CENTRE FOR ADOLESCENT RHEUMATOLOGY IMPACT REPORT

VERSUS ARTHRITIS

GREAT ORMOND STREET HOSPITAL CHARITY

MAKING SURE NO ONE WITH ARTHRITIS IS LEFT BEHIND

Adolescence is an important time in our lives when many physical, emotional and educational changes happen. Between the ages of 9 and 24, adolescents face unique challenges both in their personal lives as well as in the management of their condition. Ongoing care and treatment is required for many rheumatic conditions so it is incredibly important to make sure that young people do not fall into gaps between services.

Despite all this, 12 years ago, most research focused only on adults or younger children, including for people with arthritis and related conditions. Adolescents often 'missed out' both in research and healthcare, leaving a big knowledge gap about this time of transition. This blank canvas enabled the emergence of a new area of research called Adolescent Rheumatology. To meet the needs of these adolescents, a dedicated Centre was formed, and with it, an opportunity to support young people living with arthritis and other rheumatic conditions to independently manage their own healthcare.

ENTER THE WORLD'S FIRST CENTRE DEDICATED TO UNDERSTANDING ARTHRITIS IN ADOLESCENTS

In 2012, the research teams at University College London (UCL) teamed up with rheumatology clinical teams at University College London Hospital (UCLH) and Great Ormond Street Hospital (GOSH). Together, they created the Centre, co-funded by Versus Arthritis and Great Ormond Street Hospital Charity, where doctors, nurses, researchers and patients work together on research projects that focus on adolescent health. This unique collaboration has led the way for a pioneering commitment to enhance and transform rheumatology care and research for young people.

CENTRE FOR ADOLESCENT RHEUMATOLOGY

VERSUS ARTHRITIS

UCL

Professor Lucy Wedderburn
Centre Director

Professor Debajit Sen
Centre Co-Director

Professor David Isenberg
Centre Co-Director

Professor Coziana Ciurtin
Principal Investigator

Professor Despina Eleftheriou
Co-Principal Investigator

When the Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCLH and GOSH was launched in 2012, it was the first of its kind. We recognised that young people with rheumatological diseases have particular needs which were not well served by previous research. We were determined to fill the gaps, in partnership with patients, using discovery science and translational research to improve the health and wellbeing of adolescents, and ensure seamless research across the ages. We brought together children's, adolescent and adult rheumatology researchers and clinical teams, as well as patients. We developed new multi-disciplinary teams, skills and expertise to understand how puberty and development intersect with these conditions and impact patient outcomes.

It has been a huge privilege to serve as Director of the Centre and to work with such diverse, highly talented investigators, patients, and advisors to build this new community.

We have:

- generated deep understanding about how sex, gender and the immune system interact in these diseases
- built a unique biobank including over 3000 samples from young people with rheumatic diseases
- offered opportunities for young people to be involved in research at every stage
- delivered new clinical trials and biomarkers for children and young people
- leveraged over £38m more funding to support this work
- helped to launch UK-wide networks in the field, BANNAR and the young person's panel, Your Rheum
- trained and supported young clinicians and discovery scientists who are now becoming leaders in the field.

Now that adolescent rheumatology research is firmly embedded across the UK, we look forward to the next steps to enable better lives for all of our patients, at any age.

MEET SOME OF THE YOUNG PEOPLE WHO SHAPED THIS REPORT

Eleanor
Juvenile idiopathic arthritis and Sjögren disease

Harriet
Juvenile idiopathic arthritis

Phoebe
Juvenile dermatomyositis

Hamza
Juvenile idiopathic arthritis (undifferentiated)

Suruthi
Juvenile idiopathic arthritis

Sara
Juvenile idiopathic arthritis

HEAR FROM THE CENTRE'S SCIENTIFIC ADVISORY BOARD

"For the last 13 years we have had the privilege and pleasure of chairing two important committees (Advisory Board and International Scientific Board) underpinning the activities of the Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCLH and GOSH. We have seen the development of a successful, dynamic and productive Centre of huge international significance. The Centre has carried out truly interdisciplinary research, bringing researchers with different expertise together, making inroads into our understanding of the influence of sex, gender and the immune system as well as factors governing mental health and pain in adolescents. The Centre has generated excellent research findings that impact directly on patient care, has trained young clinicians and scientists who will become future leaders in rheumatological research, and leveraged substantial amounts of additional research funding."

Professor David G I Scott - Chair of Advisory Board
Professor Anne Cooke - Chair of the International Scientific Panel

OUR ADOLESCENT CENTRE IS INVESTIGATING WAYS TO:

1. BETTER UNDERSTAND ADOLESCENT RHEUMATOLOGY

2. CHAMPION EXPERIENCE-DRIVEN RESEARCH

3. IMPROVE CARE SO YOU CAN FEEL YOUR BEST

4. PIONEER THE FIELD AND FORGE A PATH FORWARD

OUR RESEARCH IMPACT AREAS

£3.4 MILLION VERSUS ARTHRITIS + £500,000 GOSH CHARITY FUNDING HAS LED TO

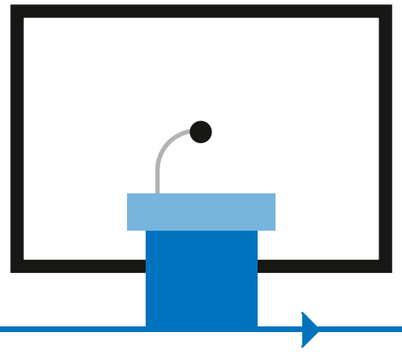
OVER 400
publications cited more than 10,000 times

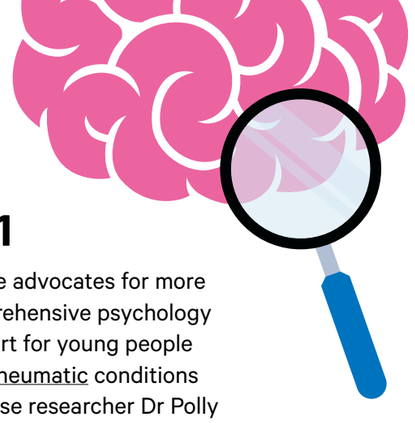
OVER £38 MILLION
leveraged funding

OVER 80
staff and students

RESEARCH ACHIEVEMENTS

at the Adolescent Rheumatology Centre





2012

The Centre for Adolescent Rheumatology is established, funded by Versus Arthritis and co-funded by GOSH Charity.

2012

Centre biobank opens, collecting biological samples from people living with rheumatic conditions as well as healthy controls of all ages and genders.

2013

Centre forms the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR), a national network of professionals working in adolescent and young adult rheumatology.

2013

Blood protein called MRP8/14 found by the Centre as a potential biomarker to predict successful treatment of childhood arthritis with methotrexate.

2014

Centre hosts the first National Adolescent Rheumatology Symposium. They become regular, highly successful events for growing the adolescent rheumatology field in the UK and beyond.

2015

Centre begins including young people with gender incongruence or with sexual development differences (intersex) in research, investigating the impact of sex hormones and sex chromosomes on immune system function.

2016

Your Rheum, a unique group of 11 to 24-year-olds living with rheumatic conditions who shape adolescent and young adult rheumatology research, is established.

2017

Muscle biopsy score tool is incorporated in routine clinical assessment and recommended in European (SHARE) guidelines for juvenile dermatomyositis patients. This tool was originally validated at the Centre.

2018

Advanced, time-efficient MRI methods to measure arthritis in the growing spine and skeleton are adopted as standard care at UCLH. These methods were designed by young people alongside Centre researchers Professor Margaret Hall-Craggs and Dr Tim Bray.

2018

CLUSTER, an experimental medicine consortium funded by the Medical Research Council, Versus Arthritis, GOSH Charity and others, is established.

2019

Signalling protein called IL-17 validated as a drug target for juvenile idiopathic arthritis by Centre researchers. This target has since led to the approval of a therapy called Secukinumab (Cosentyx™).

2019

How our immune system responds in a group of rare inflammatory diseases is found to differ between adults, adolescents and children. These age-specific immune signatures highlight the need and opportunity for more personalised disease assessment and treatment decision-making.

2020

Centre research led by Dr Lizzy Rosser shows how molecules in the gut produced after digestion of dietary fibre by gut bacteria affects the balance between pro- and anti- inflammatory B cells in arthritis patients.

2020

The Paediatric Sjögren's Cohort study and Repository, led by Professor Coziana Ciurtin, is established. It is the first study of its kind for Sjögren in Europe.

2021

Protein called ApoB:ApoA1 shown by Centre fellow Dr George Robinson as an indicator for increased risk of health and metabolism problems, and other complications, for people living with JSLE.

2021

Centre advocates for more comprehensive psychology support for young people with rheumatic conditions because researcher Dr Polly Livermore found that nearly half of paediatric rheumatology departments do not have access to a psychologist.

2022

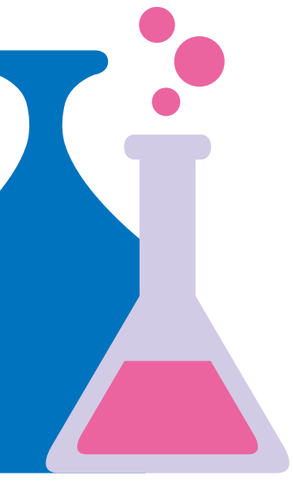
British clinical management guidelines (BSR) incorporate, for the first time, people of all ages with myositis including children. Expertise from Centre members was key to this update.

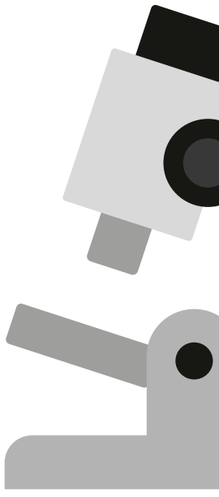
2024

Professor Coziana Ciurtin leads updates to British clinical management guidelines (BSR) for Sjögren disease that include adolescents for the first time.

2025

Centre researcher Dr Hannah Peckham leads a study which helps explain why there's a sex bias for many rheumatological conditions. Sex hormones and chromosomes are found to work in tandem to impact immune responses.





THE FUTURE

1. BETTER UNDERSTANDING OF ADOLESCENT RHEUMATOLOGY

Why is this important to young people with arthritis and other rheumatic conditions?

The Centre is unique in being dedicated to understanding what drives and controls the development of arthritis and related rheumatological conditions in adolescence. They have classified disease types, found biomarkers, and mapped biological features across many conditions which are now feeding into new treatments for thousands of young people with arthritis.

How have they achieved this?

By establishing a biobank of 3000+ specialised blood samples, it is the largest of its kind in the UK. This biobank houses linked data from young people with arthritis, lupus, myositis and related conditions, a diverse group of healthy control young people of similar ages, and also young people with gender incongruence or with differences of sexual development. It contains a wealth of information that allows researchers to investigate the health of young people dynamically over time.

ONE OF A KIND CENTRE

OVER 3000 BIOBANK SAMPLES

What has the Centre discovered?

Juvenile idiopathic arthritis (JIA)

New Product: Some immune cells that drive damage to JIA joints do so by making inflammatory proteins called cytokines. Centre research found and proved a particular cytokine called IL-17 as a treatment target. This research contributed to trials that supported the approval of an IL-17 blocker called Secukinumab (Cosentyx™) in 2022. This medicine has already treated more than 700,000 patients worldwide for inflammatory conditions and is now available in the EU to treat young people with some forms of JIA.

New Knowledge: Policing cells of the immune system, known as regulatory T cells or 'Tregs', are different in the joints of young people with JIA in comparison to healthy controls. Dr Pesenacker, funded by a Versus Arthritis Career Development Fellowship, developed a way to measure Treg fitness which is a biomarker for disease activity. With more research, it could predict and prevent flares as a disease monitoring tool in clinical practice through a small blood sample.

700,000 PATIENTS WORLDWIDE

treated for inflammatory conditions including JIA

Uveitis

New Knowledge: A genetic component to JIA uveitis was first suggested in the 2000s, then clinical indicators were found. The Versus Arthritis Centre for Genetics and Genomics at the University of Manchester, in collaboration with Adolescent Rheumatology Centre researchers, has progressed this understanding further by combining the two. They've developed a JIA uveitis integrated risk model with higher predictive power. This risk model could predict who is at most risk of JIA uveitis, help prevent unnecessary regular eye tests, and improve future screening strategies in the clinic.

Juvenile-onset systemic lupus erythematosus (JSLE)

New Knowledge: We now know much more about the immune system in a person with JSLE - in what way it goes wrong, why, and how that might affect a person's disease trajectory. This is because Centre researchers led the largest-ever direct comparison of juvenile-onset lupus with adult-onset lupus and have since been able to describe what the immune system landscape looks like in a young person with JSLE, and how it changes over time. It turns out it's extremely variable from person to person, and importantly, a white blood cell known as CD8+ T-cell is linked to severe clinical outcomes.

Juvenile dermatomyositis (JDM)

New Knowledge: Inflammatory proteins made by our immune system, known as Type I Interferon, are thought to drive the development of JDM. Dr Wilkinson showed that mitochondria, the powerhouse of our cells, are abnormal in the blood cells for JDM patients. These changes cause our immune system to make more Type I Interferon, driving inflammation. This mitochondrial abnormality could open up new drug avenues to treat JDM.

FOOD AND GUT

Our gut microbiota, the trillions of normally helpful microbes like bacteria and fungi, plays an important role in causing arthritis, affects our immune system, and can be targeted to help disease.

The Centre is the only place in the UK able to collect adolescent microbiome samples. They are uniquely positioned to investigate this further, and this has propelled an award-winning line of work, led by Dr Lizzy Rosser, to leverage over £2.5 million in grants and set up a new research group to run more dedicated studies.

SEX DIFFER-ENCES

Sex and gender differences in the immune system can affect disease risk and clinical outcomes. For example, B cells (the immune cells that make antibodies) are affected by the sex hormone oestrogen in people assigned female at birth. This may partially explain why many autoimmune rheumatic diseases such as JIA and JSLE have a strong female sex bias, and why the development of lupus is most common around the time that puberty begins.

The Centre has established itself as a leader in this rapidly evolving space because of its strong emphasis on diversity and inclusion in research.

ELIZABETH (LIZZY) ROSSER'S STORY

Understanding gut microbes and B cells

I began working at the Centre in 2016 through a foundation fellowship funded by Versus Arthritis. Following that, I became a senior postdoctoral research associate funded by the Centre. I still work at the Centre but now run my own research group, which is funded by the Kennedy Trust for Rheumatology Research with additional support from the Lister Institute for Preventive Medicine and the FOREUM foundation.

What research does Dr Lizzy Rosser do at the Centre?

I investigate how the immune system works in children and young people with rheumatic conditions. I focus on a type of white blood cells, known as B cells, to understand how they work and how they communicate with other cells like our gut microbiota.

Why is Lizzy's research at the forefront of its field?

The field of study I research is relatively niche and new which means there are so many opportunities and unanswered questions left to explore. From our research so far, we've shown that we know a lot less about what a healthy gut microbiome looks than we thought, despite what the media may portray. We also found that B cells respond to lots of different signals in healthy young people and young people with arthritis. These findings have identified new research questions which has enabled us to secure a series of successful grant applications and win awards. We hope that our research will identify new ways to treat young people with arthritis and potentially inform policies that improve child health.

Why is the Adolescent Centre so important and successful?

University College London is regarded as one of the best places to do paediatric and adolescent research in the UK because of the clinical collaborations and samples we have. It's a privilege to be at the Centre here under Professor Lucy Wedderburn's leadership. I can't speak more highly of her leadership, I'm very lucky.

Doing research about child health is just as important as it is for adults, even if sometimes it is harder to involve children in research because of special considerations. Our research is so important to make sure children, adolescents and younger adults are included in medical research studies of arthritis. Centre infrastructure funding is crucial because it pays for so much of the background work that often goes unseen - things like writing the ethics necessary to run studies; the paperwork needed to submit a publication and get it approved; gathering samples for a biobank; and creating environments where people can work well together. These Centre for Excellence grants built the foundation for great science to happen and this has been fundamental for my success as a scientist so far.

GEORGE ROBINSON'S STORY

Researching the causes, signatures and risk factors of JSLE

I joined the Centre in 2015 to work with Professor Liz Jury for my PhD, and now I am a Senior Research Fellow and Principal Investigator here.

What does Dr George Robinson research at the Centre?

My whole research career to date has been focussed on juvenile onset lupus, known as JSLE. When I first started studying JSLE, there was almost a blank canvas about the immunology and mechanisms behind the disease - very little was understood about this disease in younger patients and how it differs from adult-onset lupus.

What has George discovered?

I study JSLE from three angles, one angle is from the perspective of our immune system. Another JSLE question I study is why more women are developing the disease than men – around 8 in 10 patients with JSLE are female. I have found novel differences in both the immune system and metabolism that could help to explain this phenomenon.

The final angle I investigate relates to one of the leading causes of mortality in young people with JSLE, cardiovascular disease. There are currently no guidelines focussed on this in JSLE and yet the risk of cardiovascular disease in young patients with JSLE is up to 300 times higher than the general population. Our research has found that this heightened risk is driven by JSLE disrupting our metabolism and pro-inflammatory pathways. This leads to a 'perfect storm' where fat build-up and inflammation accelerates in our arteries, a process known as atherosclerosis, which is commonly treated using statins. This discovery led us to collaborate with JSLE experts based in the US. We pooled our resources with them and together, we've discovered a signature that can predict which patients could develop accelerated atherosclerosis, and those that continue to develop atherosclerosis despite taking statin treatment.

How has the Centre infrastructure enabled these discoveries?

These findings were discovered thanks to the Centre's biobank. It is pivotal to all this research. Without these samples, we can't do the research. The biobank houses more than a decade worth of biological samples from gender and ethnically diverse JSLE patients and healthy individuals, with matched clinical data, making it a very valuable resource to investigate these questions robustly and longitudinally.

Why is George's research so important?

Through the Centre, our discovery science research on JSLE has built an important evidence base around what drives the disease. We've helped change the way that JSLE as a disease is perceived. It is now much more respected as its own thing, an important sub-class of lupus, separate from adult-onset lupus. This is bringing to light that JSLE needs to be treated and managed in an individualised way, rather than merging it alongside existing, more generic guidelines for adult-onset lupus.

The significance of our work has won me several prestigious awards both nationally and internationally. Despite JSLE being a rare disease, the discoveries we've made have been voted as nationally high-ranking.

2. CHAMPIONING EXPERIENCE-DRIVEN RESEARCH

The Centre has launched many new platforms for young people to shape adolescent rheumatology research, and improved these opportunities, empowering them to get involved beyond being a participant. Patient experiences, thoughts and feelings are involved in every stage of research at the Centre which in turn drives higher quality, patient-centred research.

Increasing involvement opportunities

- **Centre Patient and Public Involvement and Engagement Network** - comprises of over 150 young people who provide advice on Centre research and healthcare services offered at UCLH.
- **BANNAR** – UK-wide network of 175+ professionals working in adolescent and young adult rheumatology, established with Centre funding and instrumental to the formation of Your Rheum.
- **Your Rheum** – the UK's first and only Young Persons Advisory Group for rheumatology conditions now with over 75 members. Your Rheum began with funding from the Centre and was set up between BANNAR and Dr Janet McDonagh at the Versus Arthritis Epidemiology Centre. Your Rheum is now nested within Versus Arthritis, creating a legacy for future work.
- **Adolescent Rheumatology Symposium** – regular event hosted by the Centre which brings together 100+ people each year. Young people from Your Rheum and BANNAR members are actively involved with its design, delivery and curation.
- **CAPE** – large collaborative study of pain in JIA that is part of a UK wide partnership and has already included 98 young people. Five young people from the Centre patient and public involvement network are on the CAPE advisory board.
- **CLUSTER Champions** – UK-wide patient-parent network with funding from the Medical Research Council, GOSH Charity and Versus Arthritis.
- **Young Scientist Days** - regular public outreach events where school and college students experience life in the lab. These events help to raise awareness for the importance of research in rheumatology and encourage students from all backgrounds to consider careers in science and medicine.

Improving the quality of involvement

Patient and public involvement: CLUSTER Champions co-produced a guide to PPIE, sharing their successful processes to cultivate and incorporate patient and public involvement systematically with the wider research community. This system ensures that research is both patient-centric and medically sound.

Leveraged funding: Every successful fellowship and grant within the Centre has hugely benefitted from patient input, discussion and feedback. For example, parents and patients were involved in the planning, design and management of MAPJAG, the world's first project to study synovial biopsy tissue from JIA patients at a single cell level, worth over £2 million. This in-depth study approach has shown promise for adult arthritis but has never been explored in young people before. By deepening this understanding, they hope to identify new treatment options and potentially predict young people at risk of JIA.

> "WE ASK,
> WE LISTEN,
> YOU SAY,
> WE IMPLEMENT"

PHOEBE'S STORY

Getting involved with Centre research for over a decade

I work as a doctor in Liverpool and was diagnosed with juvenile dermatomyositis aged 16, just before I was about to start my A-levels. My rheumatologist at the time recommended that I get referred to the Centre, where they specialise in adolescents and young adults like me. The London consultants offered me an opportunity to join the Centre's Advisory Board. I've been involved in Centre research ever since.

Why is patient and public involvement at the Centre a success?

To me, there are three reasons. Firstly, because of their genuine passion to involve patients. Secondly, their innovative ways to get young people to engage with their research. They're iteratively running focus groups to gauge what will appeal best to patients and using that to improve their engagement channels. Thirdly, the people. The Centre are a very approachable team. At Centre meetings with clinicians, research nurses, senior academics etc, I feel equal to everyone else. I may bring different expertise but I truly feel part of the Centre, respected, and not just there for the sake of it. These three things are why I've stayed with the Centre for over a decade.

What have been Phoebe's highlights at the Centre so far?

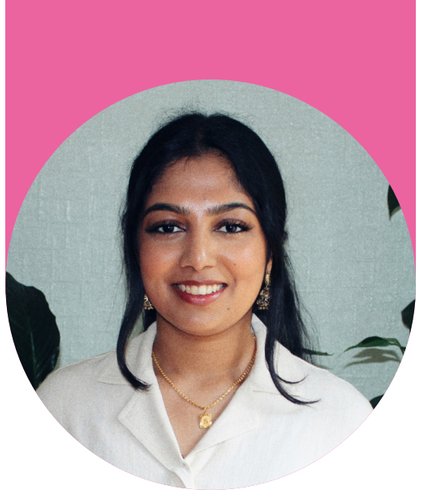
Instances where I've made a real difference. One example is when I helped to design the Centre website. I was involved in focus groups to make sure that it appealed to the target audience and when it came out, I felt very proud to have a physical thing to look at knowing I'd been a part of it. Another example is when we adjusted standard, paediatric questionnaires used in rheumatology to make them appropriate to adolescents. In the existing form, all questions were posed to parents. We helped reword the form and change the narrative, directing questions to the adolescents themselves. I know that small, thoughtful improvements like this can make a difference to patients.

Why do our young patient partners think that they should be involved in research that concerns them?

- It makes young people feel empowered and gives them a voice.
- Young people are experts in their own condition and know what is relevant.
- It provides a sense of relief and control over their condition.

SURUTHI'S STORY

With Your Rheum



When you're a young person with arthritis, you know there are others out there because of prevalence statistics, but you don't necessarily meet them. When I first joined Your Rheum and met like-minded people to sympathise with and relate to, it was a special feeling. I now help with onboarding new members. I find it rewarding to support these individuals and see them grow over the years.

Professionally, I've gained so many skills like scientific writing, communication, presentation skills and time-management. This is because I've received lots of opportunities through Your Rheum, from co-authoring publications to presenting at symposiums and judging at conferences.

What makes Your Rheum a success?

The researchers I work alongside really value input from patients. You can tell that they take us seriously because they're completely open to our responses and thoughts. The researchers are receptive to what we say, rather than just wanting us to agree with whatever they want. Part of this is because of the dedicated coordinators Your Rheum has who help select and organise the sessions.

The Your Rheum group is strong because of its diverse membership. There are so many different factors that can affect your healthcare, which are often overlooked, like geography and racial background. Our members allow researchers to learn more about these important aspects and hear a wide range of opinions.

YOUR RHEUM

Why do our young patient partners think it's important to have a dedicated adolescent rheumatology service?

- Adolescents have unique healthcare needs, different from both children and adults.
- Doctors in adolescent services understand school, exams, and life transitions better.

HAMZA'S STORY

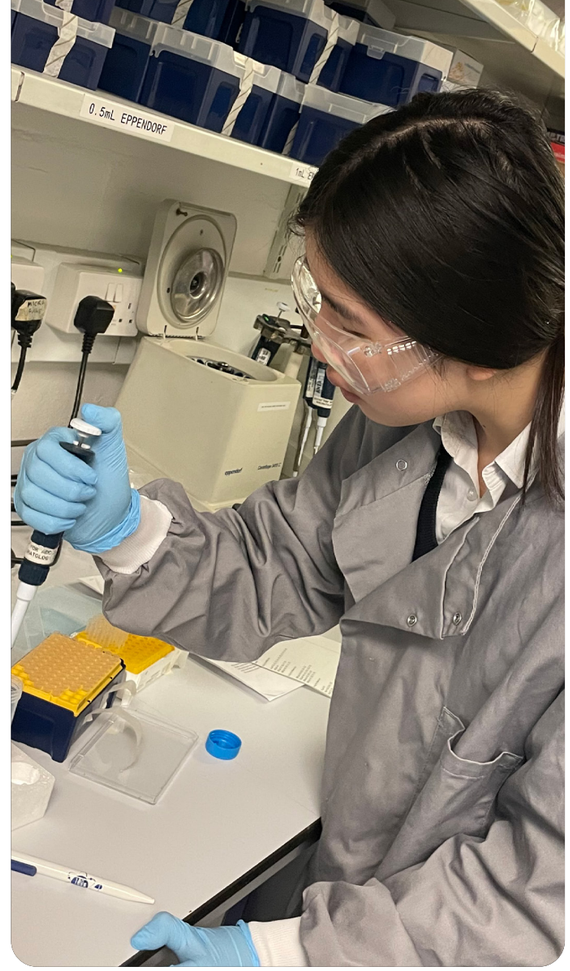
In championing inclusive research

When I was first diagnosed, I had no idea what JIA was, and I didn't know anybody else with it. I felt isolated and like my whole life had been flipped on its head. Getting involved in research has introduced me to similar people, helped me get my face out there, and given me lots of opportunities to grow both personally and professionally. Your Rheum has given me a safe space where I can get things off my chest, it feels like a weight has been lifted. I wish that everyone in my situation could have the same opportunities and benefits as me.

Why is getting involved in research so important to Hamza?

As a male South-East Asian Muslim, getting involved in research is incredibly important to make sure that a voice like mine is heard and shaping research in every conversation. Research must be inclusive. On another level, getting involved is key to get research done right and grants approved. This means that future generations of young people with rheumatic conditions can get better diagnosed and more involved.

What is one word you would use to describe Your Rheum?



YOUNG SCIENTIST DAY

8 OUT OF 10

students who attended said they are more likely to apply to university as a result of this activity.

3. IMPROVING CARE SO YOU CAN FEEL YOUR BEST

Why is this important to young people with arthritis and other rheumatic conditions?

The transition in care between paediatric and adult services is a vulnerable time for adolescents – challenges faced in this time can lead to poorer health outcomes. Centre research is mapping current care experiences and closing gaps where there is room for improvement, to make sure that adolescents are not forgotten. This is helping adolescents to feel better sooner and for longer.

Seeing arthritis in young people more accurately

New Knowledge: Centre research led by Professor Margaret Hall-Craggs and Dr Tim Bray resulted in the development of magnetic resonance imaging (MRI) tools to measure arthritis in the growing spine and skeleton. This new tool is more precise than conventional MRI methods, meaning that it can reveal arthritis at places in the body which may have previously been missed by clinical examination. Nobody had measured the spines of growing adolescents and how their arthritis changes on MRI over time before.

Practice influence: The MRI protocols were co-designed with young people. They wanted short scans, so Centre researchers reduced the time they were in the MRI machine. Several of the new methods are now adopted as standard care at University College London Hospitals (UCLH). This has led to better care and treatment whilst also saving resource by reducing time needed in MRI machines for adolescents and young people living with arthritis.

FASTER AND MORE PRECISE SCANS

which leads to better care.

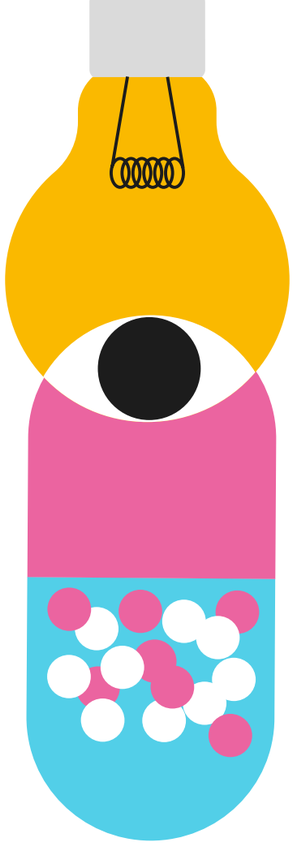
New Knowledge: Centre research has shown that clinical assessment tools for rheumatoid arthritis do not work well for young adults whose arthritis started as children. This has helped dispel the myth that when young people with JIA grow up, their condition 'becomes' rheumatoid arthritis.

Young people with arthritis and related conditions are now in the picture

Policy influence: Thanks to expertise from Centre researchers, British clinical guidelines (BSR) cover the whole life course for many adolescent rheumatologic diseases such as idiopathic inflammatory myopathy, psoriatic arthritis, and Sjögren disease, for the first time.

Patient and public involvement impact: The Centre has enabled young people to:

- co-write the "Adolescent and Young Adult Rheumatology In Clinical Practice" textbook
- participate in suitable clinical trials at any age, most clinical trials rarely allow this. The Centre successfully sought approval for young people to transition their care from GOSH to UCLH whilst contributing to the trial. This was a turning point for accessibility in clinical research for young people.



MYTH BUSTING

JIA does not become RA.

Treatment tailored to your needs and biology

Unfortunately for many JIA patients, the first treatment they are prescribed does not lead to disease control. A trial-and-error approach takes place, which means that many JIA patients have the frustration of trying several different types of treatments like biologics without success. Centre research, in partnership with CLUSTER, is improving the nuances of understanding what treatments work best for different individuals with JIA, moving towards a more personalised medicine approach.

Driving policy and practice improvements

Examples of Centre influence include:

- Defining the hallmark of autoimmune diseases known as autoantibodies, which attack the body's own tissues, that are specific to myositis in JDM. These biomarkers are now in routine clinical use for monitoring the disease.
- Advising NHS England about different biologics used to treat JIA, weighing up the risks, benefits and costs for each one through an evaluation known as a Health Technology Assessment to help inform guidelines.
- Contributing to NHS England policy for the use of a biologic called abatacept to treat myositis across the life course.

Rare but not overlooked

Centre research is improving the chances of success for young people with rare, rheumatological conditions such as myositis, Sjögren disease and scleroderma, to feel their best and get involved in research.

New knowledge: Centre researchers mapped disease activity trends in patients with juvenile dermatomyositis over time and identified distinct classes. Some patient classes showed improvement whilst others more severe disease, and these individuals could potentially be predicted based on their clinical information.

New products: New potential treatments have been found by successfully using therapies for rare genetic diseases that present with inflammation and other arthritis-like symptoms. Three examples supported by Centre Co-Principal Investigator, Professor Eleftheriou, include:

- Baricitinib to treat DNAse 2 mutations.
- Baricitinib to treat ISG15 deficiency-novel mutations
- JAK inhibitor to treat TNFAIP3 mediated neuroinflammation.

CLUES FOR NEW TREATMENTS FROM OTHER CONDITIONS

COZIANA CIURTIN'S STORY

Researching rare rheumatic conditions in young people

I'm a Professor of Rheumatology at University College London (UCL) and have been a Principal Investigator at the Centre since 2018. I'm also a clinician and spend half of my time working at UCL Hospital, looking after young people aged 13 to 24.

Which discoveries wouldn't have been possible without the Centre?

We were the first in the world to demonstrate there are certain kinds of cell sub-types that are more active, or function differently based on the sex hormones and sex chromosomal background of an individual. This helped us understand, from the time when puberty starts, why girls are more predisposed to certain autoimmune diseases than boys, and why boys have a metabolic profile that puts them at heightened risk of cardiovascular disease compared to girls.

How has being a part of the Centre helped Coziana?

Leading a research group at the Centre has helped me develop my own research interests, enabling me to focus on investigating rare, under-researched, and in some cases, under-recognised diseases such as juvenile-onset lupus (JSLE) and Sjögren disease. Working with clinicians and scientists all over the world through the Centre has allowed me to become part of instrumental initiatives that drive the research agenda and clinical management guidelines for these conditions. These opportunities have enabled my own personal growth within a specific area of expertise in adolescent rheumatology and supported my Professorship promotion.

What Centre work is Coziana most proud of so far?

Leading a research programme dedicated to working closely with young people with rheumatic diseases. We are the largest Centre that studies the molecular underpinnings of JSLE and Sjögren disease in the UK; UCLH has the largest transgender cohort of adolescent and young people in Europe enabling us to promote inclusive research and study the impact of puberty on immune responses.

More importantly, our research agenda is driven by what's important to the young people we look after in our clinical practice. Hearing their experiences, learning from them, and giving back to young people is what I absolutely love. I am proud that we have patented proteomic biomarkers predictive of cardiovascular risk and response to statin in JSLE.

What are some of the Centre's strengths?

Our Centre is globally unique, as is our biobank. This has qualified us to set up clinical trials in children and adolescents and follow them up from paediatric to adolescent and young adult services in an unprecedented way. Our biobank is incredibly valuable and underpins all our research. Another strength of the Centre is that our research is not done in silos. The funding we received enabled us to bring together two large clinical services at GOSH and UCLH and experts in many different fields to operate as one united front under the umbrella of the Centre. Out of this multidisciplinary environment, we've built national networks of healthcare professionals, researchers, young people and their families and carers to support the Centre initiatives. The voice of young people is very important.

POLLY LIVERMORE'S STORY

Researching mental wellbeing and rheumatological disease

I am a Senior Paediatric Rheumatology Nurse at Great Ormond Street Hospital and have worked in this field for nearly three decades. I've known Centre Director, Professor Lucy Wedderburn, for most of that time. Now, I lead several research projects with Centre support.

What research does Polly lead at the Centre?

I lead an experience-based, co-design study called IMPACT which is developing a verified chatbot for young people with rheumatological disease and their parents. We hope that they can turn to this chatbot for psychological support and answers, wherever they are based, day or night. The chatbot was borne out of previous research I led on which found that many families struggle to access psychological support. My research has also showed that the mental wellbeing of 8 in 10 parents and carers is negatively affected by their child's diagnosis. We believe that this chatbot could be especially valuable to parents on the weekends and out-of-hours, when clinics are shut, without needing extra manpower.

What have been the biggest successes from this project so far?

When we started this study, we planned to run eight focus groups. We ended up having 27 because there was so much interest! They were all co-delivered with our steering group members, experts through lived experience as either a patient or parent/carer. We then had a design and content workshop in May 2024 which 25 families attended. Our youngest steering group member is 12 years old, and she ran her own station to facilitate a conversation about what the chatbot should look like.

Other powerful moments in our journey so far have been our team presenting in Gothenburg and Toronto. These events have given me a platform to talk about this important research and consider cultural differences across different countries and continents. This has since led us to a successful shared grant between University College London and the University of Toronto.

How has the Centre helped Polly's research?

The Centre has been vital in bringing together patient voices to help shape our research, especially older voices. Patient and public involvement is run really well at the Centre, with so many different ways and opportunities to get involved. The older you get, the more aware you become about the impact your health has on the people around you, so getting these unique perspectives is so important to capture and shape my research focus area. I want to thank everyone that has supported this work so far.

How has the Centre helped Polly professionally?

Being currently the only UK nurse with a PhD in paediatric rheumatology, there is no clear-cut path for me to follow. The Centre's support, endorsement and recognition of my work is so valuable because it is helping me pave a path where I can continue to progress forwards.

4. PIONEERING THE FIELD AND FORGING A PATH FORWARD

Why is this important to young people with arthritis and other rheumatic conditions?

The Centre has built a world-first, critical mass in the adolescent rheumatology field by establishing networks, training researchers, supporting emerging leaders, forming multi-disciplinary partnerships, and harmonising critical cohort data from adolescents as well as children. All these things are enabling this field of research to continue progressing and grow with even greater reach.

Blank slate to fountain of knowledge

Capacity building: The field of biological sex, immunity and arthritis was entirely new when the Centre opened in 2012. Since then, Centre researchers have developed and enabled the growth of world leaders in this space who will take the programme forward. To illustrate this, the Centre has received a Centre of Excellence accolade from the Federation Of Clinical Immunology Societies (FOCIS) which will put the Centre on an international map to mark its expertise and prestige.

Expanding the reach of dedicated JIA research

New Network: Centre researchers joined the Inflammatory Arthritis Microbiome Consortium, led by Professor Fiona Powrie at the University of Oxford. It would not be possible to explore whether the microbiome can be targeted for therapy in JIA patients without them and their globally unique expertise.

Leveraged funding: The CLUSTER programme has leveraged over £21.6 million further funding into JIA research.

Capacity building: A new biobank, known as CHOIR, has been set up by Dr Rosser to investigate JIA uveitis at a deeper level than ever studied before.

Future leaders

Capacity building: Many future leaders in the Adolescent Rheumatology research field have grown and flourished through the Centre including Drs Robinson, Rosser, Livermore and Wilkinson.

Leveraged funding: Collectively, these future leaders have amassed over £7 million worth of fellowships during their time at the Centre to advance their careers.

> **The Centre has provided an incredible environment to excel into becoming a group leader with a Versus Arthritis Career Development Fellowship. The Centre has not only been critical to my research but has also provided invaluable opportunities to work with patients of all ages (children, adolescents and young adults).**
>
> Dr Meredyth Wilkinson
> Versus Arthritis Career Development Fellow

DAVID ISENBERG'S STORY

On the origins of the Centre

I am an Emeritus Professor of Rheumatology at University College London and was the Academic Director of the Adult Rheumatology Centre from 1996 to 2022. When I first joined University College London in 1984, I was one of only two rheumatology consultants. Now, we have sixteen. I was a Co-Founder of and remain Co-Director at the Adolescent Rheumatology Centre.

What were the aims of the Centre?

We wanted to marry top-class discovery science with clinical studies, and bring everything together with improved communication between patients, parents, scientists and clinicians. When the Centre began, social media was exploding in popularity. We recognised that to connect with teenagers more realistically and ultimately improve their care, we shouldn't be writing letters or calling them up, something new and innovative was needed instead. The way clinicians talk to patients should reflect the times we live in.

How has the Centre been successful?

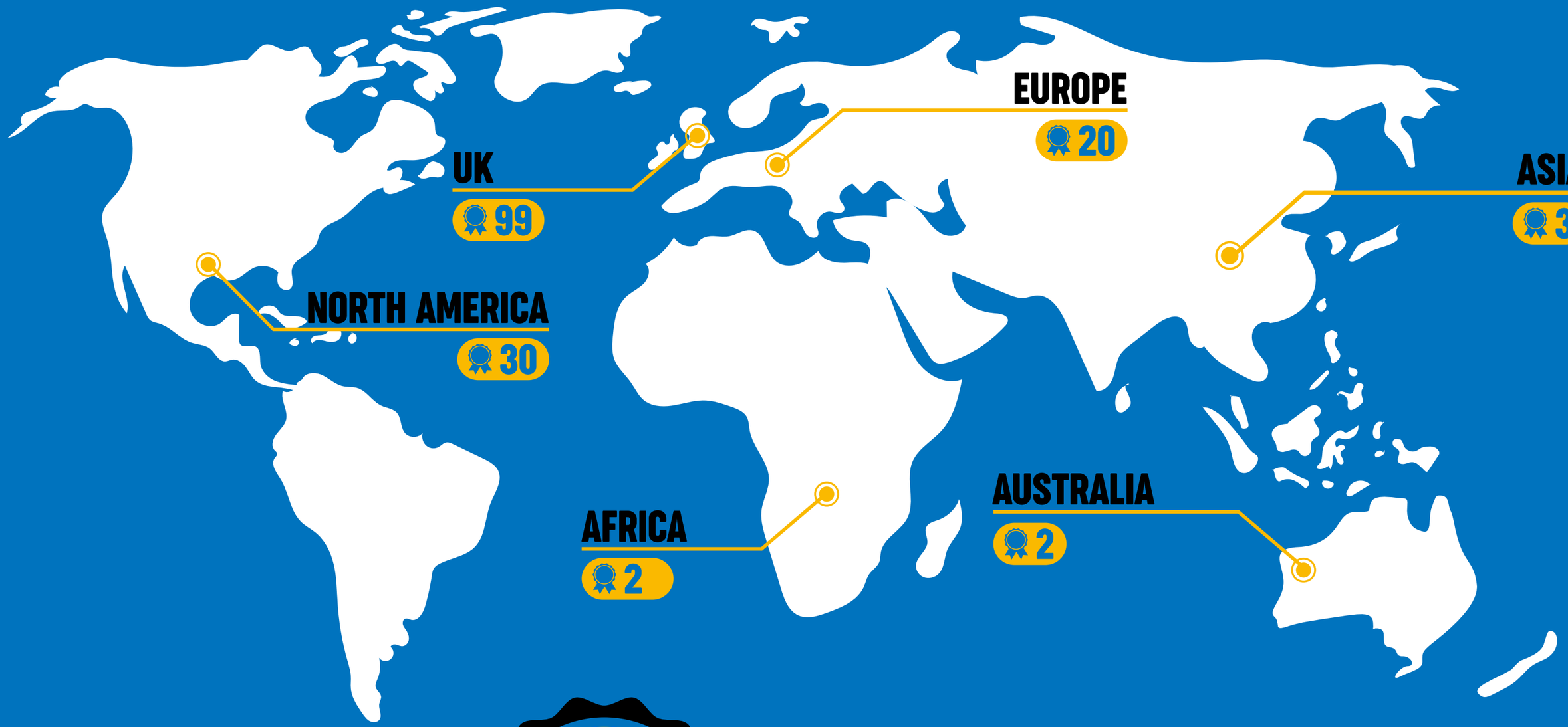
The Centre has done well to spread the word that adolescent rheumatology is an important entity that should be researched seriously. We started with a blank canvas, creating something which had never existed before. We've brought researchers together nationally and internationally who had an interest in adolescent rheumatology, but hadn't necessarily done anything about it yet. We've achieved something profound in keeping the Centre going for 12 years – a lot of determination has enabled us to go the distance, leverage lots of extra grants, set up patient groups and biobanks, and publish many great papers along the way.

Why is the Centre so important?

People too often say to me that arthritis is a disease of old people. But it's not just that, you certainly get it in children, and you definitely get it in adolescents too. The cause for arthritis is never simple – it's not due to a single cytokine or inflammatory molecule going wrong or being over-produced. It's more like a conspiracy between many factors like genetics, our lifestyle, and our sex.

It's been terrific to see brilliant, discovery scientists such as Drs Lizzy Rosser, George Robinson and Meredyth Wilkinson arrive through our doors and investigate a range of potentially important molecules involved in the development of arthritis. Doing research in this area is like a constant battle to work out what is going wrong in the immune system, and can we do anything about it, can it be blocked?

Developing ideas like these and putting them into practice though is not cheap. The support given to us by the charity has been phenomenal. From this, we now have a better understanding of adolescent rheumatic disease, better treatments, a new way for patients to talk to each other, and ultimately better success in managing patients.



RESEARCH REACH

156 GLOBAL COLLABORATORS

The centre has collaborated with 156 academics, clinical service providers and industry partners spanning 15 countries

GLOSSARY

Biobank – collection of biological samples like blood, tissue or DNA that are stored for research purposes.

Biologics - a type of treatment made from living organisms, such as those that either come from, are designed based on, or adapted from cells or molecules, instead of small synthetic molecules. Biologic therapies include anti-TNFs like etanercept.

Biomarkers – signs in the body that can show how healthy someone is or if they have a disease.

Clinical trials – research studies where new treatments or drugs are tested on people to see if they are safe and effective.

CLUSTER - UK consortium involving over 5,000 children and young people living with arthritis, plus a parent-patient network, funded by the Medical Research Council, Versus Arthritis, GOSH Charity and other.

Discovery science – early-stage, often lab-based science that explores mechanisms of disease, identifying drug targets, and how treatments work.

Differences in sexual development (DSDs), also called intersex - a range of conditions where a person's sex chromosomes, reproductive anatomy, or hormone levels develop differently from typical male or female patterns.

Drug target – specific molecule in the body that a drug interacts with to treat a disease or condition.

Gender incongruence - when a person's gender identity differs from their assigned sex at birth. Some transgender or gender-diverse people may take gender-affirming sex hormone treatments such as oestrogen or testosterone to align their physical appearance with their gender identity.

Juvenile dermatomyositis (JDM) - a rare disease that can begin during childhood which causes severe muscle and skin problems.

Juvenile idiopathic arthritis (JIA) - a group of autoimmune conditions that start in childhood, where painful, stiff and restricted joints are the main symptoms.

Juvenile systemic lupus erythematosus (JSLE) - a rare autoimmune condition that can occur during childhood where your immune system, which normally protects us against infection and illness, starts to attack the body's own tissues instead.

Microbiome – community of tiny living things that live in and on our bodies, in places like the gut.

Microbiota – trillions of usually helpful microbes like bacteria and fungi that live in a part of the body such as the gut or mouth. They help with things like digestion.

Myositis – muscle inflammation which can cause pain, weakness and swelling.

Proteomics – large-scale study of proteins to understand what they do and how they work.

Rheumatology – branch of medicine relating to arthritis and other conditions and diseases that affect our joints, muscles, bones and immune system.

Rheumatic – group of conditions or diseases that cause pain, swelling and stiffness in the joints, muscles or connective tissues.

Sjögren disease - an autoimmune condition that affects glands responsible for producing fluid like tears and saliva, as well as other parts of the body.

Translational science – late-stage research that aims to turn findings from discovery and clinical trials into results that directly benefit people with arthritis.

Undifferentiated – a type of juvenile idiopathic arthritis that does not fit into a specific category.

Uveitis – inflammation in part of the eye - a serious complication of juvenile idiopathic arthritis which if not treated can lead to sight loss.

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