# Paediatric Rheumatology CSG

## Progress Report

**1st April 2014 – 31st March 2015**

Written and complied by Professor Michael W Beresford,
Chair of the NIHR CRN: Children / Arthritis Research UK Paediatric Rheumatology CSG
Dr Eileen Baildam, Deputy Chair, and CSG colleagues, on behalf of the CSG
30th April 2015

## Overview

The CSG continues to foster and support UK development and delivery of a comprehensive portfolio of clinical studies and trials across all paediatric rheumatological and musculoskeletal conditions.
The structure of the CSG remains unchanged since the previous report in April 2014, with strong national geographical representation including: clinical and clinical academics, allied health and nurse representatives, pharmacy, basic science, trainee and consumer representation (three parents and one young person). Four members resigned from the CSG this year (Dr Khulood Khawaja, Prof Lucy Wedderburn, Dr Paul Brogan and Ali Al-Hashimi) and seven have been formally appointed through open national competition (Dr John Ioannou, Dr Dan Hawley, Dr Kiran Nistala, Dr Janet McDonagh, Dr Despina Eleftheriou, Dr Eve Smith (Trainee), Ms Claire Duong as first nurse appointed to the CSG), currently the CSG has 24 members, allowing for succession planning in the coming 12-24 months of other CSG members.
The CSG supports the proactive development of studies / trials and initiatives to address its Research Strategy through its ten "topic specific groups" (TSGs). These provide opportunities for all BSPAR Members and other key stakeholders to proactively contribute to supporting, contributing to and participating in the activities of the CSG, and in particular in taking ahead specific studies identified as priorities by Stakeholders.
The TSGs are multi-disciplinary open groups. Nurses, allied health professionals and trainees as well as established consultants are especially encouraged to get involved, as well as both NHS and university-employed clinicians and scientists.
Each of the TSGs has its own characteristics, for more details of each or a specific one, please look at the CSG's website, and contact the relevant TSG "link" person(s). In addition, the TSGs particularly welcome and seek consumer representation, which in turn feed into the CSG Consumer representatives.
The CSG's web page on the Arthritis Research UK website offers a key communications and information link for all Stakeholders:

http://www.arthritisresearchuk.org/research/our-clinical-study-groups-and-research-strategies/paediatric-rheumatology.aspx

The CSG's ten TSGs are:

- Juvenile Dermatomyositis (JDM) TSG
- Non-Inflammatory Musculo-Skeletal (MSK) Disorders TSG
- Formulations TSG
- Consumer TSG
- Scleroderma TSG
- Juvenile Idiopathic Arthritis (JIA ) including JIA-associated uveitis TSG
- Auto-inflammatory TSG
- Vasculitis TSG
- Bone TSG
- Juvenile-onset Systemic Lupus Erythematosus (JSLE) TSG

Each CSG member is encouraged to become a member of at least one TSG, and all TSGs proactively seek and appoint **trainee representatives**, in close collaboration with the RCPCH CSAC committee for paediatric rheumatology, facilitated by the two CSG's trainee representatives.

| Name | Title, role | TSG(s) | Contact Email | Start Date (Leaving Date) |
|---|---|---|---|---|
| Prof Michael Beresford | Clinical, Chair, Professor of Child Health, Honorary Consultant Paediatric Rheumatologist, Liverpool | JSLE | m.w.beresford@liverpool.ac.uk | 01/01/2008 |

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| Dr Eileen Baildam | Clinical, Deputy Chair, Consultant Paediatric Rheumatologist, Liverpool | Scleroderma TSG | eileen.baildam@alderhey.nhs.uk | 01/01/2008 |
| Dr A. V. Ramanan | Clinical, Consultant in Paediatric Rheumatology, Honorary Professor, Bristol | Juvenile idiopathic arthritis / uveitis TSG, CSG Champion for Industry | avramanan@hotmail.com | 01/01/2008 |
| Mrs Sharon Douglas | Non clinical, Consumer Representative, Scotland | Consumer TSG, CSG Champion for Consumers | sdouglas@aberlady.org | 01/07/2008 |
| Dr Jacqui Clinch | Clinical, Consultant Paediatric Rheumatology, Bristol | Non-Inflammatory MSK Disorders | Jacqui.Clinch@UHBristol.nhs.uk | 01/12/2010 |
| Prof Nick Bishop | Clinical, Professor of Paediatric Bone Disease, Sheffield | CSG Champion for External Affairs, Bone Health TSG, Link BPABG | N.J.Bishop@sheffield.ac.uk | 01/10/2009 |
| Dr Madeline Rooney | Clinical, Senior Lecturer in Rheumatology & Consultant Rheumatologist, Belfast | Bone Health TSG BSPAR Research Chair | m.rooney@qub.ac.uk | 01/01/2008 |
| Prof Wendy Thomson | Non-clinical, Professor in Complex Disease Genetics, Manchester | JIA TSG Basic Science/Genetics Advisor | wendy.thomson@manchester.ac.uk | 01/01/2008 |
| Mr Simon Stones | Non clinical, Consumer (young person) Representative, Manchester | Consumer TSG | simonstones@icloud.com | 18/10/2012 |
| Dr Ethan Sen | Clinical, Trainee, Specialist Registrar in Paediatric Rheumatology, Bristol | Trainee Representative and several TSGs | ethan.sen@doctors.org.uk | 01/05/2012 |
| Dr Clare Pain | Clinical, Consultant Paediatric Rheumatologist, Liverpool | Scleroderma TSG | clare.pain@alderhey.nhs.uk | 13/11/2012 |
| Dr Kate Armon | Clinical, Consultant Paediatrician, Norwich | Non-Inflammatory MSK Disorders | kate.armon@nnuh.nhs.uk | 13/11/2012 |
| Ms Elaine Haggart | Clinical, Highly Specialised Paediatric Physiotherapist, London | Non-Inflammatory MSK Disorders; AHP lead for CSG | Elaine.Haggart@gosh.nhs.uk | 13/11/2012 |
| Dr Hannah Batchelor | Non clinical, Paediatric Formulations Research Fellow, Birmingham | Formulations TSG | h.k.batchelor@bham.ac.uk | 01/06/2012 |
| Mrs Catherine Wright | Non clinical, Consumer Representative, Belfast | Consumer representative and Consumer TSG | CatherineW@arthritiscare.org.uk | 10/06/2013 |
| Mrs Debbie Janson | Non clinical, Consumer Representative, Bristol | Consumer representative and Consumer TSG | debbie@professionalengineeringco.com | 10/06/2013 |
| Dr John Ioannou | Clinical, Reader and Honarary Consultant Rheumatologist, London | JSLE TSG, UK Adolescent Centre representative, CSG Champion | y.ioannou@ucl.ac.uk | 07/11/2014 |

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| Dr Dan Hawley | Clinical, Consultant Paediatric and Adolescent Rheumatologist, Sheffield | TBC | dhawley@doctors.org.uk | 07/11/2014 |
| Dr Kiran Nistala | Clinical, Wellcome Trust Clinician Scientist/ Honorary Consultant in Paediatric Rheumatology, London | JDM TSG, JIA TSG | k.nistala@ucl.ac.uk | 07/11/2014 |
| Dr Janet McDonagh | Clinical, Clinical Senior Lecturer in Paediatric and Adolescent Rheumatology, Manchester | JIA TSG, Adolescent Network representative | janet.mcdonagh@manchester.ac.uk | 07/11/2014 |
| Dr Despina Eleftheriou | Clinical, Senior Lecturer in Paediatric Rheumatology /Consultant Paediatrician, London | Autoinflammation TSG, Vasculitis TSG | d.eleftheriou@ucl.ac.uk | 07/11/2014 |
| Dr Eve Smith | Clinical - Trainee, Clinical Research Fellow, Liverpool | JSLE, Trainee Representative | esmith8@liv.ac.uk | 08/10/2015 |
| Ms Claire Duong | Clinical, Nurse Specialist CYP | TBC<br>Nurse representative | Claire.Duong@nuth.nhs.uk | 03/02/2015 |
| Prof Lucy R Wedderburn | Clinical, Professor of Paediatric Rheumatology | Juvenile Dermatomyositis | L.Wedderburn@ucl.ac.uk | 01/01/2008 (01/02/2015) |
| Dr Paul Brogan | Clinical, Reader in Paediatric Vasculitis | Auto Inflammatory Diseases TSG , Vaculitis TSG | p.brogan@ucl.ac.uk | 01/01/2008 (01/12/2014) |
| Dr Ali Al-Ashimi | Non clinical, Paediatric Formulations Research Fellow | Formulations | Ali.al-hashimi@alderhey.nhs.uk | 01/11/2013 (22/11/2014) |

## Disease/disorder covered

| **Topic Specific Group** |
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| Auto Inflammatory Diseases, including periodic fevers |
| Bone Health related disorders – multiple |
| Juvenile Dermatomyositis |
| Juvenile idiopathic arthritis<br>and: JIA-associated uveitis |
| Juvenile-onset SLE |
| Juvenile Scleroderma |
| Childhood Systemic Vasculitides - multiple |
| Non-inflammatory musculoskeletal disorders |

## Community engagement

The CSG continues to work very closely with the BSPAR Board, the BSPAR Research Committee, BSPAR AHP and Nurses Group, and all members of the BSPAR, and other related groups (including the BPABG, the BAPN, the ARUK Adolescent Centre, BANNAR), to ensure maximum participation and inclusion of multi-disciplinary colleagues within the work and activity of the CSG's TSGs. The CSG Chair sits on the BSPAR Board, reports quarterly to the Board, and the CSG profiles each year at the BSPAR Annual General Meeting, co-hosts the annual BSPAR / CSG Research Day, and works collaboratively

with all the major UK-wide collaborative research networks supporting paediatric rheumatic disorders (including the JDRG, UK JSLE Study Group, other).

## Patient and Public (Lay) Input

The CSG has outstanding Consumer representatives, showing national leadership in driving forward proactive participation of consumers in all aspects of the CSG's clinical trial / research priorities. The Consumers are seeking to further foster consumer links / representatives in a range of areas of clinical / research activity, especially in each of the TSGs and to establish mechanisms through which wider consumer experience can be drawn on as necessary and appropriate. BSPAR Members have are encouraged to link them up with the Consumers on the CSG directly through their common email address: Rheumatology.parents@googlemail.com
The CSG has a strong Consumer group whose activities include the development of leaflets to be given to the all newly diagnosed rheumatology patients highlighting the opportunities and importance of paediatric rheumatology research activities in the UK. The consumer group are very active along the lines of data collection, the use of corticosteroids in children and young people and the visibility of JIA and rheumatology conditions.

## CSG activities

### (i) Regular Meetings

The CSG monthly teleconferences, and twice yearly face to face (evening, overnight and whole of next day) continue and minutes are published on the webpage, along with Annual Reports, quarterly BSPAR Board reports and an outline of the responsibilities and activities of the CSG. In addition, each of the 10 TSGs have regular meetings supported by the CSG (face to face or teleconference, variable frequency as needed to each group to take forward respective portfolios – see below).

### (ii) Workshops

The CSG continues to support and organise workshops for specific projects related to developing studies / trials – see TSG workshops / activities. Examples include a two-day workshop regarding the core data-set for research in JIA; a round-table discussing co-morbidity; developing an application for CRMO; trainee involvement in JSLE clinical studies, to name just a few.

The work of the CSG is fostered and coordinated through the ten TSGs, whose activities this year are summarised below:

| **Topic Specific Group** | **CSG link person / Email of CSG link** | **Initial developments** |
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| Auto Inflammatory Diseases | Despina Eleftheriou (previously Paul Brogan) | **Therapeutic Clinical trials:**<br>1. ***Novartis canakinumab for CAPS*** patients under the age of 4 years: UK was top recruiter (n= 3 patients); this trial and associated open label extension phase are now closed to recruitment, and going well.<br>2. ***Canakinumab for TRAPS, HIDS, and crFMF;*** this Novartis sponsored study is going ahead. CI for the UK is PB; ethics meeting occurred at the beginning of May 2014. This trial involving adults and children is a randomised controlled trial, double-blinded, of canakinumab versus placebo for the treatment of these 3 different forms of hereditary autoinflammatory disease |
| Bone Health | Dr Madeleine Rooney<br>Professor Nick Bishop | On-going studies within the paediatric bone field in the UK currently:<br><br>Directly funded by AR-UK<br>***Amalgamated paediatric bone density study.*** (ALPHABET) Led by Nicola Crabtree and Kate Ward. (Start 18/11/10. Duration 24 months)<br>Data collected so far has informed the development of a calculator that will enable cross-comparison of both clinical and research data from different machines and across different software versions. Data analysis on-going to create the final algorithms to allow data from all current and previous versions of software to be entered. The phantom used for the POPS study is now being measured on the |

machines of each of the participating centres.

***Paediatric Osteoporosis Prevention Study (POPS Trial).*** Led by Madeleine Rooney (Start: 23/10/2006; Duration: 72 months).
RCT of risedronate, 1-alphacalcidol and placebo in the prevention of loss of bone mass and prevention of fractures in children receiving steroids for inflammatory arthritis. Last patient out, data analysis now underway.

***'A randomised, double-blind, placebo controlled trial of vitamin D supplements for pregnant women with low levels of vitamin D in early pregnancy (MAVIDOS)'***. Led by Cyrus Cooper, Recruited patients through Oxford, Sheffield and Southampton. Main outcome is infant bone mass in relation to vitamin D supplementation. Recruitment complete, analysis awaited.

NIHR-funded
***Replacing conventional spine radiographs with dual energy x-ray absorptiometry in children with suspected reduction in bone density.*** Led by Amaka Offiah. (Start 1/11/11; duration 18 months. On-going project initially in a single centre, expanded to 2 centres (Sheffield and Birmingham) that aims to facilitate a reduction in radiation dose – very important in those children under long term follow-up who require monitoring of vertebral size and shape.

***Prospective fracture study in children with chronic inflammatory and/or disabling conditions*** (The SNAP study)- funded by an NIHR Healthcare Scientist Research
Fellowship (Nicola Crabtree).

**Industry-funded ± CSG/CRN support**

***Open Label Protocol to Provide Access to ENB-0040*** (Enobia's human recombinant tissue non-specific alkaline phosphatase fusion protein) in up to 6 Severely Affected Important study of infants with a severe bone disease – infantile hypophosphatasia – who showed major improvements in skeletal, motor and respiratory outcomes following institution of bone-targeted recombinant human alkaline phosphatase enzyme replacement therapy. Preliminary report published in New England Journal of Medicine 2012;366:904-913.
Enzyme now re-labelled as "asfotase alfa". On-going studies are 003-08 – the extension to the original trial – and 010-10, a new version of the infant study, with three UK centres recruiting – Birmingham, Manchester and Sheffield. A natural history study is also underway.

***A multicenter, randomised, double-blind,placebo controlled efficacy and safety trial of intravenous zoledronic acid twice yearly compared to placebo in osteoporotic children treated with glucocorticoids for chronic inflammatory conditions*** – sponsored by Novartis (CZOL446H2337) – we are also recruiting to the extension study (CZOL446H2337E1). On-going study to look at effect of a potent bisphosphonate on bone outcomes in children with arthritis and other inflammatory conditions who received glucocorticoids.

***MCRN2965 MSD Glucocorticoids MK-0822-066-01*** A Single-Dose Study to Assess the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Odanacatib in Adolescents and Young Adults Treated with Glucocoticoids. Funder Merck.
Odanacatib is a cathepsin K inhibitor that inhibits osteoclastic bone resorption. In contrast to bisphosphonates it does not bind strongly to bone and also appears to have some bone anabolic effects as judged by biomarker changes.

**Charity funded (Portfolio)**

***Acute response of bone to vibration in boys who have previously fractured.*** (Start 1/11/11; duration 18 months). Funded by Orthopaedic Research UK.
Testing the response of the skeleton to a defined mechanical stimulus (vibration) over a short period of time. We want to know if children who

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| | | have fractured respond differently to those who have never had a broken bone. This could help us understand better how to advise parents on fracture prevention. Preliminary results published in conference proceedings: http://dx.doi.org/10.1016/j.bone.2011.03.667.<br><br>**Charity funded (Non Portfolio)**<br><br>***Bone architecture and genotype relationships in children who fracture***. (Start: 01/10/2009; Duration: 48 months). Funder – The Children's Hospital Charity.<br>Preliminary study demonstrated a relationship between variation in the genes for type I collagen, the major bone protein, and risk of fracture after adjusting for other factors; published in Bone 2010 Nov;47(5):989-94. doi: 10.1016/j.bone.2010.08.014.<br>Further work looking at the volumetric imaging obtained from the 400 children in the study is still underway, in association with the INSIGNEO group, working on the Virtual Physiological Human project funded by the EU..<br><br>Fracture resistance testing of ex vivo and cadaveric bone samples from infants and children using the Reference Point Indentation device. (start 1/7/11; duration 18 months, extended for a further 2 years) Funder – The Children's Hospital Charity.<br>We are using a novel technique to assess bone strength on excised bone samples; we hope to develop a hand-held device that can be used to monitor bone strength in the clinic. Preliminary results were presented at the ICCBH meeting in Rotterdam June 22-25 2013.<br><br>The development of MRI sequences for the analysis and quantification of bone and bone marrow in children (start 1/7/11; duration 24 months). Funder – The Children's Hospital Charity.<br><br>Vibration in children with osteogenesis imperfecta. Funder Birmingham Children's Hospital<br><br>**Pharma studies in set-up/planned**<br><br>AntiFGF23 antibody in the treatment of X-linked hypophosphataemic rickets; funder Ultragenyx<br><br>Denosumab in the treatment of osteogenesis imperfecta; funder Amgen.<br><br>Other initiatives<br><br>AR-UK EATC – Bone Health theme led by Sheffield<br><br>COST Action on early onset bone fragility – EOFraB – under assessment |
| Formulations & Pharmacy | Dr Hannah Batchelor | A recent survey identified that the highest rated concern of parents caring for children with juvenile idiopathic arthritis was medication. This finding highlights the need for age appropriate medicines for children to manage their illness.<br>The pharmacy & formulation team is working closely with leading specialists in the field to advance medication in rheumatology.<br>Specific projects include optimisation of methotrexate dosing scheduled to ensure effective therapy whilst minimising side effects. |
| Juvenile Dermatomyositis | Kiran Nistala | The UK Network of JDM investigators (the **JDRG**) has grown considerably recently (3 new centres on board, 1 more applying to R and D), and we have >430 children/young people recruited to the study<br>• Key **Biomarker studies** have continued notably on novel autoantibodies which help to sub-type clinical groups of JDM patients and predict complications; these studies have been submitted for publication (Tansley et al 2014)<br>• Study defining correlations of features on JDM **biopsy** with clinical disease has been completed and published (Annals Rheum Diseases, Varsani et al 2013 )<br>• To continue these biomarker studies we have been awarded 2 grants (Great |

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| | | Ormond Street Children's Charity and Great Ormond Street/ICH BRC), PI L Wedderburn - **CSG support for these applications has been invaluable**<br>o in addition an exciting new grant has been awarded through the **NIHR Translational Research Collaboration in Rare diseases (TRC)** which will allow deep phenotyping of subtypes of JDM- a new clinical Fellowship is being appointed in next few months to take this work forward<br>o JDM has been included in the diseases which are to be the focus of whole genome sequencing (WGS) as part of the new Genomics England ( GEL) project<br>• Working with consumers, we have completed the information for the public part of the website, including **Frequently asked Questions**, in a parent and child version see http://www.juveniledermatomyositis.org.uk/FAQ.html<br>• The JDRG has moved to Web based data entry and have updated website data entry systems easily accessed an updated during a clinic visit to allow the web based resources to also create a clinical record to be printed and used in notes if required<br>• JDRG Web system now allows for long term follow up of Adolescent patients and collection of key outcomes in JDM in young people - (in collaboration with Adolescent Centre at UCL and the B Ansell National Network in Adolescent Rheumatology, BANNAR)<br>• JDM TSG, and in particular Dr L McCann, have led an International Group to define a core set of data items to be used across the world (for clinical and research), in collaboration with Euromyositis – an Arthritis Research UK pilot study grant (lead applicant L McCann) has been awarded to take this work forward with a Consensus based process to finalise a core data set for JDM<br>• JDM TSG and JDRG are very involved in **key International studies** including JDM work package of **SHARE**, (Single HUB and Access Point for Paediatric Rheumatology in Europe), the Myositis classification criteria project with **IMACS**, and the recently completed GWAS in myositis, with **MYOGEN** (Miller et al under review).<br>• The JDRG is planning a 'real life' in silico clinical study using proposed CARRA protocols, to compare outcomes in current real life practice in the UK, using the web based data system (lead N Martin Glasgow) |
| Juvenile idiopathic arthritis and:<br>JIA-associated uveitis | Professor Helen Foster<br>Prof Wendy Thomson<br>Dr Eileen Baildam<br>Dr Ramanan<br>Dr Flora McErlane<br>Dr Ramanan | The JIA TSG research priorities were initially devised through a consultation process in 2008 and updated in 2011. The research priorities have been updated during 2014/2015 and are detailed later in this document.<br><br>As previously, we remain committed to improving the evidence base informing the management of children and young people with JIA. We are keen to continue working proactively with NICE and other stakeholders to improve guidance for JIA patients. Equally, we would like to explore whether it is possible to increase the profile of the UK for future commercial clinical trials.<br><br>We would like to focus on developing new studies to answer clinically relevant questions. Such studies are unlikely to be funded by industry but the NIHR is likely to support such work. To optimise recruitment, we need to increase awareness and improve communication throughout our community (consultants to ensure all patients aware of current research opportunities, trainees to increase awareness in their teams, companies to facilitate travel). Ideally, we would like to aim towards a portfolio of studies spread across the country, accessible to all, with all Grid centres leading on at least one study.<br>General themes include:<br>- barriers to involvement in research<br>- access to care<br>- themes around medication (methotrexate associated nausea, biologics)<br>- assessment of outcomes<br>- management of early arthritis |
| Juvenile-onset SLE | Professor Michael Beresford | The JSLE TSG works through the auspices of the UK JSLE Study Group. It meets face-to-face every 12 months, along with "JSLE Young Investigator's Meetings". It has local trainees meetings to support ongoing translational initiatives related to the work |

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| | Chair of CSG, Dr Eve Smith | of the TSG. Current activities of the TSG include:<br>• Continued recruitment of inception cohort of children with JSLE or probable evolving lupus for future clinical trails<br>• Tackling issues of Transition to the adult services – and continued research follow up<br>• Improving access to care and diagnosis of JSLE<br>• Exploring revised diagnostic criteria in JSLE for their utility in future clinical trails<br>• Validation of Flare criteria in JSLE for use in clinical trials<br>• Validation of paediatric version of BILAG2004 in JSLE for use in clinical trials<br>• Analysis of the mucocutaneous manifestations of lupus in a national JSLE cohort<br>• Analysis of thrombocytopenia and cutaneous manifestations in a national cohort of lupus<br>• Supporting the development of international SHARE project – setting standards of care for JSLE<br>• Developing priorities for clinical trials in lupus<br>• Supporting translational research agenda on JSLE<br>• Working collaboratively with LUPUS UK<br>PLUTO A study of Belimumab in moderate JSLE underway with only 1 out of 5 UK promised patients currently recruited. Centres at Alder Hey, GOSH and Bristol will receive and treat appropriate patients from around the country with travel, accommodation and subsistence expenses paid. The UK had a first global recruit. PLEASE REMEMBER TO REFER PATIENTS TO UK RECRUITING CENTRES |
| Juvenile Scleroderma | Dr Clare Pain | The research priorities for scleroderma were devised through a consultation process in 2008 and updated in 2011. Through surveying members of the scleroderma TSG in March and April 2014, the current research priorities of the group are essentially unchanged. The two most pressing priorities:<br>i) Robust and widely available outcome measures<br>ii) Clinical drug trial data showing efficacy of other DMARDs and biologics apart from methotrexate.<br><br>Specific work:<br>1) BMA outcomes grant submitted March 2014 (Eileen Baildam/Ariane Herrick) Reworked proposal comparing skin scores with imaging techniques (thermography, ultrasound and laser Doppler), physician's global assessment and patient/parent reported outcome measures.<br><br>Other themes and ongoing priorities:<br>• Access to care (grant proposal led by Helen Foster to ARUK previously not funded)<br>• Definitions of inactive disease and disease remission<br>• When can treatment be stopped<br>• Controlled data via trial of efficacy and safety of mycophenolate mofetil<br>• Comparison of steroid regimes (IV versus oral, length of treatment)<br>• Use of topical treatments as adjuncts to systemic treatment<br>• Are there any environmental/genetic triggers responsible for disease onset, flare or response to treatment?<br>• Long-term outcome |
| Vasculitis | Despina Eleftheriou (previously Paul Brogan) | **Therapeutic Clinical trials:**<br>1. PEPRS trial (paediatric polyangiitis rituximab study, sponsor Roche): recruiting well, UK already well over target). Recruitment period ends May 2015; aiming for 25 patients worldwide.<br>2. MYPAN: 2nd tranche of funding now secured. Two papers submitted regarding Bayesian clinical trial design and priors setting. Study opened to recruitment |
| Non-inflammatory | Ellie Haggart Dr Jacqui | Strategy consultation identified need to develop this TSG; all interested to contact link-person. |

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| musculoskeletal disorders | Clinch<br>Dr Kate Armon | • Dr Kate Armon – hypermobility study East of England (RCT)<br>• Dr J Clinch/Prof J Tobias – ALSPAC cohort study; epidemiology hypermobility (ARUK)<br>• Dr Suellen Walker – Evaluating physiological and psychosocial changes in young people with hypermobility (Pilot finished, ARUK application for full study submitted)<br>• Dr J Clinch/ Prof Margaret Fletcher - SPACe – evaluating parental behavioural intervention in parents of children with newly diagnosed JIA (RfPB) RCT<br>• Prof Chris Eccleston/ Dr J Clinch – population based study evaluating relationship between anxiety and pain in ALSPAC population<br>• Dr Gavin Cleary – RCT evaluating efficacy of gabapentin in CRPS (Industry).<br>• Dr Richard Howard – 3 industry studies evaluating effect of Tapentadol in paediatric persistent pain<br>Lots more studies will materialise with our new relationship with Elaine Hay's group and the ongoing NIHR CRN: Children Pain/Palliative Care CSG. |
| Consumer Group | Sharon Douglas<br>Simon Stones<br>Debbie Janson<br>Catherine Wright | The consumer role on the CSG has become very purposeful, it is a prime example of an effective partnerships between consumers and healthcare professionals leading to key activities by consumers including:<br>• Development of Toolkit<br>• Membership of trial steering committees<br>• Top three concerns consultation exercise<br>• Consumer poster at BSPAR<br>• Establishing links between charities and organisations for paediatric rheumatology importance and value of research and key themes surrounding research such as barriers to research, research priorities.<br>• Establishment of relationship between consumers, parents and Organisations such as INVOLVE<br>• Ensuring the consumer perspective is given at every step of the research<br>• Comment on commissioning documentation<br>• SHARE collaborative work on the Patient questionnaire work stream<br><br>We now have a parent and patient as a consumer, gaining the two most important perspectives on treatment and research.<br>The input from consumers is critical for research to be successful - it must be applicable and suitable to the people it is going to affect and I believe the CSG does this very well.<br>We want to continue the work to ensure a better outcome for all children and families with rheumatological conditions. We want to improve the communication and collaborative work between practitioners, researchers, the CSG, charities, children and their families. This project has begun with the initiation of a quarterly email to several of the charities associated with rheumatology, spreading the word of what is happening in the world of paediatric rheumatology research and the work of the CSG. |
| Trainee Involvement | Ethan Sen<br>Eve Smith | Trainees who are interested in working with the CSG via the TSGs should contact Ethan.<br>The CSG and current Trainee Representative, Dr Ethan Sen, has continued to encourage trainee involvement in research and has created asset of competencies with the CSAC trainee representative in Research / Clinical Trials and Studies which we would expect Grid trainees to have achieved by the end of their training. |

## (iii) Horizon scans and literature reviews

These continue to be invaluable for supporting the work of the CSG and its TSGs. This year we have had the following added to our resource pool of Horizon Scans (on website):

- Paed - Horizon Scanning Report April 2014
- Paed - Horizon Scanning Report October 2014

- Paed-005 REPORT - The use of pamidronate and adalimumab in children with chronic recurrent multifocal osteomyelitis

### (iv) Publications and presentations

Publications arising directly from trials and activities led by the CSG include:

Douglas SL,
A consumer perspective on embedding research in paediatric rheumatology
Rheumatology (2014) 53 (11): 1915-1916. doi: 10.1093/rheumatology/ket461
Nov 2014

Hampson LV, Whitehead J, Eleftheriou D, Tudur-Smith C, Jones R, Jayne D, Hickey H, Beresford MW, Bracaglia C, Caldas A, Cimaz R, Dehoorne J, Dolezalova P, Friswell M, Jelusic M, Marks S, Martin N, McMahon AM, Peitz J, van Royen-Kerkhof A, Soylemezoglu O, Brogan P. Elicitation of expert prior opinion: application to the MYPAN trial in childhood polyarteritis nodosa. In Press: PLoS One, February 2015

McCann LJ, Arnold K, Pilkington CA, Huber AM, Ravelli A, Beard L, Beresford MW, Wedderburn LR. Developing a provisional, internationally agreed Minimal Dataset for Juvenile Dermatomyositis: for use in clinical practice to inform research. Pediatr Rheumatol Online J. 2014 Jul 21;12:31. doi: 10.1186/1546-0096-12-31. eCollection 2014.

Tudur-Smith C, Williamson P, Beresford MW. Methodology of Clinical Trials for Rare Diseases. Best Pract Res Clin Rheumatol. 2014 Apr;28(2):247-62. doi: 10.1016/j.berh.2014.03.004.

Ramanan AV, Dick AD, Benton D, Compeyrot-Lacassagne S, Dawoud D, Hardwick B, Hickey H, Hughes D, Jones A, Woo P, Edelsten C, Beresford MW, on behalf of The SYCAMORE Trial Management Group. A Randomised Controlled Trial of the Clinical Effectiveness, Safety and Cost-Effectiveness of Adalimumab in Combination with Methotrexate for the Treatment of Juvenile Idiopathic Arthritis Associated Uveitis (SYCAMORE Trial). Trials. 2014;15(14): doi:10.1186/1745-6215-15-14

**Presentations related to work arising from studies supported by the CSG:**

These are multiple, from each of the TSGs (above) and on going studies supported by the CSG, and in view of the breadth and range of the CSG portfolio, not routinely captured in a comprehensive manner; going forward we will endeavour to do this.

## Prioritisation activity

The CSG's ten Topic Specific Groups (TSGs) have developed the following proposed Research Priorities, building on the CSG's Research Strategy of 2008, and 2011. Throughout 2014/15, the CSG has carefully reviewed each of its research priorities in close and comprehensive consultation with the CSG's stakeholders through its TSGs, especially the BSPAR community and with robust PPI involvement throughout.
In response to evolving developments in the field, the TSG's have each been tasked to re-visit specific "next step" priorities as well as the over-arching and longer-term priorities they wish to take forward, formulating "PICOs" for all proposed priority areas. The CSG is now seeking approvals by BSPAR and other key stakeholders before finalising this as the CSG's 2015 Research Strategy. The final CSG Research Strategy 2015 will be completed and published on its website in May 2015.

## Pharma Links

Prof Ramanan is CSG Champion supporting links with Industry, working closely with the NIHR CRN: Children's Theme for PIP and new Industry sponsored studies including feasibility studies, and

developmental work on bringing other commercial trials to the UK. Over the last year, 2014 to 2015, we have had two multinational commercial trials choose to involve UK in their global trials. In conjunction with the NIHR CRN: Children Industry Unit, we are proactively engaging in discussions with industry as PIP's are filed with the regulatory bodies. Additional interactions occur through our strategic partnership with PRINTO (International Advisory Council: Beresford) and through each of the CSG / TSG leads in the development of links for individual studies being developed.

## Other Links

- Dr Eileen Baildam, Deputy Chair of the CSG supports administrative links with CRN: Children and ARUK
- Dr Sharon Douglas is CSG Consumer Champion supporting the CSG Consumer initiatives along with the other Consumer representatives and in particular links with the BSPR Parent's Group, which she chairs.
- Professor Nick Bishop is External Liaison Champion for the CSG, specifically working with RCPCH and other bodies outside of BSPAR to foster collaborations and links. He formally represents the British Paediatric and Adolescent bone Group (BPABG) and this year has been appointed President of the Academic Paediatric Association of GB and Ireland.
- Dr Kate Armon has recently become a CSG Champion supporting links with BSPAR, as has Dr Iouanou, supporting engagement and links with the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR; http://www.ucl.ac.uk/adolescent-arthritis/BANNAR) and the British Society of Rheumatology (BSR)
- All TSGs are closely linked (where relevant) to the respective adult-focused ARUK CSGs

The CSG and all of its members are entirely committed to supporting the wider stakeholder community in addressing the CSG's Mission Statement, as appearing in its Research Strategy and Website.

The CSG continues to foster links and collaborative initiatives with the international paediatric rheumatology research / trials networks, including BANNAR, and internationally with PRINTO, CARRA and PRCSG.

## Studies reviewed

### (i) Expressions of interest reviewed

The CSG has reviewed multiple studies related to the CSG / TSG activities outlined above. Additionally it has reviewed studies via the NIHR CRN, including a study involving the definition of Benign Joint Hypermobility Syndrome and the other involving Vitreous Inflammation Uveitis OCT, as well as a significant number of commercially-sponsored trials.

## Topics under discussion

These are multiple, and covered already elsewhere in the document, but include:

- All of the activities of the TSGs
- Collaborative working across multiple UK-wide initiatives to support developing a minimal core dataset in JIA
- Trainee competencies in Research
- Consumer involvement and engagement in clinical research: Coal face engagement of children and families
- Consumer-led research: Setting young person priorities for research
- Contributing to the setting of international standards of care for children with paediatric rheumatic disorders through the SHARE Initiative (EU-funded, led by Professor Nico Wulffraatt, Utrect).
- Specialist Commissioning and plugging the evidence based gaps

## Update regarding on-going supported studies (Arthritis Research UK and non-Arthritis Research UK)

The CSG continues to support and develop research projects and a list of current projects can be found below. Funders (especially Arthritis Research UK) look to the CSG research strategy and prioritisations to assess whether submitted funding requests are in harmony with this. We encourage prospective researchers to read the CSG Strategy prior to any submission.

| Study ID | Acronym | Industry (Y/N) | Study Title | Status |
|---|---|---|---|---|
| 10154 | Prevalence of Musculoskeletal Disability in Down's syndrome | N | Study of the prevalence of musculoskeletal abnormalities in children with Down's syndrome in the Glasgow population | Closed - follow-up complete |
| 13664 | Validation of a New Hand and Upper Limb Assessment Tool for Children | N | Validation of a New Hand and Upper Limb Assessment Tool for Children | Closed - follow-up complete |
| 13747 | Spreading a Health Message using Online Video - A Pilot Study | N | The Effectiveness of Spreading a Health Message using a Shareable Online Video Targeted at the Social Networks of Recently Diagnosed Individuals | Closed - follow-up complete |
| 17698 | DINOSAUR Paediatric Bone and Joint Study: Qualitative component | N | DINOSAUR Paediatric Bone and Joint Study: Qualitative component | Closed - follow-up complete |
| 14193 | DINOSAUR Study | N | Duration of INtravenous antibiOtic therapy for Septic Arthritis or acUte osteomyelitis in a paediatRic population (DINOSAUR) | Closed - in follow-up |
| 14237 | SPACe | N | Feasibility study for an RCT to evaluate a behavioural intervention for parents early in the diagnosis of juvenile idiopathic arthritis. SPACe - Supporting Parents with A Child with arthritis | Closed - in follow-up |
| 12292 | The 'SNAP' Study | N | Prospective fracture study in children and adolescents with chronic inflammatory and/or disabling conditions | Closed - in follow-up |
| 7770 | MCRN069 (CACZ885G2301E1) | Y | An open-label extension study of canakinumab (ACZ885) in patients with Systemic Juvenile Idiopathic Arthritis (SJIA) and active systemic manifestations | Closed - in follow-up |
| 15338 | Prospective study of Perthes' 8-11 | N | A prospective, multi-centre, surgeon controlled non-randomised study comparing 6 weeks vs 6 months of postoperative non-weight bearing (NWB) in patients treated with a surgical containment procedure with the onset of Legg-Calve-Perthes' disease between 8 and 11 years of age. | In Set-Up Pending NHS Permission |
| 15339 | Prospective study of role of intervention in Perthes' disease | N | A prospective, multi-center, surgeon controlled non-randomised study of the role of surgical containment in children with onset of Legg-Calv,-Perthes' disease (LCPD) between 6 and 8 years of age | In Set-Up Pending NHS Permission |

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| 16435 | Pediatric vasculitis initiative (PedVas Study) | N | Chronic childhood vasculitis: Characterizing the individual rare diseases to improve patient outcomes | In Set-Up Pending NHS Permission |
| 17284 | Adolescent hip disease. Version 1 | N | Functional outcomes in adolescents with osteonecrosis secondary to treatment of developmental dysplasia of the hip. | In Set-Up Pending NHS Permission |
| 17806 | CHIL3906 (BMS-188667) | Y | An Observational Registry of Abatacept in Patients with Juvenile Idiopathic Arthritis. | In Set-Up Pending NHS Permission |
| 18017 | MCRN3127 (20130173) | Y | Prospective, Multicenter, Single-arm Study to Evaluate Safety, Efficacy, and Pharmacokinetics of Denosumab in Children With Moderate to Severe Osteogenesis Imperfecta | In Set-Up Pending NHS Permission |
| 18021 | Young people's Opinions Underpinning Rheumatology Research- YOURR | N | The beliefs of young people with rheumatic conditions about research priorities for adolescent rheumatology and their involvement in shaping the research agenda in this area - Developing a youth involvement strategy for the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR) | In Set-Up Pending NHS Permission |
| 17342 | MCRN3165 (DAP-PEDOST-11-03) | Y | A Multicenter, Randomized, Double-Blinded Comparative Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Daptomycin Versus Active Comparator in Paediatric Subjects with AcuteHematogenous Osteomyelitis Due to Gram-Positive Organisms | In Set-Up Pending NHS Permission |
| 3227 | SPARKS CHARMS | N | A study of the immunological and genetic mechanisms of response, and psychological response to, standard disease management in juvenile idiopathic arthritis (JIA) | Open |
| 3836 | UK JSLE Cohort Study and Repository | N | UK Juvenile-onset Systemic Lupus Erythematosis Cohort Study & Repository: Clinical Characteristics and Immunopathology of Juvenile-onset SLE | Open |
| 2635 | CAPS | N | A Prospective Study of Childhood Onset Inflammatory Arthritis (Childhood Arthritis Prospective Study) | Open |
| 5904 | MCRN027 (CZOL446H2337) | Y | A multicenter, randomized, double-blind, placebo controlled efficacy and safety trial of intravenous zoledronic acid twice yearly compared to placebo in osteoporotic children treated with glucocorticoids for chronic inflammatory conditions | Open |
| 7725 | Biologics for Children with Rheumatic Diseases - The Extended Biologics Study | N | The long-term Safety and Efficacy of Biologic Therapies in Children with Rheumatic Diseases | Open |
| 7723 | JDCBS | N | Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK & Ireland) | Open |

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| 8037 | Prospective cohort study of children with hips dislocated at rest | N | International Hip Dysplasia Institute: prospective observational cohort study of children with hips dislocated at rest | Open |
| 10320 | Sycamore | N | Randomised controlled trial of the clinical effectiveness, SafetY and Cost effectiveness of Adalimumab in combination with MethOtRExate for the treatment of juvenile idiopathic arthritis associated uveitis | Open |
| 11784 | GWAS in children with DDH | N | Genome-wide association of common alleles with developmental dysplasia of the hip | Open |
| 11667 | MCRN169 (CACZ885D2307E1) | Y | An open-label extension study to assess efficacy, safety and tolerability oof canakinumab and the efficacy and safety of childhood vaccinations in patients with Cryopyrin Associated Periodic Syndromes (CAPS) | Open |
| 12382 | MCRN177 (BEL114055) | Y | A multi-centre, randomised, parallel group, placebo-controlled double-blind trial to evaluate the safety, efficacy and pharmacokinetics of belimumab, a human monoclonal anti-BLyS antibody, plus standard therapy in paediatric patients with Systemic Lupus Erythematosus (SLE) | Open |
| 12577 | Juvenile SLE Investigation | N | A Genetic Analysis of Systemic Lupus Erythematosus (SLE) in Children | Open |
| 13172 | MCRN204 (WA25615) | Y | A phase IIa, international, multicenter, open-label, uncontrolled study to evaluate the safety and pharmacokinetics of 4x375 mg/m2 intravenous rituximab in paediatric patients with severe granulomatosis with polyangiitis (Wegener's) or microscopic polyangiitis. | Open |
| 13455 | Educational Needs of Doctors in a Clinical Network for JIA | N | Developing an educational framework to facilitate optimal care delivery for Juvenile Idiopathic Arthritis within clinical networks | Open |
| 13553 | BSPAR ECS | N | British Society for Paediatric and Adolescent Rheumatology Etanercpet Cohort Study (BSPAR ECS) (Formerly British Society for Paediatric and Adolescent Rheumatology Biologic and New Drugs Register for Juvenile Idiopathic Arthritis Patients Treated with Biological Therapies (BSPAR BNDR)) | Open |
| 13561 | MCRN214 (WA28029) | Y | A STUDY TO EVALUATE DECREASED DOSE FREQUENCY IN PATIENTS WITH ACTIVE SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA) WHO EXPERIENCE LABORATORY ABNORMALITIES DURING TREATMENT WITH TOCILIZUMAB. | Open |
| 14004 | MCRN229 (CZOL446H2337 E1) | Y | A 1 year, multicenter, open-label extension to CZOL446H2337 to evaluate safety and efficacy of zoledronic acid twice yearly in osteoporotic children treated with glucocorticoids for chronic inflammatory conditions | Open |

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| 14202 | MCRN234 (WA28118) | Y | AN OPEN LABEL MULTI-CENTRE STUDY TO INVESTIGATE PHARMACOKINETICS, PHARMACODYNAMICS, AND SAFETY OF TOCILIZUMAB FOLLOWING SUBCUTANEOUS ADMINISTRATION IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (JIGSAW-118) | Open |
| 14204 | MCRN235 (WA28117) | Y | A PHASE Ib, OPEN-LABEL, MULTICENTER STUDY TO INVESTIGATE THE PHARMACOKINETICS, PHARMACODYNAMICS, AND SAFETY OF TOCILIZUMAB FOLLOWING SUBCUTANEOUS ADMINISTRATION TO PATIENTS WITH POLYARTICULAR-COURSE JUVENILE IDIOPATHIC ARTHRITIS (JIGSAW-117) | Open |
| 14794 | FAIM | N | A Cross-sectional and Longitudinal Case Control Study into the Development of Femoroacetabular Impingement (FAIM) | Open |
| 15406 | Improving the diagnosis and preventing the development of Perthes' | N | Improving the diagnosis and preventing the development of Perthes' disease. | Open |
| 16028 | MCRN2965 (MK-0822-066-01) | Y | A Single-Dose Study to Assess the Pharmacokinetics, Pharmacodynamics, Safety and Tolerability of Odanacatib in Adolescents and Young Adults Treated with Glucocoticoids. | Open |
| 16461 | Pathogenesis of autoimmune rheumatic disease in adolescents and adult | N | Pathogenesis of autoimmune rheumatic disease in adolescents and adult | Open |
| 16472 | MCRN3262 (WA29231) | Y | LONG-TERM EXTENSION STUDY TO EVALUATETHE SAFETY AND EFFICACY OFSUBCUTANEOUS TOCILIZUMAB IN PATIENTSWITH POLYARTICULAR-COURSE AND SYSTEMICJUVENILE IDIOPATHIC ARTHRITIS | Open |
| 16882 | Hip 'Op | N | Timing of Surgical Intervention for Developmental Dysplasia of the Hip | Open |
| 17395 | MYPAN | N | An Open Label Randomised Controlled Trial of Mycophenolate Mofetil Versus Cyclophosphamide for the Induction of Remission of Childhood Polyarteritis Nodosa | Open |
| 17922 | Development of an Internationally agreed Minimal Dataset for JDM | N | Development of an Internationally agreed Minimal Dataset for Juvenile Dermatomyositis (JDM) for clinical and research use. | Open |
| 11403 | MCRN154 UCB PRA JIA PASCAL (RA0043) | Y | A multicenter, open-label study to assess the pharmacokinetics, safety, and efficacy of certolizumab pegol in children and adolescents with moderately to severely active polyarticular-course juvenile idiopathic arthritis. | Withdrawn During Setup |

## Cross Clinical Studies Group activities

The CSG has close collaborative work with several of the other ARUK CSGs including Inflammatory Arthritis, Autoimmune diseases (including SLE, Myositis, Vasculitis sub-groups) and Metabolic Bone; the CSG also has links NIHR CRN: Children CSGs including the Pain/Palliative Care CSG, Nephrology CSG, Endocrine CSG and other NIHR CRN CSGs.

## Future plans

- In the very near future, once the Research Priorities have been ratified by BSPAR they will be sent to NIHR for consideration, as well as ARUK.
- We remain fully committed to improving the evidence base informing the management of children and young people with JIA and all related paediatric rheumatic diseases, especially the rare and challenging disorders that make up our portfolio, through the work of our TSGs.
- We are keen to continue working proactively with NICE/EMA and other regulators / stakeholders including the SHARE initiative, to improve guidance for paediatric rheumatic disorders. Equally, continue to work to increase the profile of the UK for future commercial clinical trials in this field.
- We will continue to foster effective engagement with an ever-broader consumer group, led by our consumer representatives, including patients especially to participate in development of research priorities and future clinical trial design. For this we will build on our established engagement with the relevant charities.
- The CSG works closely alongside and collaboratively where possible, with the other six Arthritis Research UK Clinical Studies Groups, and their various related sub-groups and this will continue, especially in the challenging issues related to transition and adolescence. This will be specifically through our links with the Barbara Ansell National Network for Adolescent Rheumatology (BANNAR)
- The CSG works will continue to work closely with the other 14 NIHR CRN: Children's Theme CSGs in sharing its experience and skills with other paediatric sub-specialities and learning from them. Examples that are specifically relevant and challenging include the advent of biosimilars, long term safety of biologics, and clinical trials in rare diseases
- The CSG will strive continue to work extremely closely with the National Coordinating Centre of the NIHR CRN: Children and especially its Industry Team, to maximise the support in delivery of the CSG's Portfolio of studies
- The CSG will continue to work collaboratively with the BSPAR Board, its members and committees to ensure the importance of opportunities to participate in clinical research and clinical trials is firmly embedded in the Service Specification for Specialist paediatric rheumatology as part of NHS Commissioning, including the importance of clinical networks, education and training for all health care professionals involved in the care of children and young people with rheumatic disease.

### (i) Forthcoming events, dates and deadlines

See TSG summary above. Our face-to-face meetings this year are 11-12th May 2015, and 7-8th December 2015, along with monthly meetings.