HOUSE OF COMMONS

Petitions Committee

Oral evidence: Brain tumour and childhood cancer research, HC 242

Thursday 27 May 2021

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Watch the meeting

Members present: Catherine McKinnell (Chair); Tonia Antoniazzi; Elliot Colburn.

Questions 11 - 30

Witnesses

Sue Farrington Smith MBE, Chief Executive, Brain Tumour Research; Ian Walker, Executive Director of Policy, Information and Communications, Cancer Research UK; Professor Richard Gilbertson, Chair, Tessa Jowell Brain Cancer Mission, Director, CRUK Cambridge Centre, and Head of Department of Oncology, University of Cambridge; Professor Chris Jones, Professor of Childhood Brain Tumour Biology, Institute of Cancer Research.

Written evidence from witnesses:

- Brain Tumour Research
- Cancer Research UK

Examination of witnesses

Witnesses: Sue Farrington Smith, Ian Walker, Professor Gilbertson and Professor Jones.

Q11 **Chair:** We are now going to move on to our second panel. Please briefly introduce yourselves, and tell us about your interest and work in brain tumours and childhood cancers.

Sue Farrington Smith: I am Sue Farrington Smith. I am co-founder and chief executive of Brain Tumour Research. I have a passion for finding a cure for brain tumours, having lost my sister's little girl, Alison Phelan, to a brain tumour 20 years ago, three weeks before her eighth birthday. Having met so many devasted families since, we really have to do something now, so that in the next 20 years we do not have the same story.

Ian Walker: My name is Ian Walker. I am executive director for policy, information and communications at Cancer Research UK. As people will be aware, CRUK is the largest medical research charity dedicated to saving lives through research. Our interest here is that in 2014, through our strategic review, we highlighted four cancers of unmet need, one of which was brain cancer. These are cancers that had bucked the trend of progress and therapeutic advances. Brain cancer in particular, as we heard very eloquently from Fiona and Peter, has not seen any substantial progress in therapeutic options for those patients in the last 40 years.

Since 2014, we have approximately tripled our spend of the amount of money that we have allocated to researching brain cancer. Since 2018, when the task and finish group report was published and we had committed that we would try to spend £25 million, we have now committed approximately £28 million-worth of new research in a ring-fenced, targeted way towards brain cancer. We can perhaps talk more specifically, as we go through the questions, if helpful, about the paediatric components of that.

Professor Gilbertson: My name is Richard. I chair the Department of Oncology at the University of Cambridge. I also direct the CRUK major centre at Cambridge and the Children's Brain Tumour Centre of Excellence at Cambridge. I am a children's cancer doctor by training, and a children's brain tumour specialist. For the last 30 years, my research has focused on developing the understanding of children's brain tumours and new treatments for that disease. I spent 15 years in the States, where I was the director of the US's largest children's cancer research hospital, St Jude Children's Research Hospital. I was a scientific director there before coming back to the UK in 2015. I chair the Tessa Jowell Brain Cancer Mission, which we have already talked a little bit about today. I would be happy to answer questions on any of those aspects.

Professor Jones: My name is Chris Jones. I am a basic scientist and cancer biologist based at the Institute of Cancer Research in London, at

our Sutton campus. My lab is focused on the biology of childhood brain tumours, like Richard. We focus particularly on a group of tumours called high-grade glioma in children and young adults. These include, and we have a particular interest in, DIPG. You have already heard some powerful testimony about that.

Thank you for the opportunity to participate in this important discussion, particularly just a few days after DIPG Awareness Day, when we heard so many moving stories from families who have lost their child to DIPG.

Q12 **Chair:** Thank you all for being here today. We very much appreciate it. I will come back to you, Sue, first of all. You have been involved with both the Government working group on brain tumours in 2018 and now the Tessa Jowell Brain Cancer Mission. Is there more momentum behind brain tumour research today than there has been previously, in your view?

Sue Farrington Smith: Yes. It is definitely moving forward. I think the centres for excellence for patient care will really benefit brain tumour patients. Richard knows this; for me, we can give all the care in the world, but we absolutely have to do something about funding research to find the cure. That is what families want to hear. They do not want to hear that there are no treatment options. We are still in that position; there are no treatment options.

Q13 **Chair:** Have you seen improvements in UK brain tumour research? Have you seen improvements that could be attributed to the work of the Government working group or the Tessa Jowell mission? Where have you seen improvements, if you have? What could you attribute them to?

Sue Farrington Smith: I know there is increased investment. Ian talked about increased investment in Cancer Research UK, but it is still small steps at this stage. I am not seeing anything that will be life-changing, going forward.

Q14 **Chair:** Where can we focus the effort? There is some momentum now, as you said in answer to the first question. What could drive the momentum? Where do we best focus our efforts?

Sue Farrington Smith: Thinking about investment in clinical research, I am not so sure that we have done the basic research yet. At Brain Tumour Research itself, at the moment we can only fund £1 million a year. There are much bigger budgets around, but the Government are not putting the money behind it. We probably need to look at joined-up thinking across the spectrum. We need to focus on what needs to be done to find a cure, and then address it all in a joined-up way.

Q15 **Tonia Antoniazzi:** My questions are mainly to Ian. Cancer Research UK has made significant commitments on brain and childhood cancers in recent years, including an extra £25 million for brain tumour research in 2018. Why have you decided to invest specifically in those areas?

Ian Walker: As I mentioned in my introduction, and if we take them in order and think about brain cancer particularly first, it is a terrible collection of diseases, as we have heard. There are many different types of brain tumours, central nervous system tumours and intracranial tumours that we capture in that grouping. Looking across them as a whole, survival for these diseases is pretty poor; five-year survival, as an average, is around one in 10. There are certainly subsets of disease within that where survival is much less. We have already heard that for paediatric brain cancers, the biggest killer of children from disease in the UK, we do not have the right therapeutic interventions.

In terms of the CRUK investment, we have focused on trying to address some of the systemic problems that Sue was beginning to speak to in her response. We are trying to focus on the fundamental biological problems that we need to address, and to think about how we build and grow capacity within the research community, and, with that, bring diversity of thinking to the problem—multidisciplinary thinking—so that we really can drive innovative steps forward, as opposed to incremental progress.

At CRUK, we have had specific highlight calls around those kinds of innovative biological questions, with multidisciplinary awards where we spent something like £17.8 million across three of our innovation awards. We have partnered that with the Brain Tumour Research charity as well. Those are three specific programmes of research looking at novel ways of treating cancer, and at some of the biological questions and even how we evolve some models to help us think more effectively.

We have also invested in centres of excellence. That has multiple elements. It is thinking about how we create an environment that is conducive to the positive training of the next generation of researchers, and how we bring our clinicians and scientists through in an environment that is enriched and focused on specific areas of brain cancer.

I guess we have taken a longer-term, strategic view of how we make our investment. I would view it as a pipeline of innovation. The clinical trial funding aspect is also important. We have to have opportunities for people to enter clinical trials, as we find novel therapies. I think the NIHR world is synergistic with ours. It is a really complex system, and everyone has a part to play in the system in how we continue to make progress.

Q16 **Tonia Antoniazzi:** Does the novel discovery research that you are doing, and that is going on in understanding brain tumours, include brain tumours in children?

Ian Walker: I am just checking through my notes. I might have to come back to you specifically. I can tell you the headlines of what they are, but Richard may be able to comment on whether they have specific relevance to children.

Tonia Antoniazzi: Yes, Richard was nodding.

Ian Walker: One of the awards is his, actually. Of the three headline areas, one is about how we develop novel drug combination approaches and how we use nano-technologies to think about more effective ways of delivering novel therapies into the brain; how it gets across the blood-brain barrier. That is a fairly unique circumstance, if you like, within the body where we have to think differently about how we address it.

I will not speak to Richard's projects. He is much better placed to do that. The third project is thinking about biological vulnerabilities that are very specific to glioblastoma. Some cells, essentially, become dormant, which makes them much more resistant to therapies. It is thinking about how we might target those mechanisms. If you will allow me, I will hand over to Richard to speak about his project.

Professor Gilbertson: Very briefly, the CRUK founded a centre of excellence for children's brain tumours, based in Cambridge, which I oversee. It is specifically directed at developing completely new treatments for children's brain tumours and is done in partnership with the ICR. Chris, who is on the call, is one of the members of that, based at the ICR.

Rather than the typical way that drug developments are done for children, which is to wait for the crumbs to fall off the table of adult cancer and see if we can try that in children, we are actually developing treatments specifically for children's brain tumours. In concert with that, we have assembled a team of international experts across mainland Europe and North America, who are focusing on the basic biology of children's brain tumours, with the specific intent of finding vulnerabilities that are unique to children's brain tumours.

Kids' brain tumours, like all cancers in children, are biologically very distinct from those that occur in adults. It is incredibly important that we focus on the biology of children's cancer, rather than trying to extrapolate observations from adults to children, which rarely works.

Q17 **Tonia Antoniazzi:** That leads me nicely on to my questions for Chris. Thank you, Richard. Chris, much of your research specifically focuses on DIPG. Can you tell us why this disease is still so hard to treat, and what is your experience of seeking further funding for your research in the UK?

Professor Jones: Yes, absolutely. There are several fundamental challenges with trying to treat DIPG, if I can go through some of them. The first is that it occurs in the brainstem, which is an area of the brain that controls many critical functions such as breathing, swallowing, mobility and so on. The tumours do not form a distinct lump. They are very invasive, so surgery in that region of the brain is just not possible. That means that you cannot just take it out as a treatment option. Historically, it has also had the impact of there being no tissue to study. Until relatively recently, we had no idea what this tumour really was.

I mentioned that it is diffusely infiltrating. It spreads throughout the brainstem, but in other parts of the brain as well. Studies from post-mortem tissue of children who have passed from this disease have shown that it is everywhere throughout the central nervous system at the time that they die. Our own work in this area has tried to reconstruct the evolution of the tumours and suggests that actually some of the cells have already spread outside the brainstem when the child is diagnosed.

Biologically, it is a very complex tumour. It is made up of multiple different sub-types or sub-clones of tumour cell that allow it to evade treatment and to rapidly develop resistance to the therapies that we are trying. It is also now apparent that these tumour cells interact with normal brain cells to grow, spread and probably suppress an immune response as well.

Its biology is unique. As Richard said, these are not just the same as similar looking tumours in adults. In fact, DIPG has a genetic make-up unlike any other form of human cancer. As Richard said, for decades we were trying clinical trials based on ideas from adult tumours, which did not work then and, unsurprisingly, did not work in DIPG. The only thing that is effective at all is radiotherapy, which provides a temporary palliative response at best, and has increasing risk, the more you use it, of damaging the brainstem.

Finally, it has already been mentioned once or twice that it sits behind what we think is a very intact blood-brain barrier. This is the border of blood vessel cells that limit chemicals getting into the brain as a protective mechanism, but also stop potentially effective drugs getting in as well. Part of the centre of excellence is designing drugs that can more readily cross the blood-brain barrier. Other innovative drug delivery techniques will be required as well.

Q18 **Tonia Antoniazzi:** Are there any changes you would like to see in how research funders like NIHR allocate their funding, and that you think could help to promote research into DIPG and other cancers with poor survival outcomes?

Professor Jones: One thing that has been mentioned already is that the NIHR primarily funds clinical research. There is still a real gap in funding for the basic, biological research that then forms the platform on which we build translational efforts in getting things into trial. I am not aware of huge amounts of research spend in this area, via the MRC, for example.

Q19 **Tonia Antoniazzi:** How can we plug that gap? How can we address it?

Professor Jones: At several levels. We have already heard about outstanding initiatives such as the centres of excellence. Obviously, I fully support them. They are a really good way of accumulating expertise in a single centre or in a virtual network.

It will probably come up later, but I think we need to promote the careers of young outstanding scientists who may be attracted into this area

through all levels of their career progression, training them as PhD students, and training not just clinicians but basic scientists as well. We should provide a route for their post-doctoral studies through the outstanding labs we have in the UK. They should have a pathway for them to establish their own labs, either within the centres of excellence or elsewhere in the UK.

The centres of excellence perform an outstanding job, and will continue to do so in the long term, but there are some very good research pockets around the country, particularly people who have not necessarily been studying DIPG previously, for example. In the last few years, I have had a substantial uptick in people approaching me from outside the field, wanting to get involved and wanting to apply their kind of ideas, and looking for connections, advice, model systems and data that might facilitate them in entering DIPG research. That needs to be supported more readily.

Tonia Antoniazzi: I can see that Richard wants to come in.

Professor Gilbertson: Very briefly. I completely agree with what Chris has just said. The real problem with DIPG and with many of the difficult-to-treat brain tumours is that they are intrinsically horrible diseases. That seems like a vague and rather odd statement to make, but if we look at the history of medicine, any problem like this has been solved by disruptive science, by people outside the field coming up with an idea. It is not the continued, important ongoing research that happens in other centres.

There is a very clear possibility, and that is pressure on UKRI or funders like Wellcome or MRC to engage with what we have in the UK as a fantastic opportunity. We have arguably the world's best neuroscience community here. One thing the Tessa Jowell Brain Cancer Mission has done is to work closely with some of the leading neuroscientists who work on dementia, motor neurone disease, multiple sclerosis and how the brain is fundamentally knitted together, and to say to them, "If you had the opportunity to have a PhD student or a post-doc who worked on brain tumours in your lab, would you take that chance?" They said, "Absolutely." They do not need to do this. They do not need to pivot their research. They are automatically already world leaders in their field, but if relatively modest amounts of funding were available to put PhD students and post-docs in those labs, it could be transformative because we would access that expertise.

The reason for setting up the Tessa Jowell centres, which we might get to talk about, is that allied NHS institutions will be treating patients right next door to the academic health science centres that are doing that kind of research. We have a real opportunity in this country to transform the landscape with relatively modest and focused investment.

Tonia Antoniazzi: Thank you, Richard. Ian?

Ian Walker: I agree 100% with what Chris and Richard have just said. That is absolutely right. The other point I was going to make is that we felt it was pretty important to have specific ring-fenced money for target areas. When we are thinking about these kinds of small research communities, there is inherent disadvantage in a fully open court because they do not necessarily have the long-term sustainable funding behind them that breast cancer or bowel cancer would have, for example. What that means is that they do not have the tools or the models. They do not necessarily have all the tools in the toolkit so that they can effectively compete in a fully open system.

You can still honour the principles of independent peer review and quality by having a ring-fenced and targeted funding allocation for areas that you want to prioritise your efforts around. We found that was an important part of our model from a CRUK perspective in where we increased our spend in these areas.

Tonia Antoniazzi: Thanks, Ian.

Q20 **Elliot Colburn:** Thank you to our second panel for coming along. It is particularly great to see Chris from the ICR. The ICR is in my borough in Sutton in south London, and I highly recommend it to colleagues for a visit if they are ever in my part of the world.

Richard, the Tessa Jowell Brain Cancer Mission describes itself as a convening body. Could you explain a little bit more how that works in practice and, in particular, what your relationship with Government is like?

Professor Gilbertson: Thanks to the legacy of Tessa, we have a very good relationship with Government, and that has been transformative.

It is a convening body because my experience in the States and here is that often we have all the right pieces of the jigsaw, but they never talk to each other or work together effectively. Basically, we have brought together the key stakeholders like charities, represented on the call here, the clinical arena and the academic research arena, along with patients and families, to focus on the issue of brain tumours, and really target what are the key issues that we need to address. In doing that, we have identified in a very short time—three years—the five key areas, which are in training, clinical trials, research, patient outreach, and the NHS care system. In the last year, we have run the world's most intense and detailed landscape view of brain tumour research and treatment in any country. We engaged all 26 of the UK's NHS centres treating brain tumours; 20 of those applied to be centres of excellence, and nine of them have been launched as centres of excellence.

That has given us a granular view of what excellence looks like. That is a key starting point for understanding where the capacity needs are. As I mentioned, we are bringing alongside that the research elements, so that people who are not in brain tumours at the moment but are interested in doing that can ally with clinical activity in those centres. They are a focus

for training as well. In this country, we have no neuro-oncologists apart from one. That is a medical oncologist and cancer physician focused on brain tumours. In the US, every routine hospital has a neuro-oncologist, so that gap is a bit bizarre. We are starting a training programme that the NIHR is going to partner with fellowships, which is fantastic.

We have had great support from James O'Shaughnessy previously and then Lord Bethell's office in bringing this together. The good will that was created by the intrinsically good person that Tessa was, and now carried forward by her daughter Jess Mills, has brought attention to this across the different political parties interested in making things better for both children and adults with brain tumours.

The previous panel quite rightly pointed out that the mission has focused in its first three years on adult cancers. That was very purposeful because that is where the initial drive was. However, our next focus, which will be happening in the next few months, is to open Tessa Jowell centres for kids. Basically, that is to launch centres in NHS hospitals, often based in children's hospitals, with the same kind of principle. What is excellence like in children's brain tumour care? What does it look like? That will go all the way through treatment and through to community care, and will then raise all boats by launching that activity. They will provide a nidus for all the activity around clinical trials, research, community care, patient care, outreach and training.

Q21 **Elliot Colburn:** Thank you very much, Richard. Sue, Ian and Chris, how has the convening role that the Tessa Jowell Brain Cancer Mission brings transformed the brain tumour research environment in the UK? What impacts have you seen that convening body model have?

Sue Farrington Smith: I think it brings clarity and a road map to what we need to do. We often talk about the funders, and of course the funders are the people who are sat round the table and are reliant on the British public giving us money in order to fund research. Yes, Cancer Research UK funded the £28 million, but because of what has happened in the last year with Covid, they are saying that they may not be able to commit to that beyond the next five years. It is what is coming down the line and what finances we can be assured of.

We are incredibly grateful to our supporter base, who have kept us going in the last year. Of the £15 million that was spent on brain tumour research through the NCRI partners, £11 million came from Cancer Research UK and £1 million came from us. Was the other £3 million from Wellcome or from the Government? We need to see the Government contributing a lot more in the research space for brain tumours.

Elliot Colburn: Thank you, Sue. Ian, I will come to you next on the question of how the convening body of the Tessa Jowell mission has changed the landscape in the UK.

Ian Walker: I do not have a huge amount to add to what you have heard from Richard and Sue. There is definitely an important part of the convening aspect in bringing focus and strategic alignment where investments are happening. Just thinking about Richard's comments about the paediatric centres that will follow over the course of the next few months or year, it is how we make sure that those things are really aligned to other paediatric investments, whether that is clinical trial units or our experimental cancer medicines centre network, where we have a paediatric network co-funded with the four devolved Departments of Health. It is making sure that all of the different pieces of the jigsaw, to use Richard's words, are stuck together, speaking to each other and aligned in what they are trying to achieve. From that alignment perspective, I think there is a clear role and a clear advantage in the work that has been done.

Elliot Colburn: Thanks, Ian. Finally, Chris, over to you on the same question.

Professor Jones: Picking up on that a little bit, I am really glad to hear that the mission will start focusing on childhood brain tumour centres in the coming months. That is terrific news. As Richard knows, for some of these very rare and complex childhood brain tumours, you need specialist expertise. Of course, what has happened in the UK because of that rarity is that by necessity, but also by choice, we have worked in international collaboratives for some time. It would be great to understand how the mission can intersect with some of the large, international collaboratives that are running some of the innovative trials right now, but which we are struggling to open in the UK.

There are several consortia, some of which I am involved with, such as ITCC—Innovative Therapies for Childhood Cancer. This is a European consortium that opens stratified clinical trials, such as the ESMART trial in the UK. We are developing a specific ITCC brain network to open brain-specific trials, including for DIPG, across specialist centres in Europe, including the UK. It would be great to know how that intersects.

There are others as well, which the UK either is or could be part of, but it has proved really difficult to open those trials. One I am involved with is Connect, which is a network of clinical centres and research labs across North America, Europe and Australia. They are running early phase trials, including trials for DIPG, but to date they have only been based in the US. Another is PNOC—the Pacific Paediatric Neuro-Oncology Consortium—again primarily based in North America, but now beginning to open studies in Europe—in Zurich—and elsewhere internationally.

There are plenty of ideas coming through those networks but, as I understand it, there is not the capacity to deliver some of these complex international trials through the specialist centres in the UK. This is not my area of expertise, but my colleagues tell me that there is simply not enough resource for the clinical trial delivery teams to go through the

difficult, practical, regulatory, governance issues to open these international trials.

It would be really great if something like the mission could actually intersect with some of those and allow us to open some of the trials that are already extant—we would not have to reinvent them—via networks we are already part of, so that families and children in the UK could benefit from that kind of choice of innovative trials.

Q22 **Elliot Colburn:** Thank you, Chris. Everyone touched on funding. I will move on to talk about the Government's commitment to invest £40 million in brain tumour research over five years. We are now three years into that commitment.

I am keen to understand how much difference that has made. Is there concern that more has not been allocated? Have the processes and criteria for the funding been the right ones? Is there anything that you would like to see done differently or prioritised differently in the remaining two years of that commitment? That is quite a lot to pack into one question, but I hope you will forgive me. Sue, I will come to you first on the question of funding.

Sue Farrington Smith: You know what I am going to say: it is not enough. I do not know if you have seen our petition report; 112,000 people signed that, and we are not seeing that money. We know that only 25% has been spent. It is at the clinical end. Do we need £40 million spent at the clinical end? Do we need £800 million spent at the basic end? We need to understand what we need across the spectrum, and what the Government are doing to help move that forward. None of us can do it alone. If Cancer Research UK changes strategy in another five years' time, who will be left to keep this going? We want parity with other cancers. We want to see the Government levelling up, basically, in the same way as they did with Covid. Let's throw some money behind this, obviously in the right way, as has been outlined by the Tessa Jowell Brain Cancer Mission. We have to see it moving forward now, or we will be in the same position 20 years down the line.

Elliot Colburn: Chris, I will come to you next on the question of funding.

Professor Jones: I obviously agree that more funding is necessary. As has been mentioned several times, these are complex diseases. They are really going to take a village to try to improve survival for these kids. We need to be funding at all levels: career levels and all levels of risk and innovation. We have talked about some of the out-of-the-box-type approaches that will be needed to move the dial. We also need to support some of the more laborious and painstaking preclinical type work that will be required to take some of those innovative ideas and do the grunt work to show that they are robust treatments that can be trialled in the paediatric oncology setting.

You asked about Government funding specifically. I do not have much to add to what has already been said. Primarily, it has been apportioned, as I understand it, through the NIHR. I think much more needs to be filtered through UKRI, MRC and the basic science end of things.

Elliot Colburn: Richard, I will come to you next.

Professor Gilbertson: I think the £40 million commitment is a bit disingenuous. What I mean by that is that, hopefully, the Olympics will happen in Japan, but it is a bit like saying to somebody who has not trained and has been chronically under-trained for years, "Yes, you can join the race at the start," but they have no hope of winning. That is basically the brain tumour community. It has been chronically underfunded and under-resourced for many years. As a consequence, when the NIHR says, "Yes, you are eligible to apply for this money," it is an underfunded and under-resourced arena that has little capacity to respond.

The mission has brought together those individuals so that we now have a fantastic opportunity and a landscape ready and poised for that. The Government have to invest smartly—we get that—and we also understand that everybody cries for money and says, "Our cause is important," but we have a fantastic opportunity in this country, in its basic neuroscience community, which is world class. You have an opportunity to direct money specifically to the neuroscience community to work on brain tumours.

The one thing that has to happen is that this cannot be an open call for all diseases, or even all cancers. There needs to be a ring-fenced amount of money for brain tumours, but invested smartly in the UK's neuroscience community. If you put those two elements together, it will be highly potent and transformative. That is what needs to be done. A simple open call by the NIHR to say you can apply for this is unhelpful. If it goes to the neuroscience community, it will be superb, but for brain tumour research it will be transformative.

Elliot Colburn: Thanks Richard. Ian, finally to you on the question of funding.

Ian Walker: I agree with everything that has been said. The only comment I would add is that when we think about the areas that need long-term strategic investment, £40 million over five years is not going to solve the problem. It is definitely a step in the right direction. If it is allocated and spent in the right way, in a strategic way, in the way that you have just heard from others, it can definitely have real impact. The reality is that to build novel capability to bring new insight into an area, you are talking about building careers and researchers. We are talking about multi-year—five, 10, 15 and even 20 years—long-term investments before we really start seeing those things feed through.

There needs to be longevity thinking about how we might address these issues going forward. It is not going to be fixed in five years.

Elliot Colburn: Thank you all very much for your time this afternoon.

Q23 **Tonia Antoniazzi:** In 2018, the Government working group on brain tumour research suggested that the main barrier to more research was not a lack of funding—I know we have just been talking about that—but a lack of fundable research proposals. Would each one of you say whether that is still the case, and what can be done to resolve it? I will start with Richard because he is nodding.

Professor Gilbertson: Yes. Thanks, Tonia. It goes back to the training analogy. It is true that the capacity is limited for good applications. That is not unique to the UK; it is a global issue. That is because if you put us alongside the racehorses, the experienced deep broad communities like breast cancer, prostate cancer, lung cancer or even leukaemia, there isn't a competition.

We have to see it in the context of how this has come about culturally. Basically, brain tumours are intrinsically bad diseases. They are relatively rare. That does not attract, and has not attracted, people to work on them. That leads to few breakthroughs, so you get into the vicious cycle that has happened for decades. That needs to be broken.

Simply to offer opportunities to a brain tumour community, which is small, has fewer skillsets and is less developed, is inevitably going to fail. You need disruptive investments that need to be smart, of the kind I have suggested, where you invest in areas where you really have disruptive science, world class and ongoing, that can partner in brain tumour research. Throwing money at a poorly resourced, underfunded and limited capacity field will have limited benefit; it should have ring-fenced investment in a smart way.

Yes, there have been poor applications going forward, but it is not acceptable to sit back and say as an excuse, "Well, we can give you money but I'm sorry, you're just no good at doing science." There are good pockets of that around, but it is about holistically building capacity and the community generally. That is what the mission is focused on. I think we can do that, and there is an opportunity to do it, but it is a global problem; it is not just in the UK.

Tonia Antoniazzi: I will go to Chris, because then I have more for Ian afterwards.

Professor Jones: Obviously, I agree with what Richard says. I also think that that perception is perhaps a little bit outdated. Maybe historically it was true. When I started in this field, there were no samples available. There were no studies done on human tissue from any of these rare tumours. There were no model systems. We did not know anything about the biology of the tumours. Researchers putting in applications were just trying to extrapolate from the adult situation, as we described before, or

taking shots in the dark. That is simply not true any more. We know an enormous amount about all kinds of different brain tumours, particularly childhood brain tumours. We know about their complexity, and we also have very clear research hypotheses to follow up now.

Saying that there are no good applications is a bit circular, with the money being there to attract the highest quality and highest calibre applications in the first place. Connecting the disease biologists with the specialists in the other, more fundamental areas of biology that we have discovered are important in these brain tumours is where we are going to get high-quality applications. As Richard said, that is out there in the UK and worldwide. The situation has changed dramatically, even in the last five years.

Tonia Antoniazzi: Thanks, Chris. Ian?

Ian Walker: I do not feel that I have a huge amount to add. I agree with what both Chris and Richard have said. The only other example I can think of from CRUK's perspective, where we have looked in a similar kind of way, is specifically in the paediatric cancer setting. It is very similar to brain more generically, in that it is a relatively low incidence disease, with lots of different rare diseases and a small, compact community.

To drive innovations we have put in a sequence of innovation funding, which is proactively designed to encourage researchers from the developmental biology field to come and apply their wares with the paediatricians—the paediatric doctors and researchers—and bring that differential thinking. We have huge depth and breadth in developmental biology in the UK. We need to try to turn their attention to the paediatric cancer question.

At a fundamental biology question level, there are very similar themes. They are asking about the fundamentals of how cells develop and how the mechanisms within cancer, where they go wrong, are not controlled or do not stop. Fundamentally, there is a huge opportunity for us to tap into the broader expertise across the UK, whether it be for brain cancer research or for paediatric research.

Tonia Antoniazzi: Sue, do you have anything to add?

Sue Farrington Smith: The approach the Tessa Jowell Brain Cancer Mission has taken at their centres is more about mentoring. There might have been only nine centres accepted this time around, but they are helping the other 11 to get up to that standard. I wonder if there could be a better mentoring approach to brain tumour scientists.

I was at the brain proposal guidance meeting this morning with the NCRI and this occurred to me there. Who are on the panels of the NIHR helping people to bring forward good applications and helping them to make their applications better? I think there should be mentoring across the piece.

Q24 **Tonia Antoniazzi:** Thanks, Sue. Ian, it was interesting today to see that the Government have announced £20 million for medical research charities as part of the BEIS R&D budget allocations. The Government have said that one reason why they have not been able to spend more on brain tumour research is the limited research workforce and the lack of basic science in this area. That does not tally with what Chris and Richard have been saying has been going on recently. Or does it? What is your experience?

Ian Walker: I think there are probably a couple of different things. In the first respect, it is important to acknowledge that within the UK we have quite a unique environment in how medical research charities contribute to the research environment in the country. It is very different from many other European countries and, indeed, the US. We have a vibrant research community. From a CRUK perspective, overall we fund something like 50% of non-commercial cancer research in the UK.

That is very positive, but there is a consequence. We have seen the impact of Covid on various sectors, but specifically on medical research charities. We have not been able to do our fundraising events. Many of the retail chains have been closed for much of the year. It has had a massive impact on our ability to fundraise, and because the system is somewhat reliant on the medical research sector, the knock-on effect is that funding to that system will decrease. For us, since the start of the pandemic, that means we have funded about £121 million less than we would have done against our pre-Covid plan. It means that our income for last year was about £100 million less than we had planned pre-Covid, so there are some significant impacts for us and for the broader sector. While the £20 million is welcome, it is clearly not going to fix the problem at a system level. I hope that it is the first of many conversations that we will be able to have with Government about continued support for the sector, which ultimately mean continued support for our research community and our research environment.

I have not quite heard it phrased in the way that you did—that there just is not research capacity in the system. We have talked about some of the complexity. If we really want to address the problem, it is about finding the right expertise, but it is also about thinking innovatively about how we bring in people from other areas and other multidisciplinary teams, whether it is neurodevelopmental biology, immunologists or whatever it might be. It is how we bring those people to bear on the question that we are trying to address, and then how we think about long-term strategic investment. It is about training, capability and capacity-building, and—to Richard's previous points—how we drive an innovative next step.

If we just have a call and say, "We've made some money available and we'll see what happens," my sense is that it will not be sufficient to fix the problem. It is a good start, but we have to think longer term. We have to think strategically about where we can invest money in the right way.

Q25 **Tonia Antoniazzi:** That is interesting, Ian. It is complex. It is not just one area. It is not something you can just throw money at—we know that. The initiatives we have been discussing are affecting researchers' perceptions of the opportunities for funding and career progression in brain tumour research. Are you able to say that we are getting these people working in neurology and sparking their interest? Is it all coming together? Listening to what Chris and Richard have been saying, it is something that is moving forward. What can we do to move it forward quicker and get more people involved?

Ian Walker: Again, I do not think I can speak for Government funding and for the broader system. I can speak from a CRUK perspective, which is just our perspective. It is not necessarily reflective.

If we take the paediatric innovation awards, in order to drive multidisciplinarity, we have proactively engaged with different scientific communities that would not routinely come to CRUK. We have had to partner; we have worked in collaboration with other organisations, engaged with different communities and been proactive in bringing people to bear. I think we still have some way to go, if I am honest, at a system level. It does not feel like we are quite there yet. I encourage you perhaps to ask a similar question of Chris and Richard. I think they will probably be closer to it than I am.

Q26 **Tonia Antoniazzi:** Thanks. That is where I was going next. Chris, Richard and Sue, do you want to make a contribution?

Professor Jones: I think we have touched on it before, but we need to grow the brain tumour research workforce as well. We need funding at all levels of their career pathway. It has been highlighted many times that many researchers do not view a viable career pathway existing in brain tumour research in the UK, particularly around paediatric brain tumours. We are losing people, and I think we need to address that.

We need to do the training in the first place, but we need to provide funding schemes and mechanisms to have our trained researchers stay in the UK and move between labs and get the expertise they need, believing that the most successful of them will be able to form a long-term career in this area, whether they have come from another research environment first or whether we are training them up directly from university. I think that is what is lacking. In a long-term strategy, we need to do that to provide the sort of high-level, thriving research community that will then allow us to attract the world's leading scientists to the UK to set up their labs here as well.

Q27 **Tonia Antoniazzi:** Who should be driving that forward?

Professor Jones: Good question. I guess it has to come from all the stakeholders. We are identifying people in all of our own labs and through all our collaborative networks. We are seeing the kind of people we would like to retain in brain cancer research. It is working in partnership with the funders to see how we can put money into small, short-term

fellowships with the institutes to create faculty positions where there will be a renewed focus on brain tumours and childhood cancers. It needs to go hand in hand, I guess.

Tonia Antoniazzi: Thanks. Richard?

Professor Gilbertson: If the question was, "What could Government do?", I would say that the Government are empowered to change policy to direct efforts and to bring funding into certain areas. Maybe that is naive, but that is what I think they do.

Often, the availability of money, in my experience, has not always been the problem. It is the policies or systems in place that prevent flexible investment. In an area like brain tumours, which is rare and a niche area in healthcare, there are limited individuals available, so the capacity in the system is small. When you put that alongside the existing policies that govern research funding and how it is directed, it does not fit, so it falls away.

There needs to be some transformative thinking where you say, "Look, there's money available here. This is a system facing capacity issues. It needs to be built up, but there are pockets of excellence. How can we just take some of that money and flexibly invest it?", even if it is associated with a bit of risk, which is minimalised by putting it in neuroscience centres where there really is world-class excellence and a proven track record.

The turgid nature of the system sometimes stops that money flowing. It is a rather rigid system whereby it cannot go into brain tumours for this or that reason, if that makes sense. We need more flexibility and more innovative thinking with UKRI and other funders to direct some money, even in the short term, into brain tumours to get the pump-priming going. That would be very helpful.

Tonia Antoniazzi: You have practically answered my next question. Sue?

Sue Farrington Smith: I obviously agree with what everybody has said. Our call was to ring-fence a pot of £105 million. Rather than go the other way round, "What do we need to do?", it would be to say, "Here is the money and how can we best spend it using the brains around the table?"

You may recall that even the Prime Minister himself, answering Chris Bryant's question on brain injury, said spontaneously that "brain cancer is an area that is too often neglected in our system and may fall through the cracks." Even the Prime Minister recognises that. If we could make money available, and the brains then decide how best to spend it for the best effort, that is where we need to be.

Q28 **Tonia Antoniazzi:** Thanks, Sue. Ian, as a charity you have been very vocal about the impact of Covid-19 on your income. You have spoken in

previous questions about the impact it has had on your income and future research budgets. What is it going to mean for future research? Basically, do you think that the Government have supported you enough throughout the pandemic?

Ian Walker: To reiterate, because the numbers are big and it is important that we get a sense of them, from a CRUK perspective we have some new numbers, which I have to say are not yet audited, so my caveat is that they are subject to change. Our current best estimate and forecast is that, for us, we are going to be around £250 million behind where we were pre-Covid to plan over a three-year window. That is a significant decline in our income. As I said, since Covid started, we have taken £121 million out of what we would have spent on research otherwise.

Clearly, these are big numbers, and the impact will be mid to long term. They are difficult numbers to bounce back from. What I would say, and what I think came up earlier, is that we will do our very best to honour the commitments we have already made. We think we have now taken the cuts out of the live grants that we need to do. We have re-established our new baseline and we are moving ahead in that light. It is important to acknowledge that.

Have the Government done enough to support the sector? In the messaging from the AMRC campaign, which was very clearly trying to articulate the scale of impact and reduction across the system—Sue might know the numbers—I think they were looking at a shortfall of around £300 million in a year, which will come directly out of the research community. The announcement today was for £20 million, so you can see that there is a differential.

Again, it is important to recognise that it is a complex system. There are lots of interdependencies. Everyone has a part to play in the system and in how we move things forward. I do not want to be overly critical. All support for the sector is welcome, but clearly if we want to mitigate the impact of Covid on the research community more broadly, we hope that that is the first of a number of conversations that we will be able to have with Government over coming weeks and months and, I suspect, years.

Q29 **Tonia Antoniazzi:** I have one last question, because I know we need to move on. Richard and Chris, how important has voluntary sector funding been in supporting your research?

Professor Gilbertson: It has been absolutely invaluable. If you are referring to charity funding, CRUK, Brain Tumour Research and Brain Tumour Charity have been the backbone of funding for brain tumour research, particularly in paediatrics. That is true in the US as well, where I was before; much of the funding comes through the voluntary sector because the other cancers swamp the budgets when it comes to Government and federal funding.

If you look back, Chris referred to the fact that in children's brain tumours we have made remarkable strides in the last 20 or 30 years in understanding these diseases, and we have transformed them, between a few labs in the world. If you look at the proportion in those labs that comes from foundation funding, it is massive; at least half, if not more, has come from foundation funding, but that is not a reason to not get funding from Government. The answer to that would be, "Look at what more could be done if more money was provided from Government." What we have done with that modest investment has been highly significant. What could be done with a modest investment from Government could be dramatically transformative.

Professor Jones: I completely agree. My lab is currently about 90% charitably funded. Most of that is probably from the larger peer-review bodies like CRUK and Brain Tumour Charity. A substantial proportion, maybe 20% or 25%, is from very small foundations. They give small, or sometimes rather large, amounts of money directly. They are usually very small charities led by parents who have lost a child due to one of these terrible diseases and want to do something to catalyse the research.

That is a really important point. It is not just about funding. They really have catalysed the whole research endeavour going back five, 10 or 15 years, as Richard knows. In the early days of my lab and DIPG research, it was those small foundations that got researchers together and gave some modest funds to get us going. They demanded that we work together and start tackling this disease. It shows the impact that charitable sources can have, both in advocacy and in driving the research agenda, as well as funding. Now, it seems that that is something the Government could do much more effectively at the current time.

Q30 **Chair:** We are running out of time. It is important that we put some of this to the Government as well, to get their response. Before we say goodbye to this panel, I want to ask about international collaboration. You have talked a lot about it, and it is very obvious that working in a collaborative way internationally is hugely important for this area of research, as it is for much medical research. From my own visits to Cancer Research in Newcastle, I have seen how multinational the team is, and how the ease of being able to collaborate in that way is important for the work that they have achieved.

Are there any concerns about our exit from the European Union at the moment in terms of its impact on your research? If so, what can we do to try to mitigate that? I know that cancer is one of the five missions identified under the EU's new Horizon Europe programme in 2027. It would be interesting to hear your views on where you see the opportunities for, in particular, brain tumour and childhood cancer research as part of that.

Would anyone like to respond? No? Apologies for bringing the tone down and talking about Brexit.

Ian Walker: I am happy to start us off. First, I agree with you; international collaboration is important across all parts of life sciences. We have seen some great partnerships across Europe, and between the UK and the US. There is a specific initiative between CRUK and the NCI around our cancer grand challenges, which is looking to solve some of the biggest international cancer problems through a challenge-based approach.

Specifically in this area, there is almost even greater importance in international working for what are, essentially, rare cancers. The reality is that, if you are thinking about this at the clinical trial end, we simply do not have sufficient numbers of patients. That is clearly a good thing, but in terms of how you demonstrate real impact through clinical research we do not have sufficient patients within country who can participate in those trials. The vast majority of our paediatric trials are international and work across Europe.

At the minute, that seems to be working fine, but there are some key moments coming up on Brexit in particular. There are the upcoming EU clinical trial regulations, which we will not be part of as the UK. Clearly we will have our own view on what the UK regulations will look like going forward, but it will be critical to make sure that we do not diverge and make things more difficult in international clinical research.

There are other things around the clinical trial information system, which is a new EU portal around improving how quickly trials are set up and started across Europe. Again, the UK will not be part of that, so we will have to have a parallel system. If it diverges from that system it will create additional challenges.

Finally, on Brexit, there is the ongoing issue around data adequacy and the flow of information. From a clinical trial perspective, if those things do not align and if we do not get them right, it will have a direct and damaging impact on our ability to contribute to international clinical trials across Europe and the UK. We think that is all progressing quite positively in the right direction, but they represent real risks and we absolutely need to keep a close eye on those things.

Finally, and then I will pass to others, on Horizon 2020 we were really pleased, as was the rest of the community, to see Government support for that, but recognising that it is a one-year settlement. There still remains significant uncertainty about the future sustainability of interaction with Horizon 2020. Fundamentally, the crux of your question is what opportunities there are if we do not resolve that longer-term engagement across European funding. There are clearly some constraints that would be a concern for us.

Chair: Thank you very much. Unless anyone has anything to add, I think that was a fairly comprehensive response.

Thank you so much to our panel members. We really appreciate you

taking the time to be with us today. We appreciate how important your work is, and it has been vital to get your input today. We will put some of these issues directly to Ministers and officials from the Department of Health and Social Care.