Great Ormond Street Hospital:

A Pioneer in Research

Research Hospital

As Deputy Director of Research and Innovation at Great Ormond Street Hospital (GOSH) I know how much of a priority research is here. We know that patients treated at hospitals that carry out research have better outcomes – they have more confidence in their care, they feel more informed and they tend to survive longer.

At GOSH we connect multi–disciplinary teams of healthcare professionals and scientists to improve the lives of children with rare and complex diseases. Our dedicated staff are often researchers themselves and we have more than 500 active research projects underway at any one time.

Underpinning all research at GOSH is the National Institute for Health Research Biomedical Research Centre (NIHR GOSH BRC), the only centre of its kind in the UK that specialises in child health research. Heading four major themes (Genomics, Gene, stem and cell therapies, Novel therapies, and Structural malformation and tissue damage), much of the research you are about to read about is spear-headed by BRC leaders.

GOSH is also home to the Zayed Centre for Research into Rare Disease in Children, bringing together pioneering research and world-leading clinical care under one roof to drive impact from lab bench to a child's bedside. The Centre is also Europe's largest academic facility dedicated to cell and gene therapy.

Our NIHR Clinical Research Facility provides specialist day care accommodation for children and young people taking part in clinical research studies. This state–of–the–art facility is also available to all staff undertaking clinical research, in particular early phase and experimental medical trials, where teams investigate the safety and effectiveness of new treatments in small groups of patients.

Successful research that starts in this facility eventually becomes integrated into the wider hospital translating seamlessly into benefits for patients .

But we know we do not do this alone.

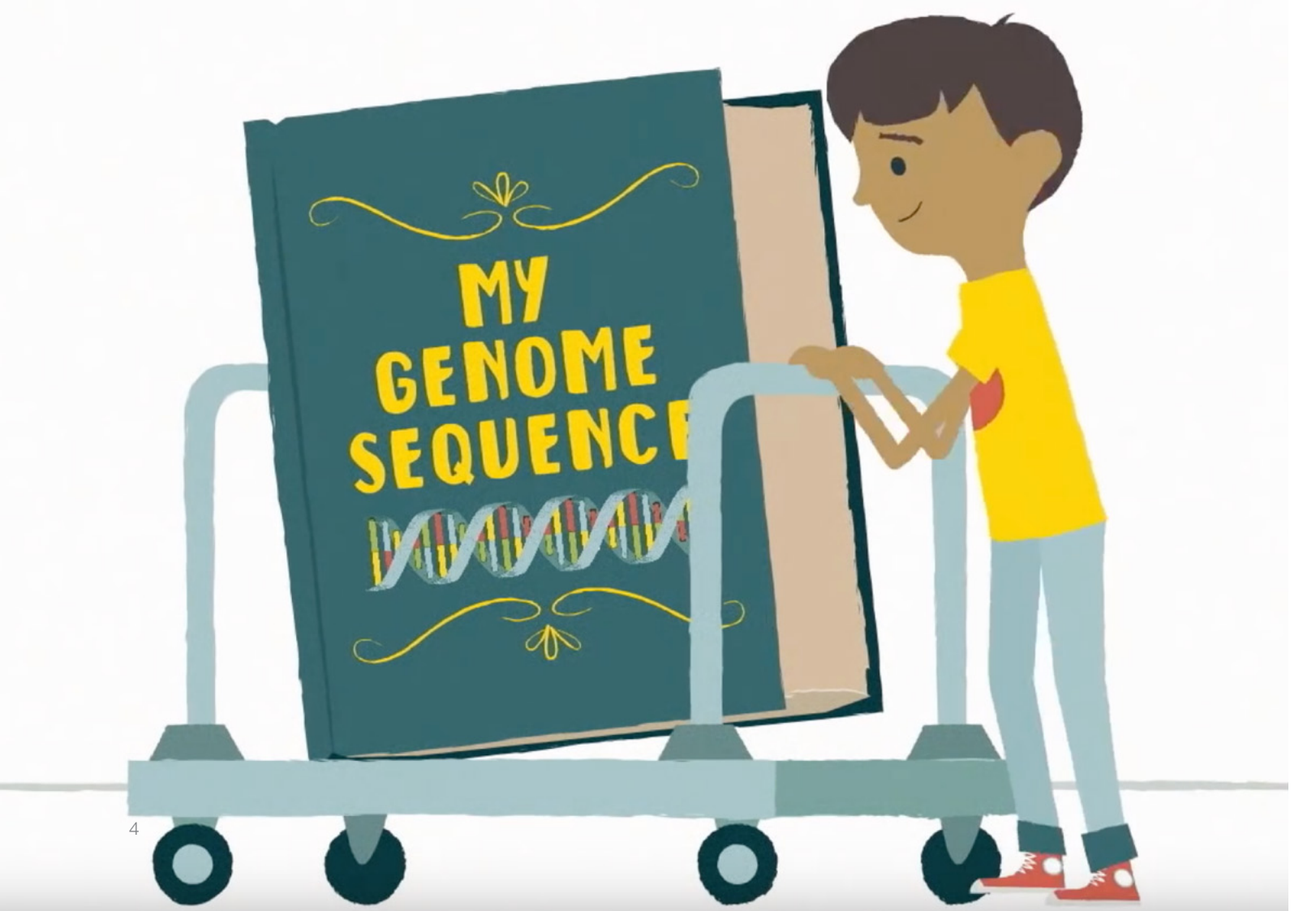
We work closely with Great Ormond Street Hospital Children's Charity (GOSH Charity) and the UCL Great Ormond Street Institute of Child Health (UCL GOS ICH) to develop cutting–edge research. We collaborate with national and international hospitals and research institutes across the world to share expertise as quickly and broadly as possible, including within the NHS in the UK.

Wherever possible, we involve our patients, families and members of the public in our research design – high quality research depends on listening to lived experiences, priorities and perspectives. This process of joint working is vital to how we design and carry out research.

We are focused on embedding research into everything we do, aiming to offer participation in research to every patient, and better understanding of our research to every staff member and volunteer – making GOSH a true Research Hospital.

Throughout this guide we'll be introducing you to just some of the incredible GOSH staff that make research possible.

Dr Jenny Rivers
Deputy Director of Research and Innovation



Genomics

Our genome is made from DNA - the code of life that makes us what we are.

Whether we're talking about people, insects or viruses, we all have our own individual genomes, which are different to each other. Modern genomic sequencing now allows us to examine genomes and identify changes, known as variants, which can be linked to different features. For example, if we have blue eyes, are predisposed to a certain condition or if a particular virus is more dangerous to humans.

GOSH is a world–leader in genomics, delivering research, supporting care by guiding treatment, and working with national and international partners to find answers hidden in our genetic code.

In 2012, the UK Government launched the 100,000 Genomes Project. This was an initiative that aimed to sequence 100,000 genomes from families with a rare condition or cancer in order to better understand their conditions. GOSH recruited around 2,000 children with a rare condition and their family members. GOSH also leads the North Thames Genomic Medicine Centre, a consortium of hospitals in the local area, which ultimately recruited 28% of all participants with a rare disease in the project. Recruitment ended in 2018 and the research is already bearing fruit with some of our patients receiving new diagnoses. Others have seen their prognoses improve dramatically, from taking less toxic cancer medication to understanding more about their condition.

"While we are rightly proud of our huge contribution to the 100,000 Genome Project, our involvement goes way beyond recruitment. We took this opportunity to examine the views of people being offered genomic sequencing by speaking to them to understand and improve the consent process. Almost immediately, we found that genomic sequencing was hard to explain and therefore poorly understood. By working closely with the GOSH Young Persons' Advisory Group for Research (YPAG) and local schools we developed animations that answered questions of young people."

Professor Lyn Chitty
GOSH Consultant, Lead of the NIHR GOSH BRC Genomics Theme and Medical Director of the North Thames Genomic Medicine Centre

Genomics research is also allowing us to help children, even before they are born.

If a parent has a gene for a genetic condition, we sometimes need to test their unborn baby's genetic material, their DNA. This is usually done by putting a needle into the womb to sample the placenta (chorionic villus sampling) or amniotic fluid (amniocentesis) – but both have a small miscarriage risk.

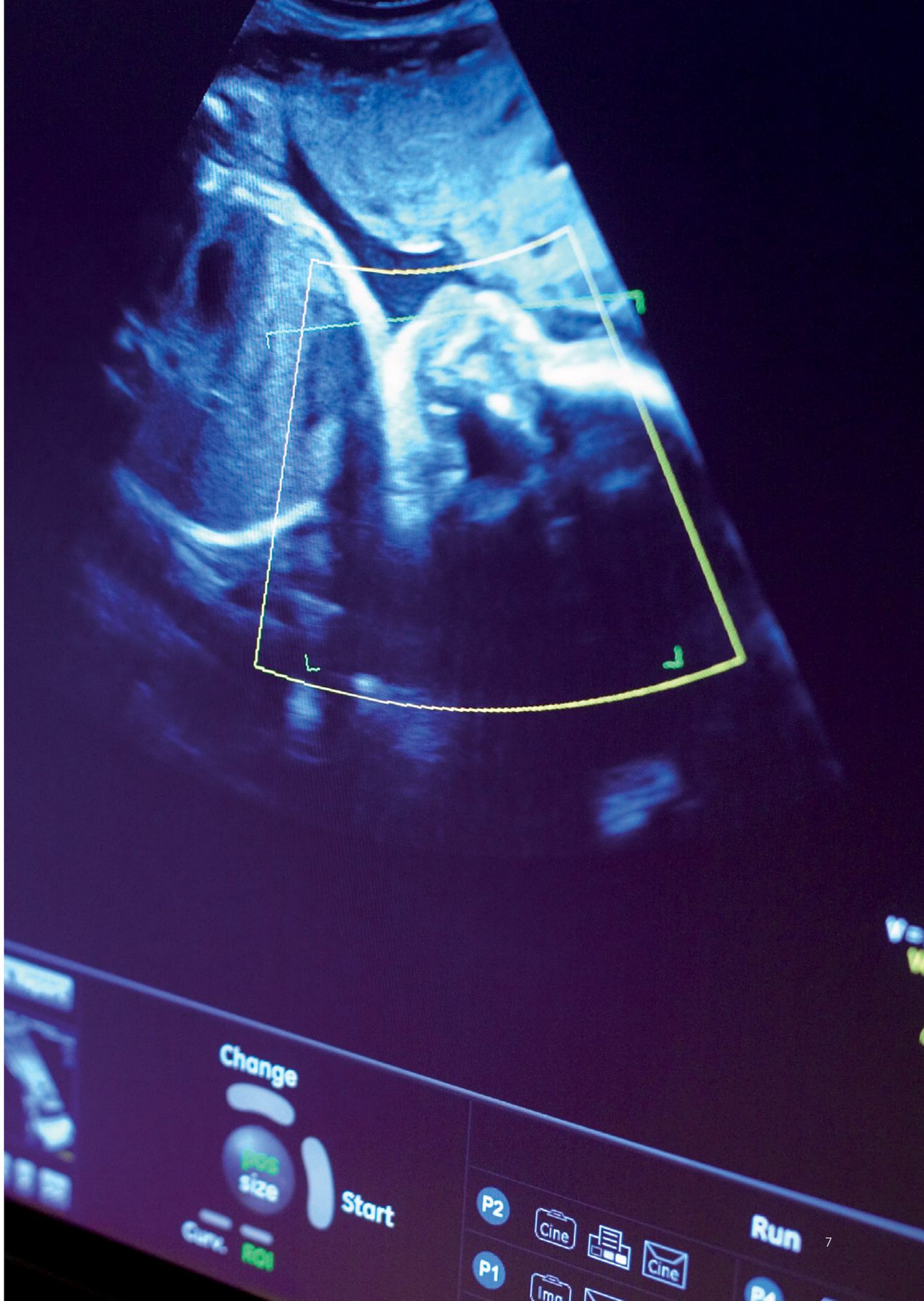
Using sophisticated genomic techniques and careful analysis, GOSH researchers have developed tests to analyse the DNA of a baby in the womb from a simple test of the mother's blood. This Non–Invasive Prenatal Diagnosis (NIPD) presents a safer option for parents to find out about the health of their baby and has led to a rise in families seeking out such information. This allows support to be offered much earlier, to all involved.

Our research has also helped speed up the results of genomic testing, whether during pregnancy or after birth. This allows us to intervene as early as possible, so families are not waiting on a long diagnosis before treatment can begin. These studies have helped NHS England include rapid genomic sequencing and NIPD in the National Genomic Test Directory (the register of approved genomic tests for NHS use) so everyone in England can access these tests if needed, while GOSH also offers genomic services to patients around the world.

Over the coming years, researchers will be looking at how these new tests are being used across the country and what patients and health professionals need to make sure everyone who may benefit has access to, and understands, these tests.

Genomics to tackle a global pandemic

Sequencing DNA of organisms like viruses and bacteria can have a huge impact on how we track infections and treat patients. For example, during the COVID–19 pandemic, GOSH expertise was essential to the development of fast methods to sequence the whole SARS–CoV–2 viral genome, the virus responsible for COVID–19. Through a programme of work led by Professor Judith Breuer, in close collaboration with research groups across the UK, this has allowed teams to track the virus in London, support the Government to manage the pandemic and change the way viral infections are treated – all by studying the genome of the virus.



Gene therapy

20 years ago, GOSH pioneered the development of stem cell gene therapy, paving the way for research, clinical trials and gene therapy to become available in the NHS for a number of rare diseases with a genetic cause.

Gene therapy involves altering the genes inside your body's cells to stop or treat disease. For example, it can include adding a working copy of a faulty gene or 'switching off' a gene that causes disease. The aim is to 'fix' whatever condition is being caused by faulty or missing genes. But it is a tricky science. Early trials of gene therapy appeared to cure the conditions they were targeting but some had the serious side effect of causing leukaemia. Even with this serious potential side effect, some families still chose to have the treatment, but our researchers did not stand still.

For the last two decades, we have been working with national and international collaborators dedicated to improving gene therapy's delivery system – the 'viral vector'. By using different types of virus to deliver the gene therapy, we have treated patients born without an immune system, children with degenerative muscle conditions and children who are losing their sight – all due to genetic conditions – without the risk of leukaemic side effects. Gene therapy research at GOSH is life changing and life–saving.

Sarah's story

One child treated under a gene therapy research programme at GOSH, led by Mahboubian Professor Claire Booth, Deputy Lead of the NIHR GOSH BRC Gene, stem and cell therapies Theme, was Sarah from South Yorkshire. She was less than ten days old when her mum Maria became concerned about her daughter's weight loss and sore, bleeding nappy rash that wouldn't heal. Tests revealed Sarah had ADA–SCID – a rare immunodeficiency that meant she had no working immune system. Maria says:

"I remember the exact time I saw the paper that had the blood test results on and the diagnosis. I saw it was SCID and I was incredibly upset... I wasn't allowed to kiss my daughter or sleep next to her. Everything had to be highly sterilised to keep her safe. It was horrible to not be able to do normal things with my own daughter."

Sarah was referred to us for gene therapy and several years after her treatment is doing very well. Maria adds:

"Six months after she was given the gene therapy her skin was clean and healthy and the other symptoms got a lot better. She's doing so well now and does all the things you'd expect for a child of her age."

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While there are some conditions that we can now treat with gene therapy, others are still waiting while our teams work tirelessly to find a treatment or even a cure.

Professor Manju Kurian discovered a rare condition called Dopamine Transporter Deficiency Syndrome (DTDS) when she was getting her PhD. Previously doctors thought it was a form of cerebral palsy but her work showed it was caused by a single faulty gene. Children with DTDS are rarely able to learn to walk or speak. As they grow, they develop 'parkinsonism' – so called because of similarities to Parkinson's Disease. This includes slow movements, involuntary twisting postures of their arms and legs and whole–body stiffness.

There are currently no effective treatments or a cure and most children with DTDS sadly die before reaching adulthood, often from respiratory infections or other complications.

But in 2021, using a mix of laboratory tests and animal studies, Professor Kurian, working closely with colleagues at the UCL GOS ICH, was able to cure mice with DTDS. She was also able to use the cutting–edge facilities of the Zayed Centre for Research to grow human brain cells with DTDS – so–called 'brain in a dish' – and cure them of the condition. She'll soon be applying to start a clinical trial that will offer hope of a treatment for DTDS and other degenerative brain disorders like it.

Cancer

We've come a long way in treating children's cancers but it remains the leading cause of death in children aged five to 14. Four or more children die from cancer each week in the UK*.

GOSH treats children with the rarest and most complex types of cancer. Some have exhausted their treatment options and are facing the most heart–breaking of outcomes.

Many children with cancer at GOSH are on clinical trials as they desperately need new treatments. Researchers at the hospital are working on ground–breaking scientific ideas to make these treatments a reality.

With some of the rarest cancers affecting only a few children a year, it's vital our teams work together to gather data and understanding from as many patients as possible. There are incredible systems in place across the globe making it easier than ever for doctors and scientists to connect and share knowledge.

Advances in genomic sequencing are not only helping us to understand a person's genome, instead we can now also understand the genetic makeup of cancers. A UK-wide collaborative study called Stratified Medicine Paediatrics – led from the Institute of Cancer Research – has been sequencing all childhood relapse cancers and, via a National board led by Professor Darren Hargrave at GOSH, feeds back this genetic information to clinicians all over the UK. This allows a targeted therapies approach, with several led by Professor Hargrave showing early promise in paediatric brain tumours.

Drug repurposing

Developing completely new drugs is an expensive and time–consuming process, so researchers at GOSH are also working to understand if there are drugs that are already approved for other conditions that could be used to treat cancer. This is known as drug repurposing. The team, led by Professor Owen Williams, are just one group working on a different approach. They have already shown that mebendazole, a drug originally prescribed to treat parasitic worms, shows promise in treating children with acute lymphoblastic leukemia.

GOSH has big ambitions for cancer research. This includes creating state of the art facilities which we hope will be a national resource that offers holistic, personalised and co-ordinated care to children with rare and difficult-to-treat cancers.

"A decade ago, our primary diagnostic tool for cancer was looking at the cells under a microscope. Genetics is revolutionising the way we diagnose and treat these and other diseases. Studies have shown that for virtually every 'type' of cancer, there are many sub types, each with different genetic characteristics. That's telling us incredibly valuable things about which existing treatments are likely to work for which types, as well as giving us new ideas for treatments."

Professor Darren Hargrave
Consultant Paediatric Oncologist

*www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers#heading-One

Image used with permission: Guilhem Baker, The Times

Ayaan's story

Ayaan was diagnosed with acute myeloid leukaemia (AML) in 2020 after becoming unwell with a fever, unexplained bouts of exhaustion, and a lack of appetite. Her family were told she had a 60 per cent chance of survival but, after advanced genomic testing, the Genomics Laboratory Hub based at GOSH found a gene that was associated with a different cancer, acute promyelocytic leukaemia (APL). This changed things drastically for the family. The new diagnosis called for less intensive treatment, so she could be at home with her family, and APL has a long-term survival rate of more than 90 per cent.

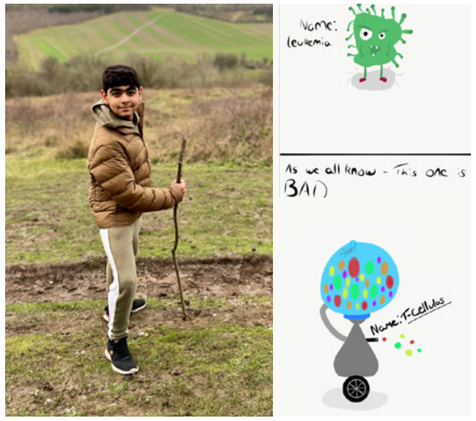
CAR-T cell therapy

One particular area of interest at GOSH is utilising the body's own immune cells – T cells – to fight cancer. T cells are specialised immune cells that patrol our body, seeking and clearing up cells that are infected, for example, with a virus. But cancer cells can go unnoticed as they often look very similar to healthy cells. To use T cells as a cancer treatment, we reprogramme them with a cancer 'detector' called chimeric antigen receptor, or CAR for short. The CAR enables T cells to spot cancer cells and spring into action, directly destroying cancer cells and alerting other immune cells of the cancer threat.

Yuvan was the first person to receive Kymriah - a type of CAR-T cell therapy, in the NHS, to treat his leukaemia at GOSH when he was just 11 in 2010. Yuvan said:

"I remember a few flashes of this time at GOSH, like talking to the consultants and some of the good news we received but it's mostly a blur. To anyone else undergoing this kind of research treatment, I'd advise them to keep calm: Just let the hospital teams work their wonders and hang tight.

I worked with the team in the Young Person's Advisory Group for Research to design a game to help children to understand more about leukaemia and treatments in a fun and interactive way. It's really important how the hospital involves children and young people in their research design."



Years later, Yuvan is doing well

While promising for some forms of childhood cancer, CAR–T cell therapy can lead to life–threatening side effects and the cancer often returns as the treated T cells disappear from the body. Furthermore, obtaining children's cells and returning them requires harsh, invasive procedures that some children simply aren't well enough for.

Our research is tackling these issues head on.

For example, in blood cancers like acute lymphoblastic leukaemia (ALL) Professor Persis Amrolia and his team, in a project part–funded by GOSH Charity, have developed a new CAR molecule that can bind more rapidly to the cancer cells and remove them, reducing side–effects and improving cancer symptoms. They're working out why CAR–T cells last longer for some patients and not others (important because loss of CAR–T cells means the treatment doesn't work), how they can make CAR–T cells persist in the body and have found that a special group of T cells are essential for destroying cancer cells. In parallel, Professor Waseem Qasim and his team are leading research that uses 'off–the–shelf' CAR–T cells that work for anyone, so children don't need to go through all the harsh measures to remove their cells.

Research at GOSH is also working to tackle cancers with solid tumours, particularly neuroblastoma, a cancer that comes from the nervous system outside the brain. A team led by Dr Karin Straathof, part–funded by GOSH Charity, developed a special CAR that instructs T cells to recognise a protein present only on the surface of neuroblastoma cancer cells. They've shown this works, leaving healthy cells untouched, and now plan to start a clinical trial of CAR–T cell therapy for children with neuroblastoma who aren't responding to standard treatments. GOSH teams are also now working towards developing CAR–T cell therapy for tumours inside the brain, as part of a clinical trial.

Intensive care research

As a specialist hospital, GOSH doesn't have an Accident & Emergency department but this doesn't mean that children here are not in need of urgent care.

For those in immediate need, there is a specialist team of intensive care professionals who lead research and incorporate new findings into their work in innovative ways. The team includes doctors, nurses, data managers, physiotherapists, pharmacists, psychologists, dietitians and mathematicians, to name just a few.

Intensive care covers all manner of conditions, diseases and specialties. Whether caring for a child after a heart transplant or providing support to a child receiving experimental gene therapy, researchers in intensive care must try and find the interventions that can make a difference in a group of patients that may seem to have nothing in common beyond the severity of their need.

Due to the nature of this work, intensive care research often spans across hospitals, across the UK and across international borders – a true team effort to recruit large numbers of patients through multiple hospitals and study sites. We have played a major leadership and recruitment role in international paediatric intensive care trials for many years.

Intensive care, by its very name, may suggest that all patients need intensive treatment, all of the time. But ongoing research at GOSH is starting to uncover how being more gentle with our treatments can improve recovery, benefitting patients and creating a more effective and efficient ward.

For example, the Oxy–PICU trial, led by Dr Mark Peters, is looking at how patients may benefit from using less extra oxygen for breathing. Getting this right could have implications across healthcare, as patients receive oxygen in many settings and could be beneficial in locations where oxygen is in short supply.

In another collaborative project called SANDWICH, led from Queen's Hospital in Belfast, the team has looked at how best to help bring patients off sedation and pain relief. They found that a structured approach, centred around nurse–led care, is the best way to support children to come off ventilation. Within months, the recommendations from this study were already in place in two–thirds of UK paediatric intensive care units – immediately benefitting children in need.

The research team are also interested in how they can improve the long–term outcomes of their patients and recently led a study by Dr Kate Brown that looked at complications for children after heart surgery. This gives much better support and a deeper understanding than merely looking at survival.

"As a research team here at GOSH, we worked incredibly hard to recruit patients to the SANDWICH study, which demonstrated the importance of bedside nursing input for reducing ventilator hours.

Managing a study like this across three busy ICUs is very complex and requires a lot of resource from everyone. However, to see the positive outcome for the patients at the end of the study made it very worthwhile!"

Lauran O'Neill
Critical Care Research Nurse

Nursing staff on the Paediatric Intensive Care Unit

A responsive and embedded team

Due to the agile nature of the intensive care team at GOSH, in 2020 they were able to support intensive care research into the SARS–CoV–2 virus, working on urgent national and international public health studies on patients hospitalised with coronavirus–related illness, and looking for biomarkers to work out who might be most affected.

The Unit
Every child that is admitted to the intensive care unit at GOSH is carefully screened to see if there is a research programme they could benefit from and, with the advent of digital technology and the close involvement of the Children's Acute Transport Service (CATS) in research, this sometimes happens before the children make it through our doors.

Once at the hospital, the intensive care research team is physically based on the intensive care unit, allowing research best practice and training to inform and improve a child's care at any time, day or night.

Under the expert care of often nurse–led teams, we are changing paediatric intensive care practice.

Imaging

Children come to GOSH with rare and complex conditions. Sometimes asking them and their families questions and carrying out tests simply can't give the answers healthcare teams need, and we need to take a look inside their body to see if we can work out what is going on. For this, GOSH has a host of options that can look 'inside' the body called imaging.

Imaging encompasses a range of different techniques, from X–rays for looking at broken bones to Magnetic Resonance Imaging (MRI) for examining the brain and ultrasound for examining the abdomen. Most children in our care require a scan as part of their clinical care and most research trials require imaging to see whether treatment is working. But Radiology at GOSH is now a world–leader in its own research.

For example, Radiographer Dr Ian Simcock has shown how to use non–invasive imaging to help families following miscarriage and still birth, a painful topic that can sometimes be overlooked. To find answers, families are usually offered an autopsy but, in most cases, this requires an incision in their child that some feel is just too much to consider. To address this, the team has developed imaging techniques to perform an examination without incisions. In their experience, imaging like this can give answers to around half of the families who choose this method, which is similar to a full autopsy. GOSH uniquely offers an Imaging Autopsy (or Non–invasive autopsy) to parents of children of all age ranges – from babies all the way up to older teenagers who have sadly died.

Non–invasive imaging research is also shedding light on how to best look after children who have broken bones or suffered suspected abuse and give them the best care. Children's fractures are hard to spot, are different to adult fractures and what sometimes looks like a fracture may actually just be a child's growing bone. A new research project led by Radiologist Dr Susan Shelmerdine, and working with the GOSH Young Person's Advisory Group for Research, is studying whether artificial intelligence can help find fractures so that patients receive the best care at the right time. This will allow children's radiologists around the country to access the best healthcare, even when they don't have immediate access to specialist centres.

"Paediatric radiologists have expert knowledge to help them spot fractures in children quickly and accurately, but not all hospitals will have these sorts of specialists. I'm hoping my research will bring that expertise to every hospital in the country, meaning all children will have access to the best care."

Dr Susan Shelmerdine
Consultant Paediatric Radiologist

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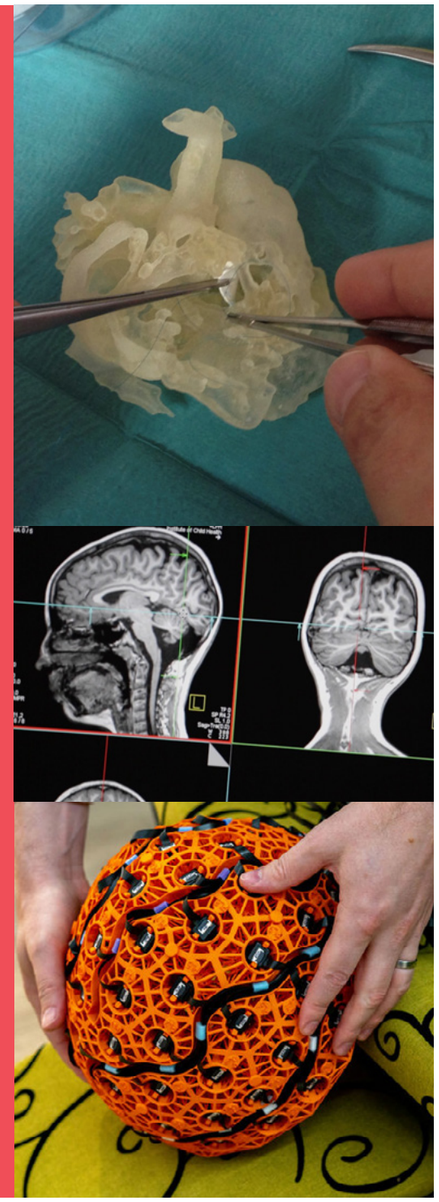
Reimagining imaging

When it comes to the heart, we are using imaging to explain complex heart conditions to patients, families and even doctors in training. Led by Professor Silvia Schievano at UCL Institute of Cardiovascular Science, a team of medical engineers have 3D–printed personalised hearts so doctors can use these models to explain surgery to young children and their families. They now regularly use virtual reality to train budding heart surgeons and have also used complex computer modelling to work out how the blood flow in major arteries and veins may be affected by an intervention like surgery or a stent, before the patient has the operation.

Making our way up to the brain and we are driving innovation in MRI – particularly in complex neurosurgery (e.g. conjoined twins), brain tumours and in epilepsy. The team at GOSH and UCL GOS ICH, led by Professor Chris Clark, are exploring a kind of MRI - called diffusion tensor imaging and tractography - that carefully maps the 'white matter' of the brain. This allows them to reconstruct important structures in the brain responsible for learning, memory and language and work out what is happening when something goes wrong, such as during an epileptic seizure.

Magneto encephalography (MEG) scans allows hospital teams to look for regions of high electrical activity in the brain and can help healthcare teams locate the source of epileptic seizures. The standard machine requires children to stay very still for prolonged periods of time and, as this often isn't realistic for small children, general anaesthetic to take the MEG scan needs to be used. Now, working with the Institute of Neurology, Nottingham University and the charity Young Epilepsy, a project led by Professor Helen Cross at GOSH is developing the first 'wearable' (MEG) machine. While a child can play and move around in a specially–designed room, the device – which looks like a large helmet – can be taking detailed scans of the electrical activity in their brains to help specialists understand more about the child's condition.



New treatments

GOSH researchers have a long history of contributing to new ideas impacting patients. Solely between 2017 and 2022, our researchers have contributed to 11 life-changing new treatments obtaining regulatory approval in Europe and the USA, with the potential to affect many millions of people worldwide.

From leading lab-based drug development and running clinical trials, to collaborating with global teams and providing evidence that supports drug approval, GOSH has played so many pivotal roles in developing new treatments supported by our NIHR Clinical Research Facility.

NIHR GOSH Clinical Research Facility

Zolgensma

Zolgensma is a new gene therapy that, when injected, reaches brain cells responsible for muscle function. Children with a degenerative and eventually fatal muscle disorder called Spinal muscular atrophy (SMA) can now receive Zolgensma to improve their movement and breathing thanks, in large part, to our research.

Zolgensma is now approved for use in the NHS and results show we need to find a way to identify children with SMA as early as possible, so they can receive this treatment before symptoms develop and permanent damage has taken place.

In fact, ongoing studies at GOSH, led by Professor Francesco Muntoni, Consultant Paediatric Neurologist and Lead of the NIHR GOSH BRC Novel therapies Theme, are showing that genetic screening can be used to find children likely to be affected by SMA, even before they show symptoms. Giving children Zolgensma early is allowing them to meet all the normal walking and movement milestones for healthy children their age. Our teams are now working to include SMA screening as standard within the new-born 'heelprick' test.

Pre-screening

Sadly, Amelia didn't undergo gene therapy before she lost the ability to walk, but through screening her sister Lena did.

"We only knew that Lena would develop SMA because her sister, Amelia, has it. None of us thought Lena's treatment with Zolgensma would be this successful. We hoped of course, but not even our hopes went this far. We couldn't expect just one injection to make this much difference."

Amelia and Lena's mum, **Dorota**

Brineura

For some treatments, gaining regulatory approval is just the start of the journey to achieve patient impact. For example, our researchers were involved in a drug called Brineura being approved by the European Medicines Agency in 2017, and finally becoming available for use on the NHS in 2019. It is an enzyme replacement therapy for children with CLN2 type Batten's disease (CLN2). CLN2 disease means that children don't produce a specific enzyme that is responsible for recycling waste materials in cells in the central nervous system. Without this enzyme, there is a waste build-up that first causes seizures, then gradual decline in ability to walk, speak and see, as well as progressive dementia. The life expectancy for a child with this disease without treatment is 10–12 years old.

Brineura is a life-changing treatment and has been shown to restore enzyme activity and slow the onset of disability. However, although it's effective in preventing movement and speech loss, this brain infusion does not prevent children losing their sight. The treatment cannot cross the blood-retinal barrier meaning the nerves in the eye cannot function and children lose vision. In follow-on research at GOSH, Retinal Surgeon Rob Henderson and Professor Paul Gissen, Consultant in Paediatric Metabolic Diseases and Lead of the NIHR GOSH BRC Gene, stem and cell therapies Theme, are now using the tiny amount of the drug leftover from the brain infusion and injecting it directly into the eye as part of a compassionate use programme at GOSH.

This eye injection is a quick and common procedure and, with no effective treatment option for blindness in CLN2 disease, this treatment could help preserve children's sight for longer, transforming their quality of life.

"Brineura has already helped stabilise Kavyansh's condition and we feel extremely lucky that we may have some hope of saving his sight in future."

Kavyansh's dad

Surgery

Today, more than one in three of the patients that visit GOSH undergo a surgical procedure so it should come as no surprise that our surgical research is just as progressive as elsewhere in the hospital.

Multiple teams can be involved in a patient's journey to surgery and our use of research and innovation means many disciplines can be brought together by using state–of–the–art imaging such as MRI and computerized tomography (CT) scans, virtual reality and complex 3D–modelling, so the surgical teams are better equipped than ever before.

Nowhere is the need for close collaboration felt as keenly as when our teams take on one of medicine's most challenging situations – separating conjoined twins.

We are internationally renowned for being one of only a few hospitals in the world to have the infrastructure, facilities and team of experts to meet this challenge and give these twins the best chance of survival. Interdisciplinary teams including general surgeons, neurosurgical, urological, orthopaedic surgeons and anaesthesiologists, have successfully treated more conjoined twins at GOSH than any other hospital in the world.

Among the most complex separations, craniophagus twins are fused at the cranium (the part of the skull that holds the brain) and their division is led by a large team involving radiologists and engineers who, under the leadership of Neurosurgeon Owase Jeelani, have designed innovative imaging and 3D–printing to guide the difficult and challenging surgery.

Surgeons at work

Surgery in the womb

In the earliest surgical intervention, one of GOSH's most complex pieces of research carries out life–changing surgery on babies that are still in the womb.

Babies born with severe spina bifida have a gap in their spine. They are often unable to walk, control their bowel or bladder and need operations to drain fluid from their brain. Surgery to close the gap can be carried out soon after birth, but this has its limitations in what it can solve.

In 2018, the first UK prenatal surgeries for spina bifida were performed by a 30–strong team from UCL Hospital and GOSH. The operation involves opening the womb to expose the defect in the spine, repair it, then closing the womb, without delivering the baby. Previously, expecting mothers in the UK had to travel abroad for this surgery.

This innovative procedure has now been carried out in the NHS on more than 25 babies, with some already starting to see the incredible impact of this treatment.

Through a collaboration of NHS and international hospitals, charities and research institutions, we are now looking to develop fetoscopic surgery. These are operations carried out using tiny 3–4mm incisions that do not need to open the womb and so may reduce complications for mother and baby. The hospital has already successfully used this approach in a small number of patients.

Many surgical interventions, such as the one described above, are also exploring an area of research that sounds more like something from science fiction: regenerative medicine.

Heart Surgery

Right now, around 50 children are waiting for a heart transplant in the UK but hearts of the right size are especially hard to find for a child. The agonising wait to find out if a suitable heart is available for an urgent transplant is over twice as long for children and babies – an average wait of 88 days compared to 35 days for an adult, while children deemed 'non–urgent' will wait over a year, on average.

Our surgical teams are constantly researching new ways to increase the chances that a child could find a new heart and, in 2021, two such techniques made headlines. In the first, donated hearts were kept beating outside the body – in a collaboration between GOSH, Royal Papworth Hospital (RPH) in Cambridge and NHS Blood & Transplant – allowing more hearts to be donated and giving surgical teams time to assess and plan for this vital surgery.

In the second breakthrough, research led by Perfusionist (someone who carefully controls the machines that support patients during a heart and lung transplant), Dr Richard Issitt, has used a special 'filter' during heart transplants that allows children as old as eight to receive hearts that don't match their blood type – a solution that was previously only available to very small children.

A new heart

The oldest child to receive a transplant using this technique was eight-year-old Lucy, who was double the age of the oldest child treated previously. Her mum Jenny explains how the transplant has impacted their lives:

"Since the operation, she's been so eager to try everything and catch up with her big sister, Freya - she's missed out on a normal childhood.

It's the simple things that make me well up – the other day she just ran ahead of me like any child would and she'd never done that. Lucy said to me recently, "I don't feel left out any more" and that's all you really want as a parent, isn't it?

"I think about the donor and their family a lot. It is incredible that a family made such a decision at the most devastating time. We are so very grateful for the gift and are determined for Lucy to live her life to the full, she has a second chance at life and no words can fully convey how amazing that is and how grateful we are.

"Even after three and a half years on the transplant waiting list, she was only able to get the heart because of this new research. I dread to think how much longer we would have waited without it."

Right: Lucy on the first anniversary of her heart transplant

Regenerative medicine

Regenerative medicine is defined as any treatment that restores normal function to tissues or organs, with an emphasis on harnessing the body's natural ability to repair itself. It tells us that we can tackle the root cause of disease and not just the symptoms.

Surgical teams at GOSH are working at the very forefront of regenerative medicine – they are looking at ways to use stem cells to 'grow' different kinds of human tissue, exploiting the healing powers of stem cells to aid healing after surgery and even reprogramming the body to heal itself.

For example, our teams developed research programmes to repair mis-formed trachea by combining patient stem cells with a donor trachea, limiting rejection of the new organ. The team now hopes to produce a range of organs, from simple ones like intestines to complex functioning organs like kidneys, and is getting ever closer to those goals.

More than 50 children have been treated in a GOSH Charity funded project that uses revolutionary thymus transplants and the power of regenerative medicine to 'grow' thymus tissue. The thymus is responsible for the body's response to infection and babies born without a functioning thymus are likely to die before the age of two. In this new technique, GOSH teams use healthy thymus tissue that has been removed from another child during heart surgery – tissue that would otherwise be discarded during the operation. The thymus tissue is then 'grown' in the laboratory before implantation into the thigh muscle of the child without a working thymus.

Around 75% of children who received a thymus transplant at GOSH had a successful outcome, developing the ability to fight common infections, coming off treatments such as antibiotics and immunoglobulin injections, and were able to attend nursery and school normally.

We are the only centre in Europe – one of two worldwide – where children born without a thymus are receiving this treatment, which has been led by research. There is now the possibility to scale the treatment up to adults.

The team is also looking at using stem cells to grow 'matching' thymus tissue for when a child is receiving a new major organ, like a heart or kidney. While it is essential for a functioning immune system, the thymus can also cause the body to reject transplanted major organs, as it recognises them as 'foreign'. By receiving lab–grown thymus tissue and a major organ from the same donor, rejection could hopefully be avoided.

They now hope to develop other organs and are already making great steps on using intestinal tissue to rebuild the gut.

Professor Paolo De Coppi Paediatric Surgeon and Deputy Lead of the NIHR GOSH BRC Structural malformations and tissue damage Theme

"As a paediatric surgeon at GOSH, I can see regenerative techniques in surgery changing and improving all the time. Along with advances in technology, we're developing a better understanding of different tissues in the body and how we might better heal or replace them. Because younger tissue is more able to regenerate and repair, regenerative medicine holds huge potential for children.

Alongside clinical work, I'm passionate about research. We're using new ways of sourcing stem cells, growing tissue from scratch in the lab and modifying DNA inside cells to make them work better. We're seeing a shift away from a reliance on organ and tissue donors – a process that often requires finding a good match fast – towards a future in which the same, or perhaps better, results could be achieved using the child's own cells, or ready–made banks of patient–matched cells and organs."

Future hospital

GOSH was one of the first hospitals in the UK to make all patient health data digital. It's now easier for clinicians to look up information, and share what's needed in a safe and secure way.

We have also developed a hospital app, called MyGOSH, where patients and families can pull up their health record, check appointments and, coming soon, find out about research studies they are eligible for.

As a world–leading children's hospital with a unique group of patients with rare diseases, we have a special opportunity to use data in a way that can improve healthcare and drive research. We have already established international collaborations with leading children's hospitals in the USA, Canada and Australia to help harness the power of data.

But we are also aware of the great responsibility we have as we grow into a hospital fit for the future of healthcare.

The Data Research, Innovation and Virtual Environments unit (GOSH DRIVE), headed by Sue Connor, part–funded by GOSH Charity, provides a physical space, meeting rooms and technology to enable collaborations in innovation, development and rapid use of digital medicine within the NHS. Patients, the public and researchers can be contacted, engaged and consulted in this space, developing research and feeding back as projects develop. We have supported more than 100 collaborative projects with UCL computer science students, connecting them to NHS patients and real–life healthcare problems.

In fact, GOSH DRIVE was highlighted as a best example of how a hospital's data infrastructure has the potential to improve healthcare, in a 2019 UK Government–commissioned independent report (Topol Review).

Collective data can help doctors and scientists improve care for patients both here at GOSH and across the world, make new discoveries and find better treatments. It can even help develop new technologies that allow healthcare teams to make more informed decisions about a child's care, drawing on information from healthcare teams, the children themselves and wearable technology.

For this research, information that identifies patients can be removed, so anonymity is protected while still harnessing the power of data.

The real-world patient benefits of GOSH's Future Hospital ambitions have already been shown. For example, we were able to rapidly show the impact of COVID-19 on children, we were the only UK site able to contribute to a global consortium that identified and tracked different SARS-CoV-2 variants and, led by Dr Pia Hardelid at UCL GOS ICH, we have combined hospital data with that from GPs to investigate the best antibiotics to prescribe during pregnancy.

Dr Cho Ng, Lead Consultant in GOSH Cardiac Intensive Care Unit

"We have collaborated with GOSH DRIVE to develop an app that helps us to collect and collate information on how the unit runs, creating easy to view and search dashboards, allowing us to identify incidents like organ failure or infections.

Through working with DRIVE, we've been able to get the most out of health information that we are already routinely collecting, using digital platforms, to advance our care and investigate research to improve practice."

Leaders of tomorrow

All our clinical directorates and services at GOSH are developing their own research agendas to improve treatment options, outcomes and experience for the children and families we see.

A team of dedicated clinical research nurses facilitate research and offer research opportunities to other nurses, developing the research nurses of the future.

Healthcare professionals at GOSH, like dietitians, physiotherapists and radiographers are also often research active, supported by our allied health professionals research strategy.

We are constantly looking at how we can better embed research in our teams and services. But we also know that our people are at the heart of our big ambitions for Research and Innovation and we want to do all we can to support them, individually.

This is why we have a GOSH Learning Academy for staff education and training, a Research and Innovation team to offer advice and coaching on research careers, and online resources to support individuals inspired to turn research ideas into research reality.

We also look for innovative ways to support our staff with research careers. All healthcare professionals are potential researchers and we are committed to ensuring all staff – whether doctors, nurses, dietitians or perfusionists – can get involved in research and are supported in doing so.

One way we do this is through the Centre for Outcomes and Experience Research in Children's Health Illness and Disability (ORCHID). It specialises in research that looks at the overall impact of health, illness and disability on children, young people and their families, and supports our nurses and other healthcare professionals to start or develop their research careers, plan and deliver research projects and apply for research funding.

The GOSH NIHR BRC Experimental Medicine Academy also has an established track record in supporting the career development of the next generation of high–calibre researchers in translational research for children. They have supported more than 100 researchers since 2016 through a programme of pioneering schemes.

For example, the BRC's Catalyst Fellowship awards, designed by early career researchers, address gaps to support junior researchers looking to transition to independent research careers, the Internship Scheme for nurses and allied health professionals nurtures and enhances research culture in these varied fields, and the Knowledge Exchange Programme funds researchers to bring back knowledge and expertise from other global leaders in their specific field.

The many and diverse ways we support our staff have huge impact on our workforce, allowing us to motivate, train and retain the best research–interested staff. Many staff who took their first steps through schemes like this are already forging leading research careers.

We know it is through building up the next generation of researchers that we will cement our place as a Research Hospital.

Dr Amy Mctague
Principal Research Fellow and Honorary Consultant Paediatric Neurologist

"I was a fully qualified children's epilepsy doctor before I started on my research path but I knew I wanted to investigate the link between genetics and epilepsy.

I studied for a PhD in the genetics of early onset epilepsy and then I returned to GOSH where I was supported as a GOSH NIHR BRC Catalyst Fellow.

This gave me 18 months to devote to new stem cell models of epilepsy and meant I had the right experience to apply for a substantial fellowship from the Medical Research Council.

By leveraging early support like this, I am now in a place where I have my own growing team based at the Zayed Centre for Research. In this unique building we can collaborate with others and capitalise on stem cell and gene therapy expertise.

Patients and families can look into our sunken labs through the open ceiling, often waving as they go, and this is a constant reminder of why we do what we do. As the sign on the wall says "together we can do so much".

Together we can do so much

Dr Kiki Syrad
Director of Impact and Charitable Programmes, GOSH Children's Charity

"At GOSH Charity we have built a phenomenal legacy of helping to transform the lives of seriously ill children by raising vital funds so the hospital can deliver life-changing care and discover new treatments and cures. Together, with our supporters we have already saved and touched the lives of so many and will continue to support the children who will need us in the future.

It is not only those treated in the hospital itself who benefit from this care. The world-class research that takes place at GOSH, alongside its research partner UCL Great Ormond Street Institute of Child Health, helps seriously ill children from across the globe.

Through the work we have funded, we have already saved and touched the lives of so many. But we know that diagnosis can be difficult, and the burden of disease can have a profound impact on the child and their family. Gifts left to us in Wills today will help to fund future areas of work that will enable us to have the greatest possible impact on the lives of those we support. It is only through the generosity of our supporters that we will be able to continue to do this for generations of children to come. Thank you."

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