FREE

SPRING 2024 | ISSUE 102

Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

contact

SUPPORTING FAMILIES THROUGH CHILDHOOD CANCER

MAGAZINE

Innovations and developments

What research is happening to support new treatments? How is care being improved?

+ USING AI TO PROPOSE NEW DRUG COMBINATIONS

+ NEW PROJECTS AND INITIATIVES

Family Story

Michelle Aldred, mum to Amelia who was diagnosed with osteosarcoma aged seven, tells us how a pioneering procedure helped her daughter remain active **Page 6**

BACK TO BASICS:

From bench to bedside

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THE ONCOLOGY GUIDE

Charley Scott and her husband Jon have developed an accessible new information resource influenced by their own experiences during their daughter's cancer treatment

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ON THE COVER

Contact

is a free, quarterly magazine for families of children and young people with cancer.

Contact aims to reduce the sense of isolation many families feel following a diagnosis of childhood cancer.

Children's Cancer and Leukaemia Group brings together childhood cancer professionals to ensure all children receive the best possible treatment and care. **Contact magazine was founded by The Lisa Thaxter Trust and CCLG and first published in 1999.**

Past issues of Contact: The wide variety of articles published during the year in Contact adds up to a valuable and informative reference archive. If you would like any back issues, please contact the Editor. Details of key articles in previous editions are listed on our website.

Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

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KEEP IN TOUCH

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Your messages...

On Contact's last edition:

"Really diverse and helpful articles. Thought the breastfeeding during your child's cancer treatment was really important, and great to highlight."

"Having evidence-based, family friendly resources to share are pure gold, and so deeply appreciated."

CCLG's award-winning information resources continue to support families

"Thank you for all the work that you do, especially all the literature about the disease and supporting siblings, which we really benefitted from."

Praise for CCLG's research blog tackling important subjects

"A terrific piece by CCLG. It is incredibly important to have trusted organisations and voices counter harmful misinformation and conspiracy theories."

Read our research blog here ▲

CCLG research webinars continue to provide valuable insight

"More webinars like these please! Parents often complain they have so little time with consultants, so webinars like these and especially the Q&A opportunity are so valuable."

If you would like to **SHARE YOUR STORY** in Contact or have an idea for a theme for us to cover, please let us know. **Email us at editor@cclg.org.uk**

Hello!

Innovation is the key to progress. Without us having creativity to think up new ideas or bravery to go where no one has gone before, innovation doesn't happen and we stagnate. Nothing changes and we stay the same. This is true for most things but particularly so in the medical and healthcare fields. The reason we are seeing such good survival rates now is because a handful of concerned doctors decided to break the status quo, create a new expert organisation (the origin of today's CCLG) and push for better treatments so more children could survive. Innovation has stayed at the heart of our childhood cancer community and this issue showcases the many areas where it has transformed treatment, care and support for young patients throughout their cancer experience.

Claire

MEDICAL ADVISER

Professor Bob Phillips

Candlelighters Chair of Supportive Care Research for Children and Young People with Cancer, University of York, Consultant Paediatric Oncologist at Leeds Children's Hospital and CCLG member

In this issue of Contact, we hear about lots of new ideas that are helping to improve many aspects of both treatment and care for children with cancer, across a wide spectrum of ages and needs. Some of these have the potential to make a massive difference, such as monitoring the exact amounts of chemo which are present when we give a particular dose, or allowing for treatment to be delivered outside of a hospital setting to lessen some of the upheaval for families. Artificial intelligence is also being harnessed to come up with better guesses at which chemicals might be more effective or less unpleasant chemotherapies.

All of these will need careful introduction and assessment - as with anything new, we need to be sure it's better than what came before. This most certainly applies to treatment, for example, where we need to find out if it's as effective, or has fewer side effects, than current methods. We've got a description of this process and how good ideas flow - or don't – from laboratory through to clinical trials and into everyday practice.

Exactly how to deliver things we already know need to be done, like informing families about the treatment ahead, can also be improved. New ways of making information accessible are coming along all the time through developments in media. We can use them to make health information clearer and better understood, too.

We can also learn from our families and colleagues where it comes to understanding how our special skills overlap. There are families and clinical teams who spend their time caring for children with learning disabilities and neurodiversity, such as autism spectrum disorders and ADHD. When children who already have these and other conditions also develop cancer, we need to blend all that expertise together to help them as best as possible.

In children's cancer, we're constantly striving to find new and pioneering ways of supporting patients and will continue to do so for as long as needed. So, let's embrace the new stuff, be prepared to walk away if it doesn't work, and keep looking for ways to move forward.

NEWS IN BRIEF

App improved outcomes for pain among children with cancer

A home pain monitoring app led to less clinically significant pain in children with cancer, as well as improved parental wellbeing, according to a recent study. Children who were receiving active treatment (chemotherapy/radiotherapy) with access to a smartphone/tablet were recruited for the study, with researchers using the 'KLIK Pijnmonitor' app developed by the Princess Máxima Center for Pediatric Oncology in the Netherlands as their pain monitoring for the investigation. This app allows patients and their families to report moments of significant pain, and to set up daily reminders if desired. The research team said the results open up a range of opportunities for digital symptom monitoring.

(Source: Hematology Advisor)

Potential of new treatment strategies for most common childhood cancer

Researchers in America have made a key discovery about how childhood acute lymphoblastic leukaemia evolves and responds to targeted therapies. Their study found that some treatable aspects of a child's cancer present at diagnosis still remain if the disease returns. This suggests clinicians can begin looking for precision treatments for a child's cancer immediately after diagnosis, rather than waiting until relapse.

(Source: University of British Columbia)

Promising new treatment combination for relapsed or refractory neuroblastoma

Birmingham researchers have found a more effective combination of drugs for treating children and young people whose neuroblastoma isn't responding to standard chemotherapies. The clinical trial found that adding bevacizumab to standard chemotherapy made tumours shrink 8% more than without. This treatment will be taken forward into the next stage to find out how it works and how best to use it.

(Source: Journal of Clinical Oncology)

Research increases understanding of medulloblastoma

Dutch and American researchers have discovered a tiny protein essential for the survival of MYC-driven medulloblastoma brain cancer cells. The MYC gene is found in several cancers, helping cancer cells survive and spread. However, this work has found a micro-protein that cancer cells with MYC are dependent upon, suggesting MYC has functions beyond known genes in cancer cells. Understanding these roles could support the development of treatments.

(Source: News Medical Life Sciences)

Therapeutic drug monitoring: A novel approach to improving treatment

***Gareth Veal**, Professor of Cancer Pharmacology at the Newcastle University Cancer Centre, leads a team helping doctors to personalise treatments through an innovative process called 'therapeutic drug monitoring'. Here, he tells us more about his work.*

Advances in the development of anti-cancer drugs or chemotherapies have come a long way since the pioneering work of Sidney Farber at Boston Children's Hospital, where some of the first rationally designed drugs were developed for children's cancer well over 50 years ago. While overall survival rates for childhood cancer are now above 80%, it's telling that many of the drugs commonly used for treatment have been around for several decades.

Indeed, drugs developed by Sidney Farber such as methotrexate and actinomycin D are still widely used today for the treatment of acute lymphoblastic leukaemia and Wilms tumour, respectively. While we need to maintain or even improve on the excellent survival rates that have been achieved, more needs to be done to try and reduce the wide-ranging and common side effects of treatment that can severely impact the quality of life of childhood cancer survivors.

Professor Veal and Dr Barnett receiving the CCLG Innovation in Practice Team of the Year Award

Our work

Alongside Dr Shelby Barnett, I lead a programme of work at Newcastle University that's been focusing on this area for several years. I fittingly spent two years training right around the corner from Boston Children's Hospital, at the Harvard Institutes of Medicine, before establishing the Newcastle Cancer Centre Pharmacology Group. The group run a national service, currently generously supported by The Little Princess Trust and Cancer Research UK, providing information on individual patient drug exposure for particularly challenging patients including babies being treated in the first days and weeks of their life.

For these patients, doctors often have to make difficult decisions about the most appropriate dose of a drug to give, often with limited scientific information to base the decision on. The team at Newcastle leads a novel approach to treatment which involves collecting a small number of blood samples from a patient on the first day of treatment with a particular chemotherapy. They're then sent to the Newcastle research laboratories to determine the actual drug exposure that the patient is achieving at a particular dose level.

The idea behind this is that there's an ideal concentration of drug that we want to achieve in the bloodstream of the patient, to target the cancer cells without causing damage to healthy cells. This can be likened to the 'Goldilocks principle', where just the right amount of something is sought. In our case, we want to make sure the drug exposure is high enough to lead to a response to the treatment and, ultimately, survival, but isn't so high that it risks causing excessive harm to the patient and long-term side effects.

Personalised treatment

By collecting blood samples during and following treatment, our research team is able to measure drug levels in patients and work out whether they may benefit from more or less drugs. The information is then used to adjust the dose they receive, either within or between treatment cycles. This pioneering approach to the personalisation of patient treatment has resulted in the Newcastle team receiving several national awards, including CCLG's Innovation in Practice Team of the Year Award in 2022. Data generated from this work is also being used to propose novel dosing regimens based on clear pharmacological reasoning, for some of the most challenging-to-treat groups of childhood cancer patients.

Looking ahead

In addition, the group are involved in an exciting collaborative project with scientists at University College London and the spin-out MedTech company Vesynta, to develop point-of-care drug monitoring devices to facilitate the current approach at the patient's bedside. It's hoped that this venture will allow a markedly increased number of patients to benefit from drug monitoring treatment approaches in the coming years.

How embracing innovation has helped Amelia inspire others to stay active

Michelle and Richard Eldred, with Amelia

***Michelle Eldred's** daughter, **Amelia,** was diagnosed with bone cancer in 2017 on her seventh birthday. Here, Michelle tells us about a pioneering procedure which helped Amelia remain active after a leg amputation.*

Amelia was diagnosed with osteosarcoma in her left thigh bone. She received a few months of chemo before we were told the high-grade tumour wasn't shrinking, and she needed to have her leg amputated from her hip or another type of amputation called 'rotationplasty'. Amelia chose rotationplasty, which was a quite rare procedure in the UK. It involved amputating her femur and knee to remove the tumour but saving her lower leg and foot and reattaching to the top of her thigh, backwards.

When we were told about this procedure, it was difficult to fully understand, so we went home to research it. We googled rotationplasty as there simply wasn't enough information on the procedure without looking for visuals. We found a YouTube video of a girl in America, who also had osteosarcoma and had this procedure when she was nine. We were blown away with how active this girl was following the procedure and how she fitted a prosthetic leg and how she could dance.

Amelia was always an active child and loved dancing and sports. We were inspired to see this young girl, called Gabi, with great mobility and showed Amelia the same video. I'll never forget Amelia's words after watching the video. She simply said, "Wow, I'm going to be like her", and the decision was made. We're so thankful to Gabi for sharing this video and, through the power of social media, I've been able to say "thank you" to her myself.

> "Amelia chose rotationplasty, which was a quite rare procedure in the UK. It involved amputating her femur and knee to remove the tumour but saving her lower leg and foot and reattaching to the top of her thigh, backwards."

Amelia never complained about having to have the operation. She said she wanted to be like Gabi, and as she went into surgery, the last thing she said was, "bye bye, tumour, see you, loser".

It's quite a controversial procedure and people do a double-take if they've never seen it before, because her foot is backwards. But we knew that she had a much higher chance of survival and being able to walk again with a prosthesis, if the procedure went well.

▲ Amelia after her procedure

> "Amelia now enjoys rock climbing, running, archery, dancing, swimming - there's no stopping her!"

We're so grateful that the surgery proved to be very successful, and Amelia is now using her fourth prosthetic leg, plus a sports blade leg. She first challenged herself to dance again as soon as she could use a prosthesis, with her first dance taking place at an awards ceremony with her surgeon, Professor Lee Jeys! Then, last year, she was able to have a sports blade leg that allowed her to run for the first time.

Amelia now enjoys rock climbing, running, archery, dancing, swimming - there's no stopping her! She went to a children's amputee camp in Tenerife last summer, which is a funded group that provides holiday camps for children and their families who have gone through an amputation. Amelia loved this and has grown more confident from her Amp Camp Kids experience. She's now fundraising to help other amputee children from the UK to attend this life-changing camp.

She's also doing musical theatre with a group called The Wings Family, and her blade has given her so much more confidence to get on stage. She's danced in a production of Peter Pan last Christmas, where a little girl was watching the production who also had a prosthetic leg. After the show, she told Amelia that she had inspired her so much, and that she was going to join the theatre group, too.

We're so proud of Amelia's determination and attitude to always push herself and, as she says, "anyone can achieve their dreams if they challenge themselves". Her main goal now is to inspire other children with disabilities and help them become confident and proud of who they are, just like Gabi in America did with her YouTube video. Through her fundraising, performances and some public speaking, Amelia is certainly achieving this.

▲ Amelia taking part in an array of physical activities

'From bench to bedside': How the latest treatments come about through clinical trials

▲ **Professor Pamela Kearns (left), Dr Sarah Al-Jilaihawi (middle), and Dr Jessica Douglas-Pugh (right)**

New and innovative cancer treatments go through many steps to make their way from 'bench to bedside'. ***Professor Pamela Kearns, Dr Sarah Al-Jilaihawi*** *and* ***Dr Jessica Douglas-Pugh*** *from the University of Birmingham's Cancer Research UK Clinical Trials Unit (CRCTU) explain more about this process.*

Globally renowned for academic excellence, the Birmingham CRCTU is responsible for the majority of academic-led children's cancer trials in the UK and plays a crucial role in improving clinical practice and outcomes for children with cancer.

All new medicines and treatments must be thoroughly tested before they're licensed and available for patients. Experimental medicine is hugely important in discovering and testing new, cutting-edge cancer treatments that have the potential to be more effective or cause fewer side effects and long-term health issues. When looking at children's cancers, these 'new' treatments could have previously been found to be effective in adult cancers but hadn't yet been explored in children's cancers, or they may be entirely new treatments.

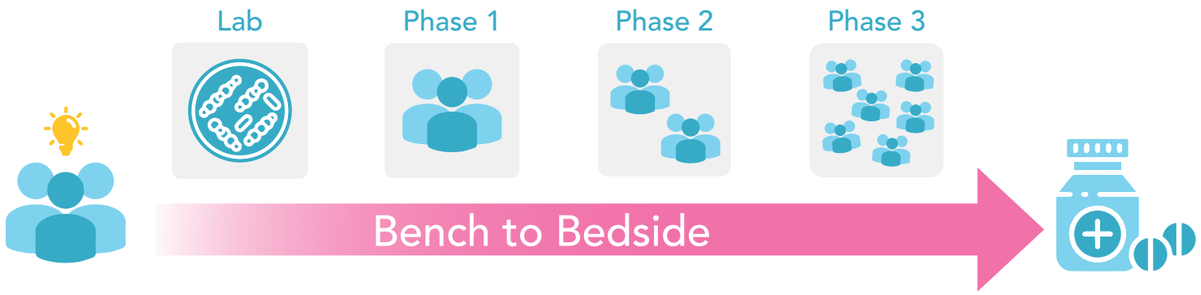
Laboratory research

Preclinical or 'lab-based' researchers first explore the potential of a new anti-cancer treatment through testing 'in-vitro' on cancer cells in a laboratory dish or test tube, or 'in-vivo' on living organisms. The aim of laboratory testing is to investigate whether these novel treatments work in killing cancer cells before they're studied in people.

So, how do we know that these new promising treatments are going to be safe or effective in our patients? How do we decide if they are going to be better than, or help to enhance, our existing established cancer treatments? The answer is through clinical trials.

Clinical trials

In the last 40 years, vast improvements have been made in survival rates for children and young people with cancer, largely driven by clinical trials. Clinical trials are vital to carefully studying the effects of new medicines or approaches to treating cancer in children. If a new medicine is shown to work well without too many side effects, it may then be licensed and become available as a routine treatment for patients. The time that it takes for a medicine to be tested, approved and licensed can vary widely. It may take more than 10 or 15 years to complete this process. So, why does it take so long?



Clinical trials generally have three main stages, known as 'phases 1 to 3', that must be completed to show a medicine is safe and can work in a certain cancer.

Phase 1 > Trials only test a new treatment in a few people. The aim is to see how much of the treatment is safe to give and the side effects it can cause. If deemed safe, it will be tested in a phase 2 trial.

Phase 2 > Trials test the treatment in more people to continue to find the best dose, collect information on side effects, see how well the medicine works in treating a particular cancer or group of cancers and whether it's good enough to continue to be tested in a larger phase 3 trial.

Phase 3 > Trials are tested in larger group of patients to test if the new medicine is better than the best existing treatments. These trials are often 'randomised', where patients taking part are put into treatment groups at random to be able to compare the new treatment with the best standard treatment.

There are many factors that can influence how long these phases take, as we detail below.

Designing, funding and setting up trials

Clinical trials are designed by a research team which includes clinicians, clinical trials specialists, statisticians and patients, parents and members of the public. It ensures that trials are set up properly and safely, according to strict standards, and that trials meet the needs of patients.

Before the trial can happen, the research team must obtain funding from a research or charitable funding body or a pharmaceutical company. This money is necessary to make the trial possible and is used to fund the new medicine(s), the expertise required to design and manage the trial, the opening and recruiting of patients onto the trial in hospitals, the collection and storing of data about trial patients, and the analysis and reporting on the results.

With funding in place, the team can prepare the trial protocol and the regulatory and supporting documents such as patient information sheets. It will decide:

- who can take part in the trial
- what the different treatments are
- an appropriate trial design
- what tests the patients will have
- how the results from the study will be assessed

Once the protocol is finalised, the team will need to get approvals from regulatory bodies. In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) must review and authorise the protocol according to strict regulations. Trials must also meet ethical standards to protect the safety and wellbeing of patients who take part and be reviewed by a Research Ethics Committee. Once these approvals are in place, it's necessary to ensure each recruiting hospital has the appropriate facilities and staff who are trained and able to deliver the trial safely. All these reviews can take many months before it is possible to open the trial.

As children's cancers are rarer than adult cancers, research teams from several different hospitals and countries have to work together to recruit enough patients onto these trials. This can affect how long it takes to organise the trial and set it up.

What happens next?

Once a clinical trial is open in a hospital, doctors and research nurses can begin to recruit eligible patients into the trial. They must make sure that children and families receive information about the trial and understand what taking part means.

Information about the patient taking part in the trial, and how they respond to the treatment, is collected in a secure database which protects the identity of the patient. To ensure the safety of patients on the trial, processes are put in place for doctors to report any unexpected side effects or reactions to treatment back to the research team. An independent committee will also review the data collected during the trial to make sure it's safe.

After trial treatment finishes patients are followed-up for some time, usually for several years but this depends on the type of treatment and group of patients. Data collected during the follow-up period will show the research team how well the treatment works over a longer period and allow them to learn about longer-term side effects. Once this follow-up period is complete for all patients on the trial, the research team can analyse the results and determine if the new trial treatment should be used as the new 'standard of care' or if further research needs to be completed.

We hope that this has shed some light on how cutting-edge science in children's cancer is translated into improved patient care, and the importance of clinical trials in pushing boundaries when it comes to research into children's cancer.

New online resource supporting children and their families


Charley and Jon

Charley Scott's daughter was diagnosed with cancer as a two-year-old. She tells us about an accessible new information resource that she and her husband **Jon** have created to help other children and families, influenced by their own experiences.

When our daughter, Jess, was diagnosed with T-cell non-Hodgkin lymphoma, we were given some information about her cancer, but we wanted to read and understand more. We were also extremely conscious of trying to explain to Jess the procedures she was going to have and what they would entail so she wasn't frightened. We looked for visual aids to help us but couldn't find anything that would connect with a then two-year-old. Both my husband and myself are filmmakers and creatives and could see the value video content could have to children going through treatment. So, we made it our mission to try and help, and The Oncology Guide was born.

How it will help families

We've carefully designed the resource so it's accessible everywhere on all devices and it's free for everyone to use. The written medical information is provided by the wonderful CCLG and the medical information in the films is from Kings College Hospital NHS Foundation Trust. We wanted to create visual aids of procedures and treatments to help explain to the children what was happening, hopefully reducing their anxiety. We understand children who are going from school, clubs and playdates with friends to being thrust into cancer treatment can be extremely daunted and frightened, and so can the parents and families, too. So, we hope this resource will be able to inform and help guide the whole family.

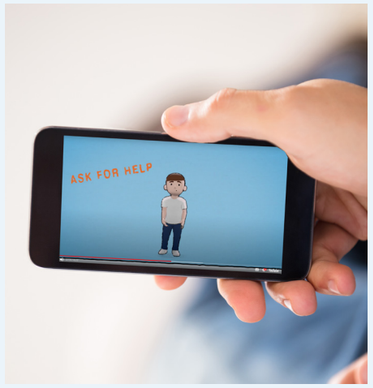
Why it's innovative and different

The Oncology Guide is a first-of-its-kind web resource that brings reliable information from trusted resources into one place. It's the only place dedicated to providing specialist, child-focused oncology guidance. The videos that feature are presented by children who have either been on, or are going through, treatment, and therefore have experienced much of what they're talking about. This gives them a unique perspective and one that will help resonate with those newly-diagnosed children and families that may watch them.

We feel we've been incredibly blessed to have had some incredible support by organisations and charities who shared our passion for creating this resource. CCLG for the written information, Kings College Hospital NHS Foundation Trust for their medical expertise and filming location, Chartwell Cancer Trust as main funders, Kingfishers Charity for further funding, Design Bridge for the incredible design and Arcade_xr for building the app for us. We also need to give a special mention to the wonderful children who took part in the films. We're very proud of them and of what we've all achieved. We hope it can go some way to helping families like ours in their time of need.

We want to continue to develop the app with further written information, podcasts, more video content and localisation for other territories and languages making it accessible to even more children and families. We're also already working on an adult version of The Oncology Guide.

For those families reading this who are going through treatment, we are so sorry you are on this journey. Our biggest piece of advice is to go one day at a time. We hope the app will go some way in helping your family, and we send lots of love.



www.theoncologyguide.co.uk

New initiative supports young cancer patients with additional needs

*Children with cancer who also have learning difficulties and autism often have additional needs when it comes to their care. **Jeanette Hawkins**, CCLG's Chief Nurse, tells us more about a project aiming to improve support for this group of patients.*

In early 2023, I joined the NHS England Cancer Experience of Care Improvement Collaborative (CIC) expert advisory group. The CIC brings together cancer healthcare professionals and people with lived experience from different organisations to work in a structured way to improve services.

The group translates findings from the annual National Cancer Patient Experience Survey (CPES) for adults, and the Under 16 years CPES into themes where improvement is needed. They offer hospitals the chance to apply to be part of a quality improvement programme, giving teams the opportunity for training and support in quality improvement (QI) methods.

Last year's improvement theme was 'people diagnosed with cancer who had a pre-existing condition of learning disability, autism, mental health condition or dementia', because data showed their experience of care scored lower than for other groups across a range of areas. We know that children with Down syndrome are predisposed to cancer, particularly leukaemia, and all have a degree of learning disability (LD), so they're represented in children and young people's cancer services. We also see children with autism on a regular basis. It made sense that this group of children and young people should be a focus for us.

The project

We knew from the outset that you can't fix everything about the cancer experience for these patient groups and their families through just one project. So, our next step was to identify where there were struggle points for them, as well as areas that professionals felt could be improved. It quickly became apparent that scans, tests and investigations were a particularly challenging part of care.

Guided by the CIC, we established a project team of multiprofessionals with an interest in QI or in LD and autism from the UK's children and young people cancer centres. We were privileged to get Sue North (MBE), the lead for children and young people in the Learning Disability and Autism Programme of Care at NHSE, as our project sponsor.

Importantly, we appointed parents with lived experience to the project team. The CIC provide workshops and one-to-one support sessions which helped the team learn about QI approaches and helped us further refine the project to ensure it would be achievable and make sustainable change. As a result, we're now focusing on the experience of having an off-the-ward X-ray, and is likely to illuminate areas for improvement that will be transferable to other tests, scans and investigations. We're also working with representatives from the Society of Radiographers.

Vital baseline data is collected before making any assumptions about where improvements might be made. Our lived experience partners have been amazing at informing the data collection tool and testing it with other families to ensure it's suitable. The tool collects data which helps us understand patients and families' experiences of having an X-ray.

Next steps

We're gathering real-time data from families presently going through services whose child has had an X-ray in the last six months. This will be used to identify areas for improvement. We already have indications of what these might be and have an 'ideas car park' for possible interventions to test.

We're looking at small practical changes, that can have a big impact. Like improving how an X-ray department is notified that the patient has additional needs so that they can plan non-urgent X-rays for in-patients at a quieter time of day. Or implementing checklists to ensure a child and family's needs have been adequately assessed for the procedure. Perhaps simple guides or training tools for radiology staff on supporting those with additional needs.

We estimate the project will take another 18 months to have tried out some changes and completed robust testing to make sure changes are positive and sustainable.

How is ambulatory care improving young people's experiences of treatment?

***Dr Alison Finch** is a nurse and researcher from University College London Hospitals NHS Foundation Trust (UCLH). She explains how ambulatory care is positively impacting young people's experiences of treatment and how a CCLG Special Interest Group has been formed to develop this care nationally.*

In the UK, intensive cancer treatment has long centred around inpatient care. However, since the 1980s many cancer pathways in the USA have been delivered on an outpatient basis. Ambulatory cancer care, or simply ambulatory care, has since become a mainstay in many NHS adult treatment centres. Founded on offering choice and a more personalised experience, it offers systemic anti-cancer therapy that traditionally requires inpatient care, in an outpatient environment, with patients staying in a residential setting overnight. This could be their usual home, or in a nearby hotel, apartment or home-from-home close to the hospital. Ambulatory care has been made possible since the advent of programmable portable infusion pumps and more sophisticated supportive care medication.

Development

An ambulatory care service was set up at UCLH in 2012 to support young people aged 13-24 and their families. It drew on the expertise of adult colleagues who'd established the first NHS ambulatory care service in the early 2000s, modelled on a children's service at Memorial Sloan Kettering Cancer Center in New York. It works by getting young people actively involved in self-monitoring and self-surveillance during cycles of treatment (for example, recording fluid input and output) – clinical checks that, if staying in hospital, would usually be done by the healthcare team. Young people attend the ambulatory care unit each day for an infusion change or clinical review – after which, if they remain well, they return to their residential setting overnight.

Research

With over a decade of ambulatory care experience, the team at UCLH wanted to better understand the benefits of this care pathway for young people and their families. I received funding from the National Institute for Health and Care Research (NIHR) as part of a doctoral fellowship to research the experiences of young people, families and staff receiving and delivering ambulatory care. We wanted to see if changes were needed to better meet the needs of families at UCLH, and to inform the development of this care pathway UK-wide. My research team included young people and family members who became co-researchers, actively involved in every stage, with charities Young Lives vs Cancer and Teenage Cancer Trust becoming collaborators.

The research found that ambulatory care contributed positively to young people's experience of cancer treatment. It helps keep young people rooted in their usual lives and communities, and together with the support of an accompanying parent, sibling or partner, fosters young people's sense of self and their autonomy – particularly important at this developmental stage of life.

The research, however, also evidenced the need for greater psychosocial support for companions – those accompanying a young person – with a widening of healthcare professionals' delivery of 'age-appropriate care' to be more encompassing of young people's support networks.

What's happened since?

Since the research finished in 2022, a national Special Interest Group has been set up by CCLG, bringing together health professionals interested in developing both children and young people's ambulatory care. Since it's first meeting in October 2022, it now has over 80 members.

Ambulatory care is in the process of being launched, piloted or considered within many principal treatment centres in England and Wales. The Christie, in Manchester, already has an established teenage and young adult service, and is increasing the number of protocols they can offer in ambulatory care.

Further research, funded by CCLG and Young Lives vs Cancer, and led by Dr Jess Morgan, at Leeds Children's Hospital, and Dr Gemma Bryan, at the University of Surrey, aims to understand how ambulatory care is currently used across the UK and how to help hospitals design their ambulatory care services for children.

Further details about Alison's research can be read in an online resource called **'Re-defining cancer care with young people'.** Scan the QR code to find out more.

How at-home treatment has helped us

***Jess Formby's** daughter, **Arabella,** was three years old when she was diagnosed with acute lymphoblastic leukaemia (ALL) in 2023. Jess tells us how being trained to deliver Arabella's IV chemotherapy at home helped her family.*

A short time into Arabella's treatment for ALL, my husband Eric and I asked one of the advanced nurse practitioners (ANPs) whether there was any financial help with travel to and from hospital as we were finding it financially hard, and we were visiting the hospital near enough every day for chemo and appointments. One of the IV chemos Arabella was going to start, cytarabine, was going to be given every day for four days with a three-day break. So, the ANP suggested training us to give the IV chemo at home. We were a little hesitant at first, but if it meant less time at hospital for Arabella, then it was worth trying.

We found the process easy – all the nurses were supportive, and we were both trained and signed off over a couple of weekends (the chemo started on a Friday). The nurses were so helpful and thorough, they showed us what to do from setting up the tray, drawing up hepsal and saline, to administering the chemotherapy. Then we both separately set up the tray and administered the chemo while being supervised before being signed off. We were given everything we needed to take home, from sterile wipes to a sharps bin, and we would collect the chemo every weekend. Arabella has a portacath so we still needed to have a gripper placed before the chemo could be administered, which the nurses did, but this was no problem as we would get her gripper inserted on the clinic day and then take everything we needed home.

How it's helped our family

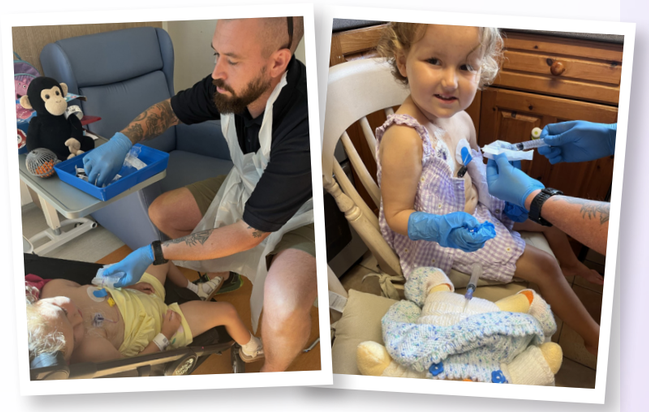
Being able to administer chemo at home was a massive help. It really helped Arabella as she was more relaxed in her home environment. It meant less time travelling (it takes us approximately 45 minutes each way) and less time in the hospital. It also helped financially, as we were using less fuel than we had been travelling to and from hospital.

Thankfully, we found no major challenges. We felt well prepared and well equipped, and we knew the nurses were only at the end of the phone if we needed help. Sometimes, a line doesn't bleed back initially when accessing, but we were made aware of this and knew to flush the line with saline first then bleed the line back so when it did happen, we didn't panic and could handle the situation.

If you feel you'd be able to administer chemotherapy at home, then I'd say please ask your team. It isn't as scary as it first sounds, and it's a much nicer experience for your child, especially in the beginning when you might feel like you live at the hospital! I also felt it gave us some sort of control in a situation where you feel like you have none. If you're newly diagnosed, try to remember there's light at the end of the tunnel. Keep going and stay positive. You'll get through this. We're seven months into treatment now and we're hoping things will be so much easier. We're due to go into our maintenance stage, which for Arabella means at-home oral chemotherapy.

We want to raise awareness of ALL and money to fund further research to understand it and develop new treatments. We believe CCLG is doing an amazing job in raising awareness and funding research, and we – and our friends, family and supporters – wanted to help. That's why we set up Arabella's Leukaemia (ALL) Research Fund with CCLG to support other families in the future.

Scan to find out more about Arabella's fund



COVER STORY

Harnessing artificial intelligence to identify new drug combinations

▲ Professor Chis Jones (left) and Dr Fernando Carceller (right)

Artificial intelligence (AI) has helped scientists propose a promising new drug combination for DIPG brain tumours. **Prof Chris Jones,** Director of the Brain Tumour Research Centre of Excellence at the Institute of Cancer Research (ICR), and **Dr Fernando Carceller**, Paediatric Neuro-Oncology Consultant at The Royal Marsden Hospital, tell us more.

Diffuse intrinsic pontine glioma (DIPG) is a challenging brain tumour affecting the brainstem of children, usually around five to seven years of age. Unfortunately, for many years we knew little of the underlying biology of these tumours because, due to their location, obtaining tumour samples wasn't common practice, and clinical trials based upon similar-looking gliomas in adults made little difference to the outcome of these patients.

The last 10-12 years have led to an enormous increase in our understanding of what makes DIPG so different to other cancers. However, for many of these new biological targets we've uncovered, there aren't yet any drugs available in the clinic that can be given to these children.

An example of this is a gene called ACVR1, which was discovered to be associated with around a quarter of DIPGs nearly 10 years ago by Chris' team at the ICR in London, along with several other groups worldwide. This gene had never been linked to human cancer but was instead known to play a key role in the development of a congenital malformation syndrome called fibrodysplasia ossificans progressiva (FOP). This exceptionally rare disease sees the soft tissue of an affected patient gradually turn to bone. Working with researchers in the FOP field, Chris' team demonstrated that laboratory models of DIPG may respond to drugs targeting ACVR1, but none of these were yet suitable for administration to patients.

How AI helped us

Hearing this story presented at an international meeting in the US, an AI company called BenevolentAI approached Chris with a proposal to use their proprietary technology to search for drugs already in the clinic which might also target ACVR1.

Their platform scoured all available drug databases and scientific publications to look for such a drug, but there was a problem. As well as hitting ACVR1, any drug to be 'repurposed' in this way would also have to reach the tumour tissue, crossing the protective blood-brain barrier – and it appeared there weren't any such drugs available.

> **"It's a discovery that we wouldn't have made without AI."**

The flexibility and benefits of such a computational approach compared to manual sifting of the vast amount of information out there then became clear. The platform was subsequently tweaked to look for a combination of drugs such that one may increase the brain levels of the other.

The combination proposed were two drugs readily available for other indications – one of which targeted ACVR1, and another which blocked a cellular 'pump' which would otherwise limit the ability of the first to reach the brain, like bailing water from a boat. Most promisingly, this combination was already being tested in adults with brain metastases from certain forms of lung cancer.

Chris' team first validated the use of these drugs in the lab, and then joined forces with colleagues in the Paediatric & TYA Neuro-Oncology and Drug Development Unit at the Royal Marsden Hospital, led by Fernando, to see if this was something that could be safely given to children. Both teams are currently working to translate these findings into a clinical trial to assess the efficacy of this drug combination in DIPG with mutations in ACVR1.

A glimpse of the future?

This drug combination is extremely promising for these children, who otherwise have few options for these types of tumours. It's a discovery that we wouldn't have made without AI. It's exciting to think that there may be other new treatment possibilities for children with these tumours that we may uncover this way.

As AI gains a foothold in various parts of a patient's pathway from helping analyse pathological specimens to reading radiological scans – it's tantalising to think it might make the biggest difference in uncovering new and effective treatments for children with cancer.

The GRANS trial: Pioneering a novel treatment

***Prof Robert Wynn**, Consultant Paediatric Haematologist and Director of Bone Marrow Transplant at Royal Manchester Children's Hospital, leads the GRANS clinical trial. He tells us how this innovative treatment is showing promising results for children with hard-to-treat leukaemia.*

When leukaemia isn't cured with chemotherapy, we use cell therapies including transplant. Many children with leukaemia are cured by having a transplant when it would have been incurable with drugs. During a transplant, we give a donor's bone marrow, and the immune cells of the donor reject and kill the patient's leukaemia cells. We call this graft-versus-leukaemia (GVL) and understanding, refining and redirecting this GVL will make a transplant even more effective and safe, and extend its use beyond leukaemia to children with solid tumours, for whom there are no effective treatments once chemotherapy fails.

We noticed that when we use cord blood – surplus blood taken from the placenta of newborn babies – then the transplant works better than using bone marrow, and fewer children relapse afterwards. There's also less graft versus host disease (GvHD), which is where the donor immune cells don't just kill leukaemia cells but attack healthy tissues in the body, too.

For children with acute myeloid leukaemia (AML) and residual disease (MRD positive after standard treatment), only 10% were cured with a transplant using bone marrow, but 50% were cured, without GvHD, using cord blood. These are remarkable differences.

Why does using cord blood work better?

Firstly, when we do cord transplants the donor is less well matched to the recipient and the immune cells can see the leukaemia cells better, using this mismatch. Secondly, we infuse more immune cells during cord transplants so there are more immune cells to reject and kill leukaemia cells. We noticed that when we give granulocytes (a type of white blood cells) to children having cord blood transplants then we see a surge of donor immune cells (called T-cells) stimulated by the infusion.

We noticed this by accident at first, but it happened every time we gave such an infusion to children receiving cord blood and granulocytes. We reasoned that as GVL is mediated by T-cells and is better with cord anyway, then this massive surge of T-cells might further decrease the chances of relapse in those with the highest risk leukaemia.

We opened the GRANS clinical trial for children, referred by a national multidisciplinary team, who had a transplant but had relapsed or refractory disease. During this trial, we gave granulocytes to children receiving a mismatched cord blood transplant. We have already published the results from the first ten children, and we continue to recruit children at Royal Manchester Children's Hospital (RMCH).

Some key findings:

- GvHD rates and risks of serious complications are very low – the transplant is safe, despite the mismatch and the immune expansion
- Some children reject the transplant, which is unusual in normal cord transplant
- Almost all children go into remission and in many, this remission is sustained, and some are cured

What's next?

We'll evolve our protocol and we're looking to extend the protocol to adult patients. We'll use an expanded cord (increasing the number of stem cells) to reduce the risk of rejection. We'll add a top-up of cells from the donor to try and prevent later relapse.

In the labs at the University of Manchester, we're looking to see if these cord blood T-cells can see and reject solid tumour cancer cells. We've learnt about a lot of immune responses against leukaemia, but solid tumours are also killed by donor T-cells. With oncology colleagues here at the RMCH, I want to see if we can cure children with brain tumours and other solid tumours whose lives are currently lost to disease, and for whom drugs don't work.

The Little Princess Trust, in partnership with CCLG, funded the lab science of this work, which helped us greatly. I think this project has the ability to cure more young patients, since it's a refinement of a technique – bone marrow transplant – that's already saved so many lives.

Molecular radiotherapy for children's cancers

Molecular radiotherapy (MRT) is an evolving form of children's cancer treatment. ***Dr Mark Gaze, Caroline Elmagrahi*** *and* ***Georgia Azzopardi****, of University College London Hospitals NHS Foundation Trust, tell us more about what it is and what work is being done to develop its usage.*

▲ Caroline Elmagrahi (left), Dr Mark Gaze (middle) and Georgia Azzopardi (right)

MRT is a less well known form of cancer treatment, but can be highly effective, even when the cancer has spread widely. Its uses are growing, and there are increasing numbers of clinical trials of MRT in a variety of types of childhood cancer. There's a lot of ongoing work in this field to improve, personalise and discover new uses for MRT, aiming for better outcomes for children affected by cancer.

What is MRT and how does it work?

Unlike 'conventional' radiotherapy, where a beam of radiation from a machine is directed at a cancer, MRT is a treatment given either by mouth or injection. A radioactive drug accumulates in the cancer cells in a much higher concentration than in most healthy cells. In this way, it delivers a high radiation dose directly to the cancer, sparing healthy, normal tissues. When taken up by the tumour cells, the radiation destroys them. This is a highly targeted treatment.

What is MRT used for, and what trials are there?

The oldest and most common form of MRT is the use of radioactive iodine for the treatment of thyroid cancers. Most patients have a single dose following surgery, to destroy any remaining thyroid cells.

Children who have advanced disease – for example, spread to their lungs – may require multiple treatments over time, and this may still cure the cancer completely. This is an established treatment.

MRT with 131-Iodine mIBG is already an established treatment for high-risk neuroblastoma which has not responded well to initial chemotherapy or has relapsed. 131-Iodine mIBG is currently included in an American front-line high-risk neuroblastoma trial. There's a range of clinical trials (past, present and future), which try to optimise its use in different ways. These include trials with:

- radiation sensitisers to make tumour cells easier to kill e.g. VERITAS trial
- immunotherapy combinations e.g. MINIVAN trial
- combination with targeted drugs so cancer cells cannot repair themselves e.g. MINT trial

"Unlike 'conventional' radiotherapy, where a beam of radiation from a machine is directed at a cancer, MRT is a treatment given either by mouth or injection."

The radioactive drug 177-Lutetium DOTATATE targets a cell surface receptor on some cancers. It's been shown to improve outcomes for neuroendocrine cancers in adults, and its use is being evaluated in children with the same disease in the ongoing NETTER-P trial. The same drug is being tested in children with neuroblastoma. Previous LUDO trial data formed the basis for the current LUDO-N trial, which gives an increased amount of 177-Lutetium DOTATATE over a shorter period, hoping to improve outcomes.

Patients with leukaemia needing bone marrow transplants traditionally receive conditioning with external beam radiotherapy which, although effective, does have long-term side effects. MRT with a monoclonal antibody (immune system protein created in the lab) directed against leukaemia cells has been shown in the RIT trial to be safe, and now the RIT-2 trial will study a much larger number of patients to see how effective it is.

Side effects and isolation?

MRT in general is a very well-tolerated treatment. There's no hair loss or severe sickness and fatigue, as seen with some chemotherapy regimens. There are some side effects depending on the type of treatment, while another challenge for patients is that they have to be isolated in hospital. Their stay will be a week or more, depending on the treatment. The room is large with an ensuite, as well as a separate side room for a parent to sleep in. As long as comforters and carers follow simple safety measures to keep their personal radiation exposure as low as possible, they can spend as long as necessary with the child during treatment

Although this treatment may seem daunting for children, with the support from the multiprofessional team including play specialists, nurses, radiographers and physicists, they're able to cope very well.

Understanding the evolution of neuroblastoma to improve treatment

Dr Alejandra Bruna

- **PROJECT TITLE:** Single-cell transcriptomics linked to lineage tracing to interrogate the role of intra-tumour heterogeneity in shaping therapeutic susceptibility and resistance in paediatric cancer
- **LEAD INVESTIGATOR:** Dr Alejandra Bruna
- **INSTITUTION:** The Institute of Cancer Research
- **AWARD APPROX:** £500,000 (funded by The Little Princess Trust in partnership with CCLG)

Neuroblastoma is one of the most common types of childhood cancer and is particularly good at adapting to resist treatment. When we take a closer look at a neuroblastoma tumour, we discover something extraordinary – they're made up of lots of different types of cells, each with unique traits and behaviours. Due to this, there are a wide range of outcomes for patients, with some rare cases of neuroblastoma spontaneously curing themselves, while others can be incurable.

Neuroblastoma cells can adapt to their surroundings using a trait called 'phenotypic plasticity', which lets the cells change how they look or behave without affecting their genetic code. The cancer cells seem to exploit their differences to navigate the challenges posed by treatment. By doing so, they persist, adapt and ultimately re-emerge as a relapsed disease, often with limited treatment options.

What this means for neuroblastoma treatment

The diversity hidden within neuroblastoma tumours holds a key to improving their treatment. Understanding this diversity could help doctors target specific cell types within tumours, potentially significantly improving outcomes. However, if neuroblastoma keeps changing over time, a truly effective approach could be one that prevents this transition process. Understanding the dynamics of cancer evolution is a key priority according to recent studies, especially in childhood cancers like neuroblastoma. These studies go against traditional beliefs that mutations in the genetic code are the primary drivers of cancer evolution and suggest that non-genetic variation like phenotypic plasticity play a crucial role.

By understanding the types and origins of neuroblastoma diversity, researchers are better equipped to devise strategies that target the tumour's adaptability. We predict that targeting the most adapted cell state and the process of adaptation itself would be an effective way to cure neuroblastoma.

Our mission in the lab

In our laboratory, we want to understand how neuroblastoma evolves. We're harnessing a cutting-edge technology called 'single-cell barcoding', which allows us to look at the cells we have grown in the lab and see how they evolved with treatment and other stages of neuroblastoma. Our goal is to gather evidence of the non-genetic drivers behind cancer evolution.

Additionally, we're in the process of developing special tools that can identify biomarkers in the body linked to non-genetic treatment responses. These biomarkers could significantly impact outcomes by helping doctors choose more effective treatments.

Anticipating progress and personalised care

Our research not only aims to uncover the mysteries of cancer evolution but also holds the promise of personalised care for neuroblastoma patients. By understanding which patients are likely to be unresponsive to treatment, experience progression, or face relapse, we aim to provide doctors with vital predictive information. Armed with this knowledge, we can work towards strategies to prevent resistance and relapse.

In conclusion, the significance of understanding non-genetic diversity in childhood cancers like neuroblastoma can't be overstated. Our journey into the complexities of cancer evolution has the potential to transform the way we approach treatment, prediction and patient care. Through a combination of advanced technologies and innovative thinking, we hope to pave the way for improved outcomes and brighter futures for young patients and their families.

www.cclg.org.uk/our-research-projects

60 SECONDS WITH

Pritesh Patel

Pritesh Patel, Senior Specialist Pharmacist in Paediatric Cancer at Great Ormond Street Hospital for Children and CCLG member

Q: Tell us about your career so far?

A: I qualified as a pharmacist in 2009. After a few years working as a junior pharmacist, rotating in different areas of pharmacy, I moved to Great Ormond Street where I developed an interest in cancer. I then moved to the cancer team and have been a senior pharmacist in paediatric cancer for 10 years. Throughout the past decade, I've worked mainly in patient-facing areas in inpatient and outpatient wards, but also in the chemotherapy manufacturing unit and have trained as a non-medical prescriber.

Q: Tell us about your role in supporting young people with cancer and their families?

A: Pharmacists have a wide range of roles supporting young people with cancer. On a day-to-day basis, we're responsible for the safe and effective use of medicines to treat paediatric cancer. This includes making sure chemotherapy is prescribed and tailored to each individual patient, the patients have had the right tests and investigations before having the chemotherapy, and supportive treatments are as effective as possible.

Where patients have side effects, we'll help manage those as well as optimise future treatments. We also work with the wider pharmacy team to prepare chemotherapy in a safe manner, ready for giving it. Where patients need to take medicines at home, we'll go through those medicines with patients and their carers to make sure they fully understand how to give them, but also importantly what side effects to look out for.

We also work with colleagues from different hospitals to coordinate the care of each patient so they can also have treatment closer to home. Medicine is ever evolving, and we're constantly working to improve treatments, reduce side effects and improve outcomes. The way we treat cancer is progressing as we better understand the genetic causes of it. We work on introducing new drugs and treatments for cancer, often in clinical trials. We also work with our medical and nursing colleagues to develop national guidelines for treating different types of cancer.

"Where patients have side effects, we'll help manage those as well as optimise future treatments. We also work with the wider pharmacy team to prepare chemotherapy in a safe manner, ready for giving it."

Q: What is the proudest moment of your career so far?

A: I particularly enjoy working on improving the way we do things and have worked on many improvement projects. I was proud to receive my Trust's Improvement Champion of the Year after leading on a project to improve the tracking of chemotherapy within the Trust. The project revolutionised a previous paper-based system and made the process of manufacturing chemotherapy safer.

Q: What's the most rewarding part of your job?

A: I have the great honour of witnessing many patients ring their end-of-treatment bell. I'm genuinely touched each time I see a child do it, surrounded by their loved ones. I'm humbled every day seeing this. The small part I play in the process of helping get patients to ring that bell helps keep me motivated.

Q: What is most challenging?

A: We're often working without a lot of evidence behind what we do. Finding the time to do research and fill those evidence gaps is challenging in a busy environment, but it's important to think about the patients in the future as well as the ones in front of you.

Q: Do you have any advice for children with cancer and their families?

A: No question is too silly. You have a team of highly-trained healthcare professionals who are there to support you. Make the most of the time you have with them, but also find out how you can get in touch with them if you have any questions later on. You'll be given a lot of information throughout your treatment journey, and we all understand that it is impossible to digest all the information immediately.

ASK THE

Expert

Caroline Brown, Lead Complementary Therapist for Paediatrics, Teenagers and Young Adults at The Royal Marsden Hospital

What is story massage?

Complementary therapies are used alongside conventional medical treatment. They can help relieve symptoms and side effects of cancer treatment and provide positive self-help and coping strategies. Story massage is a fun way to introduce the benefits of positive touch through storytelling and simple massage strokes.

What happens?

It consists of 10 easy-to-follow massage strokes, each with a child-friendly name and symbol, which are used to represent different parts of the story. Story massage can be adapted for all ages, abilities and backgrounds and sessions can be tailored to suit each child's individual needs. Massage stories are given through clothing, without the need for massage oil and always with respect and consent.

How does story massage help children with cancer?

Story massage is an enjoyable, meaningful and safe activity. It provides the experience of positive touch, which is important for children having stressful and painful procedures. Story massage can be practised by everyone in the family, from patients, siblings, parents and grandparents. During long and exhausting hospital stays, it's a helpful alternative to screen time, allowing families to share time together, having fun and connecting. Story massage is relaxing for both mind and body, easing tension and stress and allowing dedicated time to recharge and feel calm.

What does story massage entail?

Favourite stories, poems, songs and nursery rhymes can be adapted as massage stories. Health professionals, family members and children themselves can also write their own massage stories which can be a creative and therapeutic activity. The choice of 10 massage strokes makes this a simple activity that can be done together and repeated often! The strokes have names like 'The Wave', a zig-zag movement in a downward direction, and 'The Sprinkle', a light tapping of the fingertips as if playing the piano. Story massage stickers can be added to books, showing the different massage strokes.

What other types of complementary therapies are there?

Aromatherapy, therapeutic massage and reflexology are examples of other complementary therapies. These are safe and effective, working on both a physical and psychological level. Complementary therapies promote the release of endorphins and oxytocin, the body's natural pain killing and feel-good hormones, allowing for pain reduction and a feeling of general wellbeing. They can be effective for symptoms such as muscular aches and pains, headaches and nausea and help improve sleep and boost mood, motivation and self-esteem, as well as reducing stress and anxiety and providing a helpful distraction.

How do people find out more?

A free service may be available within your child's hospital. Your child's nurse specialist will be able to tell you more. Alternatively, you can search for local practitioners on the government backed Complementary & Natural Healthcare Council website, cnhc.org.uk. It's a good idea to check the therapist has had the correct training and experience of working with cancer patients. For more information, visit storymassage.co.uk.

Have a question to ask one of our experts?

Please get in touch by emailing **info@cclg.org.uk** or via DM on our social channels.

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13 July
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7-8 September
South Coast Ultra Challenge

8 September
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