cancer patients on the European Commission's Expert Group on Cancer Control.

Leanne Prichard, Patient



Leanne is a patient who lives in London. She got involved with this project as she is passionate about making a difference and improving research, care and treatment for those with brain tumours. She has been involved in charity projects with the luxury and corporate sectors to raise awareness and directly touch the lives of patients. As a die-hard health and fitness enthusiast, within a financially strained health system, she wants to see how lifestyle changes can positively affect outcomes for brain tumour patients.

Isabella Prichard, Relative



Bella is a teenage carer who lives in London. She got involved with this project as she had a lot of exposure to the brain tumour sphere through her mum (Leanne), best friend's mum and a teenage friend – all with brain tumours. She is campaigning to get her school behind brain tumours as their charity for the coming academic year. She wants to be heard as a young person and her voice to make a difference.

David Smith, Patient



David is a spinal cord tumour patient representative. He recovered after surgery to become a Paralympian rower who achieved a gold medal in 2012 with the rowing team. He was made MBE in 2013. He is particularly interested in nutrition and positive mental attitude to illness.

Maddie West-Nelson, Patient



Maddie has lived in London all her life. She enjoys sport, drama and music. She began having epileptic seizures at around age 8, but wasn't formally diagnosed until age 10 with epilepsy, and this was also the time she was first given an MRI and diagnosed with a low grade brain tumour. The tumour was surgically removed in July 2013 as the epileptic seizures increased and could not be controlled by medicine. The operation was a success. She was back at school 6 weeks later and playing sport not long after.

Claire Wiseman, Patient



Claire is a Partner at Apex Executive, an Executive Recruitment Consultancy. She is one of the brain tumour patient representatives and is passionate about raising awareness about brain tumour support and Ehlers-Danlos Syndrome.

Health professionals

Nazia Ahmad, Occupational Therapist



Nazia is a Highly Specialist Occupational Therapist at the National Hospital for Neurology and Neurosurgery in London. She has a keen interest in neuro-oncology and rehabilitation and is doing a research Masters on vocational rehabilitation and brain tumours.

Keyoumars Ashkan, Consultant Neurosurgeon



Ash is Professor of Neurosurgery at King's College Hospital, London with a special interest in neuro-oncology. He is chief or principal investigator on a number of studies, including a phase III immunotherapy trial for glioblastomas.

Sebastian Brandner, Professor of Neuropathology



Sebastian is a Professor of Neuropathology at UCL and Honorary Consultant Neuro-pathologist at the National Hospital for Neurology and Neurosurgery in London. He is a BNOS Executive Member and advises on neuropathology at a national level. His department serves the local population and a wider population in the UK.

He represents North West London as a member of the NHS Clinical Reference Group “brain tumours”, and this gives him insight into commissioning of specialist services. He is also a member of the North London Cancer Network, which has implemented a consolidation of brain tumour services in North East London, and resulted in a significant benefit for patients.

Lucy Brazil, Adult Neuro-Oncologist



Lucy is an oncologist at Guys and St Thomas’ and Kings College Hospitals in London. She is a member of the NCRI brain tumour Clinical Studies Group (and previously Chairperson of the NCRI Brain Tumour Palliative Care and Quality of Life Subgroup) and the European Organisation for Research and Treatment of Cancer (EORTC) Brain Tumour Group.

I have a busy NHS brain tumour practice and I am Neuro-Oncology Research Lead at Guys and Thomas’ Hospitals, with an active trial portfolio.

Robin Grant, Consultant Neurologist



Robin is a clinical neurologist at the Edinburgh Centre for Neuro-Oncology. He believes that more funds should be directed to practical, important clinical neuro-oncology research that can improve quality of life and survival of people with brain and spinal cord tumours. He established the Cochrane Neuro-Oncology Group and leads the Neuro-Oncology Section of the Association of British Neurologists. He is on the BNOS Executive and was Lead Clinician of the Scottish Adult Neuro-Oncology Network (SANON).

Paul Grundy, Consultant Neurosurgeon



Paul is a neurosurgeon in Southampton and Chair of the NHS Commissioning Brain CRG (Clinical Reference Group) and Chair of NHS England CNS Tumours Clinical Reference Group. He is also a member of the Society of British Neurosurgeons.

Diz Hackman, Physiotherapist



Diz is currently working as a physiotherapist at a specialist neurological rehabilitation centre, working with residential and outpatient clients requiring subacute rehabilitation and long-term management. She is supporting the JLA Neuro-Oncology PSP because of her broad experience, including her own research, in the rehabilitation and

management of neuro-oncology patients through her previous post as Specialist Physiotherapist at the Royal Marsden Hospital.

Kirsten Hopkins, Adult Neuro-Oncologist



At the time of the project, Kirsten was an adult clinical oncologist in Bristol. She is a member of the NCRI CSG, EORTC Radiation Oncology Group and Brain Tumour Group, in addition to being a member of the Royal College of Radiologists/Oncology.

Kat Lewis, Speech and Language Therapist

Kat is the Team Leader for Speech and Language Therapy at University College Hospitals NHS Foundation Trust in London. She became involved in the PSP project having worked in an acute neurosurgical unit and then a charity-funded support and information service. She has observed the reality for patients and their families of what living with a brain tumour really involves – and it is not always the medical aspects that create the greatest challenges.

Jamie Logan, Neuro-Oncology Nurse Specialist



Jamie has a wealth of experience in clinical neuro-oncology and at the time of the Priority Setting Partnership final workshop, was a Clinical Nurse Specialist in Neuro-Oncology at King's College Hospital in London.

Jane Neerkin, Palliative Care Consultant



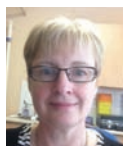
Jane is a Palliative Care consultant at UCL and National Hospital for Neurology and Neurosurgery in London. She is a member of the National Cancer Research Institute Brain Clinical Studies Group Palliative Care section and several other palliative care societies.

Gail Quinn, Cochrane Neuro-Oncology Group Managing Editor



Gail works in Bath as the Managing Editor of the Neuro-Oncology Cochrane Group and the Cochrane Gynaecological Cancer Group. The Cochrane Collaboration is funded by the National Institute for Health Research (NIHR) and publishes systematic reviews of evidence of effectiveness of treatment interventions or the identification of harms related to treatments in clinically controlled trials.

Julie Read, General Practitioner



Julie is a GP in Edinburgh and the wife of a brain tumour patient who was diagnosed with a low grade glioma in 1999 and died in 2012. She is interested in the effects of brain tumours and their treatments on the patients and carers. Even those who survive many years often have to give up promising careers due to the brain injury, and the impact on families is immense

Ally Rooney, Psychiatry Fellow



Ally is a psychiatry trainee in Edinburgh with an interest in the neuropsychiatry of brain tumours. He chairs the SANON Supportive and Psychological Care group, which connects clinicians, researchers and charities in the Scottish brain tumour community.

David Walker, Professor of Paediatric Oncology



David is professor of Paediatric Oncology and Co-Director of the Children's Brain Tumour Research Centre at the University of Nottingham. He is currently president of the British Neuro-Oncology Society (BNOS). He has played a variety of leadership roles in clinical trials in children and young people with brain tumours in the UK and Europe. His particular research interest is accelerating brain tumour diagnosis by raising awareness, preventing focal tumour related brain injury to optic pathways and cerebellum and developing novel drug delivery systems for brain tumours. He works with brain tumour charities on funding and research strategies and contributes to political lobbying to optimise access to novel diagnostic techniques and therapies.

Support team

Julia Day, Assistant Manager/Data Analysis Lead



Julia is an Assistant Psychologist working in the Department of Clinical Neurosciences in Edinburgh for NHS Lothian. She has an MSc in Clinical Psychology and is a Cochrane author and peer reviewer.

Catherine Fitton, Graphic Designer

Catherine is a freelance Graphic Designer based in Winchester. She is a Trustee of *brainstrust* and provides a pro bono design service for the charity.

Niall Grant, Technical Support



Niall is Founder and Chief Executive Officer of WorkbaseHR, an online human resource management software company. He is Chairman of Volunteering Development East Lothian; a Royal National Lifeboat Institution (RNLI) crew member; founder of Tilitonse, a project to get Malawi into the Homeless world cup.

Jane Hayes, Information Specialist

Jane is the Trials Search Co-ordinator for the Cochrane Gynaecological Cancer Group and Cochrane Neuro-Oncology Group.

Laura MacDonald, Manager

Laura is the Managing Editor of the Cochrane Oral Health Group. She has a Masters in Applied Psychology. She has worked with children and families in a therapeutic capacity and as a researcher on a project for people with alcohol dependence.

Richard Morley (pictured), Tessa Clarke and David Crowe, JLA Advisors



Richard has extensive experience of public engagement and partnership working in the voluntary, public and education sectors. He co-chairs the University of York, Department of Health Sciences Patient and Public Involvement Committee, and is a James Lind Alliance Adviser and Consumer Network Co-ordinator for Cochrane.

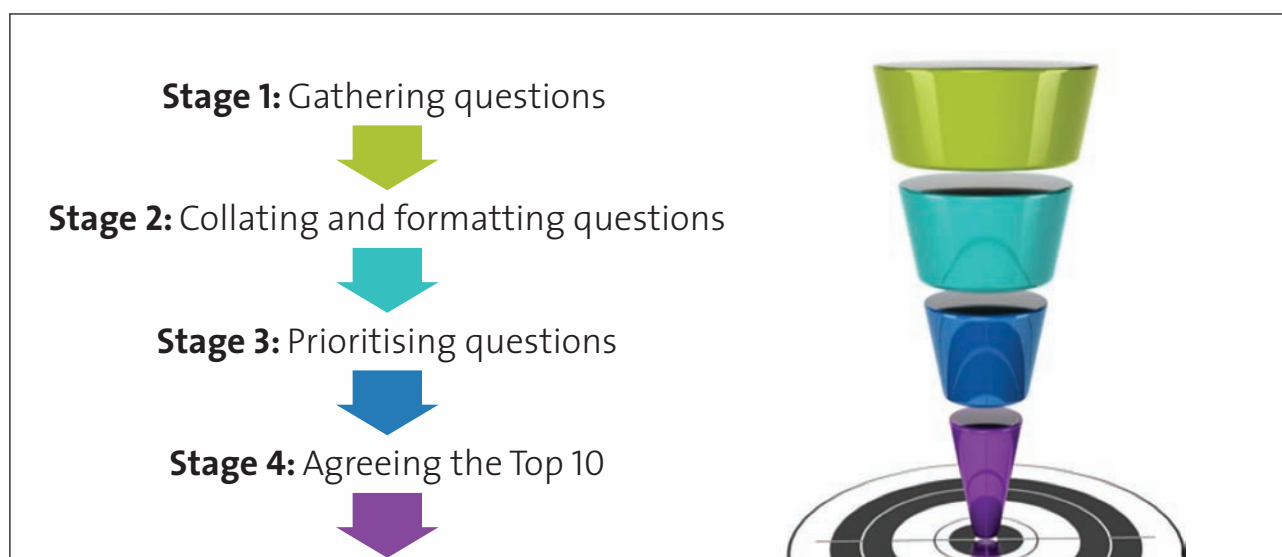
Karolis Zienius, Researcher



Karolis is a doctor in Edinburgh with a psychology degree and has Cochrane systematic review experience.

Everyone who was invited to take part in this Priority Setting Partnership completed a declaration of interest form so that any bias could be minimised. No relevant interests of any financial nature were noted. Further details available if required by contacting jlagroup@exseed.ed.ac.uk or visit www.neuro-oncology.org.uk

Process



Stage 1: Gathering questions

After the period of planning, the Neuro-Oncology Group invited questions from the public in March 2014. We timed the launch of our survey to coincide with the UK Brain Tumour Awareness Month and issued a press release, as well as providing articles to relevant magazines such as *Brain Tumour*. We also used social media to advertise that patients, carers, relatives, friends and professionals with experience of or an interest in brain and spinal cord tumours were being given the opportunity to influence the research agenda. We contacted a long list of relevant charities and governmental, health and research organisations to ask them to alert their members to the opportunity to contribute. Our stakeholders involved their multidisciplinary teams and other contacts, with some charities adding links to the survey on their websites and mentioning the project in their electronic newsletters. Publicity was therefore through a variety of means, with ‘snowballing’ being the main technique used to get the word out.

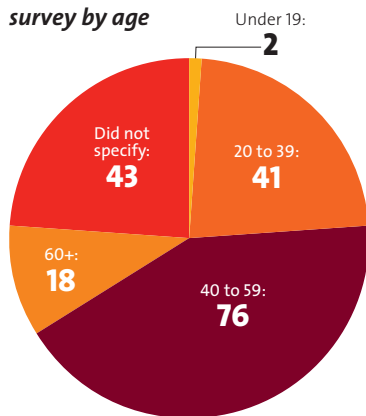
Our JLA PSP website invited people to submit ‘unanswered questions’ about any aspect of diagnosis, treatment or care; however, we anticipated there could be potential participants with cognitive difficulties or without internet access and so paper copies were available as well. This also meant we had a contingency for the inevitable technical problems that we did encounter periodically. To ensure this did not limit anyone from contributing, we extended the survey for an extra month until the end of May 2014.

The survey was open-ended and people could submit as many or as few questions as they wanted. We asked for some basic demographic data if people were happy to provide it, which included age, sex, type of contributor (patient, relative/carer/health professional/other) and place of residence, but submissions could also be made anonymously.

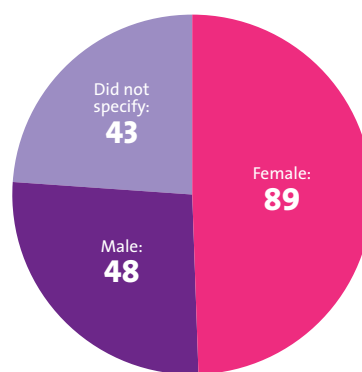
In accordance with JLA guidance, we also gathered questions relating to brain and spinal cord tumours from UK DUETS (The UK Database of Uncertainties about the Effects of Treatments, <http://www.library.nhs.uk/duets/>), which publishes treatment uncertainties about a wide variety of health problems, as submitted by patients, carers and clinicians, and gleaned questions from research recommendations in clinical guidelines and other publications. In addition, to increase the patient representation, particularly from those unlikely to go online to complete a survey, we decided to gather questions from patient forum events run by *brainstrust*.

In total, over 600 individual questions were gathered from around 200 people, 180 of these submitting questions through our online survey. Survey submissions were primarily from the UK but there were a few submissions from Australia, France, Ireland, Italy, the Netherlands and the USA.

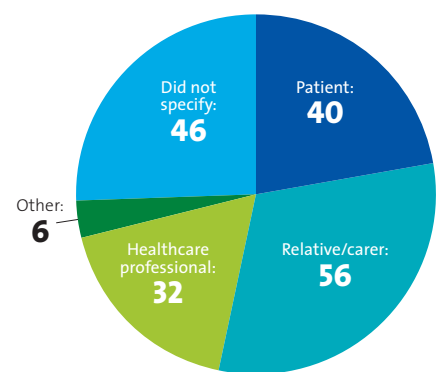
Respondents to initial survey by age



Respondents to initial survey by gender



Respondents to initial survey by type



Stage 2: Collating and formatting questions

When the survey closed at the end of May 2014, all submissions were downloaded into an Excel spreadsheet, with the questions sourced from the patient forum and UK DUETS added. Many submissions had multiple questions within them so these were separated out and the questions categorised for ease of analysis.

a. Rejecting out of scope questions

Two people read through all the questions and those that were considered to be ‘out of scope’ were removed. These might have been submissions that were comments rather than questions or were too personal; were more suited to audit or NHS education; were not clinical questions or were simply too broad. The questions removed from prioritisation were checked over by another stakeholder to confirm their exclusion. Those about which there was uncertainty were put to one side for discussion at a full stakeholder meeting. There was agreement that no questions submitted through the process would be ‘lost’ but that we would look for other ways to use them after the end of the PSP.

b. Formatting questions

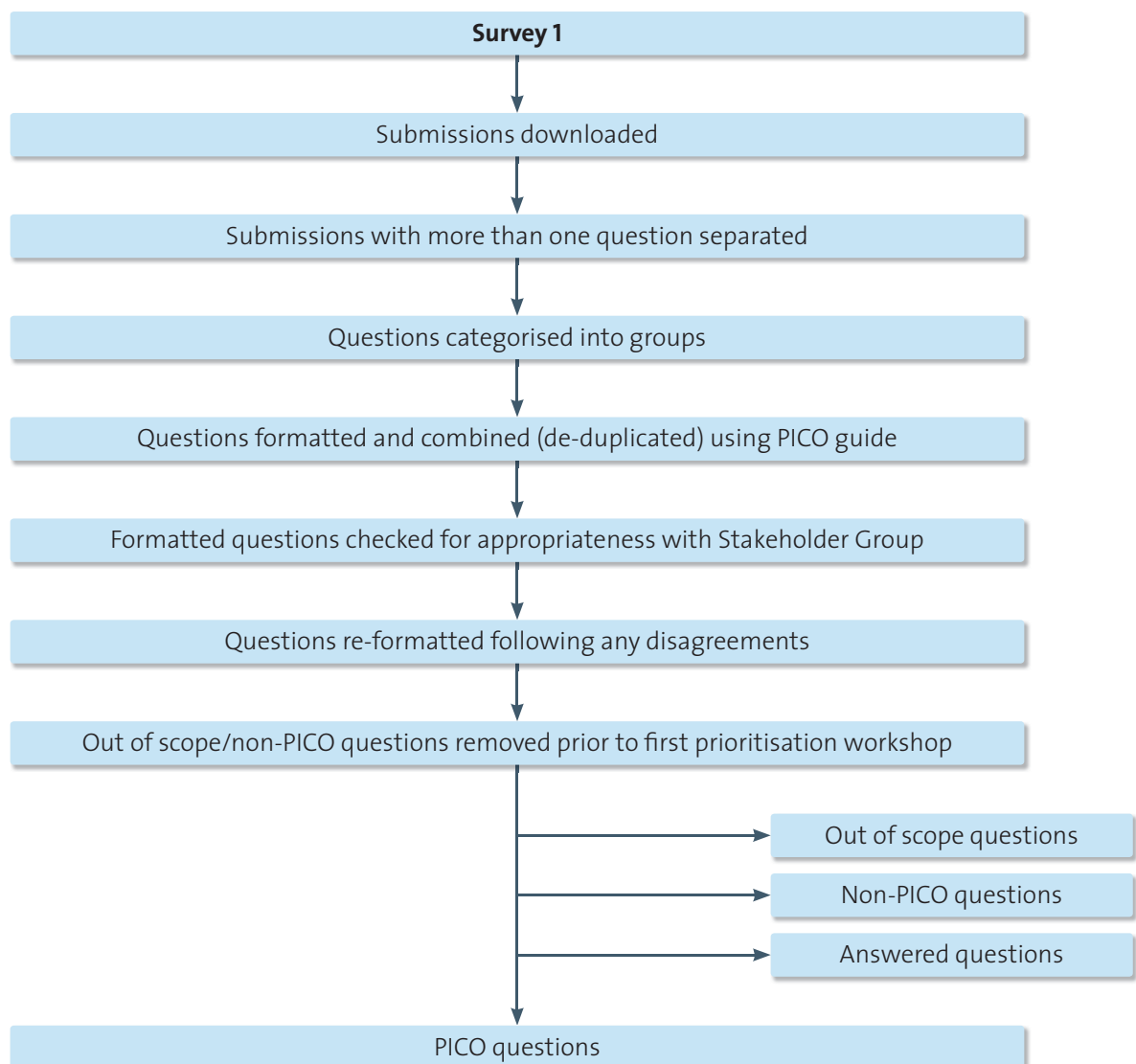
In accordance with guidance from the JLA, we wanted to focus primarily on questions that could be researched within the framework of a randomised clinical trial. We standardised each question into a PICO (p**ar**ticipant, i**n**tervention, c**om**parison, o**ut**come) format to facilitate this.

The PICO format allows specification of the participants to be involved in the experiment, the intervention(s) to be tested, the control (comparison) condition to be used and the outcomes to be measured. Where asking essentially the same thing, questions were combined. Where questions clearly could not fit this format, they were removed from the selection. One or two stakeholders checked that each formatted question reflected the original(s). Questions were reworded where necessary. Where there was uncertainty, these questions were put to one side for discussion at a full stakeholder meeting.

c. Searching the literature

In the survey, we invited people to submit the “probably unanswered questions you think researchers need to investigate”. In accordance with the James Lind Alliance definition of a ‘treatment uncertainty’, i.e. no systematic review has been carried out in the last three years addressing the uncertainty or a recent systematic review has confirmed there is uncertainty, we conducted literature searches to identify all systematic reviews on brain or spinal cord tumours undertaken in the last three years. Any submitted questions that were, in fact, already answered were removed.

A summary of this stage of the process is illustrated in Figure 1.



Stage 3: Prioritising questions

Stakeholder input

In July 2013, a stakeholder meeting, chaired by our JLA advisor Richard Morley, was held to take forward the prioritisation of the questions. This was a challenging task as we had to reduce a still large number of questions to 50 or less, a number we considered would be manageable for people to vote for in a second survey. Questions that had caused difficulties at the previous stage were discussed by the whole group. The main principle that guided us was balance. While we agreed it was very important to acknowledge those questions that were very common, we did not want to rely solely on 'majority vote'. We also wanted to ensure that both patients and professionals made equitable contributions to the selection, that we had questions relevant to children and to the elderly, and that questions relevant to spinal cord tumours, despite being so much rarer than brain tumours, should be included.

The stakeholder group therefore agreed to:

- Reject questions that are about the causes of brain tumours
- Reject questions difficult to put in PICO format
- Take forward questions submitted more than once (excepting the few the group agreed were unimportant questions)
- Take forward the majority of the child-specific questions (as prioritised by a patient and professional stakeholder)
- Take forward the majority of the spinal cord specific questions (as prioritised by a patient and professional stakeholder)

At the end of the meeting, we had not achieved our goal of having the questions for the second survey determined. The questions that remained after applying the 'rules' agreed above, were sent to each stakeholder individually and we asked them to vote for the 10 additional questions they thought should go into the second survey. Once these responses were collated, the core team agreed to take forward those that were voted for by three or more people if they included both a patient and a clinician representative. They also included the small number of questions that were voted for by four clinicians. Where combining or rewording questions had been suggested by one or more stakeholders, this was discussed and a decision made as to whether this was justified.



Stakeholder meeting in Liverpool in July 2014

“As a patient who hears very little in the media about the devastating affect that brain cancer has on so many people in the UK, it is extremely satisfying to be part of this ground breaking initiative, which attracted support from dedicated clinical professionals, patients and carers, all sharing a common goal: to find answers to questions about treatment and prevention coming from the brain tumour community.”

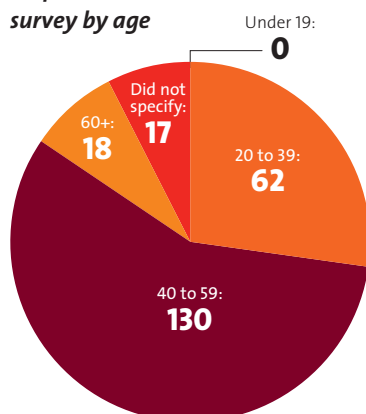
Keith Knight, Patient

Second survey

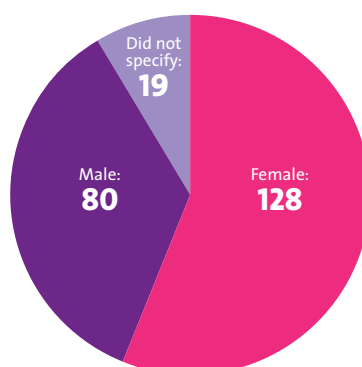
In September 2014, we launched our second survey, aiming to involve at least 200 people and to reduce the 44 questions still further to a number that would be manageable for the final priority setting workshop. The survey was available online for two months, with paper copies also available for those who needed them. The opportunity to take part was publicised in much the same ways as for the first survey, with the addition that all those who had provided their email address were sent a personal copy. Participants were asked to select their Top 10 by ‘ticking’ next to a question. They were not asked to rank them and were advised that they could not select more than 10 or we would be unable to use the submission.

We received votes from 227 people. We were pleased with the response though disappointed that we may have had no voters under age 19 and only one spinal cord tumour patient. This is impossible to know, however, as some people exercised their right not to disclose demographic data when completing the survey. The majority of respondents were from the UK but we did have 32 people taking part from further afield in Australia, Canada, Chile, Denmark, France, Germany, Ireland, Italy, Netherlands, New Zealand, Singapore, Spain, Tunisia and USA.

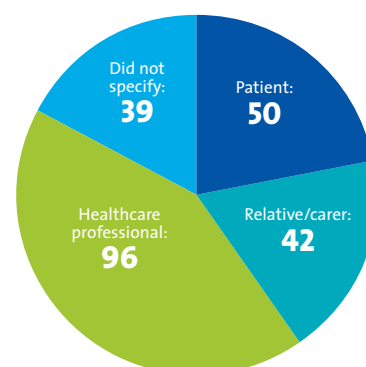
Respondents to second survey by age



Respondents to second survey by gender



Respondents to second survey by type



After analysing the results, the core group of the stakeholders agreed to take forward questions receiving more than 20% of the total vote (at least 46 votes) and any question receiving at least a third of either patient, relative or health professional votes.

Stage 4: Agreeing the Top 10

In November 2014, stakeholders were approached to write lay summaries for each of the remaining 25 questions to help people (especially the patient representatives) prepare for the final priority setting meeting. These lay summaries were issued to all stakeholders, along with details about the reason the question had been selected from the second survey and the results of voting in the second survey. In keeping with the methodology of the James Lind Alliance for this stage of the process, stakeholders were asked to individually rank the 25 questions in order of importance prior to the final workshop to serve as a starting point for discussions. Biographies of the participants were also circulated before the day.

Our final workshop took place in central London in November 2014. Eighteen of the stakeholders were able to take part in the day, in addition to Laura MacDonald and Julia Day who co-ordinated the event. An observer from NIHR and another from CancerWorld magazine attended. The day was facilitated by JLA advisors Richard Morley and David Crowe using the now well established JLA format, which employs the nominal group and modified Delphi technique to encourage discussion and move towards consensus.



Debating what's most important at the Neuro-Oncology PSP final workshop in November 2014



Reaching consensus about the Top 10 at the Neuro-Oncology PSP final workshop in November 2014

The participants were divided into two groups, which had been pre-arranged to ensure there was a balance of patient and professional representatives and a mix of disciplines and of ages. The groups were given a set of 25 laminated A5 cards, each printed with one of the questions. In the two smaller groups, we discussed all 25 questions, aiming initially to identify the most important and least important three. Once these were agreed, debate continued in order to place the remaining questions in order of importance. At lunchtime, the ranking of the 25 questions from the two groups were combined so that in the afternoon session, in a new group composition,

the consensus ranking was the starting point for discussions about priority. After the second round of rankings were collated, the two groups came together in the final portion of the day to agree the Top 10 and debate their order.

There was disagreement and dissension but within a respectful atmosphere, where participants actively engaged and each person was given equal opportunity to contribute freely. At the end of the day, there was a great sense of satisfaction that consensus was reached and we achieved our goal of agreeing the Top 10 clinical research priorities in brain and spinal cord tumours.

“It was so interesting working together at that meeting to determine the priorities from amongst the questions considered and impressive that so much agreement was evident in the process involving people coming from different angles. I was glad that spinal cord tumours were represented since these are relatively rare compared with brain tumours.”

Marilyn Monk, Patient



Stakeholders at the Neuro-Oncology PSP final workshop in November 2014

Priorities

From the earliest stages of the process, we had established an ethos of inclusivity and stressed that it was important the Top 10 questions finally identified should represent both brain tumours and the much rarer spinal cord tumours, as well as including questions of relevance to children through to those over age 60. We aimed to ensure that selection was not dominated by clinicians' views but that genuine consensus between patient and professional viewpoints was reached. We are pleased to say that we believe this has been achieved.

Top 10*

- 1 Do **lifestyle factors** (e.g. sleep, stress, diet) influence tumour growth in people with a brain or spinal cord tumour?
- 2 What is the effect on prognosis of **interval scanning** to detect tumour recurrence, compared with scanning on symptomatic recurrence, in people with a brain tumour?
- 3 Does **earlier diagnosis** improve outcomes, compared to standard diagnosis times, in people with a brain or spinal cord tumour?
- 4 In **second recurrence glioblastoma**, what is the effect of further treatment on survival and quality of life, compared with best supportive care?
- 5 Does **earlier referral to specialist palliative care** services at diagnosis improve quality of life and survival in people with a brain or spinal cord tumour?
- 6 Do **molecular subtyping** techniques improve treatment selection, prediction and prognostication in people with a brain or spinal cord tumour?
- 7 What are the **long-term effects** (physical and cognitive) of surgery and/or radiotherapy when treating people with a brain or spinal cord tumour?
- 8 What is the effect of interventions to help **carers** cope with changes that occur in people with a brain or spinal cord tumour, compared with standard care?
- 9 What is the effect of additional strategies for managing **fatigue**, compared with standard care, in people with a brain or spinal cord tumour?
- 10 What is the effect of **extent of resection** on survival in people with a suspected glioma of the brain or spinal cord?

*priorities relate to any age

Next steps

“This PSP has been a truly collaborative effort and everybody has had a voice. It has widened horizons and will shape clinical research for brain cancer patients and the people who look after them. This means that in the future clinical research will be relevant, focused and cohesive. It’s been a fabulous experience.”

Helen Bulbeck, Director of *brainstrust*

Where are we now on the research journey⁹? The JLA PSP has taken us halfway. We are now committed to handing the baton to those who can ensure that these priorities are not merely interesting but are pro-actively investigated, that researchers and those who fund them are motivated to address these vitally important uncertainties and that they find answers that will bring reliable evidence to the clinicians who care for neuro-oncology patients. Most importantly, as a result of this research, we look forward to seeing much improved outcomes for people living with a brain or spinal cord tumour.

The research journey



⁹ http://www.lindalliance.org/pdfs/7_Cycle%20or%20Train.pdf (accessed 12 June 2015)

In March 2015, we began highlighting our Top 10 questions to key organisations. Several abstract and poster presentations at cancer and neuroscience/neuro-oncology meetings in the UK and Europe have been accepted and more are planned. A poster we designed to describe our Priority Setting Partnership was submitted to the National Cancer Intelligence Network (NCIN) conference where its patient focus was praised and it won third prize. We have published articles in a number of magazines and newsletters.



JLA poster presentation at the European Association of Neuro-Oncology, Istanbul March 2015

Three systematic review titles based on questions 5, 8 and 10 of our Top 10 priorities have been prioritised by Cochrane:

- Early referral to specialist palliative care services for improving quality of life and survival in people with a brain or spinal cord tumours (priority 5)
- Interventions to help carers cope with changes that occur in people with a brain and spinal cord tumour compared to standard care (priority 8)
- Biopsy versus resection in spinal cord tumours (priority 10)

Also under consideration is a review on the ketogenic diet in primary central nervous system tumours, which is based on our top question “Do **lifestyle factors** (e.g. sleep, stress, diet) influence tumour growth in people with a brain or spinal cord tumour?”

To determine where the questions are best directed for potential funding, we have discussed the Top 10 clinical research priorities with:

- a) National Institute for Health Research (NIHR)
- b) Scientific Director, Cancer Research UK Clinical Trials Unit in Birmingham
- c) Health Foundation Chair in Health Economics and Chair of the Joint Economic Methods Group of the international Cochrane and Campbell Collaborations
- d) Senior Research Manager of Experimental & Translational Research at Chief Scientist Office

In the run up to our ‘launch’ of the questions at the British Neuro-Oncology Society conference on 1 July 2015, we have organised a meeting in the offices of the National Institute for Health and Care Excellence (NICE) in London entitled: “Strategy to Support Collaborative High Quality Clinical Neuro-Oncology Research Applications to Inform Guidelines”. We have invited key influencers in funding organisations and charities to discuss how we can develop the questions to give them most chance of success when submitted against all the other types of submissions to organisations such as the National Institute for Health Research, Wellcome, Cancer Research UK and Chief Scientist Office.

As for the questions that did not make the Top 10, we appreciate the time each contributor took to submit their questions and we would like to see that wherever possible each is used to improve the care and treatment of people with brain and spinal cord tumours. Questions suitable for PICO formatting will be submitted to UK DUETS. It is hoped we will have resources to revisit non-PICO questions to see how we may use these to develop other forms of research. Overall, we would like to use the information gathered in the process to improve information accessibility and support for people with a brain or spinal cord tumour and their families.

“We are delighted to have achieved our goal of identifying the top 10 clinical research priorities in brain and spinal cord tumours, as selected by a people diagnosed with a brain or spinal cord tumour and those who care for them, whether personally or professionally. These final 10 questions cover a wide range of topics including diagnosis, treatment and support; they cover brain and spinal cord tumours, and they apply to the very young through to the over 60s.”

Project Lead, Consultant Neurologist **Dr Robin Grant**

Over to you


The project is over, but in many ways the work is just beginning.

Will you join us in calling for high quality research to answer these priority questions in clinical neuro-oncology? With your help we can make life longer and better for people diagnosed with a brain or spinal cord tumour.

For more information, see our website www.neuro-oncology.org.uk
or email jlagroup@exseed.ed.ac.uk

Notes

Notes



**Top 10 priorities for clinical research in primary
brain and spinal cord tumours**

Final report of the James Lind Alliance
Priority Setting Partnership in Neuro-Oncology

June 2015