

The Brain Tumour Charity's Response to the James Lind Alliance Report

This document outlines how the JLA 'Top 10 Neuro-Oncology Uncertainties' align both with The Brain Tumour Charity's five year strategic plan 'Defeating Brain Tumours', which includes our new research strategy, 'A Cure Can't Wait', as well as the research The Brain Tumour Charity is currently funding and previously funded projects.

'Defeating Brain Tumours' was developed through consultation with patients, carers and the very best global minds in brain tumour research. This strategy has two clear goals – to double survival and halve the harm caused by brain tumours. To achieve these goals we will be funding extensive research, both clinical and laboratory-based, as we seek to get better treatment to patients faster and improve outcomes.

Critically, by integrating our research funding, influencing and advocacy activities we will be able to accelerate progress to benefit patients, as lack of research alone is not the only thing holding us back. Our influencing and advocacy work will seek to optimise the environment in which research is conducted and the standards of treatment and care received, thereby facilitating the rapid translation of fundamental research discoveries and treatments to benefit patients. This integrated approach to our work is reflected in this strategy.

To achieve our ambitious goals, we will focus our efforts on six priority areas that we believe will have the greatest impact for everyone affected by this disease:

1. A Cure Can't Wait
2. Every Patient is a Research Patient
3. Early and Accurate Diagnosis
4. Equal Access to the Best Treatment and Care
5. Improving Life Today
6. United in our Battle to Defeat Brain Tumours

'Defeating Brain Tumours' can be read in full at: www.thebraintumourcharity.org/defeatingbraintumours

Our work will provide a significant contribution towards answering some of these 'Top 10 Neuro-Oncology Uncertainties'.

You can read 'A Cure Can't Wait' in full here: www.thebraintumourcharity.org/researchstrategy and our 'Research Impact Report', highlighting previous breakthroughs here: www.thebraintumourcharity.org/impactreport

If you would like any further information please get in touch: research@thebraintumourcharity.org

The Top 10 Neuro-Oncology Uncertainties as identified by the James Lind Alliance

What is the influence of lifestyle factors (e.g. sleep, stress, diet) on tumour growth?

We have committed in our new research strategy to identifying and analysing long-term survivors to see what we can learn from the biology of their tumours and response to treatment, as well as other environmental impacts such as diet and lifestyle.

Researchers we are currently funding^{1,2} are conducting a study in which healthy volunteers on a low-carbohydrate, high-fat diet will be given MRI scans to track metabolic changes in the brain.

Previously we have funded research at the University of Manchester and the University of Leeds which looked at factors including maternal experiences during pregnancy, childhood illness and family history of disease and cancer to see if they had an effect on brain tumour incidence in children. This led to a larger international study into the causes of childhood brain tumours³. Earlier research we funded found that certain vitamins and minerals may have potential to help prevent brain tumour growth⁴.

¹<http://www.birmingham.ac.uk/staff/profiles/cancer/tennant-daniel.aspx>

²<http://www.birmingham.ac.uk/staff/profiles/cancer/peet-andrew.aspx>

³<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3922821/>

⁴<http://www.ncbi.nlm.nih.gov/pubmed/14520549>

We will track the impact of lifestyle on tumour growth over time through a new data registry, to inform future learning and potential research in this area.

What is the optimal scanning interval to detect tumour recurrence?

Through 'A Cure Can't Wait' we are committed to funding pioneering research that will help make sure brain tumours are diagnosed as early and accurately as possible. We have also committed to investing in pilot studies designed to transform the NHS experience for brain tumour patients through testing different models of service delivery.

One of our funded researchers, Dr Adam Waldman is currently testing an improved MRI technique that could help to detect progression earlier⁵. In addition, we are co-funding Professor Andrew Peet², in partnership with Action Medical Research, to develop a new imaging technique to gauge the severity of brain tumours in children to help select the most appropriate treatment⁶.

Previously, our researchers found a way of using scans to help detect when low grade gliomas will become malignant⁷, while work we funded has led to advances in using magnetic resonance spectroscopy (MRS)⁸ to gauge treatment response and tumour type.

Our work to ensure equal access to the best treatment and care, one of our six strategic priorities, will include developing an optimal patient pathway (which includes imaging) and a new quality standard of care to be adopted throughout the UK.

We also recognise the need for rapid scan results for patients to reduce fear and anxiety and our Support and Information Team have highlighted where this has not been the case in specific neuro-centres and worked with them to ensure changes in practice that benefit patients.

What is the effectiveness of earlier diagnosis?

At present we do not know the average time taken to diagnose an adult brain tumour in the UK nor the impact that an earlier diagnosis could have on outcomes and quality of life. As part of our new research strategy, we issued a funding call for research applications in December 2014 that will provide us with the evidence we need about the journey to diagnosis and the impact of earlier diagnosis for adults⁹. This funding will be awarded in July 2015.

For childhood brain tumours, funding from The Brain Tumour Charity enabled Professor David Walker and his team at The University of Nottingham to promote the early detection of symptoms and that prompt treatment does help save lives and reduce long-term disabilities. The work led to our HeadSmart early diagnosis campaign, which has brought down average diagnosis times for childhood brain tumours from over 14 weeks to 6.7 weeks and saved children's lives¹⁰.

What is the effectiveness of further treatment in relapsed glioblastoma?

We have committed in our strategic plan to investing in research that will contribute to doubling survival for all brain tumour patients within ten years.

We support investigating the repurposing of drugs that have been successful in other disease areas. We will develop closer partnerships with the pharmaceutical industry and bring together researchers, clinicians and industry leaders to facilitate clinical research and accelerate access to new drugs.

At our Centre of Excellence at UCL, researchers in the lab discovered that hydroxychloroquine, variants of which are used to prevent malaria and are therefore safe and tested drugs, could help radiotherapy get to the brain more effectively in patients over the age of 70¹¹. This has led to a clinical trial in an unprecedented 2.5 years.

Responsible innovation should entail access to treatment options that may not be clinically proven, but are clinically safe and for which there is evidence of potential for efficacy, such as the Government's proposed Early Access to Medicines scheme¹². There should, however, be clearly defined guidelines on what constitutes a suitable evidence base on which to prescribe treatment for a condition for which it is not clinically proven.

Such an initiative would mark a step forward for terminally ill patients who have no other option available to sustain their lives, by streamlining appraisal processes so that medicines can be accessed at phase two clinical trials. We call on

⁵ <http://www.thebraintumourcharity.org/research/current-research-projects/testing-new-treatments/New+MRI+techniques+to+measure+response+to+treatment>

⁶ <http://www.thebraintumourcharity.org/news/news-articles/pioneering-mri-technique>

⁷ <http://www.thebraintumourcharity.org/Resources/SDBTT/the-research/documents/the-research-impact-report-v2.pdf>

⁸ <http://www.thebraintumourcharity.org/research/research-news/breakthrough-could-help-reduce-need-for-biopsies>

⁹ <http://www.thebraintumourcharity.org/research/for-researchers/Funding-opportunities/adult-brain-tumour-diagnostic-pathway>

¹⁰ <http://www.thebraintumourcharity.org/awareness/the-headsmart-campaign>

¹¹ <http://www.thebraintumourcharity.org/research/our-discoveries/testing-new-treatments>

¹² MHRA, "Early Access to Medicines Scheme". Accessed at:

<http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm>

legislators of the Medical Innovation Bill to consider measures about how medicines can be accessed at an earlier stage of clinical development.

At the Brain Tumour Charity, we are committed to improving patient safety and quality of life for brain tumour patients, particularly at the end of life. To retain our support, the Bill must ensure the strongest possible safeguards against professional malpractice, and protect vulnerable patients from clinically unsafe treatments.

We believe that every innovative treatment under the provision of the Medical Innovation Bill should be recorded in a compulsory and properly maintained Open Access database, which will subject the treatment option to greater scrutiny from regulators about safety and efficacy.

What is the impact on quality of life of a referral at diagnosis to a specialist palliative care service?

As part of our new research strategy, we have commissioned the most comprehensive and significant research report to gather evidence and quantify the impact of brain tumours on people's quality of life. The report "Losing Myself: The Reality of Life with a Brain Tumour"¹³ builds on a survey we carried out in 2013 and will be published in summer 2015.

Following this research, we have launched a funding call for researchers to investigate aspects of quality of life highlighted as the key issues in the report¹⁴.

This is supported by our influencing and advocacy work, driving change to ensure that every patient has equal access to the very best treatment and care, regardless of postcode, age and cancer or tumour type, through the adoption of an optimal patient pathway in future.

Longitudinal data on quality of life and the patient pathway will be captured through a new data registry.

We have also committed to investing in studies designed to transform the NHS experience through testing different models of service delivery.

Our 2013 quality of life report¹⁵ revealed that almost one in four of the patients we surveyed had no single point of contact for information about their treatment.

What is the effectiveness of new molecular subtyping?

We have committed in our new research strategy to create and fund a centralised biobank for collection of adult brain tumour tissue. The biobank will have an internationally standardised list of core data including tumour subtypes so these can be compared as part of future studies. We also hope an improved understanding of the molecular mechanisms behind different tumour subtypes will help drive forward more accurate diagnosis and more personalised, targeted treatments in the future.

As part of our policy work, we will call on NHS England, NHS Wales, NHS Health Scotland and NHS Northern Ireland to ensure that there is equal access to molecular diagnostic services for brain tumour patients across the UK.

Currently, we are funding Professor Denise Sheer, Dr Thomas Jacques and Dr Colin Watts to pave the way for more targeted treatments by investigating tumour subtypes⁷. We continue to fund Professor Steve Clifford¹⁶, whose work on the unique characteristics of different childhood medulloblastoma brain tumours molecular subtypes has already led to a Europe-wide clinical trial offering personalised treatments to children with the disease.

Previously, research we funded has led to new state-of-the-art tests that detect biomarkers and mutations in the genetic material of individual tumours to determine a more accurate diagnosis and the best treatment for patients. We funded Professor Sebastian Brandner's work to implement routine testing for 1p/19q¹⁷. It also gives patients a more accurate prognosis. Our researcher Professor Peter Collins¹⁸ was responsible for the ground-breaking identification of an abnormal form of the BRAF gene, which is now being used in a diagnostic test and could help us develop new treatments in future.

What are the long-term physical and cognitive effects of surgery?

As part of our new research strategy, we have commissioned an in-depth research report on quality of life¹³ to ensure that future treatment decision making helps to reduce the long-term and late effects of a brain tumour.

We are also calling on researchers to take toxicity and effects on quality of life into account when new treatments are developed and tested, rather than just focusing on survival, and we are calling on the NHS to do the same when they are considering whether to adopt new treatments.

¹³ <http://www.thebraintumourcharity.org/research/for-researchers/Funding-opportunities/life-with-a-brain-tumour>

¹⁴ <http://www.thebraintumourcharity.org/research/for-researchers/Funding-opportunities/quality-of-life-project-grants>

¹⁵ <http://www.thebraintumourcharity.org/policy/quality-of-life>

¹⁶ <http://www.thebraintumourcharity.org/NR/exeres/661CB175-207C-4694-BA26-FFD66406306D>

¹⁷ <http://www.thebraintumourcharity.org/research/our-discoveries/Understanding-brain-tumours>

¹⁸ <http://www.thebraintumourcharity.org/research/research-news/research-helps-lead-to-pilocytic-astrocytoma-clinical-trials>

Previous work led by Professor Colin Kennedy and funded by us showed how an alternative radiotherapy technique could help improve quality of life for children with a brain tumour⁷, while our funding of Dr Howard Ring to study aspects of quality of life in long-term survivors of childhood brain tumours showed reduced IQ as a consequence of treatment¹⁹.

We will be able to further investigate the long-term effects through the data registry.

What is the effectiveness in carers of interventions to support coping with changes in a patient, including memory loss?

We have committed in our new research strategy to enhancing care and quality of life for everyone affected by a brain tumour, including patients and carers.

The quality of life survey we conducted in 2013¹⁵ showed that caring for someone with a brain tumour has a negative impact on the emotional wellbeing of over 80% of carers. The survey also showed that 95% of carers feel better informed after using our fact sheets.

We offer a comprehensive range of Information and Support Services available to anyone affected by a brain tumour, including carers. We continue to develop information that is identified by our beneficiaries as the most important and provide online, phone and face to face support, so that they can support changes in a patient.

Additionally, we are backing research to tackle memory loss in brain tumour patients. Currently, we are funding a clinical trial led by Dr Gillian Whitfield involving targeted radiotherapy to reduce memory loss in adults with secondary brain tumours²⁰. Meanwhile, the alternative radiotherapy technique highlighted by Professor Colin Kennedy⁷ was shown to have a lesser impact on children's memory compared with conventional radiotherapy.

What is the effectiveness of fatigue management strategies?

We have committed in our new research strategy to investigate approaches such as epilepsy and fatigue management to enhance the quality of life of those affected by brain tumours.

Our funded research conducted by Dr Howard Ring¹⁹ showed the need for further work in this area by highlighting that long-term survivors of early childhood brain tumours often have an increased risk of significant clinical apathy compared with their siblings who were not diagnosed with a brain tumour.

Our 2015 quality of life report "Losing Myself: The Reality of Life with a Brain Tumour"¹³ identifies fatigue as one of the biggest issues that impacts on quality of life, affecting two-thirds of respondents. The Information and Support team offers guidance on fatigue management, including online information and talks from fatigue specialists at Information Days and Way Ahead Days for newly diagnosed patients and carers.

The long term impact of fatigue will be measured through the data registry.

What is the effectiveness of the extent of resection in glioma on survival?

We have committed in 'A Cure Can't Wait' to investing in research that will double survival for all brain tumour patients within ten years, not just through surgery but also through catalysing new drugs and helping to enhance service delivery.

Our equal access to treatment and care work will investigate current standards of care.

Previously, we funded a phase II clinical trial with Cancer Research UK led by Dr Colin Watts¹¹, which involved a substance called 5-Amino-Levulinic Acid to make glioblastoma brain tumours glow under ultraviolet light during surgery, in combination with the use of Gliadel wafers. This allows more accurate and complete tumour removal whilst leaving healthy tissue intact. Patient outcomes are being monitored and results appear to be positive.

¹⁹ <http://www.thebraintumourcharity.org/news/news-articles/SurvivorsofchildhoodbraintumourscansufferreducedIQandclinicalapathy>

²⁰ <http://www.thebraintumourcharity.org/Resources/SDBTT/the-research/documents/28-203-lay-summary-whitfield-manchester-adult-rt-trial.pdf>