

UNLOCKING THE BIG BREAKTHROUGHS OF THE FUTURE

Research and Innovation Strategy
2016–2021

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OUR CHARITY MISSION

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Our mission at Great Ormond Street Hospital Children’s Charity is to enhance Great Ormond Street Hospital’s (GOSH) ability to transform the health and wellbeing of children and young people, giving them the best chance to fulfil their potential.

OUR RESEARCH AMBITION

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Our ambition is to put the child and the adult they will become at the centre by focusing on supporting the delivery of personalised medicine for children with rare and complex conditions.



A MESSAGE FROM OUR CHIEF EXECUTIVES



GOSH is no ordinary place. Extraordinary things happen every day, and every year, more and more children benefit from the hospital's specialist care. Thanks to the generous contributions of the charity's supporters, transformational changes are being made to the lives of our patients and their families.

But we know that there is more that we can do to enhance the work already taking place in the hospital. For many seriously ill children, research is their only hope. That's why the hospital and the charity have worked together to develop an ambitious five-year strategy, which will ensure we continue to invest in the areas where we will have the greatest impact. Along with the national and international paediatric research community, we have identified key priorities and outlined approaches to maximise the charity's research investment. We're delighted that we can now share them with you.

The main focus will be on translational research, with personalised medicine being the ultimate goal. Our ambition is that, thanks to charity funding, researchers will be enabled to discover more precise and faster diagnoses, targeted interventions, and cures, and improve long-term outcomes. Behind this will lie an ethos of 'translation and reverse translation' or 'bench-to-bedside and back again'. We hope this will increase the number of children that GOSH can treat, ultimately resulting in an improvement to overall survival rates and quality of life, helping more children reach their potential.

Our six priority areas represent the strengths of GOSH and its academic partner, the UCL Great Ormond Street Institute of Child Health (ICH),

and the particular opportunities that the demographic of the patients that come to GOSH provide. They are:

- **cancer**
- **inflammation and immunity**
- **neuroscience**
- **endocrine and metabolic**
- **reconstructive, regenerative and development**
- **cardiovascular**

The charity is the largest dedicated funder of paediatric research in the UK, and we know that investing in the right way will be key to our success. This is why we've also identified three cross-cutting themes that we believe will enhance the research efforts of the hospital and the ICH:

- **genetics and genomics**
- **information and data integration**
- **partnership**

The funds we raise will primarily go towards building research capacity in our six priority areas by investing in outstanding researchers, supporting clinical trials and exciting new ideas, and providing the infrastructure required to build on the excellent research platform that currently exists.

To make this strategy a success, we will need the continued support of the researchers and clinicians we fund, our funding partners and the wider academic research community, patients and their families, and our generous supporters. Research carried out by GOSH and the ICH is saving young lives every day. In developing this strategy, we will be in the best position to enable more extraordinary things to happen for more children and their families.



Dr Peter Steer
Chief Executive
Great Ormond Street Hospital



Tim Johnson
Chief Executive
Great Ormond Street Hospital Children's Charity

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AN URGENT NEED TO IMPROVE CHILD HEALTH



Many of the children that pass through the doors of our hospital have rare and complex conditions that are life-limiting or life-threatening. We know all too well that diagnosis can be difficult, treatment options are often imperfect, and the burden of disease can have a profound impact on the child and their family. Even for the children that do survive, current interventions can have lasting, permanent effects, requiring continued support and treatment into adulthood. There is an urgent need to improve this situation with new solutions and treatment approaches.

While each rare disease alone impacts fewer than 30,000 people, when grouped together they represent a significant medical burden – one in 17 will be affected by a rare disease at some point in their life. In the UK, that equates to around 3.5 million people, and 75 per cent of rare diseases present in children. Sadly, around 30 per cent of children with these rare diseases die before their fifth birthday. And the pool of rare diseases is growing. Genetic research has broken down many conditions into multiple subtypes, and those previously considered ‘common’ are now better understood as a collection of rare diseases.

We know that children are not just small adults – the priorities for their care and the needs of child health research are different. Children under 18 represent approximately 22 per cent of the UK population, yet dedicated funding for paediatric research stands at only five per cent. Although some funding does also come from other sources, this demonstrates that there is still an urgent need to invest more into childhood disease research.

The issues and the imbalance in the investment into paediatric research need to be addressed, which is why we’re delighted that the charity are launching a Research Strategy that aligns with the needs of the hospital, but also national and international research.

THE OPPORTUNITY

As GOSH is often a place of last resort for children with rare and complex conditions, research is built into our fabric. We make extraordinary life-changing differences to a child’s quality of life and can even offer the hope of cure. And the effects can be far reaching: it’s not just children and their families who benefit, but wider medicine, the NHS, the economy and, most importantly, future generations.

The partnership between GOSH, the ICH and the wider University College London (UCL) creates the perfect environment for problem-solving and offers an unrivalled opportunity to make a global impact on children’s health. Together, we form the largest concentration of paediatric research expertise outside of North America and host the only National Institute of

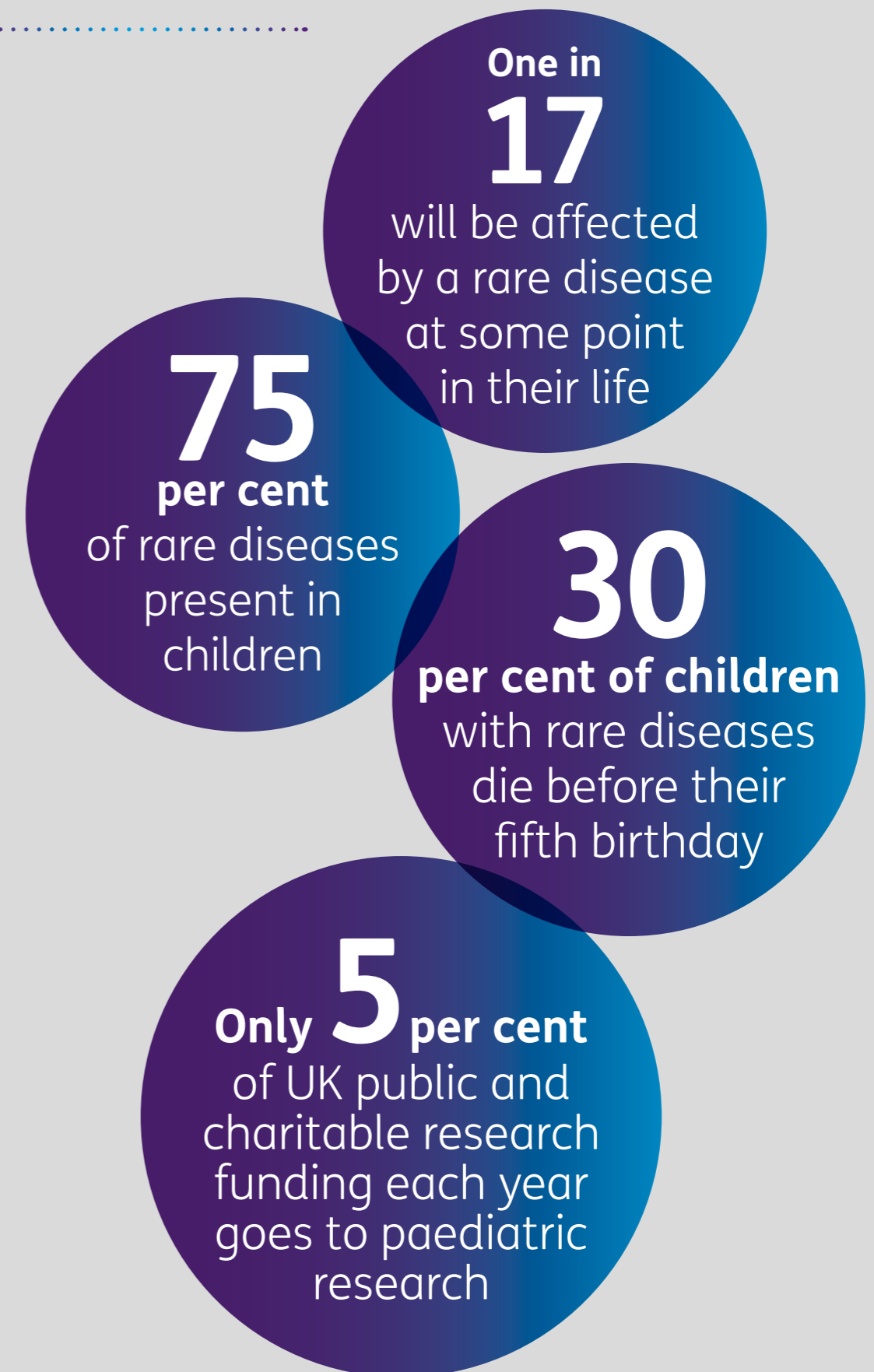
“We want to see an overall improvement in survival rates and quality of life for children with rare and complex conditions.”

Health Research (NIHR) Biomedical Research Centre (BRC) in the UK that focuses on paediatric research. Charity funding allows to build on this, by enabling us to do things we would not otherwise be able to do.

Together, our ambition is to put the child and the adult they will become at the centre, by focusing on delivering a personalised approach to treatment for every child. We hope this will lead to great strides in paediatric research and I look forward to seeing the difference it will make over the coming years.

Professor David Goldblatt
Director of Clinical Research and Development
Great Ormond Street Hospital

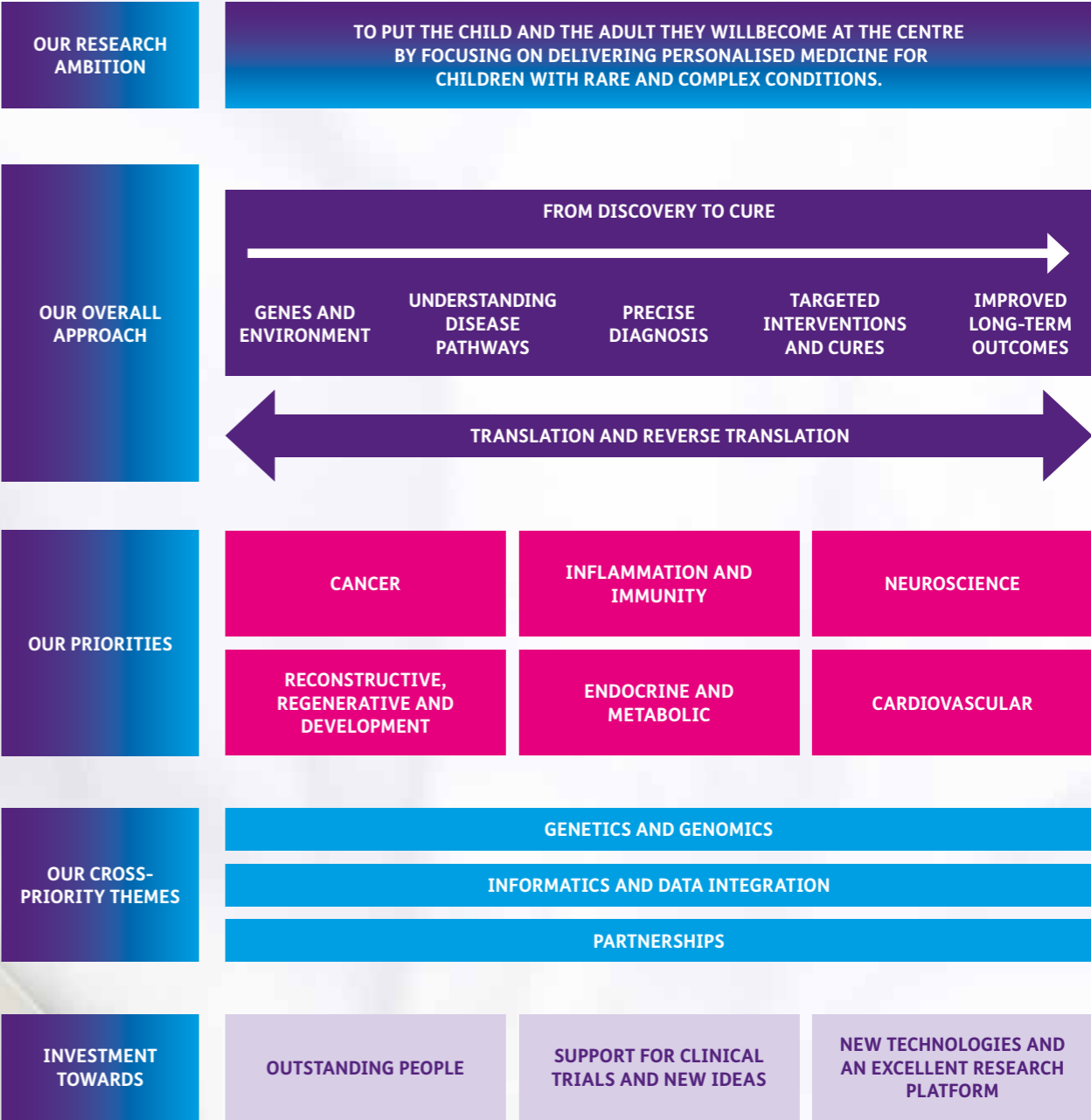
THE REALITY





OUR STRATEGIC FRAMEWORK

Our new strategy, drawn up in collaboration with the paediatric research community, outlines our plan to create a step change in child health research. Over the next five years, we will match this research ambition with increased investment. During this period, our direct research commitments towards rare and complex diseases are likely to exceed £50 million, but we will also be supporting research in other ways, such as funding the building of the Zayed Centre for Research into Rare Disease in Children. This framework outlines our approach.



OUR OVERALL APPROACH



From discovery to cure, our research strategy ethos will be ‘translation and reverse translation’. Three cross-cutting themes will also enhance the research efforts in our priority areas.

FROM DISCOVERY TO PERSONALISED CURE, AND FROM BENCH-TO-BEDSIDE AND BACK AGAIN

Discoveries in the lab will be moved into the hospital to benefit patients as quickly as possible, taking advantage of the full discovery pathway, from understanding genes and environment to mechanisms of more precise diagnosis and developing targeted, personalised interventions. This will be complemented by ‘reverse translation’ – taking clinical learnings back to the lab. We are in the privileged position of being able to facilitate this by taking advantage of the co-location of the ICH and hospital. We will also continue to promote the collaboration of scientists and clinicians working closely together, many with dual roles that involve looking after children as well as undertaking research.

We will also maintain the flexibility and agility to react to opportunities that may arise and that will directly support delivery of the strategy. We will also consider establishing new initiatives that accelerate innovation in paediatric care and keep the hospital and Institute at the forefront of medical innovation.

CROSS-PRIORITY THEMES

Three cross-cutting themes are essential to progress in each of our priority disease areas as well as underlying the future of medicine. Advances in these cross-cutting themes will be accelerated by pooling resources, sharing ideas, cultivating productive partnerships,

capitalising on the significant investment in nationally led infrastructure, and leveraging the excellent local environment.

Genetics and genomics

About 80 per cent of rare diseases are of genetic origin, so there is huge potential for children to benefit from the genetics revolution.

Eventually, GOSH hopes to be able to sequence the genome of every child that comes to them and link their genomic data to their other ‘-omics’ profiles, building a dynamic map that explains how each child’s body is functioning. This will help determine the best approach for treatment and the likely trajectory of their disease. The foundations for this ambition are being set by nationally led infrastructure that is being developed through Genomics England and selected Genomic Medicine Centres (GMC) – of which GOSH is one – as part of the 100,000 Genomes Project.

Informatics and data integration

Informatics is an essential part of modern-day research, allowing us to make sense of the vast amount of biological and clinical data being generated. IT infrastructure is also needed to link clinical and scientific databases and realise the possibilities of big data. In particular, molecular, phenotypic and genotypic information, and treatment-related outcomes will be crucial.

Partnership

No one will solve the tough challenges in paediatric healthcare alone. That’s why partnerships are

an integral part of our strategy. Partnership allows us to do things that we otherwise could not do. The relatively small number of patients affected by each rare disease demands a national and international collaborative approach and the scientists and clinicians we support will continue to build creative durable relationships at a local, national and international level, resulting in new discoveries and improved care.

Our strategy will be a catalyst for national and international partnerships with pharmaceutical, biotechnological and other industry partners and funders, fuelling greater and faster innovation, moving discovery science into clinical trials that further advances the hospital’s and the ICH’s precision approach.



Key principles will underpin all of our investments, ensuring the highest standards most likely to drive advances in rare disease research. In our six priority areas, funding will primarily go towards building research capacity to accelerate progress.

INVESTMENT PRINCIPLES

Across all our investments, we will provide the resources and capacity needed to make a significant impact. All investments will be defined, and judged, by the following four principles:

EXCELLENCE

We will continue to fund exciting and novel research, and outstanding people of the highest international quality.

INNOVATION

We will continue to support an enterprising research environment that promotes innovation and nurtures innovators.

LEVERAGE

We will continue to leverage our funding to maximise the impact of our investment.

PARTNERSHIP

We will continue to work in partnership and support collaboration to quicken the pace of our research.

IN OUR SIX PRIORITY AREAS, WE WILL TARGET INVESTMENT TOWARDS:

Outstanding people

We know that to deliver our research strategy, we will need to support the recruitment of outstanding world-class leaders. We also need to help attract and develop younger researchers – the leaders of the future – particularly focusing investment in areas where there is a need to build capacity or bring in new talent and expertise. Prestigious fellowships will be offered to individuals in these areas, who will drive forward translation. This will include professorial-level appointments, fixed-term Senior Career Fellowships and the

establishment of a surgeon-scientist academic training programme. The support provided will enable these individuals to develop momentum, with the aim of becoming self-funded in the future.

Clinical trials and new ideas

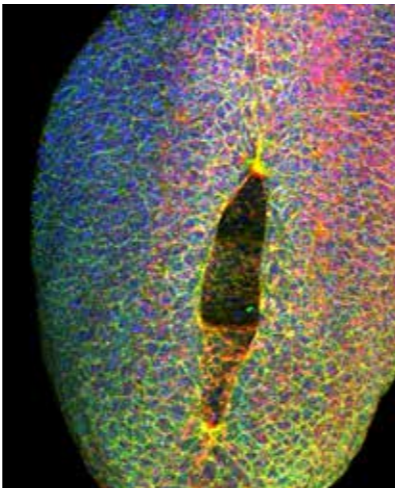
Support for clinical trials and new ideas will continue to underpin our investment in outstanding people. Clinical trials are no longer seen as a last resort for patients who have no other treatment choices. We see our investment in this area as vital, and through our strategy, we will work to increase the overall number of trials offered to children across our six strategic priorities. Funding will be provided for research nurses, data managers and trial co-ordinators,

facilitating an increase in the number of clinical trials that can be safely established.

Our research strategy will also continue to offer pump-prime funding and support exciting and novel trials and projects through our Clinical Research Starter Grants and our National Call, with the latter providing funding to paediatric research across the UK.

New technologies and an excellent research platform

The strategy will build on what is already an excellent research environment. We will invest in new, cutting-edge technologies and infrastructure, essential for strengthening the overall research platform, catalysing developments in research, and driving improvements in clinical care. In particular, IT infrastructure will be essential to link clinical and scientific databases in order to realise the possibilities of big data.



ICH Imaging Facility, Sarah Ivins and Dale Moulding



OUR PRIORITIES



Our research strategy focuses on supporting the delivery of personalised medicine across six priority areas. Within each priority, we will target and concentrate our investment towards key areas where we have the greatest chance of making a step change.

The hospital has some of the largest cohorts of rare disease patients anywhere in the world, giving us an unparalleled opportunity to study these diseases. But focusing on our six priorities does not limit us to discoveries in those areas. The study of rare diseases can progress the understanding of more prevalent diseases that have a wider medical burden, such as obesity and diabetes. Unlocking this invaluable information could help more children and even adults.

PRIORITY: CANCER

Our funding will help pioneer the development of new and kinder treatments for difficult-to-treat childhood cancers. In particular, researchers will focus on the development of personalised treatment approaches for high-risk brain cancers, chemotherapy-resistant leukaemia and relapsed solid tumours that cannot currently be treated.

250
CHILDREN
LOSE THEIR LIVES TO
CANCER
EVERY YEAR IN THE UK

THE SURVIVAL RATE
FOR MORE DIFFICULT-
TO-TREAT CANCERS IS
ONLY ABOUT 40-50
PER CENT (COMPARED
TO 80-90 PER CENT FOR
THOSE CONSIDERED
'EASIER' TO TREAT)

THE PROBLEM

Around 1,600 new cancer cases are diagnosed in children each year in the UK, which represents about four children every day. The most common childhood cancer is leukaemia, followed by cancers of the brain and spinal cord. As a result of investment in research and treatment, survival has increased dramatically, and now more than 75 per cent of children survive for 10 years or more.

However, cancer remains the leading cause of death in children in the UK, with around 250 children losing their lives to the disease every year. The burden of short- and long-term toxicity also remains high. There is an urgent need for more innovative and gentler treatments, especially as the overall number of children surviving cancer in childhood is increasing, meaning more children are living with the long-term effects of their medication.

WHY GOSH?

GOSH is the largest children's cancer unit in the UK and has one of the largest cohorts of childhood cancer patients in the world, meaning it is ideally positioned to make the transformational progress needed in this area.

OUR APPROACH

We want to see improvements in cancer survival and better long-term outcomes, as well as an increase in the number of clinical trials available to children. We will invest in studies that are centred on targeted treatments, such as immunotherapies and innovative 'kinder' treatments to achieve long-lasting clinical responses in patients currently considered incurable.

GOSH will lead on linking clinical outcomes with data about each child's disease, here and across the UK. This data will include information on imaging, genetics and pathology, so that children can be stratified into the most appropriate clinical trial based on the specific characteristics of their disease – a truly precision medicine approach to treatment.

HARRY'S STORY

When Harry's acute lymphoblastic leukaemia (ALL) returned for the second time, further conventional treatment offered little chance of success. Following a landmark clinical trial at GOSH, the future looks very different for the football-loving 10-year-old.

"Making the decision to take part in the clinical trial was easy for us," says Harry's dad, Steve. "We had two options. One was a total dead end, the other – hope. You'd take the second option every time."

Two years later and Harry is still all clear. However, after many years of intense treatments, Harry has developed osteoporosis and currently uses a wheelchair. Research will be vital in ensuring that children in the future have fewer side effects from treatment.



PRIORITY: NEUROSCIENCE

We commit to funding research that will discover new life-changing treatments that target both cognition and muscle function in rare degenerative neuromuscular conditions.

THE PROBLEM

Neuromuscular diseases, including muscular dystrophies and motor neurone diseases, are an unmet health need. More than 100,000 people in the UK are living with untreatable muscle-wasting diseases. There are many subtypes with a wide range of symptoms, from minimal weakness and the progressive loss of muscle function, to severe disability and paralysis, which, in some cases, can lead to premature death.

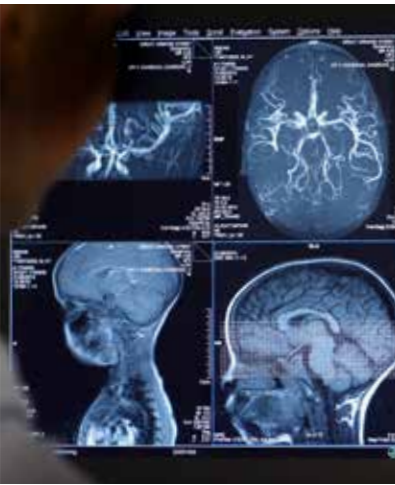
WHY GOSH?

Every year, GOSH treats more than 1,600 patients with these challenging conditions. Diagnosing some of the rare variants of degenerative neuromuscular conditions was extremely difficult even five years ago and there were no therapies available. But thanks to the work of GOSH and the ICH, this is now beginning to change.

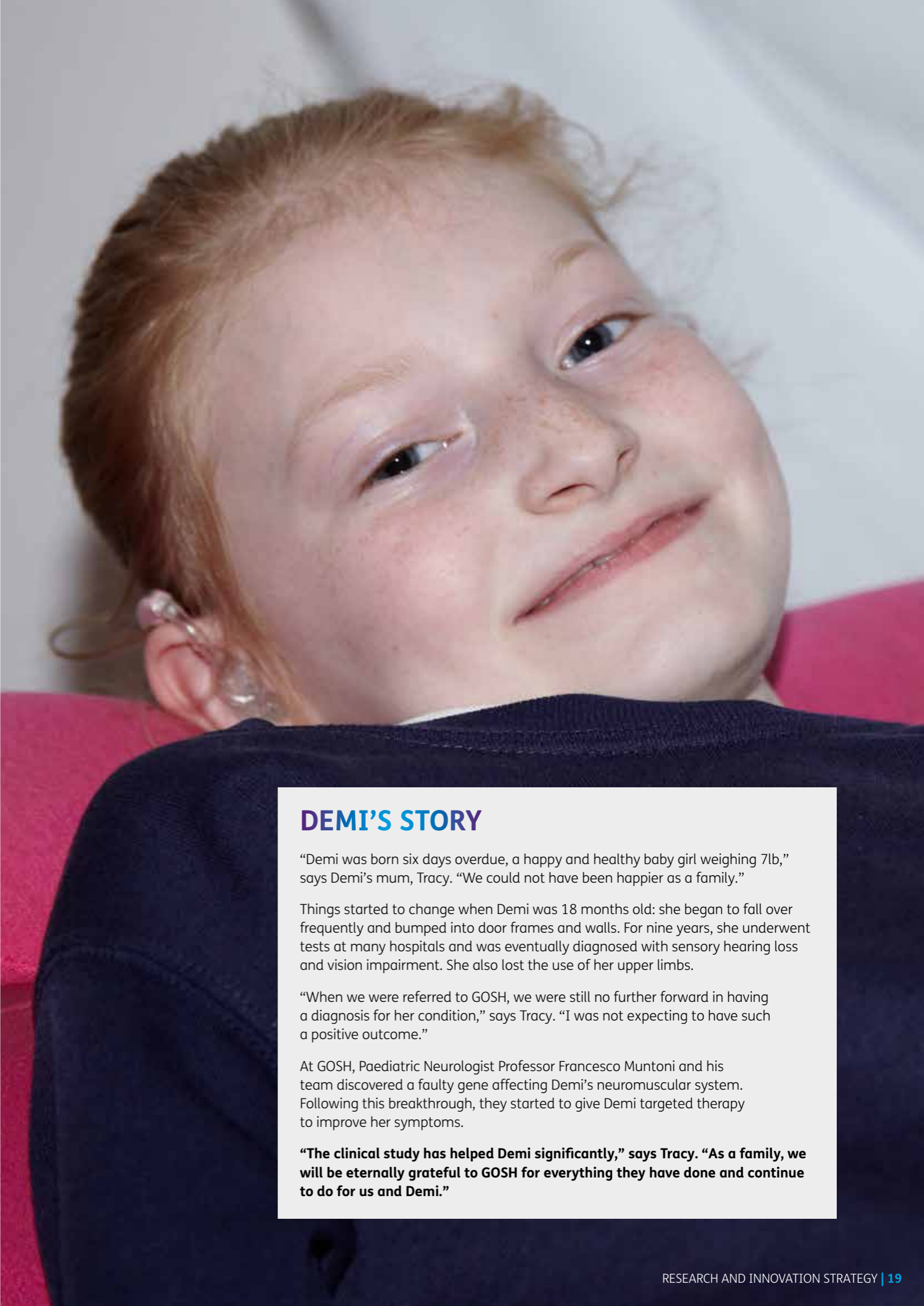
Our ultimate aim is that our funding helps researchers to develop targeted treatments that improve strength, function and overall survival in degenerative neuromuscular conditions.

OUR APPROACH

Our funding will continue to support the accelerated development of novel therapies for neuromuscular conditions by furthering understanding of the genetics of these diseases and increasing the number of new trials that can be offered to children and their families. The development of novel therapies will focus on a new generation of antisense oligonucleotides that can switch off defective genes. These will be far more potent and able to cross the blood-brain barrier, meaning that cognition and muscle and cardiac function can be targeted at the same time. These novel antisense oligonucleotides could also be developed for other conditions for which there is currently no therapy.



MORE THAN
100,000
PEOPLE IN THE UK
ARE LIVING WITH UNTREATABLE
MUSCLE-WASTING DISEASES



DEMI'S STORY

"Demi was born six days overdue, a happy and healthy baby girl weighing 7lb," says Demi's mum, Tracy. "We could not have been happier as a family."

Things started to change when Demi was 18 months old: she began to fall over frequently and bumped into door frames and walls. For nine years, she underwent tests at many hospitals and was eventually diagnosed with sensory hearing loss and vision impairment. She also lost the use of her upper limbs.

"When we were referred to GOSH, we were still no further forward in having a diagnosis for her condition," says Tracy. "I was not expecting to have such a positive outcome."

At GOSH, Paediatric Neurologist Professor Francesco Muntoni and his team discovered a faulty gene affecting Demi's neuromuscular system. Following this breakthrough, they started to give Demi targeted therapy to improve her symptoms.

"The clinical study has helped Demi significantly," says Tracy. "As a family, we will be eternally grateful to GOSH for everything they have done and continue to do for us and Demi."

PRIORITY: INFLAMMATION AND IMMUNITY

We will support curative gene therapy trials for children with rare immunodeficiencies and other disorders, and transformative clinical trials and personalisation of medicine for children with autoimmune diseases – specifically arthritis and juvenile dermatomyositis.

GENE THERAPY: RARE IMMUNODEFICIENCY DISORDERS AND BEYOND

THE PROBLEM

Primary immunodeficiencies are a group of more than 200 different conditions that are estimated to affect around one in 2,000 people. Some forms are so mild they may go unnoticed for years, while other types are severe enough that they are discovered almost as soon as the baby is born.



WHY GOSH?

GOSH and the ICH have led global advances in treating children born with an inability to fight infections by using novel gene therapy approaches. The conventional treatment is a bone marrow transplant, but this does not work for every child. Just over 10 years ago, GOSH became one of the few centres in the world to begin trials of a new form of therapy for children born with rare genetic disorders. Since then, 45 patients have been successfully treated. These trials can be curative with minimal adverse side effects, and dramatically improve the length and quality of life for the child.

Gene therapy has opened a whole new avenue for treatment of other conditions. The focus is now to look at expanding gene therapy beyond its current scope, so that children with other conditions can also benefit from these significant clinical improvements.

OUR APPROACH

Our funding will help drive the refinement of gene therapy techniques so that they can be used to help children with a wider range of life-threatening and life-limiting genetic diseases. This will involve the establishment of five new gene therapy trials, taking the total number of conditions that can be treated up to 10, including a number of metabolic disorders and blood diseases.

OUR AMBITION FOR THE FUTURE IS THAT OUR FUNDING WILL HELP GOSH AND THE ICH TO INCREASE THE NUMBER OF NEW CONDITIONS THAT CAN BE TREATED WITH GENE THERAPY TO MORE THAN 20, OFFERING LIFE-CHANGING TREATMENT APPROACHES TO HUNDREDS OF CHILDREN

NINA'S STORY

Nina was born with severe combined immunodeficiency, a condition caused by a genetic defect that meant she did not have an immune system. She had multiple infections and was placed in isolation to stop her from coming into contact with any more diseases. Nina's future looked uncertain. However, in 2012, Professor Bobby Gaspar

and his team at GOSH and the ICH discussed the potential of using gene therapy to help Nina.

"Nina is testament to what research can do," says Nina's dad, Graeme. "We entered a trial for untested gene therapy – it was a real risk, but we had run out of options."

Now age four, Nina's life has been transformed by the gene therapy programme. "We still come to GOSH for blood tests, and will do until Nina reaches full adulthood, but things are fantastic now," says Graeme. "Nina is so full of life and mischief – she's at preschool and runs around the garden sticking things in her mouth just like any other child!"





JOE'S STORY

"I remember my mum crying when I was diagnosed with JIA," says Joe. "I thought arthritis was just something that old people get. At the time I couldn't walk, play football or go to school."

After his diagnosis, Joe was put on steroids and methotrexate, but the side effects were debilitating.

During a trip to GOSH, Joe and his family were made aware of a new clinical trial. "It was a bit daunting at first," he says, "but the alternative involved having an injection every day, so I was eager to try this new option!"

"I started the new trial and the difference the drug has made to my life is amazing. Beforehand, I could barely walk. Now, I hardly notice I've got arthritis."

"The doctors, nurses and researchers at GOSH have made such a difference. Without them working hard to develop these new drugs and treatments, my life would be very different to how it is now."

JUVENILE IDIOPATHIC ARTHRITIS AND JUVENILE DERMATOMYOSITIS

THE PROBLEM

Thanks to research, juvenile idiopathic arthritis (JIA) is a more manageable disease, but flare-ups can result in painful, swollen and stiff joints, infections, periods of stress, low mood and tiredness. Importantly, some children do not respond to the medicines currently available, and experience active JIA for many years.

Juvenile dermatomyositis (JDM) is a rare and serious condition that results in muscle pain, weakness and skin rashes, and can eventually damage the lungs, brain and bowel. In some cases, it can even be fatal.

WHY GOSH?

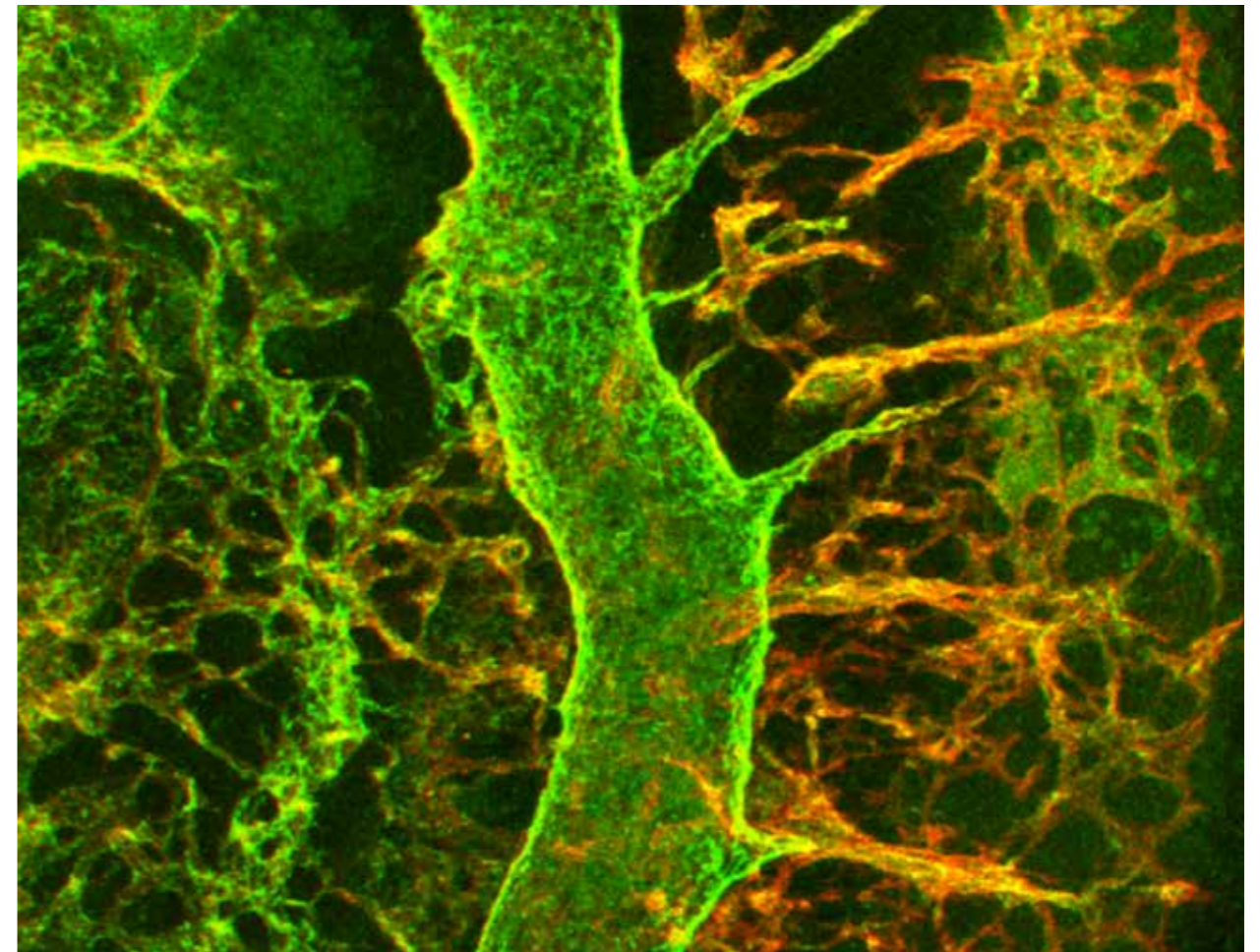
There is an urgent need to do more and GOSH is extremely well positioned to do this, with the largest cohorts of JIA (more than 1,200 children) and JDM (more than 525 children) in the world.

OUR APPROACH

Precision medicine is the key to improving the outlook for these children and there is a need to deliver more new trials more quickly. We know we can't wait for or follow the path of adult trials – children need a bespoke approach. There's also the possibility that some new drugs might actually be more efficient in children than in adults. We want to avoid any unnecessary delays by funding the development of personalised medicines for children and adolescents with arthritis, particularly in areas where current treatments are ineffective.

WE HAVE THE
LARGEST COHORTS
FOR JIA AND JDM
IN THE
WORLD

PRECISION MEDICINE IS THE KEY TO IMPROVING THE OUTLOOK FOR THESE CHILDREN AND THERE IS A NEED TO DELIVER MORE NEW TRIALS MORE QUICKLY



PRIORITY: RECONSTRUCTIVE, REGENERATIVE AND DEVELOPMENT

We commit to funding new, groundbreaking reconstructive and regenerative treatments for birth defects in utero and once the child is born. Furthermore, we will fund pioneering rejection-free organ transplants grown from patients’ own cells.

THERE ARE MORE THAN 4,000 TYPES OF BIRTH DEFECTS

THE PROBLEM

Birth defects are one of the major causes of infant mortality and childhood disability in the Western world, with one in every 40 pregnancies in Europe affected. There are more than 4,000 types – some monogenic and others multi-factorial, involving many genes and environmental influences.

WHY GOSH?

Children with rare congenital malformations are often referred to GOSH. The team at GOSH and the ICH has a strong international reputation for regenerative medicine and creating a translational environment for tissue engineering. They are also well regarded in preventing developmental disorders (eg the use of folic acid in pregnancy). As a result of the large number of patients who are treated by the teams at the hospital, and the growing momentum in this research area, GOSH and the ICH are uniquely placed to improve outcomes for children with birth defects, where there is such a desperate need.

OUR APPROACH

An area which we wish to support is early intervention — performing procedures or delivering treatment in utero, such as surgery for spina bifida. There is even the possibility of delivering gene or stem cell therapies to the foetus before birth.

We will also continue to invest in the innovative development of methods for producing induced pluripotent stem cells (iPSC) from patients’ own cells. This will help researchers to understand how faulty genes disrupt cellular processes to cause disease. iPSC research will reveal how these genetic faults may be corrected using new gene editing CRISPR/Cas9 technology. Ultimately, we want to enable the development of new preventative or curative small molecule treatments.



CIARAN’S STORY

Ciaran was born with long-segment tracheal stenosis, which caused a severe narrowing of his trachea. On the day he was born, his lungs collapsed and he was rushed to GOSH.

At six days old, Ciaran underwent major surgery. Then, when he was two-and-a-half, the metal stent that had been placed in his trachea began to erode

into his aorta, causing severe bleeding. Although Ciaran bounced back, he continued to experience complications until, in March 2010, he underwent a groundbreaking procedure.

Surgeons used Ciaran’s own stem cells to repopulate a donor trachea, which minimised the likelihood of rejection. “Ciaran was the first child in the world

to undergo a tracheal transplant like this,” say Ciaran’s mum and dad, Colleen and Paul. “His recovery in hospital was a total rollercoaster. It took a long time, but we finally got him home.

“It’s been a few years now, but Ciaran is still breathing normally on his own and he’s back at school living a normal life.”

PRIORITY: ENDOCRINE AND METABOLIC

We will support the development of a new platform of gene therapy for rare inherited metabolic conditions. This will include the establishment of new clinical trials for diseases where there is currently no treatment. In the longer-term, we aim to fund other pioneering treatment approaches, such as rejection-free organ transplants.

THE PROBLEM

Children with inherited metabolic disorders have gene faults that lead to the failure of critical chemical reactions and result in discrepancies in the body's normal functioning. This can lead to dangerous imbalances of chemicals and ultimately results in organ damage and disabilities.

Inherited metabolic diseases are rare but because there are hundreds of different types they are collectively common. Around two children are born with these conditions every day in the UK.

WHY GOSH?

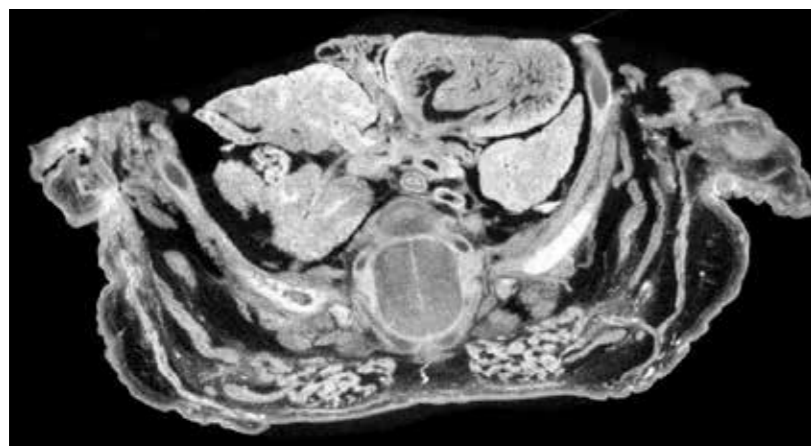
GOSH has one of the largest patient populations for metabolic conditions in the world. They can be difficult to diagnose, are often serious, and result in damage to organs and progressive brain degeneration. A smaller number are less serious but still require lifelong management through diet and medication. Early diagnosis through newborn screening and the development of novel treatment approaches is essential to ensure the best outcome for as many children as possible. We are committed to advancing this progress.

OUR APPROACH

GOSH is about to start the first gene therapy trials in the world using the adeno-associated virus (AAV) vector system to deliver the gene. Over the next five years, our support will aim to ensure that at least three new trials will be available for children with inherited metabolic diseases.

In addition, we will commit funding to exploring the potential of stem cell biology and the regeneration of organs, such as the liver. The enzymatic basis of many of these conditions means that the liver is often affected and could be amenable to regenerative techniques.

We want to focus efforts on funding the development of a new platform of gene therapy. This has the potential to be completely transformative for patients, offering them treatments that are life-saving, rather than life-prolonging or life-improving.



STANLEY'S STORY

In 2014, Stanley was diagnosed with Sanfilippo syndrome, a rare genetic metabolic disorder. "When we were given the diagnosis, we looked on the internet and found out about the research that was happening and different clinical trials which may help to treat Sanfilippo," says Stanley's mum, Mari. "We decided that the enzyme replacement therapy trial was the right one for Stanley."

"We're now six months into the trial and we're sure we made the right decision. Coming up to GOSH has become part of our family routine. When we were given the diagnosis, we had no hope. Now we have something to look forward to."



PRIORITY: CARDIOVASCULAR

For children with congenital heart disease and heart failure, we want to fund innovative and better treatments, new devices and implants, and new and better ways of investigation – such as advanced imaging – that are personalised for each individual child’s heart.

THE PROBLEM

Less invasive treatments would avoid the need for open-heart surgery, meaning shorter hospital stays and day-case procedures. Children with heart failure often do not survive unless they receive a heart transplant, but many do not get the new heart they need. As many as three out of 10 children will die waiting for a heart transplant. Developing new ways to support the heart with devices and/or stem cell treatments to boost the heart’s own recovery could hold the key to offering more children the chance of a brighter future, without the need for cardiac transplantation.

WHY GOSH?

GOSH is one of the largest hospitals in Europe for treating complex cases of congenital heart defects. It is one of the largest centres for treating paediatric heart transplantation and heart failure in the world. Every year, GOSH carries out open-heart surgery in more than 700 patients and sees more than 5,000 children with serious heart conditions.

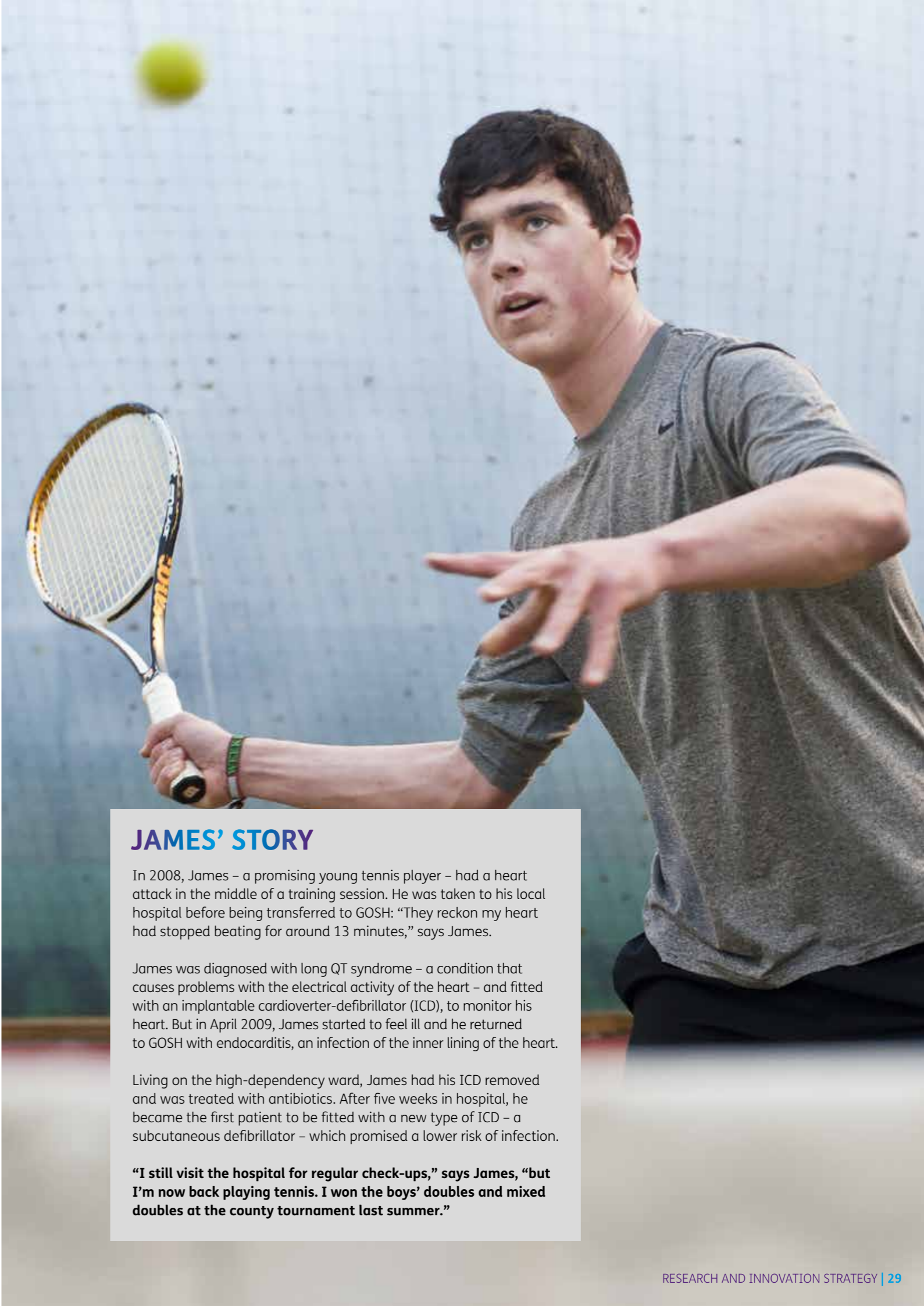
OUR APPROACH

We want to invest in a new era of patient-specific and predictive medicine, in which treatment options are tailored for the shape of each individual child’s heart. The focus will be on:

- Novel ways of designing and evaluating cardiovascular devices.
- Improving and refining imaging techniques.
- Developing new ways of supporting a failing heart.
- Monitoring long-term outcomes to determine which treatments work best and offer the greatest quality of life.

We want to ensure the development of patient-specific valves and devices that can be modelled in a virtual environment to test their suitability before surgery. We will invest in technology that is providing new ways of supporting a failing heart, including the use of stem cells, and also in miniaturised medical pumps that will mean younger children with heart failure can be supported for longer at home, and may even be able to return to school.

EVERY YEAR,
GOSH
CARRIES OUT
OPEN-HEART
SURGERY
IN MORE THAN
700
PATIENTS



JAMES’ STORY

In 2008, James – a promising young tennis player – had a heart attack in the middle of a training session. He was taken to his local hospital before being transferred to GOSH: “They reckon my heart had stopped beating for around 13 minutes,” says James.

James was diagnosed with long QT syndrome – a condition that causes problems with the electrical activity of the heart – and fitted with an implantable cardioverter-defibrillator (ICD), to monitor his heart. But in April 2009, James started to feel ill and he returned to GOSH with endocarditis, an infection of the inner lining of the heart.

Living on the high-dependency ward, James had his ICD removed and was treated with antibiotics. After five weeks in hospital, he became the first patient to be fitted with a new type of ICD – a subcutaneous defibrillator – which promised a lower risk of infection.

“I still visit the hospital for regular check-ups,” says James, “but I’m now back playing tennis. I won the boys’ doubles and mixed doubles at the county tournament last summer.”

EVALUATING OUR IMPACT

Our work is only possible thanks to the generosity of our supporters and donors. That’s why we place a high priority on the proper evaluation of our investments. Through our research strategy, we are seeking to achieve a measurable impact on the outcomes of children with rare and complex conditions. This will be central in our approach towards evaluation.

Implementation and monitoring of the research strategy, and ongoing evaluation of its success, will be monitored by the charity’s Research Strategy Advisory Board, Research Assessment Panel and Board of Trustees. This will include an annual evaluation and a more comprehensive evaluation at three years. The information will be used to refine our approach and provide an evidence base for future strategic decision-making, which will improve the likelihood of the strategy’s overall success.

Evaluation will show a clear path of how investment in a particular priority area or funding scheme is improving outcomes for patients against one or more of our organisational ‘impact’ goals:

- **treating more patients**
- **improved patient experience**
- **improved family experience**
- **improved patient outcomes**

Evaluation will be realised through the establishment of success metrics that are both scheme and priority specific, that clearly demonstrate the difference that charitable funding is making, and that provide accountability to our donors.

“If we all come together behind this research strategy, I believe we have real potential to reveal the answers to some of the most challenging questions in rare and complex childhood disease research by harnessing new technology to benefit children and the adults they will become worldwide.”

Professor Stephen Holgate
Chair of Great Ormond Street Hospital Children’s Charity’s Research Strategy Advisory Board

To develop our strategy, we canvassed the opinions of more than 200 members of the paediatric research and clinical community at local, national and international levels. We are hugely grateful for the time and insight from those who participated. Their invaluable contributions have helped to shape our research strategy and ambition.

RESEARCH STRATEGY ADVISORY BOARD

Professor Stephen Holgate (Chair)
(Chair of Great Ormond Street Hospital Children’s Charity Research Assessment Panel)

Dr Peter Steer
(GOSH Chief Executive)

Professor Rosalind Smyth
(ICH Director)

Professor David Goldblatt
(GOSH Director of Research and Development, ICH Deputy Director)

Professor David Lomas
(UCL Vice Provost for Health)

Dr Diana Dunstan
(Great Ormond Street Hospital Children’s Charity Trustee)

Mr Tim Johnson
(Great Ormond Street Hospital Children’s Charity Chief Executive)

Dr Kiki Syrad
(Great Ormond Street Hospital Children’s Charity Deputy Director of Grants)

Dr Ali Momin
(Great Ormond Street Hospital Children’s Charity Senior Grants Manager)

TOGETHER WE CAN MAKE A DIFFERENCE

We believe that now is the time to move paediatric research to the next level – the next major breakthroughs are in sight and the results will be personalised. But it’s a big and ambitious challenge, and we can’t do it alone. We hope you will stand with us and believe in this strategy as much as we do.

If we work together, we will make the best progress possible for the children who are relying on us.

“For more than 160 years, our clinicians and researchers have built an extraordinary platform to develop new treatments and find cures for children with complex and rare diseases. This strategy is crucial to continuing and expanding on this tradition.”

Dr Peter Steer
Chief Executive, Great Ormond Street Hospital

“With the continued support of the charity and the wider academic community, we hope our seamless and joined-up approach will unlock the vital breakthroughs of the future.”

Professor Rosalind Smyth
Director, UCL Great Ormond Street Institute of Child Health

**Great Ormond Street
Hospital Children's Charity**
40 Bernard Street
London WC1N 1LE
020 3841 3131
gosh.org