

NIHR Leeds Biomedical Research Centre Patient Matters Bulletin Winter 2021 edition

Welcome to the NIHR Leeds Biomedical Research Centre's Patient and Public Involvement/Engagement Newsletter.

We hope that you are all keeping well through these difficult times and we are pleased to be able to share positive news about what has been happening at the NIHR Leeds Biomedical Research Centre.

If you would like to receive this by post, please email Emma Clarke on emma.clark10@nhs.net with your name and address.

In the Winter edition, we start with a note from our Patient and Public Involvement/Engagement Core Group Chair, **Sue Watson**:

Dear All

With 2022 fast approaching I wanted to send Christmas wishes to you and your families and hope that you have as festive a time as you can given these difficult times.

Despite everything this year we have still managed to hold a large number of successful focus groups covering a wide range of topics from calcinosis of the hands to exploring how patient care can be improved for those living with Polymyalgia Rheumatica (PMR). So a big thank you to all those who were able to master the Zoom technology. Your time and effort has been much appreciated.

As ever our Ask the Researcher events continued to be well attended and it was nice to hear from Professors Emery and Conaghan on their end of year review. We are planning next year's schedule so please put forward any suggestions for topics you may have to Amy on PPIBRC@leeds.ac.uk

It is a pity that we weren't able to hold any events face to face this year but perhaps this might happen next year - we will have to keep fingers crossed that things improve and it becomes safe for us and staff to meet in person.

Some great news to share with you is that two of our researchers, Anna Andersen and Sarah Mackie as well as Amy have won awards in the University of Leeds Public Engagement with Research Awards 2021 (this award recognises those who have embraced the challenges of the past 18 months and delivered innovative projects).

Anna as a joint runner-up in the category of 'doing research ideas in partnership section' and Sarah and Amy won the award for 'development of a research idea'. It's good to get recognition of what was probably a lot of hard work and congratulations to our three winners.

I also wanted to take this opportunity to thank Amy for all her hard work in arranging the focus groups/Ask the Researcher events over 2021 and I hope you will all agree that she has done a fantastic job.

With best wishes for Christmas and the New Year.

Sue Watson
Chair
BRC PPIE Core Group



Ultrasound team update

A huge congratulations to Kate Smith, Sonographer at the NIHR Leeds Biomedical Research Centre who has been awarded an NIHR Pre-doctoral Clinical Academic Fellowship (PCAF). Kate will be looking at designing and evaluating a patient pathway using ultrasound scans to diagnose Giant Cell Arteritis (GCA).

Kate said: "The PCAF will give me the opportunity to develop a PhD application focussing on GCA and Ultrasound. I am looking forward to developing the research skills required and increasing awareness of this devastating disease. As part of the research proposal development I will be holding PPIE events so watch this space!"



Other updates from the ultrasound team -

1. Kate and Borsha are mentoring a student into research on the First Steps Into Research Program with the NIHR.
2. Kate and Borsha have been invited to act as faculty on a training event in Southend with Professor Bhaskar DasGupta, for Giant Cell Arteritis - something we have a lot of expertise with at the Leeds BRC in our Rheumatology and Research teams.
3. Over the last year Kate and Borsha have contributed to the webinar library for the British Medical Ultrasound Society with webinars on Crystal Arthropathy, Ultrasound in the Diagnosis of GCA and Ultrasound for arm DVT in point of care ultrasound.
4. Borsha had an abstract accepted at the UK Imaging and Oncology Congress (UKIO) 2021 and presented in June the engagement work of the BRC ultrasound team from Be Curious 2020 in a talk entitled Inspiring the Next Generation - what are the benefits to the researcher?

Research finds increased risk of stroke, heart disease and cardio-vascular disease for people who take steroids to treat rheumatoid arthritis

People who take steroids to treat long-term inflammatory diseases such as rheumatoid arthritis or inflammatory bowel disease have an increased risk of heart disease, stroke, and other cardiovascular disease.

New research found that the risk of cardiovascular disease increases with the dose and duration of steroid treatment. A surprising finding was that even low daily doses increase the risk. There are few effective treatment options for many inflammatory diseases. Even so, this study suggests that doctors should seek to prescribe the minimum effective dose for the shortest time.

Researchers suggest that people taking steroids, even those on low doses, would benefit from regular monitoring and extra support to reduce their risk of cardiovascular disease. With the help of their GP, many people may be able to reduce their risk through lifestyle changes such as stopping smoking or losing weight.

[Read more about this research](#)

BMJ Clinical Leadership Team of the Year 2021 winners

The Leeds Long Covid Rehabilitation service was the first community-based service to be set up in the country much before the NHS England set up 83 Long Covid clinics in the country. Clinical academics in Rehabilitation Medicine rapidly responded in the first wave of the pandemic. This was to explore the persistent symptoms of COVID-19 (which later became known as 'Long Covid' or 'Post-Covid syndrome'). From the research, the team developed a scale called C19-YRS (Yorkshire Rehabilitation Scale) to capture these symptoms and plan rehabilitation treatments.

The scale (also available as digital app) is now recommended by NICE, NHS England, and is used in many Long Covid services in the country and overseas. The unique work of the team led to Dr Manoj Sivan being appointed as World Health Organisation (WHO) consultant for Covid Rehabilitation in Europe and the team receiving a £3.4 million NIHR grant to develop a gold standard care for Long Covid in the country.



The award winning Long Covid Rehabilitation team

The clinical service in Leeds was awarded the prestigious Clinical Leadership Team of the year award for their impactful world-leading clinical and research work which has improved lives not only in Leeds but across the globe.

Award for Excellence in Inclusivity and Diversity

Dr Stefan Serban won the Award for Excellence in Inclusivity and Diversity as part of the Leeds Teaching Hospitals NHS Trust Junior Doctors and Dentist Awards 2021. Stefan was selected as the winner in the recognition of excellence in Inclusivity and Diversity as part of the in the LTHT junior doctors and dentist awards 2021.

The nomination for Dr Serban recognised his work in initiating and leading projects to improve the oral health care of vulnerable groups including the homeless and children from deprived backgrounds.

This was alongside helping to mobilise extra capacity for both flu and COVID vaccination programmes. The nomination made clear he has leadership qualities of being knowledgeable, charming and persuasive which has helped to encourage those without a voice. You are a credit to your specialty!



Dr Stefan Serban

Dr Serban said: "I am extremely grateful and humbled for receiving this award. It is a great privilege to work with a team of highly motivated and enthusiastic colleagues and this award is a result of our team effort.

I would like to thank my fabulous friends and colleagues from Public Health England, Leeds Teaching Hospitals NHS Trust, Health Education England, the NHS England Dental Commissioning Team, the University of Leeds, NIHR and especially our wonderful patients."

The Inflammation Fund

For the last 25 years the Inflammation Fund has supported work, initially this was just in early arthritis, then preventing arthritis, and has now extending into the prevention of immune mediated inflammatory diseases.

Charitable funding from the Leeds Hospitals Charity has been crucial in enabling Leeds to become a world leading centre for this approach, by enabling the retention of leading experts (including the top Oxford graduate who came to rheumatology in Leeds to complete a PhD), enabling researchers to undertake their PhDs and supporting high quality clinical service.

In prevention the team has:

- recruited the world's largest population of patients at risk of rheumatoid arthritis
- defined a Leeds risk score which accurately predicts who will develop rheumatoid arthritis and when identified a new stage of disease where patients have subclinical arthritis but no detectable arthritis, which is now the primary target for intervention
- obtained funding for an intervention study which blocks interferon at this stage



Professor Paul Emery OBE

the world's most cited rheumatologist, oversees The Inflammation Fund

Other work is enabling GPs from across the country to refer the most at-risk patient to Leeds, meaning that these patients (who are likely to develop rheumatoid arthritis) are diagnosed at the earliest opportunity and evidence shows that their outcome is considerably improved. The team has also defined which rheumatoid arthritis patients can safely reduce drugs when in remission.

MUScle Imaging in Covid-19 (The MUSIC Study)

In 2020 Leeds Hospitals Charity provided just under £24,000 to support a small but vital study towards understanding how the muscles can be affected in people who have had Covid-19. The team will scan the muscles of patients who had Covid-19 using an MRI scanner, and compare the scans with those who have not had Covid-19.

Covid-19 and related conditions are new diseases where there is much to learn to help people who are affected. The findings are likely to lead to further research related to the consequences of Covid-19 infection, such as long Covid, which continues to have a major impact on the lives of many sufferers, symptoms of which can include muscle weakness and muscle pain.



Dr Ai Lyn Tan
Research and Innovation Medical Director
at Leeds Teaching Hospitals NHS Trust

End of Year 'Ask the Researcher' Summary

As has become tradition during the virtual times we are working in, we were joined by both our Director, Professor Paul Emery OBE, and Deputy Director, Professor Philip Conaghan, for our final Ask the Researcher of 2021.

As not everyone was able to join the event, we thought we would include a summary of the discussions in our newsletter.

COVID-19 research into immunosuppressed patients and the vaccine – Professor Paul Emery OBE

This started with the obvious question of how are patients who are taking drugs to largely stop antibody formation (immunosuppressants) going to respond to the COVID-19 vaccination. In Leeds we have one of the largest groups of patients in the world who fall into this category, so we decided to explore this. We would like to thank all the patients that participated, especially at such an uncertain and challenging time.

We have most of the results now, but are awaiting complete data following the second vaccination. We would also like to note that the data gathered was mainly on the Delta virus and doesn't include data on the Omicron virus.

We contacted patients before they had their Covid-19 vaccination and asked if we could take a blood sample. Using the blood sample, we measured the antibodies to see if there had been any previous COVID-19 infection that was unknown to them. We also measured T-cell (these are the immune cells in the blood) responses to the virus. We then took further samples four weeks after each of the three vaccines were administered.

- About 60% of patients on immunosuppressants produced antibodies to the first vaccine, this is lower than the response rate for those who were not on immunosuppressives.
- After the second vaccination, a further 60% of the patients who hadn't responded, responded (although 40% of those that hadn't, still didn't).
- However, most patients, including those didn't respond with antibodies, had a T-Cell response. This means that eventually almost all patients responded.
- Thus the immunosuppressant drugs were inhibiting antibody responses, but this could be overcome by further booster doses.
- We also noted that patients who had previously had COVID-19 responded better to the first dose of the vaccine than those who responded after the second dose of vaccine.

With regards to the different types of immunosuppressant, this is a **draft proposed** for future vaccines (please note this is **proposed** and will be **discussed** with you before any decisions are made about your medication) -

- Methotrexate/ Janus Kinase Inhibitors (such as baricitinib) /abatacept – stop for two weeks after the vaccination
- Rituximab – vaccination needs to be administered ideally six months after an infusion
- Steroids –ideally have your vaccination when you are on as low a dose of steroids as possible, it needs to be a compromise, as high disease activity can compromise vaccine responses.

The CEO of AstraZeneca has suggested that we are seeing less hospital cases in the UK because we gave the AstraZeneca vaccination to our elderly population with a high uptake. Antibody responses are shorter lasting than T-Cell responses, and our observations of patients who received AstraZeneca showed that their T-cell response was five times greater than those who received Pfizer. However the reduced interval between vaccinations will reduce impact of this difference.

The overall implications of this study are that it is vitally important to get vaccinated and for it to be done in a timely manner with regards to your medications. The British Society for Rheumatology has produced guidelines for this, and we will have time to produce definite guidelines which we will follow as well.

NIHR Leeds Biomedical Research Centre activity

Workstream 1 - At risk of developing rheumatoid arthritis

We know that before the joint is involved in inflammatory arthritis there is an antibody that can be measured in the blood. This principle of immune abnormalities preceding clinical, is true for other autoimmune conditions. This will allow lessons learned in rheumatoid arthritis to be transferred to these other diseases.

We have noticed the predominance of a certain type of bacteria in the mouth, lung and the gut, and are doing a large project with the dental school treating periodontitis (around the teeth) and examining the impact on the development of rheumatoid antibodies in this area.

Complementary to this we have developed a risk score which allows to predict which patients will progress to arthritis and how quickly. We have a study for patients who are at high risk of developing rheumatoid arthritis assessing whether a drug treatment can reduce/prevent progression.

We are doing parallel work in Lupus, Sjogren's and Scleroderma where we are currently profiling patients who are at high risk of developing these conditions and understanding how drugs can prevent the development of these diseases.

Workstream 2 - Immunotherapies in rheumatoid arthritis

We are trying to predict which patients will respond to methotrexate alone, or if they will also need a biological therapy. Some patients are now offered a biologic as well as methotrexate, which should prevent the gene changes that may come from having untreated inflammation. We have now identified certain blood and imaging biomarkers which can predict which patients can successfully reduce their medication whilst in remission.

Workstream 3 - Interventions based on stratified prognosis

The identification of at-risk individuals has been extended to psoriatic arthritis.

Workstream 4 - Drug repurposing and treatment toxicity

We are currently looking at steroids with less side effects, although we won't have the findings from this until a long way off in the future.

Workstream 5 – Longer Lasting Joint Replacements

These are our bioengineering colleagues who work in the laboratory and do computer modelling to improve how long the implants used in joint-replacements last for. This can't be done in patients, so it needs to be modelled on a computer. They have recently published research about how the positioning of hip replacements may affect outcomes.

Workstream 6 – Acellular scaffolds and regenerative devices for treatment of osteoarthritis

People with osteoarthritis in their joints lose cartilage, and our bioengineering colleagues led by Professor Eileen Ingham have been exploring ways in which cartilage from people who don't have osteoarthritis, or even from animal tissues, could be transplanted into patients with cartilage loss, to regenerate without an immune response causing the body to reject the foreign tissue.

Professor Hemant Pandit, one of our orthopaedics has been awarded a large grant to explore joint distraction. This is where two pins are placed below and above the joint to pull it apart in and over a six-week period slowly bring the pins together, slowly 'reloading' the joint. Evidence from Dutch researchers studying joint distraction has shown that the cartilage regrows in the

joint and they have less pain. This would be particularly beneficial to younger patients who require a joint replacement and are likely to need a second replacement which is a more complex procedure.

Workstream 7 - Non-surgical treatments for osteoarthritis

We continue to do a lot of MRI-based work developing advanced machine learning which shows us a lot about cartilage and bone structure, and we are now looking at how this better understanding of structure can be matched to people's symptoms.

We have just finished working with a drug company called Novartis who carried out a large cardiovascular trial in people with previous heart attacks and who included patients with elevated levels of inflammation in the blood. The original trial used an anti-interleukin 1 drug to see if it reduced new heart-related events. The findings were positive when compared to the placebo; but what was interesting for us was that patients who received the active drug had many less joint replacements, suggesting an effect on their pain. So for the first time we may have identified a blood marker in certain patients (low levels of inflammation in the blood) that predicts better response to certain anti-inflammatory therapies. Higher levels of inflammation in the blood are also linked to obesity and diabetes, both of which we know lead to increased joint pain. So this is an exciting step in terms of developing pain-reducing therapies, at least in a subgroup of patients.

NIHR Leeds Biomedical Research Centre 2022-27

The goal of the BRC is that all activities are –

- Patient-led, in terms of prioritising, designing and conducting research, with a focus on patients who are in most need
- Aimed at increasing the speed at which research is adopted, is cost-effective and designed for each individual patient
- Collaborative, enabling a wide range of clinicians and researchers to maximise the quality and impact of the research
- Undertaken in respect of our values of equality, diversity and inclusion
- Developed to attract, develop, support and retain our research leaders of the future

Our themes are proposed as –

- Musculoskeletal Disease: We will identify people who are at-risk of developing rheumatoid and other forms of arthritis in order to prevent them from developing these conditions, and develop individually targeted, cost effective treatments.
- Cardiometabolic Disease: We will discover new principles for detecting and treating heart disease, particularly in terms of complications from diabetes and other diseases
- Surgical Technologies: We will develop and apply new surgical technologies to (i) monitor patients remotely, enabling them to return home more quickly and (ii) improve accuracy in surgical techniques
- Pathology: Using artificial intelligence, we will improve the accuracy and speed of diagnosis of bowel cancer, enabling early and more effective treatment

- Antimicrobial Resistance and Infection: We will accurately identify patients at risk of infections, particularly for infections that are resistant to antibiotics
- Haematology: We will improve the accuracy, speed of diagnosis and treatment of blood related cancer.

Rheumatology Advice Line

The Rheumatology Advice Line at Chapel Allerton Hospital can be accessed by calling **0113 3924444**.

During the week, calls are answered live by Rheumatology Clinical Nurse Specialists between 9am and 4pm.. Outside of these times there is an answerphone service for reporting a flare of your inflammatory condition. Due to the volume of calls received, you may hear the engaged tone when you call us - but please keep trying.

Please note there will be closures to the service over the seasonal break.