

Written Evidence from Cancer Research UK (BCCR0001) April 2021 relating to brain tumour and childhood cancer research

Summary

- Since 2018, Cancer Research UK (CRUK) has committed approximately £28m to strategic initiatives in brain tumour research, including funding calls for brain tumour research, launching centres of excellence and a radiation research network.
- CRUK has also launched a new strategy to support children's and young people's cancer research and tackle the challenges preventing progress. We have invested in the development a world-class research infrastructure for children's cancer and recently partnered with Children with Cancer UK to deliver £4.3 million in funding to support five new teams seeking to bring important advances in the diagnosis and treatment of cancer in children and young people.
- However, the COVID-19 pandemic has had a significant impact on our income, resulting in the pausing of certain funding schemes and ultimately leading to unavoidable cuts to our life-saving research in the long-term. This has had, and will have, an impact across our research portfolio, including on the available opportunities for funding research into brain tumours and childhood cancers. We have sought to protect vital elements such as clinical trials and some childhood cancer projects, but the full extent of future cuts across our portfolio is still being worked through.
- The broader policy environment is also creating challenges and opportunities for brain and childhood cancer research. While we are encouraged by measures which are beneficial to research into rare and childhood cancers following the end of the Transition Period, there are still barriers to UK-EU research that were unaddressed by the Trade and Cooperation Agreement (TCA).
- The UK has an opportunity, as it develops its new regulatory system for medicines and medical devices outside of the EU, to ensure that a balance is struck between promoting domestic innovation with our ability to collaborate internationally. Continued ability to collaborate with researchers outside of the UK will be critical to continue progress improving outcomes in rare and childhood cancers.
- Within the NHS, staff face barriers to supporting and delivering research and innovation. For example, healthcare staff lack the time, funding or skills support to undertake research. CRUK and the University of Kent recently published a report 'Creating Time for Research' analysing the situation and proposing solutions to these barriers.
- For the UK to build on its strengths and cement itself as a world-leader in cancer research, including brain tumour and childhood cancer, the contributions of medical research charities need to be preserved. The Government still has the chance to provide funding for charity-funded medical research to bridge the funding gap and protect vital infrastructure and research initiatives.

Introduction

Cancer Research UK (CRUK) is the world's largest independent cancer charity dedicated to saving lives through research. We fund research in a network of 90 research institutions in more than 40 towns and cities across the UK, which has helped to develop 8 of the world's top 10 cancer drugs. Progress over the last 50 years has transformed the prospects for people diagnosed with cancer in the UK.

Cancer is, however, still one of the leading causes of death in the UK with around 367,000 new cases of cancer in the UK each year, and sadly, around 165,000 deaths.

Around 4,400 children and young people are diagnosed with cancer every year. Today, more 0-24 year-olds in the UK are surviving cancer than ever before. Around 8 in 10 children and young people will survive their cancer diagnosis for 10 years or moreⁱ.

Despite these improvements in overall survival, cancer remains the leading cause of death by disease in children and young people (aged 1-24) in the UKⁱⁱ, with around 510 cancer deaths in children and young people in the UK each year (0-24 year olds). Brain, other central nervous system and intracranial tumours are the most common cause of cancer death in children and young people in the UK. Some of these types of cancer continue to have low survival rates and many children and young people who survive do so with serious long-term side effects.

There are around 12,000 cases of brain, other central nervous system and intracranial tumours in the UK each year, and over 5,000 deaths. Five-year survival from these types of cancers varies, but overall remains low at around 1 in 10ⁱⁱⁱ.

As an organisation committed to investing in research into brain and childhood cancers, CRUK is pleased to respond to this inquiry. We have detailed our strategic investments made in both areas in answers to questions below.

Unfortunately, COVID-19 has had a devastating impact on the income of many medical research charities, including CRUK. We have therefore been forced to announce^{iv} unavoidable cuts to its life-saving research. We now plan to introduce a new research model designed to maximise impact from a lower level of spend and will reduce research spend to £250 million per year within four to five years – a cut of up to £150m per year from what we had planned to spend.

This loss of charity research will have a long-term impact. Charities expect a major contraction in research infrastructure and capability, inability to fund new bold and innovative projects, and leaving thousands of early-career scientists unsupported. The Association of Medical Research Charities anticipates this impact may last 4-5 years due to the long-term nature of many R&D projects. Unfortunately, the impact of this will inevitably be felt in brain tumour and childhood cancer research. We are doing everything we can to find more financial support and mitigate the impact of these cuts, including calling on the Government to help.

Alongside other medical research charities, CRUK campaigned for a time-limited Life Sciences-Charity Partnership Fund to help bridge the funding gap. However, at the time of submitting this response, the Government has not made any commitments to support charity-funded medical research. The charity sector plays an essential role in supporting the UK's thriving scientific community and will be critical to reaching ambitions to be a science superpower. The UK Government should commit to transitional funding for charity-funded medical research to enable charities to effectively return to pre-COVID-19 levels of funding and increase contributions to UK R&D thereafter.

Answers to the Committee's Questions

- 1. How has Covid-19 affected your ability to support research into brain tumours and childhood cancers? In particular, do you still envisage being able to contribute the full £25 million over a 5-year period you previously announced specifically to support brain tumour research?**

In 2014, we highlighted brain tumours as a cancer of unmet need, and our spend in this field has more than tripled since then. Since 2014, we have invested £48m in brain cancer research (brain tumour research funded from 2014/15 to 2019/20).

According to the National Cancer Research Institute (NCRI) cancer research database, approximately £15m was spent on brain tumour research by NCRI member organisations in 2018/19 (this is the last year that complete data is available for from the NCRI). CRUK accounts for approx. £11m of this spend in that same financial year.

CRUK invested £12m in brain tumour research in 2019/20, and in the same period spent £8.78m on research into cancers affecting children and young people, making us one of the biggest funders of research in this area in the UK. But we know that more needs to be done to raise awareness of these cancers and to encourage more research in this area to drive and accelerate progress.

Brain tumour survival remains dismal in comparison to other cancers such as bowel or breast cancer. Between 2013-2017, the five-year survival for people diagnosed with brain cancer in England was around 1 in 10 (12.2%). However, brain cancer survival is slowly improving and has doubled in the last 40 years in the UK; we are proud that our investment has helped drive this improvement. But much more needs to be done to bring the step-change in survival statistics that is desperately needed for this hard-to-treat cancer.

Due to the cuts forced by the impact of COVID-19 on CRUK's finances, we have had to pause certain funding schemes and cut existing research projects by up to 25% in places. This inevitably has had an impact on the available opportunities for funding research into brain tumours and childhood cancers. As mentioned above, CRUK will have to reduce its baseline funding by £150m per year over the next few years.

Despite this background, we have worked hard to protect our clinical trial portfolio and maintain our commitment to fund new research for children and young people's cancers. Through forming a partnership with Children with Cancer UK we delivered £4.3 million in funding to support five new teams seeking to bring important advances in the diagnosis and treatment of cancer in children and young people^v.

For brain tumour funding specifically, the three Brain Tumour Awards had a 5% in year cut to their 2020/21 financial instalment, and the Centres of Excellence had a 10% cut to their 2020/21 financial instalment and an approx. 25% cut to their 2021/22 financial instalment. Despite these cuts, we have already committed the full £25m to strategic initiatives in brain tumours (more details on these initiatives in question 2). Currently, we do not anticipate future cuts impacting our ability to meet this commitment. However, this may change if our future financial position is dramatically impacted.

2. Can you provide an update on how much of the £25 million has been allocated to date? How do you plan to ensure the full £25 million will be allocated by the end of the 5-year period?

In 2018, CRUK announced a commitment to spending £25m on strategic initiatives in brain tumour research. Since then, we have committed approximately £28m to our strategic initiatives in brain tumour research, including ringfenced funding calls for brain tumour research (£14.8m), capacity-building centres of excellence (£5.83m) and a radiation research network with a major focus in brain tumours (two units and two centres with a major focus in brain, contributing approx. £7.69m). These figures do not include any additional funding leveraged from partnerships in these areas.

Centres of Excellence

In 2018, we launched two new brain tumour centres of excellence: The UCL and University of Edinburgh Glioma Centre of Excellence (£2.94m over 4 years), and the Cambridge University and Institute of Cancer Research Children's Brain Cancer Centre of Excellence (£2.89m over 4 years):

- The CRUK Glioma Centre of Excellence brings together world-leading experts to advance our understanding of the biology underpinning the disease and to capitalise on technological improvements in data, imaging and phenotypic drug discovery to establish a new translational pipeline. The centre is training four clinical PhD students clinicians working in neuro-oncology, who are studying for PhDs in association with glioblastoma biology, neuropathology or drug discovery groups at UCL and in Edinburgh. It has also recruited four post-doctoral researchers, some of whom have also contributed to various longitudinal health data publications on glioma.
- The CRUK Children's Brain Tumour Centre of Excellence (The CRUK-CBTCE) convenes a critical mass of expert personnel, infrastructure and global collaborations in paediatric brain tumour biology, medicinal chemistry, pharmacology and clinical trials, to support the creation of curative treatments for children with brain tumours. The CRUK-CBTCE has made significant progress in its mission to generate a preclinical pipeline of novel drugs for children's brain tumours. For example, groups at the CBTCE have successfully completed generation of a new genetically engineered mouse models to aid in studying this complex disease. With regards to building capacity, the Centre has also recruited a junior group leader, computational biologist Dr Pau Creixell, who had not previously worked in brain tumours until joining the Centre.

Multi-disciplinary Collaborative Teams

In 2019, we funded three multi-disciplinary collaborative teams through our Brain Tumour Awards, totalling £17.8m; with a £14.8m investment from CRUK and £3m investment for Prof Neil Carragher's award from The Brain Tumour Charity. These awards were established to advance our understanding of the biology of brain tumours and tackle the challenge of translating discoveries into treatments for patients in the future:

- Prof Neil Carragher at the University of Edinburgh is leading a team to develop unique drug-combination approaches specifically tailored to glioblastoma in conjunction with a novel nanoparticle-based delivery system to enhance delivery across the blood-brain barrier.
- Prof Richard Gilbertson at the University of Cambridge is leading a team of neuroscientists, developmental biologists, immunologists, and molecular biologists to building a cellular 'atlas' that details activity of normal brain cells and to use this to analyse and exploit therapeutically what is different in malignant brain tumour cells.
- Prof Stephen Pollard at the University of Edinburgh is leading a team aiming to target biological vulnerabilities in glioblastoma by designing drugs to target pathways to stop dormant cells becoming active post-treatment and leading to relapse, or to force cells out of dormancy during treatment making them more responsive to therapy.

CRUK Radiation Research Network

In 2019 we launched the CRUK Radiation Research Network (CRUK RadNet) – a planned investment of £56m over 5 years to establish a network of centres of excellence and state-of-the-art facilities to build a critical mass of radiobiology and radiation oncology activity in 7 locations. This investment aims to bring together researchers across discovery, translational and clinical research to tackle the major challenges in radiotherapy establish an effective pipeline to translate novel scientific discoveries into patient benefit in the next 10–15 years. Brain tumours (including paediatric) are a key focus area, with two Research Units in Cambridge and London (total £20.8m) and two Research Centres in Glasgow and Leeds (total £6.8m) with a major focus in brain.

Considering the proportionate focus in brain tumour research, CRUK RadNet contributes approximately £7.69m, committed over a five-year period, to strategic initiatives in brain tumour research.

Relevant activity includes:

- Utilising more clinically relevant models to understand the biology of how brain tumours, as well as normal tissue, respond to radiotherapy (including modalities such as proton or FLASH radiotherapy)
- Identifying and validating novel opportunities to combine radiotherapy with other treatment modalities, such as targeted small molecule drugs or biologics.
- Developing and validating computation approaches (e.g. AI) to predict patient outcomes, as well as toxicity, to help guide the stratification and planning of radiotherapy treatment.

While we have made great strides in honouring our commitment, and brain tumours and children's cancers continue to be a strategic priority for our research, our future commitments in this area will be contingent on our financial situation and ability to fundraise in such an uncertain environment.

3. What impact has the UK's departure from the EU had on research into rare cancers (including brain tumours) and childhood cancers (in particular those with poor survival outcomes)? Are there further steps that should be taken to protect and enhance the UK's ability to collaborate internationally on such research, following the agreement on the future UK-EU relationship?

As a basis for international research into rare and childhood cancers, CRUK sees the EU-UK Trade and Cooperation Agreement (TCA) as first step in developing a fuller, long-term relationship between the UK and EU.

International collaboration is invaluable for all forms of cancer research, nearly 50% of all UK cancer research is global,^{vi} but it's particularly important for rare and childhood cancer research. Individual countries often can't conduct clinical trials into these cancers because their patient populations are too small. To overcome this, researchers collaborate in international clinical trials that recruit patients from multiple countries and move medicines and patient data across borders.

Patients value this international collaboration. 99% of people affected by cancer we surveyed believe the UK and EU should negotiate a relationship that allows cross-border trials to operate as easily as they did during the Transition Period.^{vii} The new relationship partially delivers this, and CRUK is encouraged by the pragmatic decisions taken by the UK and EU to minimise disruption to research after the Transition Period, including:

- The UK government's unilateral decision to recognise EU/EEA Sponsors of clinical trials,^{viii} meaning UK researchers will face minimal legal and administrative barriers when participating in EU-led clinical trials.
- The TCA's provisions for UK-EU personal data exchanges to continue for up to six months, in order to give the EU time to grant the UK data adequacy status.^{ix} These data transfers are essential for running UK-EU clinical trials as they need to routinely send patient data and test results across international borders.
- Confirmation of the UK's decision to participate in the EU's research programme, Horizon Europe.^x This programme will be worth €95.5 billion (£84.1 billion) of research funding between 2021-2027^{xi} and includes a 'cancer mission' designed to fund research into cancer prevention, diagnosis and treatment.
- The UK government's unilateral decision to recognise EU batch testing and Qualified Person (QP) certification of imported EU medicines (including Investigational Medicinal Products) for a

two-year period.^{xii} Without this, UK researchers importing EU medicines (e.g. as part of a UK-EU clinical trial) would face additional tests at the border, adding to the administrative burden and cost of international research.

- The TCA's provisions for creating a Working Group on Medicinal Products that will facilitate UK-EU regulatory cooperation.^{xiii} Minimising regulatory divergence between the UK's Medicines and Healthcare products Regulatory Agency (MHRA) and the EU's European Medicines Agency (EMA) will curtail the administrative burden faced by UK-EU

Whilst these measures are beneficial for all areas of cancer research, they are particularly impactful for research into rare and childhood cancers given their reliance on multi-country clinical trials.

However, this reliance on international research also means rare and childhood cancers are more vulnerable to the remaining barriers to UK-EU research left unaddressed by the TCA. These are:

Clinical trial Sponsors

Although the UK government has unilaterally decided to recognise EU Sponsors of clinical trials, the EU has not reciprocated this measure, meaning UK Sponsors of clinical trials operating in the EU/EEA now need EU-based legal representation.^{xiv}

Insight from our research community shows that EU-based legal representation for multi-state trials can cost between £20,000 to £300,000 per year.^{xv} This would be prohibitively expensive for many non-commercial Sponsors (e.g. universities). Cancer research is particularly vulnerable to these costs, as approximately 40% of all UK cancer trials have non-commercial Sponsors.^{xvi}

In the long run, legal costs like these could make it harder for UK-based researchers to lead pan-European clinical trials, which would undermine the UK's reputation as a world leader in cancer research^{xvii} and risks reducing UK patients' access to research. This would be particularly damaging to disease areas reliant on joint UK-EU clinical trials, such as rare and childhood cancers.

To address this, the UK government should consider how it can offset the costs of EU legal representation now faced by UK Sponsors working in the EU/EEA. Doing so would minimise any impact these new legal barriers have on the UK's attractiveness as a research environment and ensure UK researchers aren't disadvantaged when leading pan-European clinical trials.

Data adequacy

To ensure UK-EU clinical trials do not face a cliff edge for data exchange after June 2021, it's essential the UK and EU confirm the UK's data adequacy status in the next two months. We welcome the European Commission's provisional positive opinion on this matter, and we encourage the European Data Protection Board and EU Member States to formally approve this opinion by the end of June. We recommend the UK government continues to work with the European Commission in facilitating this process, including via the TCA's Working Group on Medicinal Products.

Horizon European funding

Although we welcome recent announcements of additional government spending to finance the UK's participation in Horizon Europe,^{xviii} there is still uncertainty around how the costs of Horizon Europe will be met in the long run.

Specifically, there are concerns these costs could be financed using existing government R&D spending commitments, a decision that would divert investment away from the UK and amount to a cut in domestic R&D spending. To avoid this, we recommend the Government funds the UK's association to Horizon Europe with new R&D spending commitments as part of its efforts to make the UK a scientific superpower.

Medicines access

Although the UK government has unilaterally decided to recognise EU batch testing and QP certification, the EU has not fully reciprocated this measure, meaning many UK medicines exported to the EU will need to be retested and recertified.^{xix}

- Licenced medicines imported into to the EU from the UK will need to be retested and recertified by an EU-based QP.
- Investigational Medicinal Products (IMPs) imported into the EU from UK will not need to be retested, but they will need to be recertified by an EU-based QP.^{xx}

Under the TCA, if a UK-led clinical trial wants to test a UK-manufactured IMP in an EU/EEA country, that IMP will need to be recertified by an EU-based QP once it enters the EU. This could delay the IMP's shipment to EU-based trial sites, creating complications for EU researchers participating in the UK-led trial. Re-certification at the border also adds to the UK researchers' administrative burden, as they must spend time and resources managing the additional QP certification for the exported IMP.

In response, EU-based researchers may choose to avoid working with UK-led clinical trials in order to avoid the complications and costs associated with them under the TCA's provisions for UK medicine exports. If this occurred, this would lead to a reduction in UK-EU clinical trials and fewer opportunities for UK patients to access potentially life-saving research. This would be particularly disruptive to research into rare and childhood cancers, given their aforementioned reliance on multi-country clinical trials.

To address this, the UK and EU should negotiate a Mutual Recognition Agreement that covers batch testing and QP certification for both licenced and unlicensed medicines. This MRA should also include a confidentiality agreement to facilitate MHRA-EMA cooperation in monitoring medicine safety (pharmacovigilance). We'd encourage the UK government to use the TCA's Working Group on Medicinal Products to begin exploratory discussions on this matter.

Regulatory cooperation

The TCA's provisions for UK-EU regulatory cooperation on Good Manufacturing Practice (GMP) are a welcome first step towards supporting UK-EU research. However, further steps are required to establish a long-term UK-EU regulatory relationship that supports life-saving international research.

Of particular importance to UK-EU cancer research is the EU's upcoming Clinical Trials Regulation (CTR) and its Clinical Trials Information System (CTIS). The CTIS is an online portal for clinical trials designed to accelerate trial set-up and facilitate collaborative research. It plans to achieve this by making clinical trials more visible to researchers and by coordinating all EU-wide Clinical Trial Applications (CTAs) into a single platform. The CTIS will be especially valuable for rare and childhood cancer research studies as the system will simplify the process of working with multiple national research regulators, a prerequisite for recruiting patients in multiple countries.

Without access to the portal, the UK and EU CTA processes will have to run separately, in parallel to each other. If these separate processes do not cooperate well, they could eventually begin to diverge. Differences in assessment criteria, approval timelines, and other areas, would increase the administrative burden on researchers and delay the set-up of UK-EU clinical trials. This in turn could reduce collaborative research activity, resulting in fewer trials and a reduction in patient access to new treatments in both the EU and UK. These administrative costs would be particularly disruptive to disease areas reliant on multi-country clinical trials, including rare and childhood cancers.

To mitigate the risk of UK-EU regulatory divergence and the administrative burdens it would impose on international research, CRUK recommends the UK and EU use the Working Group on Medicinal Products to discuss their long-term ambitions for UK-EU collaboration in medical research. This should include discussions for expanding their current regulatory cooperation agreements, with a view to building on the TCA's GMP provisions and negotiating an MRA (see 'Medicines access').

4. What impact is the Tessa Jowell Brain Cancer Mission initiative having in supporting the brain tumour research environment, including research into childhood brain tumours?

CRUK is a member the Tessa Jowell Brain Cancer Mission (TJBCM) joint Strategy Board. We provide some operational funding, guidance and support to the mission, but do not lead on any of the initiatives. For in depth information on the achievements and impact of the TJBCM, CRUK recommends contacting the TJBCM directly.

The TJBCM is not a research grant-administering body: its mission is to unite professional, patient, charity and government groups to share information, and establish transformative clinical delivery / support programmes that will eradicate brain tumours. The mission is chaired by Professor Richard Gilbertson (Li Ka Shing Chair and Head of Oncology, University of Cambridge and Director of the CRUK Cambridge Centre).

It has recently designated Tessa Jowell Centres of Excellence for brain tumour treatment and care in all patients – an exercise designed to recognise and award neuro-oncology centres for their excellence in patient care.

Centres were measured on a range of criteria including excellent clinical practice and training opportunities; emphasis on patient quality of life; providing clinical trials and offering a high standard of research opportunities. Led by a committee of experts in the field and with virtual site visits, the assessments were backed up by patient feedback collected by The Brain Tumour Charity about the care they received in these centres.

Nine NHS hospital brain tumour centres across the UK have been recognised as a Tessa Jowell Centre of Excellence. These are:

1. University Hospitals Birmingham
2. NHS Lothian, South East Scotland Cancer Network (Edinburgh)
3. Kings & Guy's and St Thomas
4. Leeds teaching hospitals NHS Trust (Leeds General Infirmary and St James's Hospital)
5. Salford Royal & The Christie (Manchester)
6. Newcastle-upon Tyne Hospitals
7. Nottingham University Hospitals
8. St George's University Hospital, Royal Marsden & Royal Surrey
9. University College Hospital London & the National Hospital for Neurology and Neurosurgery

The NHS is one of the few health care systems in the developed world that does not train or employ experts in brain tumour treatment. Rather, brain tumour patients are cared for typically by oncologists and radiotherapists who are not formally trained in brain tumours. Therefore, another aim of the TJBCM is to establish the TJBCM fellowships. Working with the Royal Colleges and the NHS, it plans to establish programmes to train the UK's first generation of brain tumour-specific physicians. The team has now completed developing the programme and modules for the TJBCM Fellowships. The group has also established a programme faculty. The leadership team are pursuing several potential sources of funding for these fellowships and are hopeful that funding will be secured soon.

5. Are there any other recent significant developments in the research environment for brain tumours and childhood cancers with poor survival outcomes (in particular childhood brain tumours) that you would like to draw the Committee's attention to?

CRUK Research Strategy for children's and young people's cancer

In 2019, we developed a new strategy to support children's and young people's cancer research and tackle the challenges preventing progress. We've been consulting UK and international researchers in the field, as well as patients and parents who have been affected by these types of cancer. Following these consultations, we've set out a strategy that aims to:

1. Build research capacity in the UK

Working with Children with Cancer UK, we co-funded the Cancer Research UK–Children with Cancer UK Innovation Awards. Announced in March of this year, this funding is supporting five new teams of world-leading scientists, with up to £1 million each, to embark on five very distinct research projects to improve our understanding of the underpinnings of children's and young people's cancers. These include:

- Professor Richard Houlston and his team at The Institute of Cancer Research to analyse the contribution of inherited mutations in a number of solid childhood cancers, in particular Wilms tumour, Ewing sarcoma, rhabdomyosarcoma, glioma, medulloblastoma and neuroblastoma.
- Christine Harrison, along with Professor Jonathan Higgins and Professor Steve Clifford, all based at Newcastle University, to harness their expertise in chromosome biology and cell division to understand how aneuploidy can drive cancer development, and in turn, identify targets that can be exploited by new therapeutics

Working in collaboration with Stand Up To Cancer (SU2C), We delivered an international funding call^{xxi} in 2020 to drive multidisciplinary, transatlantic collaboration and knowledge sharing. We funded 3 transatlantic teams for up to \$1 million, including a team based at The Christie Hospital, Manchester. This team are building an atlas of childhood neuroradiation damage. The goal is to provide more precise radiotherapy and avoid the most sensitive brain regions which can cause long term effects in cognition and hormone production.

We will engage and collaborate with research communities not usually associated with children's and young people's cancers, encouraging them to apply their wide knowledge and expertise to this area of cancer research.

2. Develop and support a coordinated research community

In 2021 we are working with our research community to host community building workshops to support conversations and collaboration between lab scientists and clinicians, and between scientists from different research fields

3. Ensure the research community has the tools and infrastructure it needs to progress

We will build and link together resources through our CRUK for Children & Young People Network, and we will fund the development of vital research tools through our new funding award schemes^{xxii}.

By focusing on these three priority areas, we aim to support research happening into across the translational pipeline and in all types of cancer affecting children and young people – from basic research right through the translational pipeline and into clinical trials – and create a strong foundation for the research community to build upon.

Our research strategy builds on our existing strong track record and recent developments in children's and young people's research. For example:

1. Children and young people in the UK with cancers that have come back can now access new personalised treatments quicker than ever before thanks to a national tumour biopsy sequencing platform and clinical trial funded by CRUK^{xxiii}.
2. The Stratified Medicine Paediatrics (SMPaeds) programme, being led by Professor Louis Chesler at the Institute of Cancer Research, analyses the genetic make-up of children's and young people's tumours. This information is used to match them to treatments on the ESMART clinical trial, which is testing multiple new targeted drugs, and treatment combinations not previously available for children and young people. As of December 2020, more than 150 patients have been enrolled so far in SMPaeds and furthermore tumour samples and profiling data are stored for further research into paediatric cancer to identify potential targets for new therapies
3. ESMART is a European trial that is currently being rolled out across the UK, funded by Cancer Research UK and co-ordinated through the University of Birmingham Cancer Research UK Clinical Trials Unit. Currently, the trial has 10 treatment arms (plus 5 more that are waiting regulatory approval) that are testing an array of therapies on their own or in combination, including targeted drugs, immunotherapies, radiotherapy and chemotherapy. And as researchers develop promising new drugs, they are quickly rolled into the study.
4. Patients may be placed on ESMART within just a few weeks of having their tumours sequenced, offering children and young people with cancer who have limited treatment options quick access to the targeted drugs most likely to work for them.

Infrastructure investment in children's cancer research

A large amount of the money we spend on children's cancer research is outside of research grants. This money is used to develop a world-class research infrastructure to give scientists the best facilities and services needed in which to carry out their life-saving work. It also works to bring the best minds in children's cancers together.

1. As mentioned earlier, in 2018, we launched the CRUK for Children & Young People Children's Brain Tumour Centre of Excellence, supported by TK Maxx.
2. The CRUK Clinical Trials Unit in Birmingham is one of the largest cancer trials units in the UK. Led by Professor Pam Kearns, the team there coordinates over 100 cancer trials across the country and internationally, including 15 trials for children's cancers, aiming to improve patient care and outcomes.
3. The Experimental Cancer Medicine Centre Paediatric Network runs early phase trials which test the safety of new drugs for children's cancers. Co-funded by CRUK and the health departments of England and Scotland, it's made up of 11 paediatric centres and aims to offer new treatments to children with cancer who need them.
 - In 2019/20 there were 31 early phase paediatric oncology trials open/ in set up in the Network with more than 100 patients recruited to these trials so far.
 - 65% are commercially sponsored.
 - ECMC-funded research nurses ensure appropriate biological samples are collected from patients for tissue banking, pharmacokinetic studies, and the Stratified Medicine Paediatrics programme.
4. We also fund a children and young people's tissue biobank which house the largest collection of tumour, DNA and other samples from young cancer patients in the UK. The tissue samples provided by this biobank are essential for scientists to unravel key information about these cancers.

Tessa Jowell Brain MATRIX

In addition to CRUK's investments into brain tumour research and infrastructure, and the work of the TJBCM, there have also been developments in precision medicine in brain tumours. The Brain

Tumour Charity has invested £2.8m in a first-of-its-kind clinical trial platform called the Tessa Jowell Brain MATRIX trial. This trial platform will enable researchers to collect a rich genomic, pathological and imaging dataset to provide patients and clinicians with a fully integrated diagnosis of their disease. The end goal of this platform is to accelerate the development and delivery of brain tumour clinical trials and provide greater access to novel targeted treatments and improved outcomes for patients, both in terms of survival and quality of life.

6. What are the most important actions Government could take to improve the research environment for brain tumours and childhood cancers, and patient outcomes?

We have set out actions Government can take in relation to EU-Exit above. Here we provide some further views.

By improving the UK's research environment more generally, the Government can help support research charities and clinical research on brain tumours and childhood cancers.

Research charities

One of the key strengths of the UK's life sciences environment is its diversity. A combination of public, private and charitable funding sources supports innovation by fostering a network of expertise and enabling a wide range of projects with diverse risk profiles. This creates a high-quality, globally competitive medical research environment and serves as a magnet for international talent. All elements of this diverse ecosystem require adequate funding and support, including charity-funded medical research, and sustainable public research funding including increases to Quality-Related funding through Research England and research in the health service through uplifts to the National Institute of Health Research (and their devolved equivalents).

The Government has an ambition to make the UK a "science superpower" and the Spending Review recognised the critical importance of research to the UK's recovery by committing to invest £14.6bn in Research & Development (R&D) next year, and recently topped this up with £250m additional funds to ensure continued membership of the European Commission's Horizon Europe framework programme. However, there has not been clarity on whether medical research charities will receive any financial support from the government to deal with the impact of COVID-19 on their finances.

Medical research charities fund the salaries of around 17,000 UK scientists. Charities are the only source of research into some crucial healthcare challenges and otherwise underfunded conditions. In 2018, members of the AMRC invested £142m into 640 rare disease projects.^{xxiv} CRUK set up and continues to fund the International Rare Cancers Initiative that is developing clinical trials worldwide to find treatments for rare cancers. Yet our collective work has been devastated by COVID-19 leading to cuts to research budgets and the slow dismantling of our research infrastructure. CRUK has predicted a reduction in research spend of £150m per year by 2024, approximately 35% of total research spend.

Other medical research charities are in a similar situation, and in response, CRUK alongside the AMRC, has called on the government to back scientific research and jobs by committing to a Government-charity co-investment scheme that provides a level of match funding from government for future charity research over the next three years via a Life Sciences-Charity Partnership Fund (£310m in the first year). However, at the time of submitting this response, the Government had not made any commitments to support charity-funded medical research. Transitional funding will allow medical research charities to effectively return to pre-COVID-19 levels of funding and increase contributions to UK R&D thereafter.

Clinical research

Clinical research studies, including clinical trials, play a vital role in developing new ways to prevent, diagnose, and treat diseases such as rare and childhood cancers. The benefits of research extend beyond improving patient care, as participation in research has been shown to improve NHS staff retention levels,^{xxv} and every £1 invested in medical research generates 25p in additional economic value every year, forever.^{xxvi}

We believe a world-leading clinical research environment:

- Embraces scientific complexity to support high-quality, science-driven clinical trials;
- Rapidly approves, sets up, and delivers clinical trials, thereby being cost-effective;
- Effectively and carefully utilises data as a source of innovation;
- Is well-resourced, recruiting and retaining well-trained research staff and having a sufficient stock of facilities and equipment;
- Facilitates patient participation – getting the right patients onto the right studies; and
- Is collaborative, operating as a genuine network of researchers that work to rapidly distribute new trials to appropriate sites and locations.

Although cancer is the UK's strongest area of clinical research,^{xxvii} researchers still face persistent barriers to expanding their capacity to deliver more life-changing innovations, including:^{xxviii}

- **Lack of time, funding or skills support** to enable health professionals to undertake research
- **Disparities in opportunities** to develop research careers between different regions, professions, specialties, genders, and different ethnic groups
- **Lack of research expertise and training**, particularly among nurses, midwives and Allied Health professionals
- **Lack of communication** of research's role in improving the quality and safety of healthcare, patient experience, and patient outcomes
- **Lack of organisational support**
- **De-prioritisation of research**

Many of these barriers are found inside the NHS, which faces systemic and interconnected challenges to expand clinical research capacity. CRUK and the University of Kent have recently published 'Creating Time for Research', a report which analyses these barriers and proposes policy solutions to address them.^{xxix}

One of the report's key recommendations is to uplift funding for the UK's four national health research funders: the NIHR, CSO, HCRW and HSC R&D.^{xxx} These funders provide vital investment into the UK's clinical research base, including the NHS's workforce and infrastructure. However, our research found that "60% of research directors said there was insufficient funding to support research studies",^{xxxi} thus indicating the UK's clinical research environment experiences severe and widespread underinvestment.

To address this, we recommend the UK Government and Devolved Administrations should uplift long-term funding for the NIHR, CSO, HCRW and HSC R&D. At a minimum, these funding increases should be in-line with broader uplifts in public R&D investment and keep pace with future increases in inflation. We encourage the UK Government to use the upcoming three-year Spending Review to deliver this much-needed investment.

Rare disease research

Cancers in children are substantially different to those in adults and as a result need a distinct, dedicated approach. We need to improve our understanding to inform and improve our approach to

treating this disparate group of cancers. Specifically, we need to drive progress, awareness, and advocacy of children's and young people's cancers, as well as fund more research in this area.

More research is also needed in brain tumours, because compared with other types of cancer we still don't know very much about brain tumours: the brain is an extraordinarily complex organ and our understanding of the biology of brain tumours is limited.

For researchers, late diagnosis and poor prognosis allows just a small window of opportunity to study the disease, and the laboratory models currently used to study the disease don't faithfully recapitulate the human disease. Supporting the medical research charities that provide infrastructure, such as state-of-the-art research equipment, support staff, as well as resources to develop more sophisticated disease models, provides the cornerstone with which all future discoveries depend upon.

A shortage of researchers specialising in brain tumours, from discovery scientists to research clinicians, has played a huge role in hampering research. Both the brain tumour and children young people's cancer research community is fragmented, with limited senior leadership, expertise and resources. Additional resource to build capacity in both areas encourages more junior researchers to build a career in research and invites others from outside the field to pivot their research to these cancers of unmet need.

Supporting the training of brain tumour-specific physicians through the TJBCM fellowships could also strengthen the pipeline of clinician researchers in this field, who are desperately needed to support the translation of discovery research into patient benefit.

For more information, please contact Abigail Lever, Westminster Public Affairs Officer, at Abigail.Lever@cancer.org.uk.

ⁱ Cancer Research UK statistics: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers>

ⁱⁱ Public Health England (2021) Children, teenagers and young adults UK cancer statistics report 2021 [Online] Available at: http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/cancer_in_children_teenagers_and_young_adults/ [Accessed 16 April 2021]

ⁱⁱⁱ Cancer Research UK statistics: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/brain-other-cns-and-intracranial-tumours>

^{iv} Cancer Research UK (2020) *Cancer Research UK plans to rebuild and adapt to changed world following £300m drop in income* [Online] Available at: <https://www.cancerresearchuk.org/about-us/cancer-news/press-release/2020-07-15-cancer-research-uk-plans-to-rebuild-and-adapt-to-changed-world-following-ps300m-drop-in-income>

^v Cancer Research UK (2021) Meet the teams tackling 5 challenges in children's and young people's cancers [Online] Available at: <https://scienceblog.cancerresearchuk.org/2021/03/18/meet-the-teams-tackling-5-challenges-in-childrens-and-young-peoples-cancers/>

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^{vii} Cancer Research UK. (2020a). *The UK and EU.*, p. 4.

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- ^{xiv} Official Journal of the European Union. (2014). *Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*. [Online]. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf [Accessed 27 January 2021]., pp. 45-46.
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