



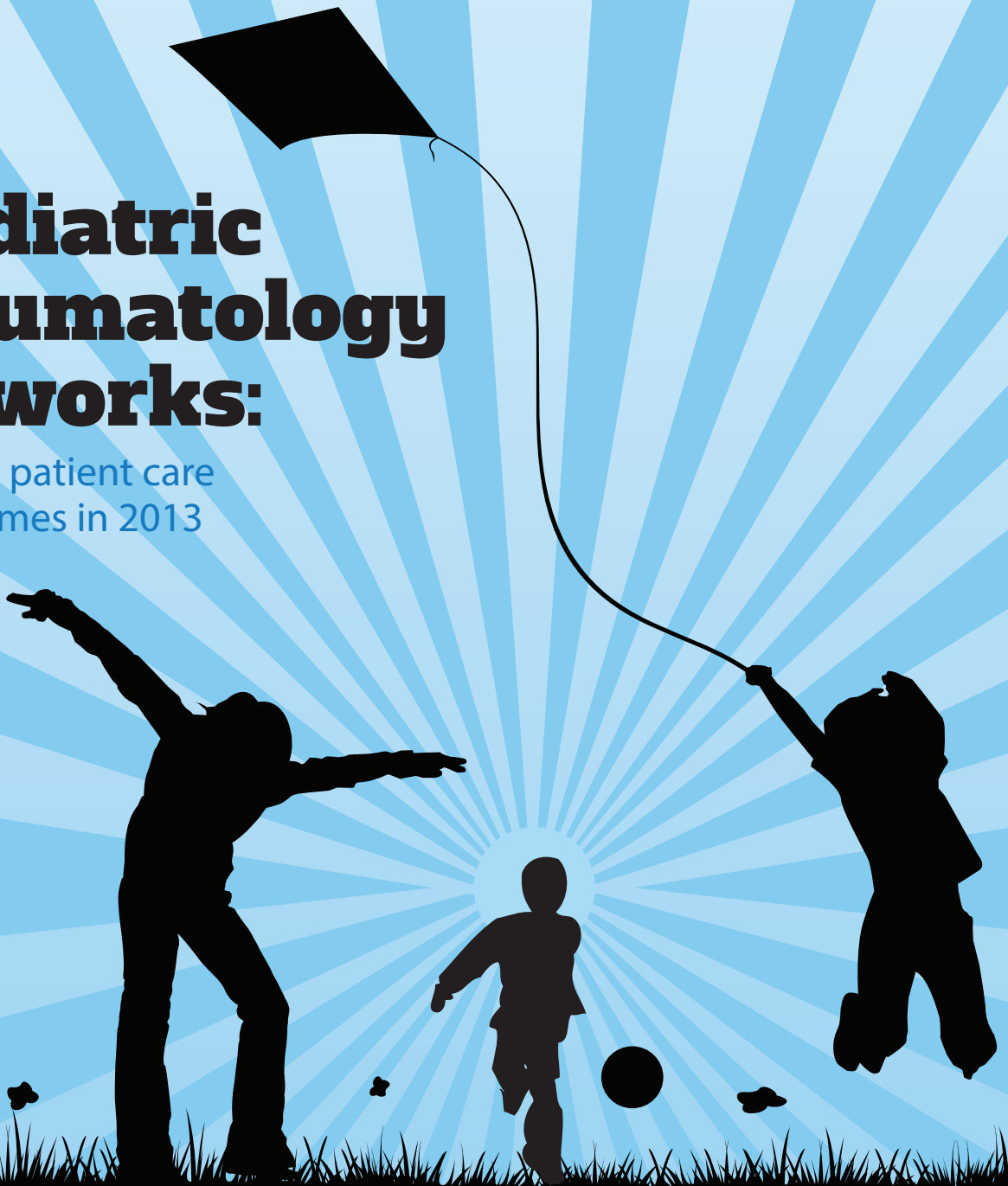
Great Ormond Street
Hospital for Children



NHS Foundation Trust

Paediatric Rheumatology Networks:

Improving patient care
and outcomes in 2013



JDRG

Juvenile Dermatomyositis
Research Group



Juvenile Dermatomyositis Cohort Biomarker Study and Repository UK & Ireland

A bright future for paediatric rheumatology research

[A panel of experts from the Royal College of Paediatrics and Child Health outline the latest research in paediatric rheumatology...](#)

Paediatric Rheumatology includes conditions which cause inflammation of the joints or soft tissues (such as arthritis), autoimmune conditions that can affect every organ in the body (such as lupus, dermatomyositis, vasculitis, scleroderma), fever syndromes, hereditary disorders of connective tissue and mechanical joint problems. We still do not know how these conditions arise in children, but recognise interplay of genetic susceptibility and environmental factors. Many of the diseases are chronic with no cure, thus having a huge impact on the child and family at a crucial time of development. Management within a specialist multidisciplinary team with expertise in paediatric rheumatology is crucial to address these issues. Children are not simply 'mini-adults'. It is important that children and young people are cared for in a suitable environment by an appropriate team to ensure that the best possible long-term outcome is achieved through early recognition and aggressive treatment.

It is a very exciting time to be involved in paediatric rheumatology with current research covering all key areas from laboratory research to clinical trials of new drugs. Basic science research is focusing on the roles of the innate and adaptive immune systems and genetics of these diseases (including gene expression pathways, genome-wide association studies and research into gene-immune phenotype of disease). Translating knowledge gained from the laboratory to new treatments for these children and determining biomarkers of disease activity is key in reducing the morbidity from these disorders. The advent of new biologic drugs offers a major step forward in the spectrum of disease modification that was not available to patients a couple of decades ago. New legislation by the European Union makes it mandatory for new drugs to have clinical trials in children if deemed appropriate. In the UK we have very good infrastructure established by the National Institute for Health and Research (NIHR) to enable us to be at the forefront of these clinical trials globally through the Medicines for Children Research

Network (MCRN). More research is needed to understand the interactions with the environment that leads to developing arthritis. Important research is looking at safe effective use of vaccines preventing infectious diseases in children on immunosuppressive medications used to treat rheumatic conditions.

The UK is leading internationally in undertaking the first large scale clinical trial in children with sight threatening eye disease secondary to arthritis. This study is supported by the research arm of the NHS (NIHR) and a charity (Arthritis Research UK). We are also pioneering new laboratory research in lupus (a disease which can affect multiple organs in the body). These and many other current and new trials and studies planned in UK mean that children with rheumatic diseases in the UK can have the best possible therapies at the earliest possible timeframe.

Each paediatric condition is rare, with some conditions only occurring in a few children per million per year. National and international collaboration is essential to answer questions such as the genetic and immunological influences on disease phenotypes and which treatment works for which patient/disease. The UK paediatric rheumatology community is exemplar in supporting collaborative research and works fully integrated with international research partners. For international collaboration, all clinicians need to be talking the same language and significant efforts have taken place through established networks to work collaboratively on diagnostic criteria for individual diseases, as well as criteria for defining disease activity and disease remission. This allows the development of standardised measures to use in clinical trials. Research needs to focus on long-term outcomes of disease, including decreasing the risk of cardiovascular disease in later life due to inflammation, and how this can be addressed and prevented in younger years.



There are many continuing challenges involving a postcode lottery regarding access to care, including early diagnosis and access to therapies. The British Society for Paediatric and Adolescent Rheumatology (BSPAR) has produced standards of care for children with arthritis in an attempt to address this issue that have been recognised internationally as exemplar. This year, EU funding has led to the establishment of a European collaboration, Single Hub and Access Point for paediatric rheumatology in Europe (SHARE), with the aim of defining a Europe-wide minimal standard of care.

Despite major advances in paediatric rheumatology, many children and young people continue to suffer significant pain and disability, with consequential significant impacts on their quality of life, sleep, education, and future employment. A key challenge is targeting research to address issues that are important to patients and their careers. In the UK, prioritisation of clinical research strategy has been developed through a comprehensive consultation process including consumer involvement through the NIHR MCRN / Arthritis Research UK Paediatric Rheumatology Clinical Studies Group (CSG). The multidisciplinary CSG itself has 10 "Topic Specific Groups (TSG)" that are disease or theme focussed that support a wider group of stakeholders who directly input into the evolving strategy of the CSG and support development of specific study applications. Patient/parent representatives are key members of the CSG and each of the TSGs, and so directly influence research priorities. Work is on-going to define better patient/parent reported outcome measures as it is recognised that current measures of disease activity do not necessarily capture all issues relevant to patients and their carers. The CSG works in close partnership with BSPAR in achieving its goals.

It is essential to ensure that we encourage the next generation of doctors to enter into this exciting specialty. The Royal College of Paediatrics and Child Health has a key role in

directing training, supported by the Rheumatology Clinical Specialty Advisory Group. In addition, involvement of Allied Health Professionals in research is vital to ensure holistic care. A clinical-academic ethos that has developed in the UK units promotes discussion for new research ideas between clinicians and academics, and ensures true translational research. This, together with patient/parent involvement, sets a fantastic platform to test research ideas through established collaborative networks. The future is bright for paediatric rheumatology and the specialty is likely to continue to grow from strength to strength.

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Paediatric Rheumatology at Great Ormond Street Hospital

The Paediatric Rheumatology Department at Great Ormond Street Hospital is the busiest paediatric rheumatology department in the UK. It has an international reputation built on the large number of patients seen and the strong research ethos, with close links to researchers at the Institute of Child Health. The department consists of a multi-disciplinary team (MDT) of doctors, nurses, physiotherapists, occupational therapists and psychologists. Our team looks after patients referred from London and the South-East, as well as accepting complex patients from other paediatric rheumatology centres in the UK and in Europe.

Paediatric rheumatologists look after conditions that affect the musculoskeletal system. This includes inflammatory and non-inflammatory conditions. Inflammatory diseases may primarily affect joints (arthritis), or may affect multiple organs including the joints, such as Systemic Lupus Erythematosus (SLE) and Juvenile Dermatomyositis (JDM). Medications are used to control the inflammation by suppressing the immune response that creates the inflammation. Paediatric Rheumatologists need to understand the diseases they treat, their effects on growth and development whilst having an understanding of the immune system and how the medications work. The

role of the MDT is to support the family and improve the patient's quality of life. Clinical Nurse Specialists help with aspects of disease education and problems surrounding medication. Physiotherapists help patients to maintain the range of movement of the joints, and help to rebuild muscle strength as muscle weakness often impacts on function and pain. Occupational therapists help overcome difficulties with function such as problems with dressing independently. Some develop specialist hand therapy skills and they often help with school and school issues. Psychologists help with the multiple psychological issues that arise for children (and their families) with disabling chronic diseases.

Non-inflammatory conditions are not due to an underlying disease process but can be due to a biomechanical problem leading to an imbalance in muscle strength. This can have a negative effect on schooling and can affect a child psychologically. An MDT approach is needed to provide a successful holistic approach. The members of the MDT work together at Great Ormond Street Hospital to care for both inflammatory and non-inflammatory patients in a child friendly- environment. The physiotherapists run group physiotherapy sessions where the children benefit from working together in the gym.





Research

Concentrating complex cases in one centre allows a level of expertise to be developed that cannot result from seeing only a handful of patients. At Great Ormond Street, there has always been a strong emphasis on improving the understanding of rare diseases through research. Close collaboration between basic science research and clinical research allows a cross-fertilisation of ideas that enables translational research.

Cohort Studies

Expertise can also be shared by collaboration with other expert centres and pooling knowledge. Clinical treatment trials recognised that drug trials need to be carried out on patients with a disease that has been clearly defined. In rare diseases, the conditions often lack enough information to delineate them clearly.

In 2001, we set up a cohort study for JDM (Juvenile Dermatomyositis) at the Institute of Child Health. The clinical team aimed to improve patient care by standardising the clinical data that clinicians asked for and by standardising the patients' physical assessments. Initially, 10 paediatric rheumatology centres agreed to participate: patients were recruited and standardised data was collected. This network of clinical researchers has become known as the JDRG (Juvenile Dermatomyositis Research Group).

At that time, I was able to take part in an international collaborative project (IMACS- International Myositis Assessment and Clinical Studies Group) to produce disease

activity and damage assessment tools, with an aim to be able to conduct international trials. These were published in 2004. The discussion amongst the experts from the UK, USA, Canada and Europe led to a consensus on the use of a standardised muscle power assessment. Dermatomyositis (juvenile and adult) is an inflammatory condition that affects muscles and requires a robust, reproducible examination of muscle power by all treating clinicians. This allows clinicians to assess whether the muscles have improved, no matter who has originally seen the patient. This is also needed to compare treatments in clinical trials. These muscle assessments are now carried out in all the JDRG centres. Currently we are undertaking research work to help assess the skin when it is affected: skin is more difficult to assess in a quantitative manner and this needs to be resolved for clinicians.

In the twelve years since the cohort study was set up, we have enrolled 427 patients, 206 of whom have come from Great Ormond Street. Outcomes for JDM patients have improved: the mortality is less than 1% within the JDM cohort. Prior to the introduction of steroids, DM used to have a mortality of 30% and caused severe disability in 50% of the survivors. JDM is so rare (incidence of around 3 cases per million children per year – this qualifies JDM as a rare disease for Horizon 20/20) that many paediatricians will only see 1 or 2 cases in their career, specialist centres will see between 5 to 40 cases, whereas we currently look after 150 patients at Great Ormond Street.

The JDRG has improved the clinical care of the patients in the participating units by standardising assessments. We also meet annually to discuss care and recent research. Advances in medication have reduced the mortality significantly, but improvements in recognition are needed as delay to diagnosis and treatment is linked to worse outcomes. At present, the most significant cause of disability is due to calcinosis (deposition of calcium in soft tissues). Calcinosis can cause foot deformities, inflamed or infected skin, and even thinning of the gut, which can be fatal. Calcinosis can be present at onset, but is often associated with ongoing active disease. Research is being carried out on the JDM Cohort which is examining potential risk markers for calcinosis: this should allow clinicians to treat these patients vigorously to control disease activity from an early stage and so reduce calcinosis and its associated problems. This research could not have been carried out without the long-term clinical data and serum samples that are collected by the Cohort study.

Cohort studies for rare diseases such as JDM are expensive to run and often take a decade before sufficient patients are enrolled to produce significant results. Research funding for these cohorts is extremely difficult to obtain, as the collection of data and clinical information cannot be done in the limited lifetime of a scientific grant. The improvement in clinical care

that is engendered by these cohort studies is incalculable, and cannot rely on the goodwill and dedication of a small number of clinicians. International collaboration for these rare diseases can only be beneficial in the long run in order to accrue large enough numbers of patients. However, sharing data poses questions around data protection, the ownership of data that has already been collected, and how large international databases can ensure ethical use of the data.

Europe: SHARE

The Single Hub Access for Rheumatology in Europe (SHARE) project is a European Union funded project. It aims to disseminate knowledge of best practice to all centres within Europe, allowing specialists who see few of these patients with rare diseases to care for them in a standardised way that is as evidence-based as possible. The project has started by exploring what paediatric rheumatology services are available across Europe. It is building on the foundation of research networks that have paved the way for international collaboration and will produce guidelines for best practice in these rare diseases.

UK Paediatric Rheumatology

In the UK, specialist centres have developed haphazardly rather than in a planned way. These centres have often been pioneered by an individual clinician with a specific interest responding to a patient need. Historically, paediatricians have not been confident at musculoskeletal examinations, as few childhood illnesses require the joints and muscles to be examined systematically. Paediatric Rheumatology is a small specialty and has recently been designated as a specialist service by NHS England. There is a compelling need for the NHS to respond in innovative ways to improve care without increasing costs. This underpins the new commissioning ethos. For the first time, the Commissioners have actively engaged the specialist societies to help steer changes to make them clinically relevant and to improve outcomes for patients. Dashboards of indicators that need to be collected and measured by all the relevant units is the start of collecting data that will allow benchmarking and should drive up care. There is a difficult balance to achieve



between what is manageable and what should be an aspiration and used to drive improvement. Quality indicators will need to be reviewed annually to ensure they are still relevant in improving front line care. The aim should be to improve the basic quality of care throughout the UK to an acceptable level, and then to drive further improvements. This is particularly daunting in areas where there is a manpower issue: there is a lack of trained paediatric rheumatologists and specialist teams in the UK.

The British Society of Paediatric and Adolescent Rheumatology (BSPAR) is a charitable organisation that grew from a handful of clinicians meeting to discuss cases, to an organisation representing all the teams from the UK and representing all aspects of the MDT. The main aim of BSPAR is to improve the care of children and teenagers with rheumatological conditions. As President of BSPAR, I have seen the passion and dedication of all the professionals involved in our activities. BSPAR relies on individuals working in their spare hours to discuss and debate how to make a meaningful difference. We are a small specialty, and the burden of the work falls onto a small number of individuals.

BSPAR and NHS Commissioners should work together to ensure a fair distribution of paediatric rheumatology teams to support District General Hospitals throughout the country. At present it is patchy.

BSPAR has worked with NHS England to produce a service specification for paediatric rheumatology which is flexible enough to fit the needs of the different regions of the UK: we need to harness the expertise and enthusiasm that already exists, but we also need to plug the gaps to ensure equity of access for all. It is important to involve all the different members of the MDT, including those working in expert centres, those working locally as well as the patients and their families. BSPAR has active groups that represent all these areas: doctors, nurses, therapists, researchers and parents. We disseminate questions on issues to all these groups and collate the responses to ensure a balanced view is obtained.

Research improves clinical care. Basic science research needs to feed translational research that moves the ideas and findings from the laboratory bench to the bedside. It is important to have Clinical Units that question practice and are involved in research. Basic scientists need to work with clinicians to understand what is clinically relevant, and to have access to clinical data and clinical samples. Results need to reach statistical significance: the numbers required can be difficult to reach in diseases that are rare, and often relies on cohort studies that are national or international. Paediatric Rheumatologists have always been interested in research as a way to understand diseases and to study available treatments. Arthritis Research (UK) has invested funds in clinical research by setting up 8 clinical study groups (CSGs). Amongst these, there is only one paediatric group (Paediatric Rheumatology CSG), and yet this is the most research active of all the CSGs. The work of this CSG is done through the members of BSPAR, and many of its topic groups are based on research networks set up by BSPAR members. An example of this is the Juvenile Dermatomyositis Topic Group, which is based on the JDRG.

Paediatricians will see many different rare diseases, but may only see one case of each in their career. Paediatricians will often share care with specialist centres with expertise in these rare conditions. Our hard won improvement in knowledge and care has relied on the dedication of NHS clinicians building up a cohort of patients and an expertise in the condition. Parents want to have access to care as close to home as possible, but they also want access to knowledgeable care. This can be achieved through shared care networks, but paediatricians with a special interest need training and continuous dialogue with the specialist centres. There also needs to be access to an MDT locally that can be supported by the specialist centres. Dialogue between the centres is essential; this needs to be supported by secure IT systems which need to be compatible and reliable to aid good communication and to prevent loss of information.





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