Rheumatology 2016

The British Society for Rheumatology, British Health Professionals in Rheumatology and the British Society for Paediatric and Adolescent Rheumatology

Annual Meeting

26 – 28 April 2016
Scottish Exhibition + Conference Centre, Glasgow, UK
The abstracts are freely available online to all visitors to the Rheumatology website (http://www.rheumatology.oxfordjournals.org).
## Rheumatology 2016 Abstracts

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### ABSTRACT REVIEWERS

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I01 CONSENT AND CANDOUR: A MEDICO-LEGAL VIEW

Sarah Devaney
Healthcare Ethics and Law, University of Manchester, Manchester, UK

In his 2013 report into the Mid-Staffordshire scandal, Robert Francis QC observed that a culture of caring in health care provision requires ‘a displacement of a culture of fear with a culture of openness, honesty and transparency, where the only fear is the failure to uphold the fundamental standards and the caring culture’. The issue of the provision of information to patients, either in advance of treatment or when something has gone wrong in their care, is a key element of such a culture. Two important legal developments in this area will be considered in this presentation. First, the 2015 Supreme Court case of Montgomery v Lanarkshire confirmed informed consent as a key legal concept in health care law. Patients are entitled to be informed of material risks posed by their treatment, as well as about alternative treatment options. Whether a risk is material will be assessed by asking whether a person in the patient’s position would think the risk is significant. Second, providers of health care (whether primary, secondary or private care providers) now owe a duty of care to patients to inform them when something has gone wrong with their care. Regulators, including the Care Quality Commission, General Medical Council and Nursing and Midwifery Council, have provided guidance on how to implement this duty as well as the implications for not doing so. This presentation will consider the implications of these legal provisions for health care practitioners when considering what information to share with patients. It will ask whether they can contribute to a culture of openness and learning from errors in health care and consider some practical issues for compliance.

Disclosure statement: The author has declared no conflicts of interest.

I02 RECENT TRENDS IN CLINICAL NEGLIGENCE AND MEDICAL INDEMNITY

Robert Hendry
Medical Protection Society, Edinburgh, UK

This session will look at recent developments in the pattern of clinical negligence litigation and the impact this has had on the cost of medical indemnity. The presentation will look at general trends and those more specifically associated with rheumatology. We will also consider ways rheumatologists can reduce their risk of claims and referral to the regulator.

Disclosure statement: The author has declared no conflicts of interest.

I03 ROLE OF THE MEDICO-LEGAL EXPERT WITNESS

Frank McKenna
Rheumatology, Trafford General Hospital, Manchester, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I04 FOOT HEALTH EDUCATION FOR PEOPLE WITH RHEUMATOID ARTHRITIS: A SURVEY OF PATIENTS’ PERCEIVED NEEDS AND EXPERIENCES

Andrea Graham
Directorate of Prosthetics, Orthotics and Podiatry, University of Salford, Salford, UK

Objective: Up to 90% of people with RA experience foot problems leading to reduced function, mobility, quality of life and social participation as well as impacts on body image, but these can be improved with general foot care, orthoses, footwear and patient education. Patient foot health education is lacking, hence the aim of this study was to identify the foot health educational needs of people with RA in relation to its content, timing, mode of delivery and perceived barriers to its provision.

Methods: People with RA completed an online survey and provided free-text comments for thematic analysis.

Results: A total of 543 people with RA completed the survey (487 females, 56 males). The majority of participants were 40-69 years of age (85.5% (n – 464)) and had a disease duration of > 5 years (67.3% (n – 365)). Of these, 183 stated they had received foot health education. The majority agreed with the stated aims of foot health education. Written and verbal were perceived to be the most effective methods of delivery and, overall, the point of diagnosis was the preferred time to receive it. Barriers to accessing foot health education included a lack of perceived opportunities to ask about foot health during consultations and a lack of clarity about what patients should ask health practitioners in relation to their foot health and RA. The survey free-text section was completed by 249/543 people. Five main themes emerged from the qualitative analysis: ‘forgotten feet’, ‘too little, too late’, ‘lacks and gaps’, ‘I am my feet’ and ‘game of chance’.

Conclusion: This is the first study to provide insight into the current status of foot health education for people with RA in the UK. ‘Patchy’ geographical provision of foot health services to people with RA remains similar to that of 10 years ago. People with RA lack awareness of foot health issues, safe self-management and service provision, driving them to seek out information for themselves. Foot pathology in people with RA has a profound bio-psychosocial impact on their lives, but despite this, foot health and related information appears to be rarely considered within the medical consultation. People with RA want access to foot health information and services, but this is limited due to a lack of patient and/or health professional awareness, leading to a detrimental impact on the prognosis of their foot health. The importance of foot health in people with RA needs reinforcing for both patients and health professionals. Opportunities to discuss foot health within the medical consultation should be regularly provided.

Disclosure statement: The author has declared no conflicts of interest.

I05 THE KNOWLEDGE AND SKILLS OF HEALTH PROFESSIONALS: THE PERCEPTIONS OF PEOPLE WITH ARTHRITIS AND OSTEOARTHRITIS

Sarah Ryan
Rheumatology, Burslem, Stoke on Trent, UK

Background: The role criteria for health professionals are often defined by professional bodies and surveys have been conducted to identify the role characteristics of nurses, physiotherapists and occupational therapists working within rheumatology. But relatively little work has been carried out to explore the knowledge and skills that people with RA and OA would like health professionals to have to address their health needs. The objective of this study was to identify the knowledge and skills health professionals require from the perspective of people with RA and OA.
Two focus groups were conducted in London in 2011. People with RA and OA were recruited nationally through patient support organisations. The condition-specific focus groups lasted for 90 min and used a phenomenological approach to explore meaningful contacts with health professionals. The focus groups were audio-taped and transcribed verbatim.

Results: A total of 13 people took part in the focus groups (8 people with RA and 5 people with OA). Shared themes identified in both groups included pain as the most challenging symptom to manage, the need for individualized care (which included being listened to, understanding the impact of the condition, receiving condition-specific information and accessing support and advice) and the absence of access to health professionals. A theme specific to people with RA was the need for psychological support, especially when symptoms of the condition were heightened. Participants in both groups wanted health professionals to have the knowledge and skills to address all of the care aspects identified.

Conclusion: For care to be meaningful and relevant to people with RA and OA, we need to ensure that health professionals have the knowledge and skills to manage pain, conduct an effective consultation that is person-focused, have condition-specific knowledge, provide appropriate advice, signpost patients to relevant services and offer psychological support.

Disclosure statement: The author has declared no conflicts of interest.

I06 WHAT PATIENTS WANT FROM A RHEUMATOLOGY SERVICE
Ailsa Bosworth
National Rheumatoid Arthritis Society, Maidenhead, UK

I have been asked to speak about what people with RA want from a rheumatology service. Having lived with severe RA for 35 years myself and having led the National Rheumatoid Arthritis Society since its launch in 2001 and spoken to many people over the last 15 years who live with the impact of RA, I believe I understand well what it is that people really need when diagnosed with RA and throughout their journey with this awful disease. I will present information that is both evidence based, and reflects the desires and needs of those with RA accessing rheumatology services in the UK today.

Disclosure statement: The author has declared no conflicts of interest.

RHEUMATOLOGY IN THE WORLD OF SOCIAL MEDIA

I07 TWITTER BASICS: PART I
Martin Lau
Arthritis Action, London, UK

Social media use is a global phenomenon, with an estimated 14.8 million users in the UK for Twitter alone. This particular social media platform was established in 2006 and allows users to engage with others in an online forum where each posting is limited to 140 characters. With > 75 000 health care professional worldwide exchanging information on Twitter, this microblogging platform is the most influential social media site for health. The ability for doctors, allied health care professionals, patient support groups and patients to network and engage provides great potential to establish relationships, influence patient behaviour and disseminate the latest clinical research. This session discusses the role of Twitter in rheumatology, along with practical tips to help delegates set up their Twitter accounts.

Disclosure statement: The author has declared no conflicts of interest.

I08 TWITTER BASICS: PART II
Elena Nikiphorou
Rheumatology, Whittington Hospital NHS Trust, London, UK

The world of social media (SM) is rapidly evolving and we are experiencing a new era of online communication and social interaction. SM platforms are being increasingly used for professional communication and for sharing knowledge and information. Having an online presence now represents the norm and can enhance an individual’s profile and social networking. Twitter is a commonly used platform at conferences and other educational events, eliminating geographical barriers and enabling rapid dissemination of information. Educational activities on Twitter include journal clubs, participation in clinical/research quizzes and problem-solving. Therefore, if SM is used appropriately, it can be an incredibly powerful means of learning and development.

Disclosure statement: The author has declared no conflicts of interest.

I09 SOCIAL MEDIA AND MODERN RHEUMATOLOGY

I09 SOCIAL MEDIA AND MODERN RHEUMATOLOGY
PRACTICE: ADVANTAGES AND PITFALLS
Av Lyn Tan
Leeds Musculoskeletal Biomedical Research Unit and Leeds Institute of Rheumatic and Musculoskeletal Medicine, Chapel Allerton Hospital and University of Leeds, Leeds, UK

Social media is the tool for modern social interaction. For most children today, this is the norm for conversation; for the rest of us, this is a new form of communication. Social media is providing us with another dimension for easier and quicker learning, networking and breaking down barriers to communication. There are unique benefits of social media in enhancing medicine and health care, and in particular, rheumatology. There are already hundreds of rheumatologists on Twitter, making rheumatology one of the most active populations of tweeters. Regular discussions and journal clubs and tweet-ups at conferences have united the rheumatology world in effective sharing and dissemination of medical science. Just as we would not say anything without care in the real world, we have to be aware of some social media etiquette, more so because what is said on the World Wide Web is even more difficult to be unsaid. Most of all, besides being an up-and-coming professional tool for communication, it is an adventure. Embrace social media, and those who dare to explore and invest their curiosity will be rewarded with a whole new exciting world.

Disclosure statement: The author has declared no conflicts of interest.

PULMONARY HYPERTENSION FOR RHEUMATOLOGISTS

I10 PULMONARY HYPERTENSION AND THE IMPACT OF CONNECTIVE TISSUE DISEASE
Robin Condliffe
Pulmonary Vascular Disease Unit, Royal Hallamshire Hospital, Sheffield, UK

Pulmonary hypertension (PH) is defined as a mean pulmonary arterial pressure $\geq 25$ mmHg at right heart catheterisation. It may be caused by an isolated vasculopathy of the resistance pulmonary arteries (pulmonary arterial hypertension (PAH)) or may develop secondary to left heart disease or in association with lung disease. Although PAH occurs in up to 10% of patients with SSc, this group of patients also has a high prevalence of lung and left heart disease. Outcomes in SSc-PAH are worse than in idiopathic PAH, which may be related to factors including age and differences in the nature of the underlying vasculopathy and ability of the right ventricle to adapt to increased afterload. PAH can also be seen in other CTDs, including SLE and anti-synthetase syndromes. SLE-PAH in particular has a superior outcome to SSc-PAH and appears to respond well to immunosuppression.

Disclosure statement: R.C. has received honoraria for lecturing and participation on advisory boards of Actelion, Bayer and GSK.

I11 SCREENING CONNECTIVE TISSUE DISEASE PATIENTS FOR PULMONARY HYPERTENSION
Gerry Coghlan
Cardiology, Royal Free Hospital, London, UK

Pulmonary hypertension is a lethal, debilitating, rare condition. The initial phase of the condition is silent and by the time the diagnosis is made based on symptoms, the disease is so advanced that few patients can expect a normal quality or length of life. Three large randomised controlled trials have demonstrated the value of pulmonary arterial hypertension (PAH)-targeted therapies in improving outcomes in PAH, with significant benefit also seen in the CTD population. As
THE THREE S’S IN RHEUMATOLOGY

I13 STIFFNESS (IN RA): WHAT DOES IT MEAN TO PATIENTS AND HOW CAN WE MEASURE IT?
Serena Halls
Academic Rheumatology Unit, University of the West of England, Bristol, UK

This presentation will focus on stiffness in RA. Stiffness is commonly reported by people with RA and it is a widely used outcome measure both clinically and in research. Despite this, until recently very little literature has focused on understanding the patient perspective regarding this symptom, and the current approaches to its assessment have been criticized. This presentation will begin by discussing qualitative research into the patient experience of stiffness. This will be considered in the context of other research performed in RA and also within the broader rheumatology literature. It will then discuss stiffness assessment from historical and current perspectives. Finally, it will consider how the patient experience fits with current assessment and will describe the development of a new stiffness patient-reported outcome measure that appropriately captures the patient perspective.
Disclosure statement: The author has declared no conflicts of interest.

I14 QUALITY OF LIFE AND SEXUAL HEALTH IN RHEUMATIC DISEASES
Kari Hansen Berg
Health and Nursing Science, University of Agder, Grimstad, Norway

Rheumatic diseases may cause multiple medical, physical, social and psychological problems; the intrusiveness of these diseases on many dimensions of life indicates a potentially wide range of sexual problems, including impairment of sexual expression and confidence. Medical treatment in itself may cause sexual problems. Rheumatic diseases can affect many organs in the body, including large and peripheral joints, the axial skeleton and enthesitis (axSpA) and other organs. This may cause significant pain, fatigue, stiffness and loss of physical function, producing a major impact on quality of life (QoL) even at a young age. QoL is a subjective and multidimensional concept with psychological, social and spiritual dimensions. Sexual activity and enjoyment are considered to be components of QoL, particularly the physical and psychological dimensions. According to the World Health Organization, sexual health is defined as a state of physical, emotional, mental and social well-being in relation to sexuality. The physical and psychological consequences of a chronic disease may also influence QoL, including sexual function and sexual perception. Despite the importance of sexual health as part of QoL, limited data are available on sexuality in patients with rheumatic diseases, including axSpA. Sexual health as a part of QoL is not an issue that is a clear part of the consultations in the outpatient clinic.
Disclosure statement: The author has declared no conflicts of interest.

I15 SLEEP: WHAT IS THE SCIENCE BEHIND SLEEP AND FATIGUE PROBLEMS IN RHEUMATIC DISEASE?
Neil Basu
Epidemiology Group, University of Aberdeen, Aberdeen, UK

Sleep disturbance and fatigue are pervasive problems among patients with rheumatic disease and are considered principal determinants of poor quality of life and work impairment. Our understanding of the mechanisms that underpin these patient priorities is limited but evolving. This lecture seeks to summarize existing knowledge and discuss potential paths for future investigation.
Disclosure statement: N.B. has received grants/research support from Pfizer.

I16 WHAT HAS THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS TAUGHT US ABOUT THE EFFECTIVENESS OF BIOLOGICS FOR RHEUMATOID ARTHRITIS?
Kimme Hyrich
Rheumatology, University of Manchester, Manchester, UK

The British Society for Rheumatology Biologics Register for Rheumatoid Arthritis has now been collecting data on patients receiving biologic therapy for RA for 15 years. Established at a time when only limited clinical trial data on the efficacy of etanercept and infliximab were available, this study has now captured data on ~20,000 patients receiving biologic therapies across the spectrum of treatments available, both as first-line and subsequent biologics. This talk will summarize the key findings looking at the real-world effectiveness of biologic therapies in routine clinical use across the UK, including real-world treatment responses, factors associated with response as well as the comparative effectiveness of therapies when used along the treatment pathway.
Disclosure statement: K.H. has received honoraria from Pfizer and AbbVie and grants/research support from Pfizer.

I17 WHAT HAS THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS TAUGHT US ABOUT THE RISK OF INFECTIONS IN RHEUMATOID ARTHRITIS?
James Galloway
Rheumatology, King’s College, London, UK

There has been a global emergence of biologic registers in the past 20 years. Almost all registers have published data on infections, each with subtle variations. The British Society for Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA) is one of the largest and longest running such registers and has an extensive publication history in the arena of infection. This talk will review the contribution of the BSRBR-RA to the knowledge regarding infection risk with biologic therapies. Key findings from the registry will be summarized, including overall serious infection risk, comparative risks in the elderly, risk of septic arthritis and opportunistic infections (tuberculosis and shingles). The findings will be contextualized in the face of the changing demographic of the rheumatoid patient as we move to an era where erosive damage is uncommon and patients are being exposed to multiple biologic agents.
Disclosure statement: J.G. is an advisory board member for Pfizer and Napp; has received honoraria for educational speaker meetings from Pfizer, Napp, MSD and Bristol-Myers Squibb and has received grants/research support from Pfizer, including a Pfizer iCRP Grant Award holder 2014.
I18 WHAT HAS THE BRITISH SOCIETY FOR RHEUMATOLGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS TAUGHT US ABOUT THE RISK OF CANCER IN RHEUMATOID ARTHRITIS?
Louise Mercer
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Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I19 SUPPORTING MEN WITH LONG TERM CONDITIONS TO SELF-MANAGE: WHAT WORKS AND WHY?
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Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I20 THE EXPERIENCES AND PHYSICAL ACTIVITY OF MEN WITH RHEUMATOID ARTHRITIS
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The prevalence for RA is 0.5–1.0%, rises with age and occurs more frequently in women, with a ratio of 3:1. It is probably the reason why research has been focusing on women and knowledge about men is scarce. RA is strongly associated with the patient’s experiences of physical, emotional and social restrictions and quality of life is poor compared with the general population. Men’s perspective on physical activity (PA) is missing from the literature. Even though research shows that people with RA acknowledge PA as beneficial and an important factor in disease and symptom management, several barriers to PA have been reported. Accordingly, the dominance of women in recent PA research within arthritis may lead to conclusions and implications that cannot necessarily be transferred to men, as a growing body of literature highlights how men’s needs and health behaviours differ from those of women. Through previous qualitative research it has been suggested that men with arthritis, besides describing PA as an essential part of being a man. Thus it could be proposed that interventions or offers based on PA could be received as a legitimate and welcomed form of health-promoting activity that acknowledges the potential masculinity in needs and preferences among male patients with RA. This presentation is based on two studies among men with RA all recruited during outpatient visits at the Centre for Rheumatology and Spine Diseases (VRR), Rigshospitalet, Glostrup. A qualitative interview study was performed based on individual semi-structured interviews with a purposive sample of 17 men with RA [average age 58 years (range 33–70)] diagnosed on average 15 years previously (range 5–34). The transcribed interviews were analysed using interpretive description. An interpretive description of the men’s experiences on PA was established. A cross-sectional study was also performed, using the Danish DANBIO registry (http://www.danbio-online.dk), where patients with inflammatory rheumatic diseases treated in routine care are followed longitudinally. Eligible participants were men, 18 years of age and diagnosed with RA. In total, 152 men were included with a median age of 60 years [interquartile range (IQR) 53–68], a median BMI of 25.2 [IQR 23.2–28.4] and a median disease duration of 9 years [IQR 4–15]. The presentation will highlight results from these two studies. From the qualitative study, conclusions will be drawn with a focus on how men perceive RA to influence their experience of losing bodily capacity as well as how a man’s masculine rationality is challenged due to limitations in being physically active. From the cross-sectional study, results on PA behaviour will be presented as well as barriers and motivators to being physically active.
knowledge of their treatment and the ability to self-manage. Generating data requires time and resources, whereas web-based systems automatically populate. Having patients enter their own data reduces clerical burden.

Disclosure statement: S.K. has received honoraria from Celgene, Novartis, AbbVie, UCB, MSD, Chugai and Roche.

I24 INPUTTING DATA BY SPONDYLOARTHRITIS PATIENTS

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Information from patient-reported outcome measures in rheumatology is beneficial for optimal delivery of care. The process has yet to be optimized, as most methods for collection of data are currently paper-based in non-specialist secondary care clinics. There has been a huge increase in the number of devices such as smartphones and tablets in our communities that can be used to measure outcomes. Challenges such as digitisation of pre-existing outcome measures and security of patient data are important considerations. Axial SpA (axSpA) has defined and validated outcomes to measure disease activity (e.g. BASDAI) and function (e.g. BASFI). The recording of these outcomes is helpful in monitoring a patient’s progress when they commence biologic therapies. This talk will demonstrate progress with the delivery of platforms that enable axSpA patients to complete their outcomes independently.

Disclosure statement: R.S. has received honoraria from AbbVie, Pfizer, MSD, Novartis and UCB and has received grants/research support from Pfizer and AbbVie.

WHY DO WE NEED A STRATIFIED MEDICINE APPROACH IN RHEUMATIC DISEASES?

I25 OVERVIEW OF STRATIFIED MEDICINE: WHAT IS IT AND WHAT EXAMPLES ARE THERE OF SUCCESSFUL APPLICATION?

Ann W. Morgan
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Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I26 STRATIFIED MEDICINE APPROACHES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract not provided.

Disclosure statement: I.B. has consulted for UCB, GSK, Medimmune, Merck Serono and AstraZeneca; has received honoraria from UCB, Medimmune and GSK; has participated in speakers bureaus for UCB, Medimmune and GSK and has received grant and research support from Genzyme and Roche.

I27 STRATIFIED MEDICINE APPROACHES IN RHEUMATOID ARTHRITIS

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Centre for Experimental Medicine and Rheumatology, Barts and the London School of Medicine, London, UK

The treatment of RA has been revolutionized by the development of biologic therapies targeting critical pathways involved in disease pathogenesis. Such a rational design approach has made a tremendous difference in the lives of millions of patients. Yet there is still a sizable proportion (30–40%) that do not respond to current medications and remission remains an elusive goal in the majority of patients. There are two main reasons for this: first, RA is a highly heterogeneous condition at both the clinical and pathobiological levels, which produces diverse responses to treatment. Second, there is still a relatively high rate of therapy discontinuation related to toxicity and/or ineffectiveness. Interestingly on a group level the response to biologic therapies appears to be stereotypically similar, with comparable ACR20 (60%), ACR50 (40%) and ACR70 (20%) response rates to all agents (TNF inhibitors, rituximab, tocilizumab, abatacept), individual patients who fail one drug with a specific mechanism of action (MOA) are not necessarily the same as those failing another drug with a different MOA. Thus, understanding the mechanisms of disease and treatment response diversity remains an absolute priority. In recognition of this, Arthritis Research UK (ARUK), the Medical Research Council (MRC) and the National Institute for Health Research (NIHR), among others, have invested considerable resources in the search for multi-omic-driven peripheral blood biomarkers. In addition, the establishment of US-guided synovial biopsy as a rapid, safe and well-accepted procedure in the hands of rheumatologists has enabled the collection of synovial tissue in most patients (both from large and small joints) to investigate the clinical utility and predictive value of synovial pathobiology in disease evolution and treatment response. Synovial tissue analysis in the MRC-funded Pathobiology of Early Arthritis Cohort (PEAC) has demonstrated that the disease can be stratified by molecular pathology (pathotype) and that specific cellular and molecular signatures are associated with diverse clinical evolution. The next challenge is to establish whether synovial pathology has clinical utility in randomized clinical trials (RCTs) and whether synovial tissue signatures can help identify peripheral blood biomarkers. This is currently being investigated in two national/international stratified health care RCTs funded by MRC/ARUK (MATURE) and NIHR (RAA). This lecture will review these ongoing research efforts by nationwide rheumatology consortia and current literature in the field of stratified medicine aimed at developing personalized approaches to the treatment of RA.

Disclosure statement: The author has declared no conflicts of interest.

OCCUPATIONAL RHEUMATOLOGY FOR THE UNINITIATED: WORK AND UPPER LIMB DISORDERS

I28 AN OVERVIEW OF THE RELATIONSHIP BETWEEN UPPER LIMB DISORDERS AND WORK

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Neck and upper limb disorders are common in people of working age. In conjunction with low back pain, these pain conditions are responsible for half of the burden of workplace disability at an estimated cost to the UK economy of £8 billion per annum. The UK is currently the nation in the Organisation for Economic Co-operation and Development (OECD) with the highest number of new disability claimants annually and musculoskeletal disorders make up more than half of these claims. As the workforce ages, it seems only likely that the prevalence and impact of musculoskeletal disorders in the workplace will increase. Epidemiological studies suggest that some occupations are associated with a higher risk of upper limb disorders, particularly when the job involves, for example, exposure to hand-transmitted vibratory tools, repetitive motions of the hand and wrist and forceful movements in awkward postures. Increased rates of tenosynovitis, de Quervain’s tenosynovitis, epicondylitis and carpal tunnel syndrome have been demonstrated in work that involves combinations of these exposures, e.g. meatpackers and slaughterhouse workers. In the 1980s, there was an epidemic of disabling forearm pain that broke out in Australia; this was labelled as repetitive strain injury and attributed by some to a new keyboard design. In some workplaces, up to 50% of the workforce reported upper limb pain and were off sick with disability. This phenomenon could not be readily explained by any physical workplace factor, particularly as the same keyboard in other locations was not associated with any illness. Clearly, psychological and psychosocial as well as cultural factors, beliefs and expectations played a role in this epidemic, and there are two main reasons for this: first, RA is a highly heterogeneous condition at both the clinical and pathobiological levels, which produces diverse responses to treatment. Second, there
The author has declared no conflicts of interest.

**I29 HOW SHOULD RHEUMATOLOGY PROFESSIONALS ASSESS WORK ISSUES IN A PATIENT WITH UPPER LIMB SYMPTOMS?**

Ira Madan
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Upper limb disorders are a major cause of suffering and disability among workers. Rheumatology professionals are in an excellent position to explore factors at work that may have led or contributed to symptoms and to advise on whether an individual should continue in their work. This talk explores how to assess if upper limb pain is likely to be caused or aggravated by work; the latest research on the importance of psychosocial factors, including cultural factors, in perpetuating disability and how to assess these in a clinical environment.

**Disclosure statement:** The author has declared no conflicts of interest.

**I30 RESULTS OF THE ARM PAIN TRIAL: EARLY RETURN TO ACTIVITY, VERSUS REST, VERSUS FAST-TRACK PHYSIOTHERAPY**

Gareth Jones
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Pain in the distal upper limb (elbow, forearm, wrist or hand) is common, yet the best approach to management is unclear. While the aetiological and prognostic factors are similar to other pain conditions, such as low back pain, management approaches differ greatly. Bed rest is no longer advocated for back pain, although patients with arm pain are often advised to rest and to avoid harmful activities while awaiting physiotherapy. This advice is without an evidence base, and the evidence supporting physiotherapy in this area is also limited. This presentation will discuss the results of a recent multicentre randomised controlled trial to examine the hypotheses that (i) advice to remain active and maintain usual activities while awaiting physiotherapy is safe and likely to result in improved functional outcome; (ii) fast-track physiotherapy is superior to normal (waiting list) physiotherapy in terms of long-term disability. Patients with distal upper limb pain were identified from 14 outpatient physiotherapy departments across the UK and, following initial screening and baseline questionnaire, participants were randomised to either: advice to remain active, advice to rest the arm while awaiting physiotherapy or immediate physiotherapy. Outcome was measured at 26 weeks using the modified Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire, which asks people to rate difficulty in performing 11 pre-specified activities over the past week because of pain in their distal upper limb. Results from an intention-to-treat analysis are presented as odds ratios (ORs) and 95% confidence intervals for the probability of recovery. A total of 538 patients [mean age 49 years (SD 14), 54.5% female, 87.6% right-handed] were randomized evenly between the three groups. Of these, 435 participants (81%) provided follow-up data at 26 weeks. The results showed that 32.1% of patients who received advice to rest were free of disability at 26 weeks, compared with 45.2% of those who received advice to remain active. Thus advice to rest was associated with a decrease in the likelihood of recovery (OR 0.54 (95% CI 0.32, 0.90)). There was no difference in the proportion free of disability at 26 weeks between those receiving immediate physiotherapy (35.8%) versus delayed (38.6%). Among patients referred to physiotherapy with distal upper limb pain, the results show that advice to remain active is associated with a superior long-term outcome compared with advice to rest the arm. However, our results do not support the provision of fast-track physiotherapy for such patients. These findings call into question current advice and provide evidence that the no-bed-rest management approaches now common in back pain may have parallels in other regional musculoskeletal pain conditions.

**Disclosure statement:** The author has declared no conflicts of interest.

**I31 EVALUATION AND MANAGEMENT OF CUTANEOUS VASCULAR MANIFESTATIONS OF SYSTEMIC SCLEROSIS**

John Pauling
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Cutaneous vasculopathy in SSc leads to a number of clinical manifestations including RP, digital ulcer disease, telangiectasia formation and calcinosis. Cutaneous vascular manifestations of SSC are common and represent a major source of the morbidity associated with SSC. Tissue ischaemia is thought to be a key driver of tissue remodelling and cutaneous fibrosis in SSc. This presentation will review putative pathological drivers of cutaneous vasculopathy and highlight the challenges we face in evaluating cutaneous vascular dysfunction in SSc, both in the clinical and research settings. The presentation will provide a practical approach to the assessment and management of cutaneous vascular manifestations of SSC aimed at clinicians and allied health professionals that draws on recent work of the UK Scleroderma Study Group.

**Disclosure statement:** J.P. has received consulting fees from Bristol-Myers Squibb; C.D. has received consulting fees from Bayer and grants/research support from CSL Behring and GSK. A.J.P. has participated in the speakers bureau for Bristol-Myers Squibb; has participated in the speakers bureau for Bristol-Myers Squibb; has received grants/research support from Actelion and has received sponsorship for educational meetings from Bristol-Myers Squibb, Actelion, AbbVie and UCB.

**I32 SCLERODERMA RENAL CRISIS**

Chris Denton
Centre for Rheumatology, University College London, London, UK

Scleroderma renal crisis (SRC) is a serious medical emergency and a life-threatening manifestation of SSC, occurring in ~1 in 20 cases overall. Typically it presents as accelerated phase hypertension in the context of SSC and this is most often a diffuse subset within the first 3 years of onset. A number of risk factors have been identified that help to identify cases at increased risk, with the most important risk factor being the presence of anti-RNA polymerase III pattern ANA. Vigilance is important to diagnose SRC as early as possible to increase the chances of a good clinical outcome. Although 12 month survival has improved dramatically over the past 30 years, from 15% to > 80%, with routine use of angiotensin-converting enzyme inhibitors in SRC, the long-term outcome is much less good in those patients that require long-term renal replacement therapy. Fortunately, about half of those SRC cases needing dialysis eventually have enough renal recovery to discontinue, but this can take up to 24 months from onset and has a major impact on quality of life. Current research focuses on defining novel treatment approaches and better risk predictors of outcome that can be used in treatment planning. Importantly, up to 20% of SRC cases occur prior to the formal diagnosis of SRC, so awareness of SSC features in the context of thrombotic microangiopathy (TMA) with renal impairment is important for all physician involved in the management of such cases.

**Disclosure statement:** C.D. has received consulting fees from Actelion, GSK, Bayer and Inventa; honoraria from Actelion and Bayer and grants/research support from CSL Behring and GSK.

**I33 MANAGEMENT OF GASTROINTESTINAL VASCULAR MANIFESTATIONS OF SYSTEMIC SCLEROSIS**

Charles Murray
Gastroenterology, Royal Free Hospital, London, UK

GI manifestations of systemic sclerosis lead to significant morbidity in this patient group. Vascular manifestations potentially have a major role...
DISSEMINATION AND COMMUNICATION THROUGHOUT YOUR DOCTORATE

I34 DISSEMINATION AND COMMUNICATION OF YOUR RESEARCH TO PATIENTS AND THE PUBLIC

Chris Macdonald
Research, Arthritis Research UK, London, UK

The ability to effectively communicate your work to a number of different audiences is becoming an essential part of a researchers skill set. Whether applying for a grant, writing an annual report or talking at an engagement event, your ability to concisely deliver research information that is understandable to the audience you are engaging with is very important; this is particularly so when you are communicating with patients and the public. Information is power, and when this information is given in the right way, an engaged and empowered patient/member of the public becomes a very powerful research ally. From participating in a study, to closely collaborating in your work, effective patient communication can mean that your research is more relevant, more sensitive to people’s needs and, ultimately, of a better quality.

Disclosure statement: The author has declared no conflicts of interest.

I35 DISSEMINATION AND COMMUNICATION OF YOUR RESEARCH TO AN ACADEMIC AUDIENCE

Anthony Redmond
Faculty of Medicine and Health, University of Leeds, Leeds, UK

This presentation will focus on how to manage the difficulties associated with trying to publish your work while juggling data collection, writing a thesis and making the transition from junior researcher to expert in your field. Publishing through your research degree is important in establishing yourself in the field, but it can be difficult to understand what precisely is required from literature review to conference abstracts, from writing styles to reporting underpinning work, there are ninefields to navigate. Presented by an experienced supervisor (and one-time PhD student himself), this session aims to forearm you with the insight, knowledge and plans to make the most of the dissemination and communication opportunities arising from your research studies.

Disclosure statement: The author has declared no conflicts of interest.

GENERAL SESSIONS

JEWELS IN THE CROWN

I38 RHEUMATOLOGY IN INTERESTING TIMES

Jane Dacre
President, Royal College of Physicians, London, UK

The delivery of health care has become increasingly difficult for all professional groups. There are more patients to deal with, and these patients have an increasing mix of co-morbidities. The health care system is under increasing strain, with aspirations from the government that appear impossible to deliver for those of us tasked with the job. Regulation of professionals, of NHS finances and the quality of care delivered feels disproportionate and onerous. On top of all this, the delivery of a 7-day service, while worthy, is viewed by many as the last straw. Are we in the middle of the perfect storm for health care? How can we navigate to calmer waters? There are no easy solutions, but there is a clear need for change. There are examples of real transformation in the delivery of care in rheumatology, and in medicine as a whole. These ideas include scientific and therapeutic advances, changes in the way we treat our patients and changes in the way we work as doctors. To steer the rheumatology ship into the future requires leadership. We rheumatology clinicians lead our local teams well, but there is a need for more of us to use our skill and knowledge to contribute to improving patient care. The way to do this is by educating for leadership, and being prepared to try it. To quote Nelson Mandela: “Young people must take it upon themselves to make sure that they receive the highest education possible so that they can represent us well in future as future leaders.”

Disclosure statement: The author has declared no conflicts of interest.

MICHAEL MASON AND GARROD PRIZE WINNERS

I39 KICKING OSTEOARTHRITIS: HOW DOES JOINT INJURY CAUSE OSTEOARTHRITIS?

Fiona Watt
Kennedy Institute of Rheumatology, University of Oxford, Oxford

OA is the most common form of arthritis, and presents us with an enormous health care burden. Joint replacements are increasing at a rate that is not economically sustainable and are not appropriate for many with early symptomatic disease. It is vital that we identify new ways of medically intervening in this disease. Any such novel specialist drug treatment is likely to be overseen by rheumatology, which would bring about a paradigm shift in how we as a specialty approach and treat OA in the years to come. Joint injury is the greatest risk factor for the development of OA. Translational studies to understand the mechanisms by which tissues respond to injury aim to increase our understanding of the initiating processes in this disease. In laboratory studies, it has been shown that articular cartilage, but also other connective tissue, responds within seconds to injury. A range of inflammatory signalling pathways were activated, in much the same way as when they are activated by IL-1 or bacterial products. Identification of the release of FGF-2 from articular cartilage by my
colleague Tonia Vincent was shown to be responsible for ~50% of the activation of these pathways on damage. The additional activating factor or mechanism remains unknown, but appears to be entirely responsible for activation of signalling in synovium. In response to injury, inflammatory signalling pathways induce a discrete set of inflammatory response genes in joint tissues that include those likely to be catabolic, such as metalloproteinases, and others such as activin A and TIMP-1, which were likely to be important in the resolution of inflammation and wound repair. Activin A, a TGF-β family member, was actively secreted by injured articular cartilage and appears to be an anti-catabolic. FGF-2 appears important in regulating much of this injury-induced gene response, including activin A. Elements of this inflammatory response, but also mechanical load, seem necessary for the development of later disease. To investigate whether this response translates to humans after joint injury, we designed the Knee Injury Cohort at the Kennedy (KICK) study. A total of 150 participants with acute knee injury are being followed with clinical, biological sampling and imaging over 5 years. Six of seven candidates from our preclinical studies were also found to be highly upregulated in the SF of those with acute joint injury. This biomarker response, best characterized by SF IL-6, was significantly associated with symptoms and function at the time of the injury. Paradoxically, a greater SF inflammatory marker response at the outset was associated with a greater improvement over the first 3 months. Studying the development of symptomatic OA in this and related cohorts may lead to better prognostic tests and much-needed novel therapeutic targets for this disease.

Disclosure statement: The author has declared no conflicts of interest.

Garrod Prize Winner

I40 LEUCOCYTE INFILTRATION DURING INFLAMMATION: WHY DOES IT GO WRONG IN RHEUMATOID ARTHRITIS?

Helen McGettrick
Rheumatology Research Group, University of Birmingham, Birmingham, UK

In RA, the inappropriate recruitment of leucocytes, in particular T cells, into the joint contributes to disease pathogenesis and joint destruction. My research focuses on identifying the endogenous regulatory pathways that control the inflammatory infiltrate during inflammation and how these go wrong in RA. Using primary human cells, we have shown that rheumatoid synovial fibroblasts activate neighbouring endothelium to inappropriately recruit neutrophils and lymphocytes. In contrast, synovial fibroblasts from healthy donors or patients with resolving arthritis have an immunosuppressive effect, limiting lymphocyte adhesion to inflamed endothelium. Interestingly, synovial fibroblasts from patients with early RA (~12 weeks symptom duration) have lost this immunosuppressive capacity, allowing endothelium to support elevated levels of lymphocyte adhesion. More recently, we have identified a novel endogenous peptide-mediated (PEPITEM) pathway that suppresses T cell migration from inflammatory sites to regions of tissues. This pathway is dysregulated in patients with RA but can be restored by the addition of exogenous recombinant PEPITEM, indicating its potential as a therapeutic agent in the treatment of RA. Collectively these studies highlight that patients with RA exhibit defects in more than one endogenous immunosuppressive pathway, leading to deregulation of the inflammatory infiltrate during the development and progression of RA. Re-establishing these endogenous regulatory cues to turn off the pathological recruitment of leucocytes to the joint represents a novel and potentially powerful approach to treating patients with early RA.

Disclosure statement: H.M has received research funding from the Pfizer-ICRP grant scheme.

I41 INVARIANT NAURAL RURAL KILLER T CELLS: A NEW PLAYER IN THE PATHOGENESIS OF ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with SLE have an increased risk of developing both clinically apparent cardiovascular disease (CVD) and subclinical atherosclerotic plaque, detectable by vascular US. Although both dyslipidaemia and immune dysfunction have been widely described in patients with SLE, their role in the development of atherosclerosis is unclear. We propose that invariant natural killer T (iNKT) cells, which respond specifically to lipid antigens presented by CD1d on antigen-presenting cells (APCs), may play a key role in linking the immune system, lipids and CVD in patients with SLE. The number and function of iNKT cells have been shown to be altered in patients with SLE, and iNKT cells are involved in atherosclerosis in murine models. Here we compare the properties of iNKT cells in patients with SLE with and without atherosclerotic plaque on US.

Methods: Carotid and femoral US carried out on 100 patients with SLE but no history of CVD showed that 36 had plaque (SLE-P) and 64 had no plaque (SLE-NP). Peripheral blood was taken from 40 SLE-NP, 34 SLE-P and 28 healthy control (HC) subjects. Phenotyping and functional assessment of iNKT cells and CD1d+ APCs were performed by flow cytometry, serum metabolomics were performed by nuclear magnetic resonance and lipids were purified from APCs by chloroform/methanol isolation.

Results: SLE-P patients had increased serum expression levels and altered lipid composition of very-low-density lipoprotein (VLDL) particles compared with SLE-NP patients (P < 0.001), whereas there were no such differences for low-density lipoprotein and high-density lipoprotein, which are more commonly measured during clinical practice. SLE-P patients had a distinct iNKT cell phenotype characterized by increased peripheral blood frequency (P < 0.001) and elevated IL-4 production (P < 0.05) compared with SLE-NP patients. These iNKT changes in SLE-P patients correlated with both serum VLDL levels (P = 0.008, r = −0.495) and plaque echolucency (P = 0.01, r = 0.475), a measure of plaque instability and lipid content. Furthermore, this iNKT cell phenotype was recapitulated in vitro by culturing peripheral blood mononuclear cells from HCs with either serum or monocyte-derived lipids isolated from SLE-P but not from SLE-NP patients or HCs, a response that was inhibited by blocking iNKT cell–APC interaction with anti-CD1d antibody.

Conclusion: The results suggest that in SLE patients with preclinical atherosclerosis, altered serum lipids are processed and presented via monocyte CD1d to iNKT cells, inducing their differential activation and the initiation of an atheroprotective immune response. This implies that in the early stages of atherosclerosis, iNKT cells could be playing a protective role. We propose that more detailed analyses of serum lipid taxonomy (in particular VLDL composition) and iNKT cell phenotype could be used to predict atherosclerosis development in SLE patients.

Disclosure statement: The authors have declared no conflicts of interest.

I42 PERSONAL IMPACT OF LOWER LEVELS OF HEALTH LITERACY ON LIVING WITH A MUSCULOSKELETAL DISEASE: A QUALITATIVE INTERVIEW STUDY

Jo Adams1, Claire Ballinger2, Wendy Lovel2, Cynthia Rowley2, Jill Luetteke1, Ray Armstrong2, Joanne Protheroe2 and Don Nubbe3
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Background: Health literacy includes the cognitive and social skills that determine the motivation and ability of individuals to access, understand and use information to promote good health. People with lower health literacy do less well in the NHS and are less likely to adopt health self-management strategies than people with higher levels of health literacy. There is no published research exploring the impact that lower health literacy levels have on individuals managing the consequences of musculoskeletal (MSK) disease. This study explored the impact of lower health literacy levels on people living with an MSK disease.

Methods: Key contacts identified potential participants from rheumatology clinics, general practitioner surgeries, colleges and community groups. Participants > 18 years of age with an MSK disease and either thought to have lower health literacy or self-identifying as having lower health literacy were included. Participants completed a Rapid Estimate of Adult Literacy in Medicine (REALM) and demographic questionnaire.

TOP SCORING ABSTRACTS (PRESENTED IN JEWELS IN THE CROWN)

I40 LEUCOCYTE INFILTRATION DURING INFLAMMATION: WHY DOES IT GO WRONG IN RHEUMATOID ARTHRITIS?

Helen McGettrick
Rheumatology Research Group, University of Birmingham, Birmingham, UK

In RA, the inappropriate recruitment of leucocytes, in particular T cells, into the joint contributes to disease pathogenesis and joint destruction. My research focuses on identifying the endogenous regulatory pathways that control the inflammatory infiltrate during inflammation and how these go wrong in RA. Using primary human cells, we have shown that rheumatoid synovial fibroblasts activate neighbouring endothelium to inappropriately recruit neutrophils and lymphocytes. In contrast, synovial fibroblasts from healthy donors or patients with resolving arthritis have an immunosuppressive effect, limiting lymphocyte adhesion to inflamed endothelium. Interestingly, synovial fibroblasts from patients with early RA (~12 weeks symptom duration) have lost this immunosuppressive capacity, allowing endothelium to support elevated levels of lymphocyte adhesion. More recently, we have identified a novel endogenous peptide-mediated (PEPITEM) pathway that suppresses T cell migration from inflammatory sites to regions of tissues. This pathway is dysregulated in patients with RA but can be restored by the addition of exogenous recombinant PEPITEM, indicating its potential as a therapeutic agent in the treatment of RA. Collectively these studies highlight that patients with RA exhibit defects in more than one endogenous immunosuppressive pathway, leading to deregulation of the inflammatory infiltrate during the development and progression of RA. Re-establishing these endogenous regulatory cues to turn off the pathological recruitment of leucocytes to the joint represents a novel and potentially powerful approach to treating patients with early RA.

Disclosure statement: The author has declared no conflicts of interest.

I42 PERSONAL IMPACT OF LOWER LEVELS OF HEALTH LITERACY ON LIVING WITH A MUSCULOSKELETAL DISEASE: A QUALITATIVE INTERVIEW STUDY

Jo Adams1, Claire Ballinger2, Wendy Lovel2, Cynthia Rowley2, Jill Luetteke1, Ray Armstrong2, Joanne Protheroe2 and Don Nubbe3
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Methods: Key contacts identified potential participants from rheumatology clinics, general practitioner surgeries, colleges and community groups. Participants > 18 years of age with an MSK disease and either thought to have lower health literacy or self-identifying as having lower health literacy were included. Participants completed a Rapid Estimate of Adult Literacy in Medicine (REALM) and demographic questionnaire.
Semi-structured interviews were audio recorded, transcribed and analysed thematically.

**Results:** Nine women and nine men 29–82 years of age participated. This group was predominantly white British, and most completed high school. Ten participants had a lower level of literacy (i.e. scored ≤6 on the REALM). Four themes emerged: (i) experiencing low health literacy as a service user—capturing the range of service users’ responses to the challenge of lower health literacy, ranging from hiding to open disclosure; (ii) the impact on living and working—where people revealed a range of understanding about their condition and frequently recounted being told by health professionals nothing could be done for their MSK pain; (iii) engaging with MSK education—where participants identified family, friends and neighbours as the most useful and frequent information resources; (iv) strategies for self-management—here people identified going over words and using practical help. In keeping with participants’ recollections of hearing that nothing could be done about their condition, they generally seemed unaware of what self-management is or how it can assist them.

**Conclusion:** People with lower levels of health literacy and MSK disease manage complex social and co-morbid medical conditions. Information provided by health professionals is not always useful and many relied on their social networks for support. People recalled that often they had been told that there was nothing that could help their pain or arthritis; it could not be cured. This impacted negatively on the incentive for people with lower health literacy to recognize and engage with self-management approaches. To better support people with lower health literacy and MSK conditions to engage with self-management strategies, all agencies need to emphasize the potential benefits and use easily accessible clear messages to communicate these.

**Disclosure statement:** The authors have declared no conflicts of interest.

**I43 DETERMINANTS OF WAITING TIME FOR PATIENTS WITH NEW ONSET INFLAMMATORY ARTHRITIS: OBSERVATIONS FROM THE NATIONAL CLINICAL AUDIT FOR RHEUMATOID AND EARLY INFLAMMATORY ARTHRITIS**

Joanna M. Ledingham1, Neil Snowden2, Ali Rivett3, James Galloway1, Jill Firth4, Elizabeth MacPhie5, Zge Ide5, Ian Rowe5, Ni jagra Kandala2 and Elaine Dennison6

1Rheumatology, Portsmouth Hospitals NHS Trust, Portsmouth, 2Rheumatology, Pennine MSK Partnership, Oldham, 3Clinical Affairs, British Society for Rheumatology, 4Rheumatology, King’s College Hospital, London, 5Rheumatology, Lancashire Care NHS Foundation Trust, Preston and 6MRC Lifecourse Epidemiology Unit, Southampton University, Southampton, UK

**Background:** Early diagnosis and treatment of inflammatory arthritis is well established as a predictor of better long-term outcome for patients. National Institute for Health and Care Excellence Quality Standard 2 (QS2) for the management of RA recommends that people with suspected persistent synovitis should be assessed in a rheumatology service within 3 weeks of referral. Non-compliance with QS2 and the influence of potential factors on this have been assessed within the National Clinical Audit for the management of rheumatoid and early inflammatory arthritis (EIA).

**Methods:** The National Clinical Audit for RA and EIA assesses care provided to individuals ~16 years of age presenting for the first time to specialist rheumatology units in England and Wales with EIA. While QS2 was developed for RA, the importance of early diagnosis is recognized for all EIA patients, so data were collected for all such patients. Data on individual unit structure, including staffing levels and the presence/absence of EIA clinics were collected from each trust along with information for all patients on the date of referral receipt and the date when the patient was first seen within the rheumatology unit. Data collected over the first year of this ongoing audit are reported.

**Results:** Data were available from 6354 patients recruited from 1 February 2014 through 31 January 2015 via 135 (86%) eligible secondary care rheumatology trusts across England and Wales. Nationally, just under two-fifths (38%) of patients were seen within 3 weeks of referral receipt. The national average waiting time for specialist review from referral receipt was 4 weeks; three-quarters of patients were seen within 7 weeks (interquartile range (IQR) 3–7). There was major variation in the ability to meet QS2 across different trusts. Twelve per cent of general practitioner (GP) referral letters did not indicate that EIA was suspected; this proportion was significantly lower (9.4%) for those waiting <3 weeks when compared with those waiting ≥3 weeks (odds ratio (OR) 2.0 (95% CI 1.6, 2.4), P < 0.001).

Fifty-six per cent of trusts had EIA clinics; those with EIA clinics were more likely to meet QS2 [OR 1.3 (95% CI 1.4, 1.7), P < 0.001] when compared with those without. Consultant numbers nationally were 1.08 per 100 000 population (range within regions 0.78–1.15). Trusts with staffing levels of more than one consultant per 100 000 population performed significantly better against QS2 than those with lower consultant numbers [OR 1.3 (95% CI 1.1, 1.4)].

**Conclusion:** The majority of rheumatologists face difficulties in offering timely appointments for patients presenting with EIA. Nationally, consultant numbers were below Royal College of Physicians recommendations of 1.16 per 100 000 population. Trusts with higher consultant numbers per individual were able to see patients more quickly after referral. The presence of EIA clinics associated with better performance against QS2; what factors lie behind this association warrant further investigation. Educating GPs on key information required in referral letters should assist appointment allocation processes.

**Disclosure statement:** The authors have declared no conflicts of interest.

**I44 HERBERDEN ROUND**

Peter C. Taylor

Rheumatology, University of Oxford, Oxford, UK

Abstract not provided.

**Disclosure statement:** The author has declared no conflicts of interest.
I45 BECOMING A CONSULTANT IN THE CURRENT NHS: WHAT YOU NEED TO KNOW

Marwan Bukhari
Rheumatology, University Hospitals of Morecambe Bay NHS Foundation Trust, Lancaster, UK

This talk will cover the essentials needed in the final transition from senior trainee to consultant. It will include assessing the suitability of the job, how to assess a new rheumatology unit, which people to contact prior to the job and understanding what is expected of you in the job. Some examples of what can go wrong are also given.

Disclosure statement: M.B. has received honoraria from Bristol-Myers Squibb, UCB, Celltech, Roche, Chugai, Abbvie, Mennarini, Janssen, Sanofi, Regeneron, Eli Lilly, BMJ Masterclasses, OnTrac Medics and Pfizer and has received grants/research support from Pfizer, Roche and Chugai.

I46 BALANCING CLINICS, RESEARCH AND TEACHING: NEGOTIATING THE CONSULTANT JOB PLAN

Hector Chinoy
Centre for Musculoskeletal Research, University of Manchester, Manchester, UK

Abstract not provided.

Disclosure statement: H.C. has received consulting fees from Momenta, aTyr and Servier; honoraria from Abbvie, UCB, Celgene, Merck, Pfizer and Roche; grants/research support and an educational grant from Novartis, funding for a clerk from Pfizer and Roche and funding for equipment from Abbvie.

I47 WHAT DO I DO WHEN THINGS GO WRONG? DEALING WITH COMPLAINTS

Nick Shenker
Rheumatology, Addenbrooke’s Hospital, Cambridge University Hospitals, Cambridge, UK

Complaints are on the increase in the NHS and are an almost inevitable part of life as a consultant. They can be distressing, time-consuming and demoralising. Accepted standards of care recognize complaints occur in <0.1% of all consultations. The three most common causes of complaints are communication, access and attitude, with medical negligence being very low in frequency. A formal complaint should be managed differently to a going concern or informal complaint. A complaint should not be confused with a serious untoward incident, which is an internal investigation triggered by the health care organization. However, both can occur over the same episode. What is the process of a complaint, including timelines? Who gets involved? How should you reply? Where do you get support? Are there things that you can do to reduce your chances of receiving a complaint? Using an actual example, this talk will cover all aspects of a complaint, including how this fits into appraisal, clinical governance and how a complaint can improve your future practice.

Disclosure statement: The author has declared no conflicts of interest.

I48 WHEN RITUXIMAB IS NOT ENOUGH: CONTROLLING B CELLS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Michael Ehrenstein
Rheumatology, University College London, London, UK

Suboptimal trial design and concurrent therapies are thought to account for the unexpected failure of two rituximab clinical trials in patients with SLE. This talk will discuss evidence supporting an alternative explanation: that rituximab can trigger a sequence of events that has the potential to exacerbate disease in a subset of lupus patients. Post-rituximab SLE flares that are characterized by high anti-dsDNA antibodies are associated with elevated circulating B cell activating factor (BAFF) and a high proportion of plasmablasts within the B cell pool. BAFF not only perpetuates autoreactive B cells (including plasmablasts), particularly when B cell numbers are low, but also stimulates T follicular helper (Tfh) cells. Moreover, plasmablasts and Tfh cells promote each other’s formation. Thus repeated rituximab infusions can result in a feedback loop characterized by ever-increasing BAFF levels, surges in autoantibody production and worsening of disease. We propose that for some patients with lupus, rituximab therapy should be swiftly followed by BAFF inhibition to delay flares and more effectively control disease.

Disclosure statement: M.E. has received grants/research support from GSK, which is supporting a clinical trial (chief investigator: Prof Michael Ehrenstein) testing the combination of rituximab and belimumab in SLE.

I49 CELLULAR AND MOLECULAR MECHANISMS OF INTERLEUKIN-10 REGULATION IN CD4+ T CELLS FOLLOWING TUMOUR NECROSIS FACTOR BLOCKADE

Leonie Taams
Immunology, King’s College London, London, UK

The main focus of research in Leonie Taams’ lab is to identify key cellular processes and molecular mechanisms involved in the regulation of inflammation in humans, with a specific interest in RA and PsA. The lab studies how inflammatory T cell responses are induced, in particular in relation to IL-17 production, and conversely how these responses are regulated. The lab has a specific interest in effector and regulatory T cell subsets and how their interaction with monocytes and stromal cells at the site of inflammation contributes to the initiation, perpetuation and resolution of inflammation. We hope to use this knowledge to identify novel pathways and/or approaches to target inflammation in humans. Our recent work demonstrates that TNF inhibitor drugs, which are widely used in the treatment of RA and PsA, can promote the expression of the anti-inflammatory cytokine IL-10 in human CD4+ T cells in vivo and in vitro. This phenomenon may contribute to the anti-inflammatory effects of these drugs. I will discuss the cellular and molecular mechanisms that underlie the induction of IL-10 in human CD4+ T cells following TNF blockade.

Disclosure statement: L.T. has received grants/research support from Novo Nordisk A/S, GSK, UCB and Novartis and has received speaker fees from GSK, UCB and Novartis.
INVITED SPEAKER ABSTRACTS

IS0 APPLIED CYTOKINE SIGNALING: FROM JAK INHIBITORS TO SUPER-ENHANCERS
Massimo Gadina
Translational Immunology Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, USA

The targeting of the Janus kinases (JAKs) has been quite successful and first-generation pan-JAK inhibitors are now used worldwide for the treatment of autoimmune diseases as well as malignancies. Studies on the mechanism of action of successful JAK inhibitors have revealed that, besides T and B cells, they act on innate immune cells and can promote tolerance. For this reason, JAK inhibitors are proving to be useful for a variety of immunological diseases ranging from arthritis to alopecia areata and to rare inflammatory diseases. More selective, second-generation JAK inhibitors are now in clinical trials and newer JAK inhibitors are being developed. Super-enhancers are genomic regions in which regulatory elements and transcription factors concentrate, resulting in exceptional activation. Notably, the JAK inhibitor tofacitinib preferentially acts on genes associated with super-enhancer structures. I will review the most recent findings related to the mechanism of action of JAK inhibitors and some of the newest diseases for which JAK inhibition is proving to be a successful therapeutic approach. In the next few years, we expect this class of drugs to establish itself as a powerful tool in the hands of clinicians treating several immune-mediated pathologies.

Disclosure statement: M.G. holds a US patent related to targeting JAKs and has a Collaborative Research Agreement and Development Award with Pfizer.

IS1 REGULATORY T CELL IMMUNOLOGICAL SYNPASE IN RHEUMATOID ARTHRITIS
Michael Dustin
Kennedy Institute of Rheumatology, University of Oxford, Oxford, UK

We have published that regulatory T cells from patients with active RA show differences in organisation of immunological synapses related to localisation of protein kinase Cθ and Disc large homolog 1 adapter protein. A severe limitation in these studies was the number of cells needed for immunological synapse analysis. I will present progress on the use of high-throughput screening technologies to analyse rare cells in small clinical samples and application to hypothesis-driven and hypothesis-free approaches to discovery of disease mechanisms.

Disclosure statement: M.D. has received grants/research support from Celgene.

IS2 REAL-TIME OPTICAL MOLECULAR IMAGING IN VIVO
Christopher Haslett
MRG/University of Edinburgh Centre for Inflammation Research, University of Edinburgh, Edinburgh, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

IS3 IMAGING IMMUNOLOGY AND INFLAMMATION IN ACTION
Paul Garside
Institute of Infection, Immunology and Inflammation, University of Glasgow, Glasgow, UK

Abstract not provided.

Disclosure statement: P.G. has received grants/research support from AstraZeneca and Bristol-Myers Squibb.

IS4 JOINT LOCALIZATION-DEPENDENT EXPRESSION OF MICRO RNAS AND LONG-NON-CODING RNAs: CAN THEY EXPLAIN JOINT TYPE-DEPENDENT PATHOLOGIES AND INFORM THERAPY?
Caroline Ospelt
Centre of Experimental Rheumatology, University Hospital Zürich, Zürich, Switzerland

Molecular mechanisms determining the anatomic susceptibility of specific joints to certain forms of arthritis are unknown. We can show that synovial fibroblasts, the resident cells of the joint synovium, exhibit significant joint-specific differences in their transcriptomes. Differential expression of HOX genes as well as of non-coding RNA appear as the major determinants of joint-specific identities of murine and human synovial fibroblasts and synovial tissues. Finding the group of long-non-coding RNA (IncRNA) in particular, the HOX-encoded IncRNA HOXAIR and HOTTIP showed strong location-dependent expression, with HOXAIR only being expressed in synovial fibroblasts from joints of the lower extremity and HOTTIP only in distal joints. Both of these IncRNAs were previously found to mediate the positioning of histone marks in the HOX locus and therefore have a key role in the maintenance of location-specific HOX gene expression. Transcriptional diversity of synovial fibroblasts translated into joint-specific phenotypes with distinct adhesive, proliferative, chemotactic and matrix-degrading characteristics and differential responsiveness of synovial fibroblasts to TNF-α, thereby creating a unique microenvironment within each joint. These findings offer a new concept that local stromal signatures predispose to joint-specific patterns of arthritis.

Disclosure statement: C.O. has received grants/research support from Novartis.

IS5 TARGETING TRISTETRAPROLIN AS A NEW APPROACH TO THE TREATMENT OF RHEUMATOID ARTHRITIS
Andy Clark
Centre for Translational Inflammation Research, University of Birmingham, Birmingham, UK

Tristetraprolin (TTP) is an RNA binding protein that negatively regulates the expression of many inflammatory mediators, including TNF, IL-1, IL-6, IL-17, IL-23 and cyclooxygenase 2. Moreover, the control of pro-inflammatory gene expression by the mitogen-activated protein kinase (MAPK) p38 is achieved via the phosphorylation of TTP. We present evidence that direct targeting of TTP itself, rather than the upstream signalling cascades, might be used to treat inflammatory arthritis.

Disclosure statement: The author has declared no conflicts of interest.

IS6 MICRORNA IN TENDINOPTHY: A TRANSLATIONAL TARGET
Neal Millar
Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, UK

Soft tissue musculoskeletal disease imposes enormous burden on the community. In particular, tendon injuries (tendinopathies) are a significant cause of morbidity and thus a health burden on human society. This lecture highlights a novel role for miR-29a as a post-transcriptional regulator of matrix genes in tendon healing and tendinopathy. Our discovery of a single microRNA-dependent regulatory pathway in early tissue healing highlights miR-29a replacement therapy as a promising therapeutic option for tendinopathy, with implications for many other human pathologies in which matrix dysregulation is implicated.

Disclosure statement: The author has declared no conflicts of interest.
I57 COMPLEX REGIONAL PAIN SYNDROME
Rachel Gorodkin
Kelgren Centre for Rheumatology, Manchester Royal Infirmary, Manchester, UK

Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I58 PSORIATIC ARTHRITIS: ANTI-TUMOUR NECROSIS FACTOR AND BEYOND
Philip Halliwell
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and Chapel Allerton Hospital, Leeds, UK

Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I59 OSTEOPOROSIS IN YOUNG ADULTS
Nicola Peel
Metabolic Bone Centre, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK

Low BMD in a young adult may reflect low peak bone mass, premature bone loss or a combination of the two. Bone mass is predominantly inherited, but many environmental factors influence whether optimal peak bone mass is reached and maintained. These include diseases affecting bone acquisition and loss, medications and lifestyle factors. Bone densitometry should be considered in young adults presenting with fragility fractures or strong risk factors for osteoporosis. Prior to achievement of peak bone mass, it is inappropriate to express BMD results as a T score; therefore use of an age-matched comparison (Z score) is recommended, providing the individual is of normal skeletal size. Even after peak bone mass is reached, interpretation of the BMD should be performed with care. The relationship between BMD and fracture risk is not well established in young adults, and absolute fracture risk is generally low, even at low levels of BMD. Consideration of risk factors acting independently of BMD is also very important in determining the individual’s risk of fracture. Investigation for an underlying cause should be undertaken in young adults with low BMD. A careful history and examination will identify the majority of underlying causes and should be followed by targeted laboratory testing. If there is a history suggestive of vertebral fracture, spine imaging should be obtained since vertebral fractures independently increase the risk of subsequent fracture. The approach to manage- ments of young adults at increased fracture risk may involve education, including patient information leaflets and patient support groups; occupational assessment; pain management (e.g. for vertebral fractures); lifestyle advice (stop smoking, moderate alcohol intake, regular weight-bearing exercise, adequate calcium and vitamin D intake, maintain healthy weight); minimising the effects of underlying disease or medication and treatment to reduce the risk of fracture. The decision of whether to introduce pharmacological treatment should be evaluated on an individual basis. There are currently no licensed treatments for use in young adults other than for glucocorticoid-induced osteoporosis. In the absence of data demonstrating efficacy and long-term safety, treatment should only be used if the benefit outweighs the potential risk, and with the patient’s knowledge that they are taking treatment outside its licensed indication. Idiopathic osteoporosis is often associated with low peak bone mass, in which case the low BMD is likely to be long-standing and stable. Unless complicated by fragility fractures, such cases probably do not require treatment, even in the presence of very low BMD. Lifestyle advice should be given, and follow-up is important to confirm that BMD is stable. It may then be possible to defer treatment for many years. The same approach may also be taken in secondary osteoporosis if the cause can be treated.
Disclosure statement: N.P. has received speaker fees from Eli Lilly and Aragen and fees for participation in advisory board meetings for Eli Lilly, ProStrakan and Internis.

I60 MY MUSCLES ARE ACHING! AN OVERVIEW OF MYOSITIS
Hector Chinoy
Centre for Musculoskeletal Research, University of Manchester, Manchester, UK

The lecture will provide an overview of what is currently known about idiopathic inflammatory myopathy (myositis), coupled with an up-to-date review of best practice and a highly clinical, practical focus on disease management. The discussion will concentrate on aspects of diagnostics and misdiagnosis, using exemplar cases to illustrate key take-home messages. Up-to-date evidence-based information will be provided, where available. The lecture will be interactive with the use of audience voting technology.
Disclosure statement: H.C. has received consulting fees from Momenta, Novartis and aTyR; has received fees for advisory board activities from Roche, Pfizer, AbbVie, Servier, UCB and Merck and has received funding for an educational grant from Novartis.

I61 MANAGEMENT OF TEMPOROMANDIBULAR DISORDERS
Jeet Rao
Oral and Maxillofacial Surgery, East Lancashire Hospitals NHS Trust, Blackburn, UK

An essential guide to temporomandibular disorders (TMDs), this lecture provides an overview of the anatomy and physiology of the TMJ. Disorders including myofascial pain, internal derangement and arthroses and the pathophysiology and diagnosis of these disorders are discussed, as well as an overview of clinical management of TMDs, both non-surgical and surgical. The objective is to enable a rheumatology physician to diagnose and advise on initial management of TMDs and make onward referral for further management.
Disclosure statement: The author has declared no conflicts of interest.

I62 VASCULITIS AND CONNECTIVE TISSUE DISEASE MIMICS
David Isenberg
Rheumatology, Medicine, University College London, London, UK

SLE is clearly not a single simple disease. It is thus not surprising that the diagnosis is often missed or only made after a number of unnecessary investigations and far too lengthy a wait. However, a number of clinical features are common to lupus, other autoimmune rheumatic diseases, infections and cancer and can cause genuine uncertainty at the outset. Individuals presenting with fever will be tested, quite appropriately, for possible classical infectious diseases. Likewise, patients presenting with enlarged lymph glands and/or weight loss with anorexia need to be tested thoroughly to exclude malignancy. It is vital in all of these cases to have a simple autoantibody screen, as this may be helpful in pointing the physician in the correct direction. However, even with positive autoanti- body tests, there are complexities. An ANA (and even occasionally anti-ENA antibodies) are found transiently in patients with a wide variety of infectious diseases. In contrast, antibodies to dsDNA and anti-Sm are very strongly correlated with the presence of SLE. Mixed connective tissue disease (MCTD) remains a widely used term, but is inherently unsatisfactory. It is said to have components of lupus, myositis and even scleroderma. Initially regarded as a mild condition affecting principally the joints, skin and circulation, it is now recognized that such patients (when associated with strongly positive anti-RNP antibodies) have widespread lung, cardiac and even renal disease. Although originally believed to require little steroid treatment and to have a good outcome, neither of these notions has held true over time. It has also become clear that many patients initially diagnosed with MCTD will evolve into more classic cases of myositis, lupus or scleroderma. Therefore, making the diagnosis of SLE is not always simple, but perhaps the most important thing is to encourage awareness of its existence, especially in women between the ages of 15 and 50 years.
Disclosure statement: The author has declared no conflicts of interest.
I63 SUSPECTED SARCOMA: WHAT DOES A RHEUMATOLOGIST NEED TO KNOW?

Lee Jeys
Orthopaedic Surgery, The Royal Orthopaedic Hospital NHS Foundation Trust, Birmingham

Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I64 PAEDIATRIC RHEUMATOLOGY: WHAT DOES AN ADULT RHEUMATOLOGIST NEED TO KNOW?

Helen Foster
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Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I65 FIBROMYALGIA IN A BENGALI POPULATION

Anisur Rahman
Rheumatology, University College London, London, UK

FM is a condition causing chronic widespread pain, which is defined according to criteria published by the ACR. Although much of the epidemiological research on FM has been done in Western populations, giving a prevalence of 2–6%, a large study in Bangladesh showed a similar prevalence there. In the UK, chronic pain appears to be a common problem in some ethnic minority communities, including Bengalis. It is not clear whether the cause of pain is different in these communities, whether patients present in a different way and what role is played by social and cultural factors. Some studies have looked at acculturation (the adoption by inomers of the cultural characteristics of the host community) as a factor that may influence chronic pain in minority ethnic communities, although this factor can be difficult to measure.

In the London Borough of Tower Hamlets, the two largest ethnic groups are white people and Bengalis. The latter come mainly from Sylhet, in the north-east of Bangladesh. In a large bilingual questionnaire study in primary care, we found that both chronic pain per se and chronic widespread pain were seen more commonly in Bangladeshis than white people. However, when the Bangladeshis were stratified into groups who had grown up in the UK or in Bangladesh, the former group had pain prevalence figures very similar to those of the white population. Acculturation was not measured in this study. Chronic pain was associated with reduced quality of life in both ethnic groups. Management of chronic pain in the community is challenging, with medications and physiotherapy often being of limited benefit. Pain management programmes involving physiotherapy and psychology may be effective but may be hampered by language barriers. A pilot study for a large randomized controlled trial of a brief self-management intervention for patients with chronic musculoskeletal pain in Tower Hamlets was carried out in both English and Bengali, showing that this is feasible. The actual trial was carried out in English only and showed improvements in mental health outcomes but not self-efficacy. In summary, although there are differences between white and Bengali subjects in these studies of chronic pain, perhaps the similarities between all people suffering from chronic pain are more important than the differences between subgroups.

Disclosure statement: A.R. is an inventor of a patent submitted for a new agent in the treatment of APS and is working with PolyTherics.
In this session, we would like to showcase our innovative idea to encourage health professionals to talk about the NRAS project in their clinics and direct suitable Asian RA patients to the NRAS website.

Disclosure statement: The author has declared no conflicts of interest.

**BSR CLINICAL GUIDELINES**

I69  **GUIDELINE ON CONVENTIONAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS**

James Galloway  
**Rheumatology, King’s College London, London, UK**

The British Society for Rheumatology guidelines for the initiation and monitoring of non-biologic DMARDs were published in 2008. These have been updated for 2016. Important new changes include review of the pre-screening recommendations before commencing DMARDs (including recommendations on respiratory screening prior to DMARDs) as well as revision of the intensity of laboratory monitoring, with recommendations to reduce monitoring frequency in some circumstances. This talk will provide an overview of the new guidelines, explaining the guideline methodology and highlighting key aspects of the evidence base from which they have been drawn.

Disclosure statement: J.G. has received speakers honoraria from Pfizer; grants/research support from Pfizer (CRP); accommodation funding from AbbVie at the ACR 2015; and has also payments for attending advisory boards for Napp and MSD.

I70  **DEVELOPMENT OF EVIDENCE-BASED RECOMMENDATIONS FOR DIAGNOSIS, ASSESSMENT AND TREATMENT OF LUPUS**

Caroline Gordon1, Maame-Boatema Amissah-Arthur1, Mary Gayed1, Ian Bruce2, David d’Cruz3, Benjamin Empson3, Bridget Griffiths3, David Jayne3, Munther Khanna1, Karen Schreiber2, Sue Brown1, David Isenberg1,  
1Rheumatology Research Group, University of Birmingham, Birmingham, 2Rheumatology, University of Manchester, Manchester, 3Rheumatology, Guy’s Hospital, London, UK

Background: There are no UK guidelines for the management of lupus. However, the disease affects nearly 1 in 1000 people and patients die on average 2-25 years earlier than the mean for the UK population.

Methods: In order to produce evidence-based guidelines supplemented by expert opinion for the British Society for Rheumatology (BSR), we set up a multidisciplinary group and undertook a comprehensive review of the literature on diagnosis, assessment and monitoring of lupus. We performed a systematic review of drug treatments used in the management of non-renal lupus. We developed and present here recommendations for the management of non-renal lupus due to inflammatory processes in adults. We determined our levels of agreement with these and the existing EULAR/ERA recommendations for lupus nephritis.

Results: More than 8000 articles were identified by our search, of which >600 met our criteria for detailed review by at least two members of the group and >400 papers contributed to our recommendations. On the basis of this literature review to June 2015, we propose that the diagnosis of lupus requires a combination of clinical features and the presence of at least one relevant immunological abnormality. To treat lupus patients appropriately, assessment should determine the level of disease activity, whether due to inflammation and/or thrombosis, damage, drug toxicity or morbidity. Regular monitoring of lupus, drug toxicity and morbidity is needed indefinitely. Evidence (see Table 1 for grades of recommendation) supports the treatment of mild lupus with HCQ, MTX and intermittent NSAIDs to minimize corticosteroid use. Moderate lupus often requires unlicensed immunosuppressive agents (e.g. MTX, AZA, MMF, ciclosporin) to reduce disease activity, the need for corticosteroids and risk of damage accrual. Severe lupus requires initial high-dose corticosteroids to induce remission, usually with MMF or i.v. CYC. Rituximab, belimumab, IVIG and plasmapheresis may be used in refractory disease or rare situations (e.g. thrombotic thrombocytopenic purpura). Levels of agreement of panel members were >90% for all recommendations.

Conclusion: Although there are still relatively few randomized controlled trials, there is increasing evidence for HCQ and immunosuppressive agents in addition to corticosteroids in lupus, with biologics for refractory disease. The BSR intends to publish the guidelines on the management of lupus later this year.

Disclosure statement: C.G. has received consulting fees from Bristol-Myers Squibb, Merck Serono and UCB, is a member of speakers’ bureau for GSK and is a member of consultants’ bureau for the same. K. Schreiber: None. S. Brown: None. D. I has received consultancy fees from Ei Lilly and UCB and received a grant from UCB, J.B. has received consultancies from GSK and Roche as is a member of speakers’ bureau for the same. D.J. has received consultancy fees from Roche and has received grants and research support from GSK, HGS and Roche. D.D. has received consultancy fees from GSK and is a member of speakers’ bureau for the same. M.K. has received consultancy fees from GSK and is a member of speakers’ bureau for the same. E. Price: None. S. Brown: None. D. I has received consultancy fees from Roche and GSK, is a member of speakers’ bureau for GSK and has received grants/research support from Roche. All other authors have declared no conflicts of interest.

I71  **MANAGEMENT OF SJÖGREN’S SYNDROME**

Elizabeth Price  
**Rheumatology, Great Western Hospital, Swindon, UK**

SS is a chronic, immune-mediated condition of unknown aetiology characterized by focal lymphocytic infiltration of the exocrine glands. Patients characteristically complain of drying of the eyes and mucosal surfaces along with fatigue and arthralgia. There is an association with autoimmune thyroid disease, coeliac disease and primary biliary cirrhosis. There is no cure for SS, but management can improve quality of life. This talk will outline our proposed update guidelines for the management of Sjögren’s syndrome.

Disclosure statement: E.P. has received grants and research support from GSK, HGS and Roche. D.D. has received consultancy fees from GSK and is a member of speakers’ bureau for the same. GSK, Roche, and has received grants and research support from GSK, HGS and Roche. D.D. has received consultancy fees from GSK and is a member of speakers’ bureau for the same. M.K. has received consultancy fees from GSK and is a member of speakers’ bureau for the same. E. Price: None. S. Brown: None. D. I has received consultancy fees from Roche and GSK, is a member of speakers’ bureau for GSK and has received grants/research support from Roche. All other authors have declared no conflicts of interest.
**INVITED SPEAKER ABSTRACTS**

**I76 ASSESSING DISEASE ACTIVITY AND DAMAGE IN VASCULITIS: AN INTERACTIVE PRACTICAL SESSION**

Alberto Floris
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

Abstract not provided.

**Disclosure statement:** A.F. has received a bursary from the Italian Society of Rheumatology in a collaborative initiative with the British Society for Rheumatology.

**COMMON MUSCULOSKELETAL FOOT PROBLEMS IN PRIMARY CARE**

This session is co-badged with the College of Podiatry

**I77 FOOT OSTEOARTHRITIS: EPIDEMIOLOGY, DIAGNOSIS AND TREATMENT**

Hyton B. Menz
School of Allied Health, La Trobe University, Melbourne, Victoria, Australia

OA is the most common musculoskeletal disorder in the world and is a major cause of disability. OA most commonly affects the knees, hips, hands and spine, and although foot involvement is also common, it has received little attention in the literature until relatively recently. The development of a standardized radiographic atlas and case definition of foot OA in 2007 enabled the population prevalence of foot OA to be estimated in the Clinical Assessment Study of the Foot (CASF), which involved 9334 adults aged 50 years of age registered with four general practices in North Staffordshire. The CASF study found the overall population prevalence of symptomatic radiographic OA to be 16.7%, with the first MTP joint being the most commonly affected site (prevalence of 7.8%). Prevalence is greater in females than males, increases with age and is higher in lower socio-economic classes, and three-quarters of those with symptomatic radiographic OA report disabling foot symptoms. A subsequent analysis of this sample identified two possible phenotypes of foot OA with different risk factor profiles: (i) isolated first MTP joint OA and (ii) polyarticular foot OA (incorporating midfoot joints). First MTP joint OA, which can be accurately identified using simple clinical tests, appears to be primarily a structural disorder, with several foot-level risk factors (including longer and wider phalanges and sesamoids) being implicated in its development. In contrast, OA affecting multiple midfoot joints appears to be more strongly related to person-level factors (possibly indicative of a generalized form of OA) and is more difficult to identify in the absence of radiographs. The management of foot OA may involve anti-inflammatory medications, physical therapy, mechanical interventions (such as orthoses and specialized footwear) and surgery. However, very few randomized trials have been conducted to evaluate the effectiveness of these treatments. For first MTP joint OA, the available evidence indicates that the addition of sesamoid mobilisation, flexor hallucis strengthening exercises and gait training to a standard physical therapy program may be beneficial. Visco supplementation using intra-articular injection of hyaluronan is no more effective than placebo (sterile saline) and prefabricated foot orthoses are more effective and better tolerated than rocker-sole footwear. This presentation will also provide an overview of a trial currently under way evaluating the effectiveness of shoe-stiffening inserts for the treatment of first MTP joint OA. In summary, foot OA is a common and disabling condition that has received relatively little research attention compared with OA affecting other regions of the body. Foot OA presents as two distinct phenotypes with different risk factors and clinical characteristics. The most commonly affected site is the first MTP joint, and although limited, the available evidence suggests that mechanical interventions such as footwear and orthoses may be beneficial in the treatment of this condition.

**Disclosure statement:** H.B.M. has received a senior research fellow grant from the National Health and Medical Research Council of Australia.
I78 PLANTAR FASCIITIS IN PRIMARY CARE: WHAT WORKS?
Anne-Marie Keenan
Leeds Musculoskeletal Biomedical Research Unit, University of Leeds, Leeds, UK

Plantar heel pain (plantar fasciitis) is one of the most common musculoskeletal problems in the lower limb, with prevalence estimates of 10% of the population. Much has recently been written on plantar heel pain. This presentation will navigate through the research to explore current issues in the diagnosis of plantar fasciitis, including clinical presentation and differential diagnosis. The presentation will focus on the pathogenesis and risk factors, where new research has provided insights into the histopathology of the condition and may offer new insights into treatments. The presentation will summarize the treatment options for plantar fasciitis using an evidence-based approach, with an emphasis on the use of imaging modalities in diagnosis and treatment.

Disclosure statement: The author has declared no conflicts of interest.

I79 ASSESSMENT AND MANAGEMENT OF ACHILLES TENDON PROBLEMS IN PRIMARY CARE
Mike Carmont
Shrewsbury and Telford Hospital NHS Trust, London, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

FOOT PROBLEMS IN INFLAMMATORY ARTHRITIS

This session is co-badged with the College of Podiatry

I80 FOOT PROBLEMS IN INFLAMMATORY ARTHRITIS: HOW COMMON ARE THEY AND WHAT IS THEIR IMPACT?
Simon Otter
School of Health Science, University of Brighton, Eastbourne, UK

Foot problems are almost ubiquitous in many forms of inflammatory arthritis. Typically foot complaints have a significant negative impact on patients’ ability to undertake day-to-day activities of daily living and their psychosocial well-being. Reports suggest that the nature and impact of foot problems is often underestimated, and this can adversely affect holistic management strategies. This presentation will explore our current knowledge of the nature and extent of foot complaints and their associated impact across a series of different rheumatological complaints, highlighting some options to enhance care and areas for further research.

Disclosure statement: S.O. has received consulting fees from Daval International.

I81 CALL THE PODIATRIST! MANAGEMENT OF FOOT PROBLEMS IN INFLAMMATORY ARTHRITIS
Anita Williams
Health Sciences, University of Salford, Manchester, UK

This presentation will focus on the research that has significantly influenced both the foot health interventions that are now provided to people with inflammatory joint conditions and the development of guidelines that directly impact on patient care. Aligned with this has been the increasing profile of podiatry within rheumatology and also the recognition within podiatry of rheumatology as a specialisation. However, the podiatrist’s role within rheumatology is currently under threat as services are driven to focus on other patient groups. This is happening despite recommendations from guidelines and support from rheumatologists. The risks associated with this decline in specialist foot care will be explored and some solutions suggested in relation to the diagnosis, assessment and management of foot problems.

Disclosure statement: A.W. has received funding for research from the Logres Trust.

I82 FOOT SURGERY IN INFLAMMATORY ARTHRITIS: WHO SHOULD I REFER, WHEN AND FOR WHAT?
Robin Rees
Orthopaedics and Trauma, University Hospital of North Midlands, Stoke on Trent, UK

No abstract provided.

Disclosure statement: The author has declared no conflicts of interest.

GROUP CLINICS IN MUSCULOSKELETAL DISEASE: BETTER TOGETHER

I83 CONSULTANT-LED MULTIDISCIPLINARY INFLAMMATORY ARTHRITIS GROUP CLINICS
Fraser Birrell
Musculoskeletal Research Group, Northumbria Healthcare & Newcastle University, Newcastle upon Tyne, UK

Healthcare delivery is a constant challenge: delivering high-quality care within or few resources. How can we deliver education with a month of an inflammatory arthritis diagnosis, see flaring patients and achieve monthly reviews when clinics are full and still treat to target? One answer is to consider implementing group clinics, where the same group clinic can be used for monthly review of early/active disease and annual review of stable chronic disease. Since winning the British Society for Rheumatology Innovation in Development Award 2009 for pilot work on single-site group clinics for inflammatory arthritis, the model has become a standard care option in two community hospitals (where 40% of review attendances are at group clinics), with plans to roll out by two other consultants to two other hospitals, including a district general hospital, in the next few months. Local commissioners have agreed that group clinic attendance is reimbursed at the standard follow-up outpatient tariff. The model has evolved with a cycle of responding to patient feedback and incorporating these ideas—embedding the ones that work well. Examples include patients going out to have intramuscular steroid injections during group discussion rather than queuing to have it afterwards; ringing a bell to celebrate low disease activity/remission; permission to make jokes and laugh and inviting members of the multidisciplinary team to give opportunistic education during the first 30–45 minutes while the consultant does joint scores, calculates DAS and has microconsults. These refinements have improved the efficiency and enjoyment without affecting the quality of care, which remains excellent. Patients complete a multidimensional HAQ on arrival and have tender and swollen joints counted, DAS calculation and treatment target stated. During this microconsult, if a DMARD change is appropriate, the patient is given the relevant information leaflet (to read and ask questions during discussion) and the review plan is made: 1 month if DAS ≥3.2 or 12 months if DAS <3.2; patients this well often leave early unless they have information needs. The group consultation itself includes ground rules, selection of topics and discussion, during which patients go out with the clinic nurse for I.m. steroids, if required. Treatment changes or confidential issues are dealt with after the main session. There have now been 105 clinics across the two sites, with 1735 attendees (mean 17 per clinic). Thirty-eight per cent of patients have low disease activity (DAS >3.2 for RA) or remission (DAS <2.6 for RA or tender/swollen joints <2 for PsA). Fifty-nine per cent of patients have I.m. steroids (or rarely, i.a. steroids). Team members participating have included specialist nurse, physiotherapist, occupational therapy, podiatry and generic assistant, with plans to extend this to include dietetics, psychology and pharmacy. In that respect, group clinics are a new answer to the same old questions.

Disclosure statement: F.B. has received research support from the National Osteoporosis Society and National Institute for Health
GROUP CLINICS IN THE COMMUNITY

Wasim Baqir
Pharmacy, Northumbria Healthcare NHS Foundation Trust, Newcastle upon Tyne, UK

Group clinics have shown promise in inflammatory arthritis. However, there is little evidence for the effectiveness of group clinics in other major musculoskeletal conditions, especially outside the USA, delivered by non-medics and in community settings. One US study showed osteoporosis patients attending shared medical appointments were more likely to have vital sign levels checked and receive treatment but it was not a randomized controlled trial (RCT) and adherence was not assessed. The objective of this RCT was to compare group and 1:1 clinics for primary care patients who did not necessarily know they had osteoporosis with a pharmacist-led intervention. Patients from a single practice-based commissioning group with high fracture risk (FRAX red zone) were randomized to group or 1:1 clinic. Patients (>50 years of age) were invited to participate if ambulatory and eligible for first-line treatment with weekly alendronate. The primary outcome measure was the median possession ratio (MPR) of bisphosphonates over 12 months (ratio of doses requested/all possible doses). The secondary outcome measure was persistence with treatment. As an equivalence trial, the hypothesis tested was of no significant difference between medication adherence measured in group versus 1:1 clinics, undertaken by the same pharmacist. Statistical analysis included Mann–Whitney U-test, χ², survival curves and Cox regression. The study was approved by the local research ethics committee. A total of 178 patients from three general practices gave consent and were invited to attend. Eighty-four patients were randomized to group clinics: 9 non-attenders, 75 attenders; 84 patients were randomized to 1:1 clinics (15 min appointment); 11 non-attenders, 83 attenders, leaving 158 attenders for the intention to treat analysis. Four 90 min group clinics were held (group 1, n = 24; group 2, n = 14; group 3, n = 13; group 4, n = 24; mean 19 patients = 4.8 min of pharmacist time per patient). The mean age of those randomized to group clinics was 74 years (s.d.; 11; range 59–90) and 74 years (s.d.; 10; range 63–90) in the 1:1 clinics; 84% (n = 63) and 82% (n = 69) were female, respectively. Fracture risk for major osteoporotic/hp fracture was 26%/14% for group clinics and 23%/10% for 1:1 clinics, respectively. MPR was 0.9 for group clinics and 0.54 for 1:1 clinics, with no statistically significant difference (P = 0.86, Mann–Whitney). After 6 months, 50 (67%) group and 56 (67%) 1:1 clinic patients remained on treatment (P = 0.82, χ²). Univariate Cox regression analysis showed group or 1:1 clinic attendance was not a significant predictor of outcome (odds ratio (OR) 0.49 (95% CI 0.25, 0.97), χ², 0.43), even after adjustment for age, sex and FRAX score [adjusted OR 0.920 (95% CI 0.636, 1.694), even after adjustment for age, sex and FRAX score [adjusted OR 0.920 (95% CI 0.553, 1.531)]. In conclusion, group clinics are as acceptable as 1:1 appointments and equivalent by the primary outcome. Since the mean pharmacist contact time per patient was lower, the group clinic was both efficient and cost effective. Clinicians with the right facilitation skills can improve service delivery for common conditions through group clinics.

Disclosure statement: The author has declared no conflicts of interest.

EDUCATIONAL FRAMEWORK FOR GROUP CLINICS

Michele Russell-Westhead
Florence Nightingale Faculty of Nursing and Midwifery, King’s College London and Faculty of Health and Life Sciences, Northumbria University, London, UK

This presentation is an evaluation of group clinics (GCs) in rheumatology developed over a period of 5 years at Northumbria NHS Trust. It addresses the acceptance of and satisfaction with GCs as an alternative model of care based on patient satisfaction data and makes recommendations for training and service delivery and potentially the transition to other long-term conditions. There are four major phases of the clinic: (i) administration—pre-clinic information, clinic arrangements and post-clinic reporting and follow-up; (ii) clinical/microconsultation—discussion of lab tests, individual concordance information and therapeutic interventions; (iii) input—consultant-led information and advice on topics raised by patients during the clinical/microconsult phase; (iv) discussion—patient-led discussion and question and answer. The GCs are consultant led, however, other team members have provided opportunistic education during the clinical/microconsult phase and in response to positive feedback from patients; this is now embedded in the model. Patient satisfaction surveys have been collected over a 5-year period in inflammatory arthritis (IA) and osteoporosis GCs, which has led to refinement of the model. A pragmatic qualitative approach using focus groups was also adopted to describe 15 patients’ experiences in the IA GCs. Data triangulation was provided from an interview with the consultant rheumatologist and focus group data from the osteoporosis GCs. The data analysis identified five main themes: efficiency, education, engagement, empathy and empowerment. At the level of service delivery, key indicators of patient satisfaction were group clinics created a more efficient system in terms of reduced waiting times, administration before and on the day of clinic and volume of patients that the health education component can be delivered to (efficiency). Most participants gained value from the GCs, including increased knowledge and awareness of their condition (education); meeting other people with a similar condition; normalizing, validating and sharing their experiences; learning from the questions of others (engagement); emotional support through listening to others (empathy) and information on how to self-manage more effectively (empowerment). Participants particularly valued the knowledge, approach and interpersonal skills of the consultant facilitator. Five Ps were thus identified as the key indicators to acceptability and satisfaction of the group clinic model: prioritisation, personalisation, participation, pedagogical approach and personality. This study has revealed a number of enabling factors needed to promote patient acceptance of, if not preference for, GCs. Particularly important is having the buy-in from all team members (prioritisation), making the discussion topics relevant and individualized (personalisation), providing an opportunity for local and peer advice and support (participation) and focusing on improving health outcomes (pedagogical approach). The personality and training of the leader of the group clinic is of paramount importance (personality). Having these in place may support translation of the model to other conditions and health care settings.

Disclosure statement: The author has declared no conflicts of interest.
skin lesions in a patient with established disease. Other disorders such as dermatomyositis may present with skin lesions that are indistinguishable from lupus, especially in the early phase before muscle disease is clinically apparent. In these circumstances, a referral to a dermatologist, with a skin biopsy, may be diagnostic. This lecture will give examples of skin manifestations where a dermatology opinion has changed the diagnosis and management of the patient.

Disclosure statement: D.D. has received consulting fees from Roche, Eli Lilly, GlaxoSmithKline, Pfizer and Actelion; is a member of speakers bureaus for GlaxoSmithKline and UCB and has received grants/research support from Aspreva.

I88 CORRELATING THE SKIN BIOPSY WITH CLINICAL FEATURES TO MAKE A DIAGNOSIS

David McGibbon
St John’s Institute of Dermatology, Guy’s and St Thomas’ NHS Foundation Trust, London, UK

The talk will highlight aspects of photosensitivity including sunlight improving cutaneous LE; solar fatigue syndrome; polymorphic light eruption as a pointer to LE, SS and polychondritis; the histological appearance of cutaneus LE and immunofluorescence; other causes of lupus panniculitis histologically besides LE; clinical and histological aspects of Degos-like lesions in APS; rashes and histology of adult-onset Still’s disease and a new entity, transient heliotrope eyelids.

Disclosure statement: The author has declared no conflicts of interest.

I89 WHAT IS SELF-MANAGEMENT: A LEAFLET, A COURSE OR A WAY OF LIFE?

Sara Demain
Health Sciences, University of Southampton, Southampton, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I90 WELL-BEING AND THE ABILITY TO SELF-MANAGE: THE SUPPORT NEEDS OF PATIENTS WITH INFLAMMATORY ARTHRITIS

Emma Dures
Nursing and Midwifery, University of the West of England, Bristol, UK

It is recognized that patients have to make behaviour changes and psychological adjustments to address the impact of inflammatory arthritis on their lives. Challenges include fluctuating pain, fatigue, flares of disease activity and emotional consequences. Meeting these challenges effectively requires patients to engage in self-management, including medical management, role management and emotional management. For some patients this can be a struggle, and the rheumatology team can be a valued source of support. However, a nationwide survey found that most rheumatology teams rate the support they can offer as inadequate and current provision is variable. This session will look at the relationship between well-being and self-management. It will include data presenting patients' views on ways in which well-being and self-management can be enhanced or diminished through clinical interactions with the rheumatology team. The theoretical bases and evidence for the models of self-management will be considered and their utility in clinical practice discussed.

Disclosure statement: The author has declared no conflicts of interest.

I91 HOW CAN PRIMARY CARE CONSULTATIONS FACILITATE SELF-MANAGEMENT? EXAMPLES FROM RESEARCH AND PRACTICE

Joanne Protheroe
Arthritis Research UK, Primary Care and Health Sciences, Keele University, Keele, UK

This lecture will discuss effective support for self-management, which requires engagement with the whole system—patient, practitioner and service organization. It also discusses the tension between evidence-based care and patient-centred consultations and how routine reviews offer a unique opportunity to promote health and support patients to better self-manage.

Disclosure statement: The author has declared no conflicts of interest.

TREATING EARLY RHEUMATOID ARTHRITIS TO TARGET: PRACTICE OUTSIDE THE UK

MTX is the cornerstone of RA treatment. Recently, updated recommendations by the EULAR show MTX as an important part of the first-line strategy in patients with active RA. The study presented here aimed to assess the clinical effectiveness and tolerability of s.c. MTX among patients with RA. Patients with RA who were naïve at baseline to both conventional and biologic DMARDs, fulfilled the ACR/EULAR 2010 criteria and had one or more follow-up visits were selected through sequential chart review for analysis of retrospective data. Patients received s.c. MTX at varying doses (10-25 mg/week). The primary endpoint was a change in the 28-joint DAS (DAS28); secondary endpoints included time to employment of the first biologic agent and cumulative MTX dose. Overall, 70 patients were in follow-up for a mean of 1.8 years after initiating s.c. MTX treatment. During this time, 37 (53%) remained on s.c. MTX without any biologics (MTX-only) and 33 (47%) required the addition of a biologic therapy (MTX-biol). Biologic therapy was required after a mean of 387 days (s.e. 404). The mean weekly MTX doses were 17.4 mg for patients in the MTX-only group and 19.1 mg for patients in the MTX-biol group. The mean baseline DAS28s were similar for patients in the MTX-biol and MTX-only groups (4.9 and 4.7, respectively). Both low disease activity state (LDAS) and remission were achieved by slightly fewer patients in the MTX-biol group than the MTX-only group (LDAS, 78.8 vs 81.1%; remission, 69.7 vs 75.7%). Over the full course of the study period, s.c. MTX was discontinued in 32 patients (46%). Among those who discontinued, the most common reason was gastrointestinal discomfort (n = 7), lack of efficacy (n = 7) and disease remission (n = 3). Severe infections occurred in three patients in the MTX-biol group and three patients in the MTX-only group. It was found that s.c. MTX is a safe and effective treatment option for patients with RA. Since s.c. MTX resulted in high rates of remission and LDAS in early disease, over prolonged periods of time, it may extend the time before patients require initiation of biologic therapy.

Disclosure statement: R.M. has received consulting fees from Antares.

I92 TREATMENT OF EARLY RHEUMATOID ARTHRITIS IN SWITZERLAND

Ruediger Mueller
Rheumatology, Kantonsspital St Gallen, Sankt Gallen, Switzerland

MTX is the cornerstone of RA treatment. Recently, updated recommendations by the EULAR show MTX as an important part of the first-line strategy in patients with active RA. The study presented here aimed to assess the clinical effectiveness and tolerability of s.c. MTX among patients with RA. Patients with RA who were naïve at baseline to both conventional and biologic DMARDs, fulfilled the ACR/EULAR 2010 criteria and had one or more follow-up visits were selected through sequential chart review for analysis of retrospective data. Patients received s.c. MTX at varying doses (10-25 mg/week). The primary endpoint was a change in the 28-joint DAS (DAS28); secondary endpoints included time to employment of the first biologic agent and cumulative MTX dose. Overall, 70 patients were in follow-up for a mean of 1.8 years after initiating s.c. MTX treatment. During this time, 37 (53%) remained on s.c. MTX without any biologics (MTX-only) and 33 (47%) required the addition of a biologic therapy (MTX-biol). Biologic therapy was required after a mean of 387 days (s.e. 404). The mean weekly MTX doses were 17.4 mg for patients in the MTX-only group and 19.1 mg for patients in the MTX-biol group. The mean baseline DAS28s were similar for patients in the MTX-biol and MTX-only groups (4.9 and 4.7, respectively). Both low disease activity state (LDAS) and remission were achieved by slightly fewer patients in the MTX-biol group than the MTX-only group (LDAS, 78.8 vs 81.1%; remission, 69.7 vs 75.7%). Over the full course of the study period, s.c. MTX was discontinued in 32 patients (46%). Among those who discontinued, the most common reason was gastrointestinal discomfort (n = 7), lack of efficacy (n = 7) and disease remission (n = 3). Severe infections occurred in three patients in the MTX-biol group and three patients in the MTX-only group. It was found that s.c. MTX is a safe and effective treatment option for patients with RA. Since s.c. MTX resulted in high rates of remission and LDAS in early disease, over prolonged periods of time, it may extend the time before patients require initiation of biologic therapy.

Disclosure statement: R.M. has received consulting fees from Antares.

I93 TREATMENT OF EARLY RHEUMATOID ARTHRITIS IN FINLAND

Tuulikki Sokka
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The treatment target of RA was set by Finnish rheumatologists decades ago. In a letter to the editor of the British Medical Journal in 1978, Finnish rheumatologists mentioned: “In our opinion gold treatment ought to be started in the early stages of RA, before the development of erosions. We are treating not only the actual inflammation of the joints but also the quality of the patient’s life for many decades in the future. Current care guidelines for RA were updated in 2015 with emphasis on
early diagnosis and prompt start of effective treatment to achieve fast remission and maintain the patient’s functional capacity and working ability. Finnish recommendations to treat early RA emphasize the following: a combination therapy with MTX as the anchor drug, together with SSZ, HCQ and a small dose of glucocorticoids (mainly prednisolone 5–7.5 mg); higher bioavailability of s.c. MTX compared with oral; the importance of treating swollen joints with intra-articular glucocorticoids; the role of biologic agents in the treatment of persistently active disease; patient education to ensure compliance with long-term treatment; consultation with a physiotherapist for engagement in regular physical exercises; prevention of osteoporosis and management of cardiovascular risks; patient monitoring as part of clinical care and every patient’s right to receive care by a multidisciplinary team in the first years following diagnosis and annual visits thereafter to a doctor with a good understanding of rheumatology.

**Disclosure statement:** The author has declared no conflicts of interest.

**I94 TREATMENT OF EARLY RHEUMATOID ARTHRITIS IN FRANCE**

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Abstract not provided.

**Disclosure statement:** V.G. has received consulting fees from AbbVie, Bristol-Myers Squibb, Chugai, Eli Lilly, MSD, Novartis, Pfizer and UCB.

**DISEASE MODIFICATION IN OSTEOARTHRITIS**

**I95 STRONTIUM RANELATE AND BISPHOSPHONATES IN OSTEOARTHRITIS: CLINICALLY EFFECTIVE AND STRUCTURE-MODIFYING**

Nigel Arden
Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

Strontium ranelate and bisphosphonates in osteoarthritis: clinically effective and structure-modifying? OA is a heterogenous disease that involves all of the tissues of the joint, including bone, cartilage and synovium. Abnormalities of the sub-chondral bone are well described in subjects with knee OA, including increased uptake on radioisotope scans and bone marrow lesions on MR scanning. This, in addition to findings of an improvement in symptoms and radiographic OA of the facet joints in trials of bisphosphonates for osteoporosis, lead to an interest in the use of bisphosphonates for the treatment of knee OA. Although early phase 2 trials delivered promising results, phase 3 studies were disappointingly negative. Strontium ranelate also showed promising early results and were confirmed in phase 3 studies, but has been associated with significant side effects. Achieving disease modification is OA is a tall order due to the relative insensitivity of x-ray as an outcome. The move towards better phenotyping of subjects entering clinical trials into those with a “bone phenotype” and the use of appropriate outcome measures, may well yield positive studies in the near future.

**Disclosure statement:** N.A. has received consulting fees from Smith & Nephew as well as Nicxo and Flexion and Freshfields; has received honoraria from Fuhumanub OA and has received research grants from Roche and Bioiberica.

**I96 METHOTREXATE AND PREDNISOLONE IN KNEE OSTEOARTHRITIS**

Anna Abou-Raya
Rheumatology and Immunology, University of Alexandria, Alexandria, Egypt

OA of the knee is a major cause of pain and locomotor disability worldwide. OA is a progressive, complex, multifactorial disease that affects all joint structures, with patients classified as heterogeneous groups exhibiting varying degrees of inflammation, in some cases more comparable with RA. The precise aetiology remains unclear. Inflammation has been implicated in the pathogenesis of OA and may be either a primary event or secondary to other aspects of the disease, such as biochemical changes within the cartilage. Synovial inflammation and proliferation is a key component of OA and a predictor of worsening disease. Synovial inflammation due to the release of prostaglandins and cytokines is associated with joint symptoms and disease progression. The unmet medical need for treatment options for patients suffering from OA is a significant dilemma. Current treatment options have had limited symptomatic effect and are associated with significant side effects. Given the limitations in terms of both efficacy and safety of the available non-specific symptom-relieving drugs, such as analgesics, guidelines acknowledge the need for medications that not only offer acceptable short-term symptom control, but also have a role in the medium-term and long-term management of OA. Thus therapeutic interventions with the ability to slow down the progressive destruction of joint tissue or possibly stop it, that is, disease-modifying OA drugs, are needed. MTX is widely used in the treatment of all inflammatory rheumatic diseases, where it seems to act primarily through a mechanism to reduce inflammation. Two open-label studies have demonstrated improvement in OA pain with MTX use. One of these, a study for erosive hand OA, showed a significant improvement in pain with 10 mg MTX. Recently, an open-label study using MTX for pain relief in knee OA reported that a high proportion of patients had considerably reduced pain comparable to that achieved with NSAIDs and opioids. MTX had an analgesic effect in patients with moderate knee pain. Moreover, in a small randomized placebo-controlled trial of MTX in symptomatic knee OA showed significant improvement in physical function associated with reduced pain and synovitis. Glucocorticoids play a pivotal role in managing inflammatory arthritis because of their anti-inflammatory and immunosuppressive roles. Additionally, systemic administration of corticosteroids may have analgesic efficacy. A limited number of studies have shown that corticosteroids given intra-articularly or orally are effective in controlling the cardinal symptoms of OA. In a randomized placebo-controlled trial, it was shown that low-dose prednisolone had both a short-term and a longer sustained effect, resulting in less knee pain, better physical function and attenuation of systemic inflammation in older patients with knee OA. Further larger scale longitudinal studies are needed to better define the role of these agents in disease modification of knee OA.

**Disclosure statement:** The author has declared no conflicts of interest.

**I97 OSTEOARTHRITIS TREATMENT IN THE BIOLOGICS ERA**

Margreet Kloppenburg
Rheumatology & Clinical Epidemiology, Leiden University Medical Centre, Leiden, The Netherlands

Abstract not provided.

**Disclosure statement:** M.K. has received honoraria from the Committee for recommendations for conservative treatment of hip and knee; is a member of speakers bureau with Pfizer and has received grants/research support from Imi, Eular, Omeract, Dutch Arthritis Foundation, Pfizer and Abbvie.

**HEBERDEN ORATION**

**I98 A RHEUMATOLOGIC JOURNEY: CURIOUSITY AT THE CORE OF CARE?**

Iain McInnes
Glasgow Biomedical Research Centre, University of Glasgow, Glasgow, UK

Historically, the rheumatic diseases have been considered chronic, disabling and incurable. Their aetiology has been obscure. Moreover, serious molecular attempts to unravel the mystery have been ambivalent at best. Recent decades have witnessed a remarkable transformation in the approaches taken to therapeutics in rheumatology, exemplified best in the management of inflammatory arthritis. This occurred based on two fundamental paradigm shifts. First, discoveries in pathogenesis provided for the first time disease rational therapeutics, particularly biologics. Such agents have
subsequently been applied across a range of diseases and disciplines to substantial benefit, provoking the notion of mechanistically common immune-mediated diseases. Second, the application of sound strategic principles in the use of such agents is increasingly driving improvements in outcome. Herein I discuss some of the pathogenesis discovery approaches that we have employed to unravel those mechanisms that drive chronicity and co-morbidity. Such studies have evolved to support a move to defining molecular taxonomies of common inflammatory diseases, seeking in turn to develop clinically useful endotypes that can confer enriched clinical responses with reduced risk to patients. Finally, I will explore parallel translational studies in which the same principles have been applied to other common rheumatic conditions with surprising results.

**Disclosure statement:** I.C. has received consulting fees for discussions with AbbVie, Bristol-Myers Squibb, Pfizer, Novartis, AstraZeneca, Janssen and UCB and has received research support for the University of Glasgow from Bristol-Myers Squibb, UCB, AstraZeneca, Medimmune and Janssen.
I99 LUNG INVOLVEMENT IN AUTOIMMUNE DISEASE: AN OVERVIEW

Chris Denton
Centre for Rheumatology, University College London, London, UK

There is a wide range of potential involvement of the lung in autoimmune rheumatic disease, including vascular and airway complications as well as involvement of extrapulmonary structures that can compromise lung function. However, parenchymal lung involvement is one of the most important challenges due to its potential severity and impact on survival. In addition, treatment options are limited. This presentation will take a case-based approach to elucidate the diagnosis and management of lung involvement in rheumatic disease with a particular focus on connective tissue disease and systemic sclerosis. Current approaches to assessment, staging and treatment will be reviewed. Current best practice for the treatment of lung manifestations in the context of autoimmune rheumatic disease will be presented and discussed with a review of recent evidence and clinical trials. The major challenge of complex multifactorial lung complications in connective tissue disease highlights the important clinical challenge for patients and the critical importance of integrated multidisciplinary care.

Disclosure statement: C.D. has received consulting fees from Actelion, GSK, Bayer and Roche; honoraria from Actelion and Bayer and grants/research support from CSL Behring and GSK.

I100 ASSESSMENT AND MANAGEMENT OF LUNG DISEASE IN RHEUMATOLOGY

Athol Wells
Respiratory Medicine, Imperial College London, London, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I101 AN OVERVIEW OF RADIOLOGY FOR RHEUMATOLOGISTS

Stephen Kelly
Rheumatology, Queen Mary University of London, London, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I102 RADIOLOGY INTERACTIVE QUIZ: TEST YOUR KNOWLEDGE

Richard Graham
Royal United Hospitals Bath NHS Foundation Trust, Bath, UK

Radiology is vital in the management of rheumatological disease. This interactive session aimed at rheumatology trainees will help prepare them for consultant practice and their exit exams. Plain film and MRI will be covered. Topics will include inflammatory arthritis and infection. The session will have an interactive radiology quiz throughout.

Disclosure statement: R.G. has shares in Circle Health; is an editor of the Oxford Handbook of Imaging in Emergencies and receives royalties from this; has received speaker fees at a Bayer Pulmonary Hypertension study day; has received grants/research support from the Bath Cancer Unit Support Group; is a medical officer in the Royal Naval Reserve; a secretary of the British Nuclear Medicine Society; president elect of the Royal Society of Medicine Radiology Section and a committee member of the Royal College of Radiologists Radionuclide Subcommittee.

I103 CURRENT REQUIREMENTS OF MUSCULOSKELETAL ULTRASOUND TRAINING

Zunaid Karim
Rheumatology, Pinderfields Hospital, Wakefield, UK

This presentation will review the current status of ultrasound training in rheumatology in the UK, identify current training requirements in Europe and suggest a British hands and feet training guideline.

Disclosure statement: Z.K. has received speaker honoraria from AbbVie, Chugai, Pfizer and Schering.

I104 NOVEL DIAGNOSTICS IN SEPTIC ARTHRITIS

Muddassir M. Shaikh
Rheumatology, Freeman Hospital Newcastle, Newcastle upon Tyne, UK

This presentation will discuss the clinical utility and application of different diagnostic modalities for diagnosing septic arthritis. Traditionally, joint aspirate culture has been the mainstay of diagnosing septic arthritis. This talk will mainly focus on non-culture methods of diagnosing joint infections. Some of the modalities discussed will include the use of PCR, matrix-assisted laser desorption ionization–time of flight and procalcitonin in the diagnosis of septic arthritis.

Disclosure statement: M.M.S. has been a speaker/chair at meetings sponsored/supported by pharmaceutical companies.

I105 ANTIBIOTICS IN SEPTIC ARTHRITIS: WHICH, WHEN, WHY, HOW LONG?

Rosie Fok
Microbiology, Royal Devon and Exeter Hospital, Exeter, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I106 SEPTIC ARTHRITIS: A SURGEON’S PERSPECTIVE

Rhidian Morgan-Jones
Orthopaedic Surgery, Cardiff Knee Clinic, Cardiff, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.
Autoimmune and inflammatory rheumatic diseases can affect women during the reproductive years, with significant impacts on family planning and pregnancy. It is important that women have the opportunity to discuss these issues and that they receive consistent advice. However, surveys have shown that ~50% of women in this age group with chronic inflammatory rheumatic or bowel disease reported ever having had the opportunity to discuss family planning concerns and only 20–25% reported this having been discussed at any of their last three clinic appointments. There is considerable variation in who provides advice, and many patients get conflicting advice from different health practitioners, causing confusion and distress. Women with rheumatic diseases such as lupus, RA, PsA and SpA often have children at an older age than their peers. They may have to defer having children due to the effects of active disease on their physical and emotional health and concerns about the impact of their disease and drugs used to treat it on pregnancy. It is important that women plan to have children when their disease is well-controlled on appropriate therapy for conception. They should be aware in advance what risks are associated with their disease, which drugs need to be stopped and when before pregnancy and which drugs should be continued and why. Active inflammatory rheumatic diseases are associated with an increased risk of adverse pregnancy outcomes, including intra-uterine growth restriction, small for dates babies and premature delivery. Some conditions and/or drugs may be associated with an increased risk of hypertension, pre-eclampsia and/or gestational diabetes that can affect pregnancy outcomes. There is little evidence for effects of rheumatic diseases on fertility, although CYP is well known to cause infertility and to be teratogenic. It is essential that MTX, MMF and LEF, as well as CVC, are stopped at appropriate times before patients try to become pregnant, due to the risk of teratogenicity. Disease control should be maintained as necessary with drugs that are compatible with pregnancy, such as HCQ, prednisone and AZA. To prevent disease flares that will affect placental function and pregnancy outcomes. Biologic agents will be discussed in a separate presentation. Patient should receive advice on contraception to ensure that they do not become pregnant when their disease is active or when they are on inappropriate drugs for conception and pregnancy.

Disclosure statement: C.G. has received consulting fees from Bristol-Myers Squibb, Merck Serono and UCB; is a member of speakers bureau; has received lecturing fees from Eli Lilly and UCB; has received research grants from Genzyme and Roche.

I107 HOW DOES RHEUMATIC DISEASE AFFECT FAMILY PLANNING AND PREGNANCY?
Caroline Gordon
Rheumatology, University of Birmingham, Birmingham, UK

I108 DOES INFLAMMATORY ARTHRITIS REALLY IMPROVE DURING PREGNANCY?
David Williams
Women’s Health, University College London, London, UK

In 1938, Philip Hench published a classic account of the amelioration of RA in 22 women during 37 pregnancies. In this study, it was recorded that RA improved in 70% of women from the beginning of the second trimester and relapsed within weeks of childbirth. Improvement in one pregnancy augured well for a similar response in a future pregnancy. Although this pioneering work identified the anti-inflammatory properties of cortisone, and led to Philip Hench becoming a Nobel laureate, subsequent studies have reported less favourable responses to pregnancy, and even a deterioration of inflammatory symptoms. Furthermore, disease severity has been linked with adverse pregnancy outcome. This presentation will review the evidence for altered inflammatory disease activity during pregnancy. The mechanism through which anti-inflammatory pathways are upregulated and how these gestational metabolic-immune regulatory adaptations may have a beneficial side effect of improving inflammatory disease activity in some mothers. Finally, I will discuss whether controlled inflammation during pregnancy can improve the outcome for the developing fetus.

Disclosure statement: The author has declared no conflicts of interest.

I109 DOES SYSTEMIC LUPUS ERYTHEMATOSUS REALLY GET WORSE DURING PREGNANCY?
Ian Bruce
Kellgren Centre for Rheumatology, Central Manchester University Hospital, Manchester, UK

Abstract not provided.

Disclosure statement: I.B. has received consulting fees from UCB, GSK, Medimmune, Roche, AstraZeneca and Merck Serono; has received honoraria from UCB, Medimmune and GSK; is a member of the speakers bureau with UCB, Medimmune and GSK and has received grants/research support from Genzyme and Roche.

I110 WHICH BIOLOGICS ARE SAFE TO TREAT RHEUMATIC DISEASE IN PREGNANCY AND BREASTFEEDING?
Monika Ostensen
Rheumatology, University Hospital of Trondheim, Trondheim, Norway

Drugs are used for an ever-increasing proportion of patients with rheumatic disease. Most biologic agents are derivatives of IgG1, either complete monoclonal antibodies of the IgG1 class or fusion proteins. IgG is actively transferred through the placenta by Fc receptors on the trophoblast. Biologic agents that contain an Fc part are also transferred actively through the placenta. Among the TNF inhibitors (TNFis), infliximab and its biosimilars, adalimumab and golimumab, are complete monoclonal antibodies with increasing transplacental passage throughout pregnancy. Etanercept, a fusion protein with an Fc part, but low affinity to the foetal Fc receptor, and certolizumab, the pegylated Fab fragment, have low transplacental passage. Published experience with infliximab, adalimumab, etanercept and certolizumab has not shown an increase in miscarriage or congenital malformations. TNFis may be used pre-conception and during pregnancy in patients with moderate or severe disease. Discontinuation during pregnancy is recommended for TNFis with extensive transplacental passage in the second trimester. TNFis with low passage to the foetus may be used throughout pregnancy. Excretion of TNFis into breast milk is minimal, therefore breastfeeding may be allowed. The B cell inhibitor rituxumab appears not to be a strong human teratogen. However, second and third trimester exposure causes B cell depletion in the foetus, with unknown long-term effects in the child. Limited pregnancy experience with abatacept, tocilizumab, belimumab and anakinra has not shown danger signals for the foetus. However, these biologics should be used only when no other safe medication can control maternal disease in pregnancy. There are no data on breastfeeding for any of these biologics.

Disclosure statement: M.O. has received honoraria from Abbott, New Bridge, Pfizer, Roche and UCB.

PSORIATIC ARTHRITIS: BEFORE AND AFTER TUMOUR NECROSIS FACTOR INHIBITORS

I111 STRATEGIES FOR THE USE OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN PSORIATIC ARTHRITIS, INCLUDING TREAT TO TARGET
Philip Helliswell
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and Chapel Allerton Hospital, Leeds, UK

PsA has multiple clinical features. This heterogeneity makes the development of simple treatment algorithms problematic. Historically there has been little work done on early aggressive treatment and the effect of traditional DMARDs on characteristic features of the disease such as enthesitis and dactylitis. MTX, the most commonly used drug in PsA, has good observational evidence for efficacy in joint disease, but the effect is confounded by improving cutaneous involvement. There are few formal studies of combination therapy to guide clinicians. Treat to target is emerging, but there is ongoing discussion about the appropriate target and if it should encompass all clinical aspects of the disease.

Disclosure statement: P.H. has received consulting fees from Eli Lilly; honoraria from Abbvie, Janssen, Pfizer and UCB and grants/research support from Pfizer and Janssen.
I112 NEW DRUGS FOR PSORIATIC ARTHRITIS: THE RHEUMATOLOGISTS PERSPECTIVE—TO INCLUDE APREMILAST, USTEKINUMAB AND SECUKINUMAB

Neil McHugh
Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, UK

Abstract not provided.
 Disclosure statement: The author has declared no conflicts of interest.

I113 NEWER THERAPEUTIC AGENTS FOR PSORIASIS: A DERMATOLOGICAL PERSPECTIVE

Nick Reynolds
Dermatology, Newcastle Hospitals NHS Trust, Newcastle, UK

The introduction of biologic therapies, primarily TNF-α inhibitors and ustekinumab (anti-p40 subunit of IL-12 and IL-23), has been transformational for patients with resistant moderate to severe psoriasis who fulfil National Institute for Health and Care Excellence eligibility criteria. Perhaps as a consequence, the global psoriasis market continues to increase, achieving $7.5 billion in 2014. Recent publications from national registries that represent real-life (rather than trial) data indicate differential persistence of biologic therapies and potentially different side-effect profiles. The recent licensing and introduction into clinical practice of anti-IL-17 biologics such as secukinumab potentially raises the bar for efficacy, with significant numbers of patients achieving Psoriasis Area and Severity Index 90 or even 100 in relatively short time periods. Other anti-IL-17 agents, such as ixekizumab, have completed phase III trials and have been filed with the US Food and Drug Administration. Gultekumab and tildrakizumab selectively target the p19 subunit of IL-23 and thereby show promise as effective psoriasis treatments with potentially fewer side effects. For example, a recent comparative trial demonstrated superior efficacy of gultekumab compared with adalimumab. On the other hand, patient surveys have shown high levels of dissatisfaction with non-biologic therapies, principally related to a lack of efficacy and/or a lack of robustness of response. Nevertheless, recent insights into disease pathogenesis, mechanisms of therapeutic action and therapeutic failure are now realizing new small molecule therapeutic agents such as phosphodisterase inhibitor 4, apremilast, dimethyl fumarate and tofacitinib (JAK3/JAK1 inhibitor) and the potential for individualization of therapy and the development of biomarkers predictive of response. Thus, currently the efficacy of therapeutic agents is variable and unpredictable, with both primary and secondary failure (caused by lack/loss of efficacy and adverse events). Recent insights offer the potential of developing tests that predict therapeutic outcomes for individual patients.
 Disclosure statement: N.R. has received consulting fees from Pfizer, Celgene, Stiefel (a GSK company) and Genentech, and has received grants/research support from a Biotechnology and Biological Sciences Research Council Case Studentship, Stiefel (a GSK company), Genentech and Novartis.

SJÖGREN’S: WELCOME TO THE BIOLOGIC ERA!

I114 IS THE ANSWER IN THE GLANDS?

Michele Bombardieri
Centre for Experimental Medicine and Rheumatology, Queen Mary University of London, London, UK

Abstract not provided.
 Disclosure statement: The author has declared no conflicts of interest.

I115 TRIALS AND TRIBULATIONS OF B CELL THERAPIES (TRACTISS)

Simon Bowman
Queen Elizabeth Medical Centre, Queen Elizabeth Hospital Birmingham, Birmingham, UK

This presentation is aimed at a general clinical audience. It will cover the following areas: background evidence supporting a role for B cells in the pathogenesis of primary SS and the potential for anti-B-cell therapy to improve the disease; initial studies of rituximab, including open-label studies and small randomized controlled trials (RCTs); recent large double-blind controlled RCTs, including the Tolerance and Efficacy of Rituximab in Sjögren’s Syndrome (TARIS; France) and Trial of Anti-B-Cell Therapy In Primary Sjögren’s Syndrome (TRACTISS) studies; available data on other agents such as belimumab and future directions for anti-B-cell and other therapies. By the end of the presentation, the audience will have a better appreciation of the role of anti-B-cell therapies in primary SS and the progress as well as some of the challenges of performing clinical trials in this disease.
 Disclosure statement: The author has declared no conflicts of interest.

I116 T CELL TARGETING THERAPIES FOR SJÖGREN’S SYNDROME

Wan-Fai Ng
Musculoskeletal Research, Newcastle University, Newcastle, UK

I will discuss the role of T cells in the pathogenesis of primary SS (pSS). This will be followed by potential strategies for targeting T cells in pSS. Finally, data from clinical trials of biologic therapies targeting T cells in pSS will be presented.
 Disclosure statement: W.N. has received consulting fees from Pfizer, Sanofi, Takeda and MedImmune and has received honoraria from Roche for speaking at an academic meeting.

I117 NOVEL THERAPEUTIC AGENTS FOR SJÖGREN’S SYNDROME

Francesca Barone
Centre for Translational Inflammation Research, School of Immunity and Infection, College of Medical and Dental Sciences, Queen Elizabeth Hospital, Birmingham, UK

Abstract not provided.
 Disclosure statement: The author has declared no conflicts of interest.

HOW TO COPE WITH STATISTICS IN A RESEARCH PAPER

I118 INTRODUCTION TO STATISTICAL METHODS

Gavin Shaddick
Department of Mathematical Sciences, University of Bath, Bath, UK

Abstract not provided.
 Disclosure statement: The author has declared no conflicts of interest.

I119 CONCEPTS IN MISSING DATA

Jamie Sergeant
Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, UK

Virtually all research studies have some data that are missing for one reason or another. How the analysis of the data is performed when some of it is missing can affect both the values of the results obtained and their validity. This presentation will explore how missing data may arise, the consequences of ignoring the problem of missing data, the pitfalls of some simple methods for dealing with the problem and the ideas behind a more sophisticated method that can satisfactorily address the problem. Delegates will learn to appraise the handling of missing data in research papers and improve the handling of missing data in their own research.
 Disclosure statement: The author has declared no conflicts of interest.
I120 REPORTING OF STATISTICAL METHODS AND RESULTS IN RHEUMATOLOGY RESEARCH
Kelvin Jordan
Research Institute for Primary Care and Health Sciences, Keele University, Keele, UK

Clear and complete reporting of studies is necessary to improve the likelihood of successful dissemination and the impact of rheumatology research. The objectives of this session are to provide an understanding of the information that should be included regarding study design, analysis methods and results when submitting rheumatology research for publication in peer-reviewed journals and the best approaches to presentation. ‘Dos’ and ‘don’ts’ in reporting research will be provided alongside examples of good and not so good practice. Links to reporting guidelines for standard study designs (e.g., randomized controlled trials and observational studies) will be included. The session will relate closely to the previous two presentations within this workshop. The outcomes will be improved knowledge of how to present the methods and results of research studies and what information to look for when reading and critically appraising research papers.
Disclosure statement: The author has declared no conflicts of interest.

I121 DO WE NEED A NATIONAL STRATEGY FOR PAEDIATRIC REHABILITATION? HOW IS THIS MIRRORED IN ADULT PRACTICE?
Anne Gordon
Paediatric Neurosciences, Evelina London Children’s Hospital, Guy’s and St Thomas’ NHS Foundation Trust, London, UK

Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I122 DUCKING AND DIVING: ESTABLISHING A REHABILITATION SERVICE FOR YOUNG PEOPLE, MOTIVATING THEM AND MAINTAINING GAINS
Nick Wilkinson
Paediatrics, Evelina London Children’s Hospital, Guy’s and St Thomas’ NHS Foundation Trust, London, UK

Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I123 REHABILITATION IN THE ARMED SERVICES: ECONOMICS, PRACTICALITIES AND LESSONS FOR THE NATIONAL HEALTH SERVICE
John Etherington
Director of Defence Rehabilitation, Defence Medical Rehabilitation Centre, Headley Court, Epsom, UK

Abstract not provided.
Disclosure statement: The author has declared no conflicts of interest.

I124 START: STRATIFYING BACK PAIN—THE SCIENCE
Jonathan C. Hill
Arthritis Research UK, Primary Care Centre, Keele University, Stoke on Trent, UK

There is no question that we need solutions to the problem of back pain, now the global leading cause of years lived with disability. In this talk, I will set out the case for improving back pain clinical decision-making through the use of the STarT Back stratified care approach. This approach is not just about assessing a patient’s likely prognosis, but is equally about providing them with an appropriate matched treatment, particularly if they have complex, psychosocial needs. I will present information on the STarT Back Trial, the IMPaCT Back implementation study, recent analysis to explore the treatment mechanisms at work in this trial and the subgroup analysis that has revealed which types of patients do not benefit from it. More information can be found at the Keele STarT Back website (http://www.keele.ac.uk/stbt).
Disclosure statement: The author has declared no conflicts of interest.

I125 PAIN PATHWAYS FOR MANAGING LOW BACK PAIN AND RADICULAR PAIN
Sanjeeva Gupta
Faculty of Pain Medicine, Royal College of Anaesthetists, London, UK

Low back pain (LBP) is extremely common and is the largest single cause of loss of disability adjusted life-years and the largest single cause of years lived with disability in England. In terms of disability adjusted life-years lost per 100 000, LBP is responsible for 2313. In contrast, the remainder of musculoskeletal complaints account for 911, depression 704 and diabetes 337. It should be borne in mind that this principally occurs in people of working age or with families. Back pain accounts for 11% of the entire disability burden from all diseases in the UK. The British Pain Society (BPS) and Map of Medicine (MOM) Pain Pathways and the National Pathway of Care for Low Back and Radicular Pain will be discussed in this presentation. I will also include information published in the draft National Institute for Health and Care Excellence low back pain pathways if this is published by April 2016. The BPS and MOM Pain Pathways include five pathways: pain (initial assessment and early management), LBP and radicular pain, chronic widespread pain, neuropathic pain and chronic pelvic pain for men and women. The Multidisciplinary Low Back Pain and Radicular Pain Pathways Committee consisted of 19 members representing general practitioners, physiotherapists, psychologists, spinal surgeon, neurosurgeon, pain medicine specialists and a patient representative. These pathways are pragmatic, representing a consensus opinion based on the best available evidence and practical common sense. Three pathways were published: LBP general management, LBP specialist management and radicular pain management. The emphasis is on the principles of supported self-management, cognitive behavioural therapy and minimally invasive approaches. The pathways include information on how to identify and manage red flags, resources for patients and caregivers, pharmacological management of LBP and neuropathic pain and diagnosing radicular pain. The pathways are pragmatic and evidence based where possible, facilitate early diagnosis and management of neuropathic and radicular pain, are time based and encourage multidisciplinary assessment and encourages use of the STarT Back tool to stratify risk and guide
INVITED SPEAKER ABSTRACTS

Thursday 28 April 2016

I127 PHARMACOTHERAPY FOR PERSISTENT PAIN: OPIOIDS INCLUDED
Shyam Balasubramanian
Acute and Persistent Pain Management, Royal College of Anaesthetists, Coventry, UK

The choice of medication depends on the type of pain (musculoskeletal or neuropathic) and co-morbidities. The type of medication can be classified as analgesic (paracetamol, NSAIDs, opioids) and co-analgesics (antidepressants, anticonvulsants). Most of the medications only have a mild to modest effect on alleviating symptoms. The objective of pharmacotherapy is not only to reduce pain symptoms, but also to facilitate functional rehabilitation. When pain is localized, judicious use of topical interventions such as topical NSAIDs, capsaicin, lidocaine or menthol can be helpful without systemic side effects. Our understanding of oral NSAIDs has considerably increased since the advent of cyclooxygenase 2 inhibitors. The choice of NSAID is determined by gastrointestinal and cardiovascular risk factors. Whatever the choice, the recommendation is to keep the dose to a minimum and the courses as intermittent as possible. There is increasing awareness of the role and limitations of opioids in persistent pain management. The Faculty of Pain Medicine has developed a resource for prescribers (http://www.rcoa.ac.uk/faculty-of-pain-medicine/opioids-aware). A small cohort of patients may benefit from a lower opioid dose, especially when used intermittently. The risk of harm substantially increases when the daily morphine equivalent exceeds 120 mg.

Disclosure statement: The author has declared no conflicts of interest.

I128 COGNITIVE BEHAVIOUR THERAPY: AN OVERVIEW
Lance McCracken
Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King’s College London, London, UK

For ~50 years people with persistent pain have participated in and benefited from cognitive and behavioural treatments for their conditions. The supportive evidence for these approaches is persuasive and is now summarized in no less than 10 systematic reviews from >50 randomized controlled trials. So these approaches are reasonably mature, established to a certain degree and known to be beneficial. At the same time, there seems to be an ever-increasing list of relevant psychological factors in persistent pain, numerous treatment methods and many different treatment brands, and this can be confusing. There are contrasting attitudes about cognitive and behavioural treatments – that perhaps they are either common sense or too complicated, that they ought to play only a small peripheral role or that they ought to be the most important thing we do for people with persistent pain. This brief talk will cut through some of this potential confusion and contradiction and focus on how to clarify and improve these approaches for the future.

Disclosure statement: The author has declared no conflicts of interest.

I129 BODY REPROGRAMMING FOR FUNCTIONAL DISORDERS: A NEW PARADIGM
Tony Davies
Pain Management, Plymouth Hospitals NHS Trust, Plymouth, UK

Overall, 20–40% of patients attending hospital clinics will have symptoms that defy an anatomical, physiological or pathological explanation. In primary care consultations, this proportion is even higher. Many still include a pain-related presentation. Chronic widespread musculoskeletal pain has a community prevalence of ~11–13% and these patients, sometimes alternatively labelled as FM or chronic fatigue syndrome/myalgic encephalomyelitis will have a significant impact on resources within the health community. There is often an uncoordinated approach to diagnosis and clinical management. Primary care and hospital physicians can be reluctant to make positive diagnoses. Typically for those at the moderate-to-severe end of the spectrum, they will have seen a multitude of senior clinicians without a formal diagnosis or else a range of functional-based diagnoses have been suggested. When the diagnosis is made, the accompanying dialogue is often unsatisfactory for both patient and physician. There is difficulty in finding the appropriate selection of an illness model or acceptable narrative. This talk will explore a novel conceptual model to explain these functional disorders and describe a therapeutic framework described as a body reprogramming intervention. The conceptual model has developed from the application of complexity theory to the body. The model is based on the following tenet. Much of physiological functioning can be understood in terms of cause and effect of biological events. However, because multiple simultaneous causality exists with the body, the body also operates as a network system. This network system exhibits some of the emergent properties that are found in parallel distributed processing (PDP) systems. This theory focuses on the body rather than just the brain functioning as a PDP system and thus explains functional disorders at a level that is intermediary to both biological and psychological approaches. Through the introduction of this model, a therapeutic intervention has been developed called body reprogramming. The focus is on lifestyle management and a reduction in centrally acting medication. Therapeutic messages are nurtured through a combination of physical exercise and psychological techniques that are individualized and consistent with the several evidence-based techniques for improving outcome in FM. Body reprogramming can be considered a large step in understanding but a small step in practice.

Disclosure statement: T.D. has received honoraria from Pfizer and Grunenthal and unconditional conference expenses from Pfizer and Grunenthal.

Discriminate, analyze, integrate, and abstract critical information from the original document.
STAYING PHYSICALLY ACTIVE WITH RHEUMATOID ARTHRITIS

I130 PHYSICAL ACTIVITY FOR THE MANAGEMENT OF RHEUMATOID ARTHRITIS FATIGUE
Victoria E. Salmon
Faculty of Health and Applied Sciences, University of the West of England, Bristol, UK

Fatigue is a major symptom of RA and has a considerable impact on patients’ daily lives. Patients report that they struggle to manage their fatigue and receive little support. Secondary outcomes for fatigue in physical activity (PA) trials in RA suggest potential benefit despite the fact that the interventions were not specifically designed to manage RA fatigue. The beneficial effects of PA have also been evidenced in other long-term conditions where fatigue is a major symptom. This session will discuss existing evidence for the use of PA to manage fatigue and will present preliminary findings from ongoing research in this area. Future directions for research and implications for clinical practice will be considered, including implementation issues and training and educational needs for health care professionals.

Disclosure statement: The author has declared no conflicts of interest.

I131 PHYSICAL ACTIVITY MONITORING IN RHEUMATOID ARTHRITIS
Norelee Kennedy
Clinical Therapies, University of Limerick, Limerick, Ireland

Physical activity (PA) is recognized globally as a key factor in health. Monitoring of both PA and sedentary behaviour patterns is complex and can be conducted using subjective or objective methods. Accurate measurement of PA is important in both clinical and research settings and both subjective and objective measures are available. Subjective methods of measurement are reported to be less accurate than objective methods, however, they are often easier to use, particularly in busy clinical environments. Many objective, wearable activity monitors are now widely used in research studies and use physiological or mechanical responses to bodily movement as signals to estimate variables that reflect PA. This presentation will examine the measurement and monitoring of PA in people with RA and will also consider the importance of measuring sedentaryness. The session will provide an introduction to the measurement of PA and key aspects of measurement as well as objective measures that have been validated in the people with RA. A review of studies measuring PA in people with RA will then be provided, with consideration of the applicability of these studies in a clinical setting. How PA measurement and monitoring can be used in changing PA behaviour will also be discussed. Finally, the presentation will identify future opportunities for research and will consider how PA can be measured in everyday situations.

Disclosure statement: N.K. has received grants/research support from the Irish Research Council.

DROITWICH MEDICAL TRUST LECTURE

I132 DROITWICH MEDICAL TRUST LECTURE
Anthony Redmond
Leeds Institute for Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

This year’s Droitwich Medical Trust lecture explores the coming of age of allied health professionals (AHPs) and nurses as part of the wider rheumatology community. Based partly on personal experience and partly on observations of the evolution, and to some extent the revolution, in rheumatology practice over the past 15 years, the lecture will explore changing practice, changing roles and the significant contributions of the British Health Professionals in Rheumatology (BHPR) constituency to musculoskeletal care over the span of the author’s professional career to date. There now exist pathways to specialist practice, research careers and post-registration qualification that were quite unimaginable to the previous generation, and the impact of these will be both celebrated and challenged. Drawing on his time overseas in the 1990s and working latterly across the EULAR community, Prof Redmond will highlight lessons learned elsewhere and their application in the UK, as well as picking out more local observations taken from hard-earned experience. Finally, the lecture will develop the theme of planning for the future, and explore where and how BHPR and audience members can prepare themselves for what the future might offer, with the aim of ensuring that the next 30 years are as exciting for AHPs and nurses as the last 30 have been.

Disclosure statement: The author has declared no conflicts of interest.

ADULT INFLAMMATORY ARTHRITIS STUDIES: THE IMPORTANCE OF LONGITUDINAL DATA COLLECTION

I133 HARMONIZING DATA COLLECTION FOR OBSERVATIONAL STUDIES IN ADULT INFLAMMATORY ARTHRITIS: A EUROPEAN INITIATIVE
Helga Radner
Division of Rheumatology, Internal Medicine III, Vienna Medical University, Vienna, Austria

Many modern day research questions in RA, such as biologic safety or genetic studies, require ever-larger study populations that exceed the size of individual cohorts or registries. These mega-populations can only be obtained by pooling data from different data sources. However, data pooling is only possible if data items are collected in a standardized way and to high standards across settings or, as a minimum, can be mapped to a common data model. Therefore, a EULAR taskforce has been convened to develop a minimum core dataset (MC2) in RA to harmonize future data collection, to act as a common data model for existing databases to map to and to serve as a template for standardized data collection for RA research in routine clinical practice. The project involved a multi-step process, starting with a hierarchical literature, an online survey to gather information from a pan-European expert panel and two face-to-face meetings. The proposed MCD should be tested across different populations for feasibility and in its ability to answer different research questions.

Disclosure statement: The author has declared no conflicts of interest.

I134 THE NATIONAL CLINICAL AUDIT FOR RHEUMATOID AND EARLY INFLAMMATORY ARTHRITIS: AN UPDATE AND REVIEW OF DATA COLLECTION
Neil Snowden
Rheumatology, National Audit Project Working Group, British Society for Rheumatology, Oldham, UK

The National Clinical Audit for Rheumatoid and Early Inflammatory Arthritis has now completed 2 years of data collection. This audit is the first comprehensive national benchmarking of care given to people with newly diagnosed inflammatory arthritis against National Institute for Health and Care Excellence (NICE) quality standards and including patient-reported outcomes. The audit aims to recruit all incident adult cases of polyarthritis in England and Wales and to capture data for the first 3 months of rheumatological care. Data were collected from clinicians and patients. It is hoped that the audit will be a powerful tool to drive service improvement in the care of inflammatory arthritis. It should also be recognized that this was a complex and difficult audit. This is the only national audit that requires real-time data collection in an outpatient setting by patients and clinicians at multiple time points, including data not collected in routine clinical practice. This presents
multiple challenges. Time is at a premium in outpatient clinics and the case mix is often uncertain. This presents difficulties with identification, recruitment and consent. Some trusts provided dedicated support, but many provided none. For these reasons, although overall participation in the audit was good, a significant number of trusts recruited only a small number of patients, and 42 of 143 participating trusts were considered not to have recruited sufficient patients to provide robust benchmarking. For all organizations, there was a significant decrease in the collection of follow-up data. Baseline data were available on 6354 patients, but clinician follow-up data were only collected on 3107, and only 1215 patient follow-up forms were returned. Follow-up data collection presents a number of challenges, particularly as there is often no reliable way of tagging patients between visits. Collecting patient follow-up data proved particularly problematic. The audit demonstrates the difficulties of sequential real-time data collection in an outpatient setting. Most care of chronic disease takes place in this setting and it is important for health care systems to understand the quality and content of this care. One of the key recommendations from the audit is that there is an urgent need for the NHS to develop better systems to support the capture, coding and integration of information from outpatient clinics. Simplification of data collection is also proposed, and an improved and streamlined information technology platform would be invaluable.

Disclosure statement: The author has declared no conflicts of interest.

FIBROMYALGIA: PREVENTING ONSET AND IMPROVING OUTCOME

I135 LONGITUDINAL STUDIES AND CLINICAL TRIALS: FRIENDS OR FOES?
Maya Buch
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

The objectives of clinical research are wide ranging and include understanding of disease outcome and treatment response, with identification of prognostic and predictive biomarkers. Randomized controlled trials (RCTs) are the gold standard approach to test the efficacy of therapeutic agents. While crucial to enable introduction of new therapies into clinical practice, RCTs do not provide information on longer-term outcomes and safety profiles that is needed to inform decision-making in real-world populations. Longitudinal observational studies have emerged as a highly effective means of consolidating RCTs to understand the benefits of therapies as well as provide long-term evaluation of outcomes of disease. In addition, the partnering of such cohorts with biosample repositories offers the opportunity to perform meaningful translational investigations to improve disease management and thus outcomes. This lecture will review the successes and challenges of longitudinal observational studies in rheumatology research to date and offer some insights into what they may have to offer in the future.

Disclosure statement: M.B. has received honoraria from AbbVie, AstraZeneca, Bristol-Myers Squibb, Pfizer, Roche-Chugai, R-Pharm and AstraZeneca and has received grants/research support from Bristol-Myers Squibb, Pfizer and Roche-Chugai.

I136 FIBROMYALGIA: CAN WE PREVENT ITS ONSET?
Gary J. Macfarlane
Epidemiology, University of Aberdeen, Aberdeen, UK

Abstract not provided.

Disclosure statement: G.J.M. has received a grant (BSRBR-AS) awarded by the British Society for Rheumatology, which receives funds from AbbVie, Pfizer and UCB and a grant (SIRAS), which has received funds from AbbVie and Pfizer.

I137 THE ROLE OF SLEEP IN THE MANAGEMENT OF FIBROMYALGIA
Ernest Choy
Section of Rheumatology, Institute of Infection and Immunity, Cardiff University, Cardiff, UK

Chronic widespread pain is the dominant symptom in FM. However, most patients also complain of non-restorative sleep, fatigue and cognitive dysfunction. Indeed, these symptoms have been included in the Symptom Severity Scale of the ACR 2011 preliminary diagnostic criteria for FM. In patients with FM, poor sleep quality is associated with severity of pain and fatigue. Furthermore, sleep disturbance could aggravate the effect of pain on fatigue and mood. Path analysis found that a night of poor sleep led to worsening of pain and mood and reduced physical functioning. Studies using polysomnography have demonstrated reduced slow-wave sleep and abnormal δ rhythms during non-rapid eye movement sleep in patients with FM. For many years it has been assumed that sleep disruption is the consequence of severe pain in FM. Moldofsky et al. first challenged this assumption by showing that disrupting sleep in healthy individuals could induce FM-like symptoms, including myalgia, tenderness and fatigue, suggesting that sleep dysfunction might be pathogenic. Recent epidemiological studies lent further support to the pathogenic role of sleep dysfunction. Poor sleep quality was a risk factor for the subsequent development of chronic widespread pain in healthy individuals who were initially pain free. In FM, the principle pathophysiology is abnormal pain processing and central sensitization, which have been demonstrated objectively by neuroimaging. Patients with FM have neural activation similar to healthy age- and gender-matched individuals, but at a lower pressure-pain threshold. Impairment of pain control has been suggested by reduced neuronal activity and μ-opioid receptor occupancy at the rostral anterior cingular cortex, which is associated with the descending pain inhibitory pathways. Restorative sleep has been shown to be important in maintaining the integrity of the descending pain inhibitory pathways. In healthy individuals, sleep deprivation can reduce activity in the descending pain-inhibition pathways. This may explain the pathogenic role of sleep dysfunction in FM. Improving sleep quality by non-pharmacological and pharmacological treatments has been associated with a reduction in pain in FM. Good sleep hygiene practices should be recommended to patients with FM with non- restorative sleep. These include avoiding stimulants (such as caffeine), large meals and alcohol too close to bedtime. Although alcohol can spread the onset of sleep, it interrupted sleep in the second half of the night. Exercise can promote sleep. Among currently available pharmacological treatments, there is evidence to suggest amitriptyline and pregabalin can improve sleep quality in FM.

Disclosure statement: E. C. has received consulting fees from Eli Lilly, Jazz Pharmaceuticals, Pierre Fabre Medicament, Pfizer and UCB; honoraria from Eli Lilly, Jazz Pharmaceuticals, Pierre Fabre Medicament, Pfizer and UCB; is a member of speakers bureaus for Eli Lilly, Jazz Pharmaceuticals, Pierre Fabre Medicament, Pfizer and UCB and has received grants/research support from Pfizer and UCB.

I138 MANAGING FIBROMYALGIA AS A CO-MORBIDITY
Geraldine McCarthy
Rheumatology, Mater Misericordiae University Hospital and University College Dublin, Dublin, Ireland

Fibromyalgia syndrome (FMS) is characterized by a multiplicity of symptoms, including musculoskeletal pain, stiffness and fatigue. The prevalence of FMS is estimated to be ~2%, and much higher among women than men (3.4 vs 0.5%). FMS often co-occurs (up to 25-65%) with other rheumatic conditions. Furthermore, some FMS symptoms are typical of other conditions commonly encountered in rheumatology, such as RA, PMR, SLE and seronegative inflammatory arthropathies including SpA. The presence of FMS can cause falsely increased scores in RA, potentially leading to the inappropriate prescription of additional DMARD therapy. Co-morbid FMS and PMR can result in more protracted and higher steroid doses than necessary. Co-morbid OA and FMS can be misdiagnosed as inflammatory arthritis such as RA. There is little evidence to guide the optimal management of FM as a co-morbidity specifically. Nonetheless, awareness of the presence of concurrent FMS in rheumatic disorders will promote optimal management of both co-morbidities. Exercise remains the key approach to management, and when necessary, pharmacotherapy and physiotherapy approaches tailored to the individual.

Disclosure statement: The author has declared no conflicts of interest.
WHAT'S NEW IN THE ANTIPHOSPHOLIPID SYNDROME?

I139 WHAT'S NEW IN DIAGNOSIS OF ANTIPHOSPHOLIPID SYNDROME?
Anisur Rahman
Rheumatology, University College London, London, UK

APS is an important autoimmune disease causing vascular thrombosis, recurrent pregnancy morbidity and strokes. It is one of the most common causes of strokes in people <50 years of age. APS is caused by aPL, which interacts with phospholipid binding proteins in the body. The most important of these proteins is β2-glycoprotein I. The aPL-β2-glycoprotein I interaction leads to activation of cell surface receptors and signalling pathways in target cells such as monocytes, endothelial cells and trophoblast. Several new ideas in APS will be discussed in this lecture. First is the concept of seronegative APS (i.e. the diagnosis of APS in the absence of positive antibody tests), which has been controversial. It seems increasingly likely, however, that there is a small subgroup of patients with APS in whom the standard blood tests (aCL, anti-β2-glycoprotein I and lupus anticoagulant) are persistently negative but in whom pathogenic aPL could be detected by other assays. In particular, tests for antibodies to domain I of β2-glycoprotein I will be discussed. Proteomics and microarray studies in cells exposed to purified β2GPI from patients with APS suggest that different protein targets may be involved in the thrombotic and obstetric manifestations of the disease. These studies may also help in identifying new thrombotic targets, although in the short term. Long-term anticoagulation is the only evidence-based treatment known to protect against recurrent thrombosis in patients with APS, but it has potential drawbacks. New anticoagulants such as rivaroxaban are being used in preference to warfarin in some other conditions associated with an excess risk of thrombosis, but there is no definitive evidence in APS. A UK non-inferiority trial of rivaroxaban against warfarin was completed in 2013 and the results are expected soon. Daily aspirin and s.c. heparin remain the standard of care for treatment of APS during pregnancy. The potential for new biologic therapies in APS is exciting and these may include peptides designed to inhibit the interaction of β2-glycoprotein I either with aPL or with phospholipids on cell surfaces. However, there are a number of hurdles to be cleared in making peptides of this kind into acceptable therapeutic agents.

Disclosure statement: A.R. is an inventor of a patent submitted for a new agent in the treatment of APS and is working with PolyTherics.

I140 WHAT'S NEW IN THE MANAGEMENT OF THROMBOTIC ANTIPHOSPHOLIPID SYNDROME?
Hannah Cohen
Haematology, University College London Hospitals NHS Foundation Trust, London, UK

Thrombotic APS is clinically heterogeneous, with thrombotic manifestations spanning a broad spectrum, from mild single to potentially life-threatening recurrent episodes and the rare catastrophic APS. Patients may develop thrombosis in one or more of any vascular sites—venous, arterial or microvascular. The current mainstay of treatment of thrombotic APS is anticoagulation with warfarin or other vitamin K antagonists (VKAs). Direct oral anticoagulants (DOACs) are established as therapeutic alternatives to VKAs and are becoming the standard of care for a wide range of indications. DOACs, unlike VKAs, have a fixed dose with predictable effects, do not require regular anticoagulant monitoring, are unaffected by changes in diet and alcohol and have fewer drug interactions, which would be expected to result in improved quality of life. The potential use of DOACs in patients with thrombotic APS, in whom warfarin presents particular problems, has sparked considerable interest. APS patients were probably included in the phase III DOAC randomized controlled trials (RCTs) in venous thromboembolism (VTE) patients. However, the presence of aPL was not systematically documented, so the results may not be directly generalizable to APS. The Rivaroxaban in Antiphospholipid Syndrome (RivAAPS) trial randomised APS patients on standard intensity warfarin for previous VTE to continue warfarin or switch to rivaroxaban. The primary endpoint was a laboratory surrogate outcome measure, the percentage change in endogenous thrombin potential, with secondary outcomes of other thrombin generation parameters, in vivo coagulation activation markers, recurrent thrombosis, bleeding and death. The results indicate that rivaroxaban offers an effective, safe and convenient alternative to warfarin. Ongoing DOAC studies include two RCTs—Rivaroxaban in Thrombotic Antiphospholipid Syndrome (TRAPS) and Apixaban for the Secondary Prevention of Thromboembolism Among Patients With the Antiphospholipid Syndrome (ASTRO-APS)—and a phase IV study of rivaroxaban. DOACs are currently unlicensed for aPL-associated arterial thrombosis. It is estimated that 14% of strokes are associated with aPL, and thus definition of the role of DOACs in APS patients with ischaemic stroke or cerebral ischaemic lesions is of high clinical as well as scientific relevance. The management of thrombotic APS may be optimized by risk reduction measures against thrombosis, active management of standard vascular risk factors and a risk-stratified approach based on aPL profile and specific laboratory markers for thrombotic risk. Several novel approaches have emerged, based on our increased understanding of aPL pathogenic mechanisms. These include B cell depletion, complement inhibition, HCQ and statins. Other modalities such as peptide therapies that specifically target aPL or inhibition of the mammalian target of rapamycin complex pathway may have future applications. Appropriately designed studies are required to establish the role of novel approaches in the management of thrombotic APS.

Disclosure statement: H.C. has received honoraria (diverted to a local charity) for lectures from Bayer; advisory board participation from Bayer and Alexion and has received institutional research support from Bayer and Alexion.

I141 WHAT'S NEW IN THE MANAGEMENT OF OBSTETRIC ANTIPHOSPHOLIPID SYNDROME?
Pier Luigi Meroni
Rheumatology, University of Milan, Milan, Italy

There is sound evidence that aPL is associated with recurrent miscarriages, particularly in the late stages of pregnancy. Animal models of foetal loss in which passive infusion can induce resorptions and foetal growth inhibition support the epidemiologic findings of human studies. While animal models of aPL-mediated thrombosis require two hits—the presence of the antibodies and an inflammatory stimulus—this does not seem to be the case for aPL-associated obstetric events. Pathogenic aPL is mainly directed against β2-glycoprotein I (β2GPI), a plasma protein detectable at high concentration. The presence of β2GPI on decidual cells, on uterine endothelial cells in non-pregnant mice and the increase of the molecule on syncytiotrophoblast both in animal and in normal human pathological placenta is the explanation for the tropism of anti-β2GPI antibodies in the reproductive tissues. Placental thrombotic events do not seem to represent the main pathogenic mechanisms and alternative/additive mechanisms have been described. In some cases, in vivo and in vitro models support local inflammatory events, which are not supported by histological analysis of abortive materials or placental tissues at delivery. More consistent with clinical findings is the demonstration of several aPL-mediated mechanisms that ultimately end in defective placentation. The pathogenic effects of aPL support their diagnostic/prognostic power. Although double/triple positivity for the diagnostic assays for APS and medium/high aPL titres identify the women at highest risk for thrombosis, still open is the question of whether low aPL titres may also display a prognostic power. The huge amount of β2GPI present in reproductive tissues in contrast with the small quantity of the molecule in resting endothelium may be the reason for the suggested predictive value of low aPL titres. Low-dose aspirin at conception and heparin during pregnancy is the standard therapy for preventing miscarriages, but the effectiveness of such a therapy is apparently unrelated to the anticoagulant effect. Up to 20% of women still display pregnancy complications in spite of this treatment. The use of a small amount of corticosteroids, IVIG and more recently HCQ has been reported to improve the outcome, but there are no specific clinical trials. As for aPL in vascular APS, the persistent presence of the antibodies is a risk factor that should be evaluated in the context of a global obstetric risk profile. Classification criteria for obstetric APS requires three or more miscarriages before 10 weeks gestation or one or more after 10 weeks gestation to treat patients. However, a more aggressive treatment is becoming common in case of a strong aPL serological profile even in the absence of the clinical classification criteria.

Disclosure statement: The author has declared no conflicts of interest.
UNRAVELLING KNOTS OF SILK: UNDERSTANDING BEHÇET’S DISEASE

I142 PATHOGENETICS OF BEHÇET’S DISEASE
Haner Direskeneli
Rheumatology, Marmara University, Istanbul, Turkey

As a chronic, multisystemic, inflammatory disorder, Behçet’s disease (BD) has immunopathogenic features of both autoinflammatory and autoimmune disorders. The clinically disparate MHC class 1-associated diseases, including BD, psoriasis and AS (associated with HLA-B*27, HLA-C*0602 and HLA-B*27 respectively, and all with ERAP1) might have a unified shared immunopathogenic basis. Common disease triggering micro-anatomical factors have been recognized for many decades, especially trauma-induced skin disease, pathergy reaction in BD and the Koebner phenomenon in psoriasis. As a unifying concept, it is proposed that target organ barrier dysfunction/aberrant reactions at sites of mechanical stress (oral microorganisms in BD) and associated interactions with innate immune lymphoid cells often culminates in secondary adaptive immune CD8 T cell responses that result in more severe and recurrent disease. Reflecting antigenic differences within target tissues, BD shows a differential immunopathology, with HLA-B*27 being linked mainly to ocular and mucocutaneous disease, but less with gut involvement. The common IL-23/IL-17 pathway genetic associations further strengthen the emerging association with conventional T cells, but also points towards the role of an array of unconventional lymphocytes in the target tissues that participate in lymphoid stress surveillance. However, some of the genetic associations, such as IL-10, IL-23R and STAT4, and clinical options for how to optimize patients’ self-management of their condition.

Disclosure statement: The author has declared no conflicts of interest.

I143 RECOGNISING AND MANAGING BEHÇET’S DISEASE
Ann W. Morgan
Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I144 CARDIOVASCULAR INVOLVEMENT IN BEHÇET’S DISEASE
Dorian Haskard
National Heart and Lung Institute, Imperial College London, London, UK

Cardiovascular involvement in Behçet’s disease occurs in a significant number of patients, with the incidence ranging from 15 to 40% depending on the case series. The most common manifestations are superficial thrombophlebitis and deep vein thrombosis, with arterial aneurysm involvement being relatively rare. Pulmonary arteries are more commonly affected than arteries in the systemic circulation. This talk will discuss possible pathophysiological mechanisms for vascular inflammation and thrombosis, focusing on the presence of endothelial dysfunction and plasma microparticles expressing tissue factor; new approaches to imaging the vessel wall and effects of treatment, with particular reference to effects of IFN-γ and anti-TNF-α antagonists on endothelial dysfunction and vascular wall structure.

Disclosure statement: The author has declared no conflicts of interest.

BIOLOGIC TREATMENT AND SPECIALIST COMMISSIONING FOR BEHÇET’S DISEASE
Robert Moots
Musculoskeletal Biology, University of Liverpool, Liverpool, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I146 HOW TO COLLABORATIVELY SET THE AGENDA WITH ANKYLOSING SPONDYLITIS PATIENTS
Claire Clark
Occupational Therapy, Powys Teaching Health Board, Brecon, UK

The aim of this interactive workshop is to explore interdisciplinary models and ideas for how to optimize AS patients’ engagement with self-management. The session will open with a brief introduction to explain the burden of AS on the individual and society, followed by four 10 min presentations. After each presentation there will be an opportunity for delegates to share their own practices and ideas in small groups around tables. By the end of the session, delegates will have gained skills in collaborative agenda setting and in facilitating useful workplace discussions with patients. They will have an understanding of the barriers to patients attending their reviews and engaging with physical activity and explore options for how to optimize patients’ self-management of their condition. 

Disclosure statement: The authors have declared no conflicts of interest.

I147 WHEN AND HOW TO DISCUSS WORK AND HOW TO FACILITATE USEFUL DISCUSSIONS BETWEEN PATIENTS, EMPLOYERS AND OCCUPATIONAL HEALTH
Debbie Cohen
Institute of Medical Education, Cardiff University School of Medicine, Cardiff, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I148 WHAT TYPES AND LEVEL OF PHYSICAL ACTIVITY SHOULD WE RECOMMEND TO ANKYLOSING SPONDYLITIS PATIENTS?
Melissa Domaille
Rheumatology, University Hospital of Bristol NHS Foundation Trust, Bristol, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.

I149 HOW DO WE MAKE SURE PATIENTS ON BIOLOGICS ATTEND THEIR REVIEWS AND ENGAGE WITH PHYSICAL ACTIVITY WHEN THEY FEEL BETTER?
Tracy French
Rheumatology Centre, University Hospital of Bristol NHS Foundation Trust, Bristol, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.
The author has declared no conflicts of interest. The most common causes of death in patients with SLE today continue to come too soon. The causes of death due to lupus have so much to be done. In the cohort of patients with SLE followed up in 1950s, SLE was reported to have a 4-year 50% survival rate. In 2016, an 85% 15-year survival would be more accurate. Thus, overall, the outlook for patients with this diagnosis has greatly improved, but there is still a long way to go. In the cohort of patients with SLE followed up between 1978 and 2015 at University College Hospital (UCH), 53 of 675 patients (14%) have died. The average age of death of these patients was 47 years and the average age of death of a woman in the UK is 80 years. Thus for a small but significant numbers of patients with lupus, death continues to come too soon. The causes of death due to lupus have changed in the past 60 years. In the 1950s, renal disease was the major culprit, but the most common causes of death in patients with SLE today are infection, atherosclerosis and cancer. Long-term follow-up at UCH has focused in particular on our patients (~30%) with renal disease. Outcome in renal lupus is very much dependent on patient compliance, and poor compliance was undoubtedly a factor in many of the 38 patients under our care who have gone into renal failure during this follow-up period. Recently published data show that the outlook for lupus nephritis has really not changed much in the past 30 years and it seems likely that conventional drugs, notably steroids and immunosuppression, are not used in ways which are as good as it gets. The future must surely lie in the introduction of biologic drugs, but here of course we face the great disappointment of many failed trials. We desperately need trials to be better designed and more successful. More optimistically, studies at UCH have shown that overall approximately one in six patients with lupus will enter a period of full remission for 3 years with no clinically active features (as judged by the loss of all BILAG As and Bs), with normal serology and off all steroids and immunosuppressive drugs. However, even among these patients, there is a 10–20% chance of a further flare occurring for several years after this 3-year period of remission.

Disclosure statement: The author has declared no conflicts of interest.

I150  BRITISH SOCIETY FOR RHEUMATOLOGY’S RESEARCHER MENTORING SCHEME
Sarah Hewlett
Nursing, University of the West of England, Bristol, UK

This presentation will outline the new British Society for Rheumatology/British Health Professionals in Rheumatology’s mentoring scheme for research, including the aims of mentorship and how the scheme will work.

Disclosure statement: The author has declared no conflicts of interest.

I151  BUILDING AN EVIDENCE BASE FOR ASSESSING AND IMPROVING MULTIDISCIPLINARY TEAMS
Lindsey Cherry
Podiatric Rheumatology, University of Southampton, Southampton, UK

Abstract not provided

Disclosure statement: The author has declared no conflicts of interest.

UPDATE ON BASIC SCIENCE AND CLINICAL ASPECTS OF SYSTEMIC LUPUS ERYTHEMATOSUS

I152  ASSESSMENT OF DISEASE ACTIVITY: MAKING SENSE OF SRI, BICLA, BST AND SBST
Chee-Seng Yee
Rheumatology, Doncaster Royal Infirmary, Doncaster, UK

The BILAG-2004 and SLEDAI-2000 (and its derivatives) indices have emerged as the standard disease activity outcome measures used in clinical studies of SLE. However, there have been some difficulties with analysis using either of these indices in longitudinal clinical studies, especially clinical trials. Various newer methodologies based on these indices have been developed for use as outcome measures in longitudinal clinical studies, including the SLE Responder Index, BILAG-based Composite Lupus Assessment, BILAG-2004 Systems Tally and the simplified BILAG-2004 Systems Tally. This presentation will discuss the analysis of disease activity longitudinally using BILAG-2004 and SLEDAI-2000 indices with a focus on the newer methodologies.

Disclosure statement: C.S.Y. has received consultancy payments from Roche, Eli Lilly, Teva and Crisalys and has received research grants from Aspreva and Arthritis Research UK.

I153  WHAT HAVE WE LEARNED ABOUT LONG-TERM OUTCOMES IN SYSTEMIC LUPUS ERYTHEMATOSUS?
David A. Isenberg
Rheumatology, University College London, London, UK

In the 1950s, SLE was reported to have a 4-year 50% survival rate. In 2016, an 85% 15-year survival would be more accurate. Thus, overall, the outlook for patients with this diagnosis has greatly improved, but there is still a long way to go. In the cohort of patients with SLE followed up between 1978 and 2015 at University College Hospital (UCH), 53 of 675 patients (14%) have died. The average age of death of these patients was 47 years and the average age of death of a woman in the UK is ~80 years. Thus for a small but significant numbers of patients with lupus, death continues to come too soon. The causes of death due to lupus have changed in the past 60 years. In the 1950s, renal disease was the major culprit, but the most common causes of death in patients with SLE today are infection, atherosclerosis and cancer. Long-term follow-up at UCH has focused in particular on our patients (~30%) with renal disease. Outcome in renal lupus is very much dependent on patient compliance, and poor compliance was undoubtedly a factor in many of the 38 patients under our care who have gone into renal failure during this follow-up period. Previously published data show that the outlook for lupus nephritis has really not changed much in the past 30 years and it seems likely that conventional drugs, notably steroids and immunosuppression, are not used in ways which are as good as it gets. The future must surely lie in the introduction of biologic drugs, but here of course we face the great disappointment of many failed trials. We desperately need trials to be better designed and more successful. More optimistically, studies at UCH have shown that overall approximately one in six patients with lupus will enter a period of full remission for 3 years with no clinically active features (as judged by the loss of all BILAG As and Bs), with normal serology and off all steroids and immunosuppressive drugs. However, even among these patients, there is a 10–20% chance of a further flare occurring for several years after this 3-year period of remission.

Disclosure statement: The author has declared no conflicts of interest.

GOUT IN THE 21ST CENTURY

I154  BETTER UNDERSTANDING CO-MORBIDITY IN GOUT: NOVEL DISEASE ASSOCIATIONS AND INTER-RELATIONSHIPS
Pascal Richette
Rheumatology, Hôpital Lariboisière, Paris, France

Patients with gout often have co-morbid conditions, including cardiovascular disease, renal failure and components of metabolic syndrome. The presence of these co-morbidities contributes to the overall excessive cardiovascular mortality in gout. The links between these co-morbidities and gout are complex. Indeed, some of the co-morbidities, such as renal failure and insulin resistance, can increase urate levels and thus contribute to the development of gout, whereas hyperuricaemia per se might contribute to the development of hypertension, metabolic syndrome and renal failure. Interestingly, recent studies have suggested that xanthine oxidase inhibitors might be cardio- and renoprotective, and that colchicine may also decrease the risk of major cardiovascular events.

Disclosure statement: P.R. has received honoraria from Ipsen, Menarini and AstraZeneca.

I155  2016 REVISED BRITISH SOCIETY FOR RHEUMATOLOGY/BRITISH HEALTH PROFESSIONALS IN RHEUMATOLOGY GOUT MANAGEMENT GUIDELINE
Edward Roddy
Research Institute for Primary Care & Health Sciences, Keele University, Stoke on Trent, UK

Gout is the most prevalent inflammatory arthritis, affecting 2.5% of adults in the UK. Despite the availability of effective and potentially curable urate-lowering treatment, management in both primary and secondary care remains suboptimal. Only 30–40% of patients receive urate-lowering therapy and many of these do not have treatment increased to achieve target serum urate levels. The British Society for Rheumatology/British Health Professionals in Rheumatology guideline for the management of gout was published in 2007. Revision and updating of this guideline is required because of the availability of new pharmaceutical treatment options; increasing incidence, prevalence and severity; continuing suboptimal management in both primary and secondary care and better understanding of patient and provider barriers to effective care. This presentation will summarize the methodology used to develop the revised updated guideline. Twenty-one new consensus recommendations covering patient education, management of acute attacks, co-morbidity, indications and options for urate-lowering therapy, treatment to target and prophylaxis will be presented and their supporting evidence outlined. Finally, a new treatment algorithm and recommendations for audit will be described.

Disclosure statement: The author has declared no conflicts of interest.
Despite the availability of effective urate-lowering therapy (ULT) for more than half a century, the incidence and prevalence of gout has increased. Control of gout could be largely achieved by careful treatment to target with long-established ULTs. While adherence to treatment is undoubtedly a problem, target serum uric acid (SUA) levels can be reached with relatively small increases in the dose of allopurinol when time is spent on patient education and careful follow-up. Studies have also shown that in patients with mild renal insufficiency, allopurinol dosage can be safely up-titrated to reduce the SUA to target levels, provided that the starting dose is low. Febuxostat can be used as an alternative xanthine oxidase (XO) inhibitor for patients in whom allopurinol is not tolerated or whose renal impairment prevents allopurinol dose escalation sufficient to achieve the therapeutic target. Flare prophylaxis with colchicine or prednisolone is typically needed when ULT is initiated with febuxostat. Uricosuric agents can be used in patients who are resistant to or intolerant of XO inhibitors. The preferred drugs are sulfinpyrazone (200-800 mg/day) or probenecid (500-2000 mg/day) in patients with normal or mildly impaired renal function or benzboromaron (50-200 mg/day) in patients with mild to moderate renal insufficiency. A uricosuric agent can be used in combination with an XO inhibitor in patients who do not achieve a serum urate target with optimal doses of monotherapy. Lelsinarud, a new selective URAT-1 uric acid reabsorption inhibitor, can be used in combination with allopurinol in patients with gout that has not responded adequately to allopurinol alone, and trials of other selective URAT-1 inhibitors and dual URAT-1 and XO inhibitors are in progress. Combining allopurinol with a purine nucleoside phosphorylase inhibitor (BCX 4208) has also been shown to be more effective in lowering the SUA than allopurinol alone in phase II clinical trials. For patients with severe symptomatic tophaceous gout in whom hyperuricemia cannot be controlled with standard ULTs alone or in combination, pegloticase, a polyethylene glycol modified mammalian uricase, can be effective. The drug is administered by i.v. infusion (8 mg in 250 ml normal saline over 2 h) every 2 weeks by physicians with experience and facilities for dealing with infusion reactions. Pretreatment with anti-histamines and steroids is advised to reduce the risk of infusion reactions, in addition to low-dose colchicine or NSAIDs for flare prophylaxis. SUA should be measured before each infusion and treatment discontinued if the SUA is > 360 μmol/l, as transient responders (~50%) are at increased risk for infusion reactions and anaphylaxis. Although pegloticase has marketing authorisation in Europe, it has not been approved by the National Institute for Health and Care Excellence or the Scottish Medicines Consortium in the UK because of concerns about toxicity and cost.

**Disclosure statement:** G.N. has received consulting fees from Savient in connection with a European Medicines Agency submission for pegloticase; honoraria as member of an advisory board for Menarini and as a member of the Independent Disease Monitoring Committee (IDMC) for Ardea/AstraZeneca trials of lesinurad and FDA/ NICE (3170); and research support from the University of Edinburgh from Menarini for the Febuxostat versus Allopurinol Streamlined Trial (FAST).

## GETTING THE MOST OUT OF PATIENT AND PUBLIC ENGAGEMENT

### I160 PHYSIOTHERAPY EXPERIENCE OF PATIENT AND PUBLIC ENGAGEMENT: DESIGNING SUPPORTIVE PHYSIOTHERAPY AND EXERCISE PROGRAMMES

Claire Jeffries
Rheumatology and Hydrotherapy, Solent NHS Trust, Portsmouth, UK

Abstract not provided.

**Disclosure statement:** The author has declared no conflicts of interest.

### I161 PATIENT AND PUBLIC ENGAGEMENT: DEVELOPING INDIVIDUAL PERSONAL CARE PLANS

Julie Ingall
Department of Rheumatology, Portsmouth Hospitals NHS Trust, Portsmouth, UK

The aim of this presentation is to introduce the concept of personalized care plans (PCPs) and the development of personalized care planning for patients with long-term rheumatological conditions with Portsmouth Hospitals NHS Trust Rheumatology Outpatient Department. In 2008 the Department of Health High Quality Care for All, NHS Next Stage Review Final Report stated that all patients with a long-term condition (LTC) should be offered a PCP over the next 2 years. Subsequent inclusion in the operating framework for the NHS in England 2009/10 confirmed that personalized care plans should be developed, agreed upon and regularly reviewed with a named lead professional for all 15 million people with an LTC. However, in 2013 a

### I157 HOW TO MANAGE TEENAGERS WITH CHRONIC PAIN

Jacqui Clinch
Rheumatology, University Hospitals Bristol, Bristol, UK

Abstract not provided.

**Disclosure statement:** The author has declared no conflicts of interest.

### ADOLESCENT AND YOUNG ADULT RHEUMATOLOGY

## I158 PAEDIATRIC VS ADULT RHEUMATOLOGY: DIFFERENCES IN NOMENCLATURE AND MANAGEMENT OF INFLAMMATORY ARTHRITIS

Debajit Sen
Rheumatology, University College Hospital, London, UK

Abstract not provided.

**Disclosure statement:** The author has declared no conflicts of interest.

## INVITED SPEAKER ABSTRACTS

Thursday 28 April 2016

### I156 WHAT'S NEW? EMERGING APPROACHES TO URATE-LOWERING THERAPY

George Nuki
Institute for Genetics and Molecular Medicine, University of Edinburgh, Western General Hospital, Edinburgh, UK

### I159 SEX, DRUGS AND ROCK AND ROLL: TIPS ON HOW TO UNDERTAKE A CONSULTATION WITH TEENAGERS AND YOUNG ADULTS

Rachel Tattersall
Rheumatology, Sheffield Teaching Hospitals and Sheffield Children’s Hospital, Sheffield, UK

### I158 PAEDIATRIC VS ADULT RHEUMATOLOGY: DIFFERENCES IN NOMENCLATURE AND MANAGEMENT OF INFLAMMATORY ARTHRITIS

Debajit Sen
Rheumatology, University College Hospital, London, UK

Abstract not provided.

**Disclosure statement:** The author has declared no conflicts of interest.

### I159 SEX, DRUGS AND ROCK AND ROLL: TIPS ON HOW TO UNDERTAKE A CONSULTATION WITH TEENAGERS AND YOUNG ADULTS

Rachel Tattersall
Rheumatology, Sheffield Teaching Hospitals and Sheffield Children’s Hospital, Sheffield, UK

Adolescence and young adulthood (AYA) is a unique and important developmental period during which young people (YP) develop their identity, autonomy and adult behaviours. YP experience profound changes, both physical and cognitive, during AYA development. Puberty usually completes by mid to late adolescence, but cognitive development continues well into the mid-20s. There is often a mismatch such that YP with adult bodies do not always think in adult-type ways. There are also hallmark features of AYA development (which are normal for AYA and indeed required to complete cognitive development), such as risk-taking behaviours, non-adherence and sexual health, that have profound implications for AYA care but which professionals can find challenging to address. This talk will outline key AYA developmental features to set the context for describing a practical approach to communicating with teenagers and young adults to improve their health care.

**Disclosure statement:** R.T. has received honoraria from Pfizer and AbbVie for educational sessions.
general practitioner survey found only 5.4% of patients acknowledged they owned a written care plan, leading the Department of Health to renew its commitment to PCPs. PCPs are a documented record of the agreed upon plan of care for a patient with an LTC. Using shared decision-making, it is both person-centred and holistic, identifying an individual’s needs and preferences, including information to support self-care and documenting goals, actions and reviews and decisions regarding medications, treatments and services. Advantages of PCPs for the patient can include promotion of independence, empowerment to self-care and informed decision-making. Benefits for the NHS are greater efficiency, reduced costs, improved risk management and quality improvement in services. Within the Portsmouth Hospitals Rheumatology Outpatients Department, PCPs have been developed to assist patients in self-managing their LTCs. The process involved the close working partnerships of health care professionals, patients, caregivers and charities. This structured teamwork approach, coordinated by the rheumatology team, enabled the production of disease-specific PCPs for rheumatological LTCs. Initial evaluation results found the PCPs were used appropriately by the majority of patients and their caregivers, with issues highlighted regarding access to results and reluctance in participation from other health care providers. Adoption of the PCPs by national charities has ensured access to the wider community and increased awareness. Resources are required for the continued patient support and review/education needed for implementation to be successful in the long term. Fostering a shared decision-making approach and by adopting PCPs, health care professionals can improve outcomes for patients and drive quality improvements within the NHS.

Disclosure statement: The author has declared no conflicts of interest.

I162 PATIENT ENGAGEMENT IN RESEARCH: DEFINING WHAT PATIENTS WANT TO KNOW FROM RESEARCH. NATIONAL ANKYLOSING SPONDYLITIS SOCIETY EXPERIENCE OF ENGAGING WITH PATIENTS—DESIGNING THE RESEARCH PRIORITIES FOR PATIENTS LIVING WITH ANKYLOSING SPONDYLITIS

Debbie Cook
Chief Executive, National Ankylosing Spondylitis Society, London, UK

Abstract not provided.

Disclosure statement: The author has declared no conflicts of interest.
ORAL PRESENTATION OF ABSTRACTS

SERONEGATIVE AND SPONDYLOARTHRITIDES ORAL ABSTRACTS

O01 DIFFERENTIAL TRANSCRIPTION FACTOR BINDING COULD EXPLAIN THE GENETIC ASSOCIATION OF ANKLYLOSING SPONDYLITIS WITH POLYMORPHISMS IN THE IL23R-IL12RB2 INTERGENIC REGION

Amity R. Roberts1,2, Matteo Vecellia1,2, Liye Chen1, Carla Cohen1,2 and B. Paul Wordsworth1,2
1Nuffield department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Botnar Research Centre and 2NIHR Oxford Comprehensive Biomedical Research Centre, University of Oxford, Oxford, UK

Background: Genome-wide association studies have revealed the polygenic nature of AS. More than 60 genetic influences have been identified, but most of these are non-coding sequences. Protection against AS is afforded by a loss of functional mutation in the cytoplasmic tail of the IL-23 receptor (IL-23R), but there is also a second independent association in this region. This study explores the functional basis for the latter association between AS and single nucleotide polymorphisms (SNPs) in the IL23R-IL12RB2 intergenic region.

Methods: We performed conditional analysis on genetic association data at IL23R and used epigenetic data on chromatin remodelling and transcription factor (TF) binding to identify the primary AS-associated SNP. Functional effects were tested in luciferase reporter assays in HEK293T cells and allele-specific TF binding was investigated by electrophoretic mobility gel shift assays. The involvement of candidate TFs in DNA binding was investigated by antibodies in these experiments. We measured mRNA expression levels of nearby genes in CD4+ T cells and compared these between homozygous for the risk A allele and the protective G allele. The proportions of IL-17A- and IFN-γ-CD4+ T cells were measured by FACS and also correlated to patient genotype.

Results: Conditional analysis identified rs11209032 as the primary causal SNP within a putative enhancer between IL23R and IL12RB2. Reduced luciferase activity was seen for the risk A allele (P < 0.001) and reduced H3K4me1 methylation was observed in CD4+ T cells from ‘A/A’ homozygotes (P < 0.02). Nuclear extract binding to the risk A allele was decreased ~3.5-fold compared with the protective allele (P < 0.001). Reduced nuclear factor binding was observed when antibody to TWIST1 was included. The proportion of IFN-γ+CD4+ T cells was increased in A/A homozygotes (P < 0.004), but neither IL23R nor IL12RB2 mRNA was affected.

Conclusion: The rs11209032 SNP downstream of IL23R forms part of an enhancer allelic variation that may influence TH1 cell numbers. Homozygotes for the risk A allele have more IFN-γ-secreting TH1 cells compared with those with the protective G allele. Further work is necessary to explain how TWIST1 contributes to these important observations.

Disclosure statement: The authors have declared no conflicts of interest.

O02 INCREASED RATES OF HYPERTENSION IN PATIENTS WITH PSORIASIC ARTHRITIS COMPARED TO PSORIASIS ALONE: RESULTS FROM THE UK BIOBANK

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Background: PsA is a chronic inflammatory arthritis associated with the presence of psoriasis. The aim of this study was to compare lifestyle factors between patients with PsA or psoriasis and a control group and to assess the association between these inflammatory diseases and cardiovascular disease (CVD) outcomes.

Methods: UK Biobank recruited 500,664 people (ages 40–70 years) in the UK between 2006 and 2010. Cross-sectional data on lifestyle, sociodemographics and health and medical history were collected at the assessment visit by questionnaire and interview by a research nurse. Participants were asked if a physician had ever diagnosed them with PsA, psoriasis or any other disease. Rates of alcohol consumption (current drinker or not) and smoking habits (ever or never) for the two disease groups were compared against a control group using logistic regression. Comparison between disease groups was performed by linear combinations of coefficients after estimation. BMI was tested using linear regression. All regression analyses included age and sex as covariates. Four CVD outcomes—heart failure, heart attack, angina and hypertension—were tested for association with the disease group using logistic regression using BMI, smoking, alcohol consumption, age and sex as covariates. Odds ratios (ORs) and β coefficients are reported with 95% CIs.

Results: A total of 470,994 participants were included; 862 PsA patients, 4,761 psoriasis patients and 465,371 control participants (Table 1). Compared with the control group, both the PsA and psoriasis groups had higher BMIs [β = 1.43 (1.11:1.75) and 0.72 (0.58:0.85), respectively], the psoriasis group smoked more [OR 1.63 (1.54:1.72)] and the PsA group had a lower rate of current drinkers [OR 0.68 (0.55:0.85)]. Comparing between disease groups, the PsA group had a higher BMI [β = 0.69 (0.32:1.06)] and lower rates of both ever smoking and current alcohol consumption [OR 0.70 (0.61:0.81) and 0.65 (0.51:0.83), respectively]. The PsA group had a higher rate of hypertension compared with the control and psoriasis groups [OR 1.71 (1.48:1.97) and 1.55 (1.33:1.82), respectively].

Conclusion: Using a large population-based cohort, we show that self-reported rates of hypertension are significantly higher in patients with PsA compared with PsA patients.

Disclosure statement: The authors have declared no conflict of interest.

O03 APREMILAST, AN ORAL PHOSPHODIESTERASE-4 INHIBITOR, IS ASSOCIATED WITH LONG-TERM (104-WEEK) IMPROVEMENTS IN ENTHESITIS AND DACTYLITIS IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED RESULTS FROM THREE PHASE III RANDOMIZED CONTROLLED TRIALS

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1Rheumatology, Toronto Western Hospital, Toronto, ON, Canada, 2Rheumatology, University of California, San Diego, School of Medicine, University of California San Diego, La Jolla, CA, USA, 3Rheumatology, University of Sheffield, Sheffield, UK, 4Rheumatology, Hospital Clínico Universitario, Santiago, Spain, 5Rheumatology, Schön Klinik Hamburg Eilbek, Hamburg, Germany, 6Rheumatology, University of Genova, Genova, Italy, 7Rheumatology, University Erlangen-Nuremberg, Erlangen, Germany, 8Rheumatology, University of Orléans, Orléans, France, 9Medical Affairs, I & I and 10Statistics, Celgene Corporation, Warren, NJ, USA, 11Rheumatology, University Hospital Southampton, Southampton, UK, 12Rheumatology, University of Massachusetts Medical School,

Table 1. Summary statistics by study group

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control group (n=465,371)</th>
<th>Psoriasis group (n=476,1)</th>
<th>PsA group (n=862)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>56.4 (8.1)</td>
<td>56.3 (8.1)</td>
<td>56.1 (7.4)</td>
</tr>
<tr>
<td>Male, %</td>
<td>45.1</td>
<td>52.9</td>
<td>48.1</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>27.3 (4.8)</td>
<td>28.1 (3.0)</td>
<td>28.9 (5.4)</td>
</tr>
<tr>
<td>Current drinkers, %</td>
<td>92.1</td>
<td>92.6</td>
<td>88.9</td>
</tr>
<tr>
<td>Ever smokers, %</td>
<td>44.6</td>
<td>57.3</td>
<td>47.8</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>26.9</td>
<td>29.2</td>
<td>37.7</td>
</tr>
<tr>
<td>Heart attack, %</td>
<td>2.2</td>
<td>2.9</td>
<td>2.8</td>
</tr>
<tr>
<td>Angina, %</td>
<td>3.1</td>
<td>4.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Heart failure, %</td>
<td>0.05</td>
<td>0.04</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Results: Compared with the control group, the PsA group had lower rate of current drinkers [OR 0.68 (0.55:0.85)]. Comparing between disease groups, the PsA group had a higher BMI [β = 0.69 (0.32:1.06)] and lower rates of both ever smoking and current alcohol consumption [OR 0.70 (0.61:0.81) and 0.65 (0.51:0.83), respectively]. The PsA group had a higher rate of hypertension compared with the control and psoriasis groups [OR 1.71 (1.48:1.97) and 1.55 (1.33:1.82), respectively].

Conclusion: Using a large population-based cohort, we show that self-reported rates of hypertension are significantly higher in patients with PsA compared with PsA patients.

Disclosure statement: The authors have declared no conflict of interest.

Tuesday 26 April 2016, 9:00–10:30
Background: PALACE 1 (NCT01172938), 2 (NCT01217277) and 3 (NCT01212779) evaluated apremilast (APR) efficacy and safety in patients with active PsA. We report the impact of APR treatment on enthesis and dactylitis, hallmark features of PsA, over 104 weeks in a planned analysis of PALACE 1–3.

Methods: Patients were randomized (1:1:1) to receive placebo, APR 30 mg twice a day (APR30) or APR 20 mg twice a day (APR20). From weeks 24 to 52, patients received double-blind APR30 or APR20 treatment; a 4-year open-label extension phase is ongoing. Pre-planned analyses examined data pooled across PALACE 1–3 at week 24 from patients with pre-existing enthesis and/or dactylitis using the Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) (range 0–13) and dactylitis count (range 0–20), respectively. Analyses at week 24 used last observation carried forward for missing values; in patients qualifying for early escape at week 16, that value was carried forward. For all others, the last post-baseline value was carried forward for missing values at week 24. Weeks 52 and 104 were based on data as observed.

Results: Among patients with enthesis (n = 915) or dactylitis (n = 610) at baseline and one or more post-baseline values, the mean MASES ranged from 4.4 to 4.8 and the mean dactylitis count ranged from 3.2 to 3.4 at baseline. At week 24, mean changes in the MASES were −1.3 (APR30 vs placebo; P = 0.0194), −1.2 (APR20) and −0.9 (placebo); the mean MASES percent/median percent changes were −23.6%/−21.6% (APR30 vs placebo; P = 0.005), −19.3%/−45.0% (APR20) and −7.0%/−21.1% (placebo). A MASES of 0 was achieved by 27.5% (APR30), 27.4% (APR20) and 22.5% (placebo) of patients. Mean changes in the dactylitis count were −1.8 (APR30 vs placebo; P = 0.0097), −1.6 (APR20) and −1.3 (placebo); mean percent/median percent changes in dactylitis count were −48.6%/−79.3% (APR30), −43.2%/−75.0% (APR20) and −38.2%/−66.7% (placebo). A dactylitis count of 0 was achieved by 46.2% (APR30), 45.9% (APR20) and 39.0% (placebo) of patients. With continued APR treatment, long-term improvement in enthesis and dactylitis severity was seen, marked by mean/median percent/median percent reductions in the MASES at 52 weeks [APR30 (n = 377): −2.0%/−34.3%/−66.7%; APR20 (n = 326): −2.0%/−27.4%/−48.7%; placebo (n = 249): −2.5%/−67.9%/−100.0%] and dactylitis counts at 52 weeks [APR30 (n = 249): −2.5%/−67.9%/−100.0%; APR20 (n = 229): −2.3%/−70.2%/−100.0%] and 104 weeks [APR30 (n = 200): −2.9%/−80.0%/−100.0%; APR20 (n = 182): −2.4%/−75.6%/−100.0%]. A MASES of 0 was achieved at weeks 52 and 104 by 37.7% and 48.7% (APR30) and 41.1% and 51.7% (APR20) of patients. A dactylitis count of 0 was achieved at weeks 52 and 104 by 67.5% and 77.5% (APR30) and 66.7% and 72.5% (APR20) of patients. Over 104 weeks, most adverse events were mild or moderate in severity; no increase was seen in adverse event incidence and severity.

Conclusion: Over 104 weeks, APR demonstrated continued efficacy in PsA treatment, including improvements in enthesis and dactylitis, and was generally well tolerated.

Disclosure statement: D.D.G. has received consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Pfizer, Novartis and UCB and research funding from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Pfizer, Novartis and UCB. A.K. has received research funding from Abbott, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene, Centocor-Janssen, Pfizer, Roche and UCB. J.J.G.-R. is on the advisory boards of Bristol-Myers Squibb, Pfizer, Roche, Schering-Plough and UCB SA; has received lecture fees from Bristol-Myers Squibb, Roche, Schering-Plough and Wyeth and has received research funding from Roche and Schering-Plough. J.W. has received consulting fees from Abbott, Bristol-Myers Squibb, MSD, Pfizer and UCB and research funding from Abbott, Bristol-Myers Squibb, MSD, Pfizer and UCB. M.C. has received consulting fees from Actelion, Bristol-Myers Squibb and Sanofi-Aventis and research funding from Actelion, Bristol-Myers Squibb and Sanofi-Aventis. G.S. has received consulting fees from Abbott, Celgene, Roche and UCB and research funding from Abbott, Celgene, Roche and UCB. E.L. has participated in speakers bureaus for Amgen, Eli Lilly, Pfizer, UCB, Celgene, Novartis and Roche; has participated in speakers bureaus for Abbott, Amgen, Biogen Idec, Bristol-Myers Squibb, Genentech, Janssen, Eli Lilly, Pfizer, UCB and has received research funding from Abbott, Amgen, Biogen Idec, Bristol-Myers Squibb, Genentech, Janssen, Eli Lilly, Pfizer, UCB, Celgene, Novartis and Roche. All other authors have declared no conflicts of interest.
**O06 SECUKINUMAB SIGNIFICANTLY IMPROVES PHYSICAL FUNCTION, QUALITY OF LIFE, FATIGUE AND WORK PRODUCTIVITY IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS TREATED FOR UP TO 52 WEEKS IN THE PHASE III MEASURE 2 STUDY**

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**Background:** IL-17A is a pro-inflammatory cytokine implicated in the pathogenesis of AS. Inhibition of IL-17A with secukinumab, a human anti-IL-17A monoclonal antibody, rapidly improved the signs and symptoms of AS at week 16 in the randomized, double-blind, placebo-controlled phase III MEASURE 2 study (NCT01649875). Here we present the impact of s.c. secukinumab on patient-reported outcomes (PROs) at weeks 16 and 52 in the MEASURE 2 study.

**Methods:** A total of 219 adults with active AS despite therapy with NSAIDs were randomized to receive s.c. secukinumab 150 or 75 mg or placebo at baseline, weekly until week 3 and every 4 weeks from week 4. At week 16, subjects randomized to placebo at baseline were re-randomized to receive s.c. secukinumab 150 or 75 mg every 4 weeks. PROs were measured every 4 weeks using the following questionnaires: 36-item Short Form Health Survey (SF-36) physical and mental component summaries (PCS and MCS, respectively), AS Quality of Life (ASQoL), Functional Assessment of Chronic Illness Therapy-Fatigue (FACT-Fatigue) and Work Productivity and Activity Impairment-General Health (WPAI-GH). Changes in the PCS and ASQoL from baseline were predefined secondary endpoints assessed at week 16 as part of a hierarchical statistical testing strategy with adjustment for multiplicity. Other endpoints were exploratory.

**Results:** Demographics and disease severity were balanced across groups at baseline, with subjects experiencing moderate - to - severe levels of fatigue and impaired health-related QoL. At week 16, secukinumab 150 mg significantly improved PCS and ASQoL scores vs placebo (Table 1); improvements in these parameters were observed from week 4. FACT-Fatigue scores also significantly improved vs placebo at week 16 (Table 1). Mean changes from baseline with secukinumab at week 16 were greater than the minimum clinically important difference (MCID) for the PCS, ASQoL and FACT-Fatigue (Table 1). Reductions in WPAI-GH were also observed with secukinumab vs placebo at week 16. Improvements in PROs from baseline were sustained or increased at week 52 (Table 1).

**Conclusion:** In subjects with active AS, secukinumab 150 mg provided rapid and sustained improvements in PROs, including fatigue, general and AS-specific QoL measures and illness-associated reductions in work productivity.

**Disclosure statement:** P.E. has received consultancy payments from AbbVie, BMS, Merck, Novartis, Pfizer, Roche, UCBB, Lilly, Samsung and Sandoz. A.D. has provided consultancy to AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer and UCB and has received research funding from AbbVie, Amgen, Boehringer Ingelheim, Janssen, Novartis, Pfizer and UCB. J.S. has provided consultancy to AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer and UCB; has participated in speakers bureaus for AbbVie, Pfizer, Merck and UCB and has received funding for research from AbbVie, Boehringer Ingelheim, Janssen, Novartis, Merck, Lilly, Pfizer and UCB. M.A is an employee of Novartis. H.R. is an employee of Novartis.

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**O06 PERIPHERAL BLOOD IMMUNOPHENOTYPING IN PATIENTS WITH ANKYLOSING SPONDYLITIS REVEALS INCREASED NUMBERS OF TH17 AND TH22 CELLS AND OF IL-17A-PRODUCING CD8+ AND γδ T CELLS**

Davide Simone, Mohammed Hussein Al Mossawi, Jelle De Wit, Anna Ridley and Paul Bowness

Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

**Background:** AS is a chronic inflammatory disease of the axial skeleton, with varying involvement of peripheral joints and non-articular sites. Significant advances have been made regarding the mechanisms of disease pathogenesis, and the processes leading to AS in the past decade. Among these, the pathogenic role of IL-17A and IL-22 in the context of type 17 immunity has become increasingly apparent. The aim of this study was to undertake an immunophenotype analysis of peripheral blood in patients with AS compared with healthy controls in order to identify differences in the frequency of specific lymphocyte cell subsets within the type 17 immune axis.

**Methods:** Peripheral blood from an observational cohort consisting of 38 patients with AS and 17 healthy donors was obtained. Mononuclear cells were analysed using flow cytometry with a multicolour panel based on surface and intracellular markers and in-depth analysis of the cytokine-producing helper and cytotoxic T cells.

**Results:** Patients with AS had a higher percentage of Th17 cells within the CD4 compartment compared with healthy controls [1.27% (0.69) vs 0.67 (0.41); P < 0.001]. The production of IL-17A in the CD8+ T cell compartment [1.30% (0.69) vs 0.40 (0.45); P < 0.001] and in γδ T cell compartment [4.86% (7.04) vs 1.01 (0.85); P < 0.001] was also higher than controls. CD4+ T cells making IL-22 were also increased in AS patients compared with healthy controls [1.37% (0.13) vs 0.58 (0.35); P < 0.001]. More detailed analysis is currently under way, including both effector and regulatory T cell subsets.

**Conclusion:** Immunophenotype analysis of peripheral blood of AS patients shows increased levels of type 17 immunity across various T lymphocyte compartments. These alterations indicate a broad dysregulation of the immune response in the peripheral blood of AS and confirm the expansion of IL-17A- and IL-22-producing type 17 cells in this disease.

**Disclosure statement:** J.D.W. has received research funding from Merck. P.B. has received research funding from Merck. All other authors have declared no conflicts of interest.

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**Table 1. Mean baseline scores and mean change from baseline in PROs at weeks 16 and 52 by treatment group**

<table>
<thead>
<tr>
<th>PROs</th>
<th>Subcutaneous secukinumab</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>150mg</td>
<td>75mg</td>
</tr>
<tr>
<td>SF-36 PCS (MCID ≥ 2.5)</td>
<td>n, week 16/52</td>
<td>72.62</td>
</tr>
<tr>
<td></td>
<td>Baseline score</td>
<td>34.4</td>
</tr>
<tr>
<td></td>
<td>Change† at week 16</td>
<td>6.08</td>
</tr>
<tr>
<td></td>
<td>Change‡ at week 52</td>
<td>7.99</td>
</tr>
<tr>
<td>ASQoL (MCID ≥ 1.8)</td>
<td>n, week 16/52</td>
<td>72.61</td>
</tr>
<tr>
<td></td>
<td>Baseline score</td>
<td>12.2</td>
</tr>
<tr>
<td></td>
<td>Change† at week 16</td>
<td>–4.00***</td>
</tr>
<tr>
<td></td>
<td>Change‡ at week 52</td>
<td>–5.23</td>
</tr>
<tr>
<td>FACT-Fatigue (MCID ≥ 4.0)</td>
<td>n, week 16/52</td>
<td>72.62</td>
</tr>
<tr>
<td></td>
<td>Baseline score</td>
<td>22.6</td>
</tr>
<tr>
<td></td>
<td>Change† at week 16</td>
<td>8.10***</td>
</tr>
<tr>
<td></td>
<td>Change‡ at week 52</td>
<td>11.46</td>
</tr>
<tr>
<td>SF-36 MCS (MCID ≥ 2.5)</td>
<td>n, week 16/52</td>
<td>72.62</td>
</tr>
<tr>
<td></td>
<td>Baseline score</td>
<td>39.8</td>
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<tr>
<td></td>
<td>Change† at week 16</td>
<td>4.04</td>
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<tr>
<td></td>
<td>Change‡ at week 52</td>
<td>6.46</td>
</tr>
</tbody>
</table>

*P < 0.001, **P < 0.01, ***P < 0.05 vs placebo; P-values at week 16 are from mixed-effect model repeated measures (MMRM) analysis. P-values for SF-36 PCS and ASQoL adjusted for multiplicity of testing. †Increase in score represents improvement. ‡Decrease in score represents improvement. ††Least square mean change from baseline. 

**Mean change from baseline using observed data. MCID: minimum clinically important difference; N/A: not applicable; PROs: patient-reported outcomes.**
Little is known about the long-term outcome of patients recruited to the Norfolk Arthritis Register between 1990 and 1994 were included in this study. Demographics, 51 swollen/tender joint counts (SJ/TJC) and the HAQ were collected at baseline. Blood was taken to determine ACPA, RF and CRP and the 28-joint DAS28 was calculated. Patients were reassessed at years 1, 2, 3, 5, 7, 10, 15 and 20 after inclusion and self-reported orthopaedic surgery and co-morbidity data were collected. The association between baseline variables and disability over time/risk of first replacement surgery was assessed using a random effects model/ Cox proportional hazard model, respectively.

**Results:** Of 1022 included patients (mean age at baseline 53.4 years (IQR: 16.3, 64.8% female), 404 (39.5%) died (mortality rate = 22.6/1000 patient-years) and 354 (34.6%) completed 20 years of follow-up. Table 1 shows baseline and follow-up characteristics. Baseline variables associated with increased disability over time, controlling for co-morbidities, were high baseline HAQ [HR = 0.61 (95% CI 0.56, 0.66)], older age [HR = 0.007 (CI 0.005, 0.009)] and female gender [HR = 0.14 (CI 0.08, 0.20)].

**Conclusion:** After early improvement, physical function deteriorated over the follow up, whereas SJ/TJC remained low. Only older age at onset predicted worse functional outcome and increased risk of first surgery. ACPA+ patients have substantially higher risk of first surgery and should potentially be treated more aggressively early after presentation.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**Q07 DISEASE ACTIVITY, DISABILITY AND SURGERY IN A PROSPECTIVE INCEPTION COHORT OF INFLAMMATORY ARTHRITIS PATIENTS FOLLOWED FOR 20 YEARS: RESULTS FROM THE NORFOLK ARTHRITIS REGISTER**

James M. Gwinnutt1, Deborah P. M. Symmons1, Alex J. MacGregor2, Jacqueline R. Chipping3, Tarnya Marshal2, Mark Lunt1 and Suzanne M. M. Verstappen1

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**Background:** Little is known about the long-term outcome of patients presenting with early inflammation polyarthritis (IP). The objective of this study was to describe the occurrence and baseline predictors of long-term outcomes including mortality, disease activity, physical function and large joint replacement surgery in a cohort of IP patients followed up for 20 years.

**Methods:** Individuals ≥16 years of age with two or more swollen joints lasting >3 weeks recruited to the Norfolk Arthritis Register between 1990 and 1994 were included in this study. Demographics, 51 swollen/tender joint counts (SJ/TJC) and the HAQ were collected at baseline. Blood was taken to determine ACPA, RF and CRP and the 28-joint DAS28 was calculated. Patients were reassessed at years 1, 2, 3, 5, 7, 10, 15 and 20 after inclusion and self-reported orthopaedic surgery and co-morbidity data were collected. The association between baseline variables and disability over time/risk of first replacement surgery was assessed using a random effects model/ Cox proportional hazard model, respectively.

**Results:** Of 1022 included patients (mean age at baseline 53.4 years (IQR: 16.3, 64.8% female), 404 (39.5%) died (mortality rate = 22.6/1000 patient-years) and 354 (34.6%) completed 20 years of follow-up. Table 1 shows baseline and follow-up characteristics. Baseline variables associated with increased disability over time, controlling for co-morbidities, were high baseline HAQ [HR = 0.61 (95% CI 0.56, 0.66)], older age [HR = 0.007 (CI 0.005, 0.009)] and female gender [HR = 0.14 (CI 0.08, 0.20)].

**Conclusion:** After early improvement, physical function deteriorated over the follow up, whereas SJ/TJC remained low. Only older age at onset predicted worse functional outcome and increased risk of first surgery. ACPA+ patients have substantially higher risk of first surgery and should potentially be treated more aggressively early after presentation.

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**Q08 BLINDNESS IN PATIENTS WITH GIANT CELL ARTERITIS AND ITS ASSOCIATION WITH VASCULAR DISEASE**

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**Background:** Visual loss is a recognized complication of giant cell arteritis (GCA); however, its rate of occurrence has not been estimated accurately and risk factors have not been firmly established. Some studies have implicated cardiovascular disease as a risk factor for blindness, but its contribution has been reported inconsistently. The aim of this study was to assess the frequency of blindness in GCA using a large international prospective cohort of patients newly diagnosed with GCA and, in particular, to evaluate the possible role of vascular risk factors.

**Methods:** The analysis was conducted among recruits to the Diagnosis and Classification Criteria in Vasculitis Study (DCVAS). Physicians from 23 countries recorded clinical data from patients referred to their service with vasculitis over a 2 year period. Visual loss was recorded by completion of the Vasculitis Damage Index (VDI) 6 months after diagnosis, which records visual impairment and uniocular and binocular blindness. Logistic regression analysis was used to assess the association of vascular risk factors and blindness.

**Results:** A total of 433 participants with vasculitis from 23 countries were considered to have GCA with >75% diagnostic certainty, of which 404 fulfilled the 1990 ACR criteria for GCA and 235 had positive temporal artery biopsy. Blindness in at least one eye was noted in 7.85% of patients at 6 months. The logistic regression model identified prevalent diagnoses of stroke [cerebrovascular accident (CVA)] and peripheral vascular disease (PVD) as being positively associated with blindness at 6 months [CVA odds ratio (OR) = 4.47 (95% CI 1.30, 15.41); PVD OR = 10.44 (2.94, 37.03)]. Prevalent diabetes was also associated with blindness at 6 months, but with borderline statistical significance [OR 2.48 (95% CI 0.98, 6.25)]. There was no association between baseline laboratory findings (anaemia, ESR, CRP, platelets) and blindness at 6 months.

**Conclusion:** This is the largest study to date of subjects with GCA and provides a robust estimate of the rate of occurrence of blindness.

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**Table 1. Characteristics of the cohort at baseline and follow-up years 5, 10, 15 and 20**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>5 years</th>
<th>10 years</th>
<th>15 years</th>
<th>20 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attended FU</td>
<td>1022</td>
<td>782</td>
<td>607</td>
<td>477</td>
<td>354</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>360</td>
<td>255</td>
<td>185</td>
<td>153</td>
<td>103</td>
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<tr>
<td>Women</td>
<td>662</td>
<td>527</td>
<td>422</td>
<td>324</td>
<td>251</td>
</tr>
<tr>
<td>Age at FU</td>
<td>1022</td>
<td>53.4 (16.3) [17/106]</td>
<td>782</td>
<td>58.4 (15.1) [24/96]</td>
<td>607</td>
</tr>
<tr>
<td>Swollen joints (51)</td>
<td>1022</td>
<td>6 (0–13) [0/47]</td>
<td>564</td>
<td>1 (0–0) [0/38]</td>
<td>601</td>
</tr>
<tr>
<td>Tender joints (51)</td>
<td>1022</td>
<td>7 (0–11) [0/50]</td>
<td>564</td>
<td>1 (0–0) [0/46]</td>
<td>601</td>
</tr>
<tr>
<td>Both swollen and tender</td>
<td>1022</td>
<td>3 (0–11) [0/44]</td>
<td>564</td>
<td>0 (0–0) [0/38]</td>
<td>601</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>817</td>
<td>4.0 (2.9–5.9) [1.2/7.7]</td>
<td>509</td>
<td>2.5 (1.7–3.6) [1.2/7.4]</td>
<td>375</td>
</tr>
<tr>
<td>HAQ</td>
<td>1010</td>
<td>0.8 (0.3–1.6) [0/3]</td>
<td>779</td>
<td>0.8 (0.1–1.6) [0/3]</td>
<td>597</td>
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<tr>
<td>RF, n</td>
<td>891</td>
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<tr>
<td>Positive, n (%)</td>
<td>252 (28.3)</td>
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<td></td>
</tr>
<tr>
<td>Negative, n (%)</td>
<td>639 (71.1)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ACPA, n</td>
<td>797</td>
<td></td>
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<tr>
<td>Positive, n (%)</td>
<td>216 (27.1)</td>
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<td></td>
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<tr>
<td>Negative, n (%)</td>
<td>581 (72.9)</td>
<td></td>
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</tr>
</tbody>
</table>
suggests that blindness remains a major clinical problem and highlights the need for urgent referral and treatment. The association with prior vascular disease indicates a need for greater vigilance in this group.

Disclosure statement: M.Y. has received travel expenses from ABBVie and Eli Lilly. P.A.M. has received research support from Roche. All other authors have declared no conflicts of interest.

**O99 ULTRASOUND COMPARED WITH BIOPSY IN THE DIAGNOSIS OF SUSPECTED GIANT CELL ARTERITIS**

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**Background:**
GCA is a relatively common form of systemic vasculitis that, if untreated, can lead to permanent sight loss. We compared the effectiveness and cost-effectiveness of ultrasound (US) with temporal artery biopsy compared with US of the temporal and axillary arteries for diagnosis of newly suspected GCA. Sonographers received training and examined 10 healthy subjects and 1 patient with active GCA before participating in the study. We recruited patients referred to secondary care with suspected new-onset GCA. The main outcome measures were sensitivity, specificity and cost-effectiveness using a reference diagnosis derived from the final clinical diagnosis, ACR classification criteria for GCA and expert review. The cost-effectiveness analysis compared treatment costs, the impact of steroid toxicity in false-positive cases and the impact of GCA complications in false-negative cases for the two tests and different testing strategies in combination with clinical judgement.

**Results:**
We recruited 450 patients with suspected GCA from 20 centres between 2010 and 2013. We included 381 patients in the primary analysis (median age 71.1 years; 72% female) and 257 (67%) were given a reference diagnosis of GCA. The sensitivity of biopsy was 39% (95% CI 33, 48), significantly lower than previously published series and inferior to US (54% [95% CI 48, 60]). The specificity of biopsy was superior to US (100% vs 81%) compared with the gold standard defined by final diagnosis that included the results of the temporal artery biopsy. Combining US with clinical judgement (sensitivity 93%, specificity 77%) was more cost effective than biopsy with clinical judgement (sensitivity 91%, specificity 81%); the incremental net monetary benefit was £493 (£456, US$703) per suspected case. A strategy of US for all suspected cases followed by biopsy in medium- and high-risk patients with a negative US was slightly more cost effective (sensitivity 95%, specificity 77%); incremental net monetary benefit £548 (£502, US$715) per suspected case.

**Conclusion:**
We compared the role of US with biopsy as diagnostic tests in patients with suspected GCA. We demonstrated that as a primary investigation of suspected GCA, US can improve sensitivity but not specificity when compared with biopsy. A diagnosis of GCA requires clinical assessment based on the patient’s history and examination; a strategy of scanning all patients, with biopsy of scan-negative cases, is effective and cost effective in evaluating patients with a medium to high index of suspicion of GCA.

**Disclosure statement:** W.S. has received funding for research from GSK and Roche. B.D. has received funding for research from GSK, Servier and UCB. A.H. has received research support from the National Institute of Health Research Health Technology Assessment programme and the Medical Research Council. All other authors have declared no conflicts of interest.

**O10 INCIDENCE OF ANCA-ASSOCIATED VASCULITIS IN A UK MIXED ETHNIC POPULATION**

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**Background:**
There are no published data on the incidence of ANCA-associated vasculitis (AV) in the UK in the black/minority ethnic (BME) population. In this study we aimed to estimate the incidence of AV in a white and a BME population.

**Methods:**
As part of an audit of AV care, incident cases of AV were identified from medical records at Nottingham University Hospitals Trust and at the Royal Derby Hospital from multiple sources. Inclusion criteria were residence in the Nottingham–Derby urban area and a new diagnosis of AAV (European Medicines Agency classification criteria) between March 2007 and June 2013. The denominator population was calculated from the 2011 census data. Data capture-recapture analysis was used to estimate the completeness of case ascertainment. Incidence rates and 95% CIs were calculated by ethnicity, age and sex and adjusted using Poisson regression. The effect of social class was estimated using Index of Multiple Deprivation (IMD) quintiles.

**Results:**
The main results are in Table 1. Overall we identified 107 incident cases of AV. The overall annual incidence of AV was 23.1/ million (95% CI 18.9, 27.9). The annual incidence of AV among the white population was 25.6/million (95% CI 21.0, 31.3) and among the BME population was 8.4/million (95% CI 3.1, 18.3). In univariable regression analysis, increasing age, male sex and white ethnicity were all significantly associated with an increased incidence of AV. When
combined in multivariable regression analysis, the effect of ethnicity was reduced and the adjusted incidence rate ratio for the BME compared with the white population was 0.7 (95% CI 0.3, 1.5; P = 0.3). Further confounding by social class did not seem to be present (P = 0.2). Data capture-recapture analysis estimated 0.9 missing cases.

Conclusion: Overall the incidence of AAV was similar to other epidemiological studies in the UK and worldwide. This is the first report to show the incidence of AAV in a mixed-ethnicity population in the UK. Crude incidence rates were lower in the BME than the white population. Once adjusted for age and sex, the incidence in the white and BME populations was similar, but the Cs surrounding the rate ratios were wide. Further studies are needed in larger populations.

Disclosure statement: The authors have declared no conflicts of interest.

O11 DRUG-SPECIFIC RISK AND ASSOCIATED FACTORS WITH VASCULITIS-LIKE EVENTS IN PATIENTS EXPOSED TO TNF INHIBITOR THERAPY: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS

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Kath Watson1, Deborah P. Symmons1,2,3 and Kimme Hyrich1,2,4
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Background: The association between TNF inhibitors (TNFis) and vasculitis-like events, possibly secondary to induction of autoantibodies, has been well reported. However, the incidence, drug-specific differences and factors associated have been poorly characterized. The aim of this study was to (i) compare the drug-specific risk of vasculitis-like events in TNFi-treated RA patients with those receiving non-biologic DMARDs (nbDMARDs) and (ii) to assess factors associated with the event.

Methods: The British Society for Rheumatology Biologics Register for RA (BSRBR-RA) is a prospective cohort study assessing the safety of biologics. This analysis included two cohorts recruited between 2001 and 2015: (i) patients starting their first TNFi (adalimumab, etanercept, infliximab, certolizumab) and (ii) a biologic-naive comparison cohort receiving nbDMARDs. To calculate drug-specific risk, biologic-naive patients at baseline on first TNFi only were included. Additional information from consultants was sought for events. Patients with baseline systemic vasculitis were excluded. Events were attributed to TNFi therapy if they occurred within 90 days of being on a drug. Follow-up was censored at the first event, switching to another biologic, death, last returned clinical follow-up or 31 May 2015, whichever came first. The risk of an event was compared between the two cohorts using Cox proportional hazards models, adjusted using propensity scores derived using inverse probability of treatment weights (IPTW). Time-varying risk was assessed using a flexible parametric spline model. A sensitivity analysis was performed excluding patients who had a possible secondary vasculitis cause (e.g. infection), were withdrawn medicinally associated with vasculitis-like events or had known baseline nailfold vasculitis.

Results: There were 95 incident cases: 14 in 3640 nbDMARD patients and 81 in 12 745 first TNFi-treated subjects, with 20 635 and 52 428 patient-years of follow-up generating crude incidence rates of 71/10 000 and 16/10 000 person-years, respectively (Table 1). After adjusting for IPTW, the hazard ratio (HR) of vasculitis-like events in patients on TNFi vs nbDMARD was 1.27 (95% CI 0.40, 4.09). Drug-specific HRs were highest in the etanercept and infliximab patients; however, following adjustment this was not significant (Table 1). Risk of event was highest in the first year of treatment. Factors associated with lower rates included methotrexate [HR 0.68 (95% CI 0.47, 0.98)] and sulfasalazine use [HR 0.46 (95% CI 0.29, 0.82)]. Other variables associated with the outcome included baseline 28-joint DAS score [HR 1.42 (95% CI 1.20, 1.68), disease duration [HR 1.03 per year (95% CI 1.01, 1.04), seropositive status [HR 1.82 (95% CI 1.18, 2.78)] and HAQ score [HR 1.65 (95% CI 1.15, 2.30)].

Conclusion: This is the first prospective observational study to assess the risk of RA patients treated with TNFi agents. The absolute risk of vasculitis-like events in both groups was low, with the highest risk in the first year of treatment. There were no significant differences in risk between TNFi agents after adjustment. Baseline use of methotrexate and sulfasalazine was associated with lower rates.

Disclosure statement: M.J. has received honoraria from Pfizer, AbbVie and UCB. I.B. has received research support from GSK, Roche, Pfizer, UCB and Genzyme/Sanofi. H.C. has participated in speakers bureau for AbbVie, Pfizer, Janssen and Novartis. A.B. has received research support from AbbVie, Pfizer, Eli Lilly and Sanofi-Aventis. K.H. has participated in the speakers bureau for AbbVie and has received research support from Pfizer. All other authors have declared no conflicts of interest.

O12 HOW HAS THE PROGRESSION OF EROSIONS AND JOINT SPACE NARROWING CHANGED IN EARLY RHEUMATOID ARTHRITIS OVER THE PAST THREE DECADES? EVIDENCE FROM THE ERAS AND ERAN COHORTS

Lewis Carpenter1, Sam Norton2, Elena Nikiphorou3, Keeran Jayakumar1, Daniel McWilliams4, Josh Dixey5, Patrick Kiey6, David A. Walsh7 and Adam Young1,4
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Background: The reduction in disease activity, disability and radiographic progression reported in RA has coincided with a shift toward earlier more intensive DMARD therapy. Radiographic scores measure the severity of erosions and joint space narrowing (JSN), both thought to be distinct but integral parts of the disease process. Clinical trial
data have shown JSN to be more closely associated with long-term disability. Previous data on secular changes in radiographic damage has focused on the total rate of progression, typically over <5 years of follow-up, and not reported on differences between the progression of erosions and JSN separately.

Methods: Data from the Early RA Study (ERAS) and Early RA Network (ERAN) cohorts were used to analyse the progression of radiographic scores over the first 9 years of the disease in patients with onset in two time periods (1986–2001 vs 2002–2011). Treatment reflected standard management guidelines at the time of assessments. All 32 outpatient clinics from the ERAS and ERAN collected yearly X-rays of the hands and feet. All 9 centres from the ERAS and 7/25 (28%) centres from the ERAN had X-rays scored using the modified Sharp/van der Heijde (SvdH) method by two trained scorers. Mixed-effects models were used to model the total SvdH, JSN and erosion scores over time. Demographic and baseline clinical variables were controlled for. Sensitivity analysis controlled for DMARD treatment by 12 months.

Results: Of 2701 patients, 1681 (62%) had 6824 X-rays scored over the first 9 years of disease (mean = 4.3). The total SvdH score at baseline for the ERAN was significantly lower than for the ERAS [7.92 vs 15.82, incidence rate ratio (IRR) 0.51, P < 0.001]. The risk of damage significantly increased with each additional year of disease (IRR 1.27, P < 0.001), with the ERAN progressing, on average, at a lower rate compared with the ERAS (4.95 vs 13.5). Sensitivity analysis suggested that the difference was mainly due to treatment, as the effect between cohorts became non-significant when controlling for DMARD use (IRR 0.71, P > 0.05). Similar results were seen for JSN, however, the erosion score at baseline for the ERAN was non-significantly different from ERAS (2.29 vs 3.02, IRR 0.73, P > 0.05). While the ERAS score did progress at a faster rate compared with the ERAN (5.42 vs 1.75), graphical displays demonstrate that the differences in erosion scores between cohorts were only significant at later follow-up.

Conclusion: The results show that the progression of radiographic damage has significantly reduced in recent years, likely due to changes in treatment strategies. Although clinical trials and observational studies have focused on total radiographic scores, our results highlight important differences in the progression of JSN and erosions over the course of the disease, suggesting that both need to be explored in the assessment of treatment response and long-term disease outcomes.

Disclosure statement: The authors have declared no conflicts of interest.
Background: The relationship between radiographic and clinical diagnoses of knee OA has been debated by rheumatologists. Although we have previously demonstrated a significant correlation between these two definitions, the specific findings on clinical examination that relate best to a radiographic diagnosis have not been fully elucidated. We explore the associations between clinical signs on knee examination and both radiological tibiofemoral (TF) and patellofemoral (PF) knee OA in a cohort of older UK adults.

Methods: The study population was taken from the Hertfordshire Cohort Study who were born in Hertfordshire between 1931 and 1939. The current study included 407 individuals recruited between 2010 and 2012. Weight-bearing AP radiographs were taken of both knees to assess for TF OA and lateral semi-flexed knee radiographs were obtained to assess for PF OA. Both were graded for OA severity according to the Kellgren–Lawrence (KL) grading scale with OA defined as a KL grade ≥2. Clinical signs at the knee were ascertained by examination. knees were excluded from the study if they had previously undergone joint replacement. Relationships between clinical examination findings and radiographic OA were assessed using multivariable univariate logistic regression. Statistical significance was defined as a P value <0.05.

Results: A total of 767 knees (383 left and 384 right) were included in the analyses. Of these, 237 (30.5%) had TF OA and 222 (28.5%) had PF OA. The prevalence of each clinical examination finding was as follows: pain on flexion 72 (9.5%), medial TF tenderness 101 (13.2%), lateral TF tenderness 61 (7.9%), joint effusion 32 (4.2%), crepitus 189 (24.8%), bony swelling 94 (12.3%) and varus deformity 167 (21.7%). Joint 8 (1.0%) knees demonstrated warmth, which prohibited inclusion of this finding in statistical models. TF OA was significantly associated with pain on flexion (odds ratio (OR) 8.4 (95% CI 3.0, 23.9), P <0.001), medial TF tenderness (OR 11.1 (95% CI 3.9, 31.5), P <0.001), lateral TF tenderness (OR 7.8 (95% CI 2.6, 23.6), P <0.001), joint effusion (OR 17.3 (95% CI 3.6, 82.0), P <0.001), crepitus (OR 5.7 (95% CI 1.8, 7.8), P <0.001) and bony swelling (mild: OR 5.2 (95% CI 1.6, 16.8), P=0.006; moderate: OR 16.6 (95% CI 2.4, 137.7), P=0.004), but not the presence of varus deformity. PF OA was only significantly associated with joint effusion (OR 10.5 (95% CI 1.8, 61.2), P=0.009) and lateral TF tenderness (OR 3.4 (95% CI 1.0, 11.3), P=0.048).

Conclusion: Clinical examination findings at the knee correlate well with TF OA. PF OA is associated only with lateral TF tenderness and the presence of a joint effusion. The latter is therefore likely to be more difficult to diagnose on clinical examination alone.

Disclosure statement: The authors have declared no conflicts of interest.

Background: Foot OA is a common and disabling condition, yet its clinical course is poorly understood. Using baseline data from the Clinical Assessment Study of the Foot (CASF), we previously examined clusters of joints in the foot with radiographic OA and identified three potential phenotypes of foot OA: no or minimal foot OA, isolated first MTP joint OA and polyarticular foot OA. The aim of this study was to investigate the natural history of these foot OA phenotypes over an 18-month period.

Methods: The CASF is a community-based cohort of adults ≥50 years of age in North Staffordshire, UK. Participants who reported foot pain in a postal health survey and underwent radiographic assessment (weight-bearing anterior–posterior and lateral radiographs of both feet) at baseline were mailed a follow-up questionnaire 18 months later. Changes in descriptive and symptomatic characteristics over 18 months were compared across the three phenotypes. These characteristics included foot pain severity (0–10 numeric rating scale), Rasch-transformed Manchester Foot Pain and Disability Index, 12-item Short Form physical and mental component summary scores, Hospital Anxiety and Depression Scale, frequent foot pain in the past month, dissatisfaction with foot symptoms persisting, hallux valgus and hip and knee pain in the last year. Within-phenotype changes over time were examined using McNemar’s test and paired t-test for dichotomous and continuous variables, respectively. Differences between phenotypes were examined using binary logistic regression for dichotomous outcomes and linear regression for continuous outcomes, using no or minimal foot OA as the reference category. Crude regression models were compared with estimates adjusted for baseline scores alone and also with estimates adjusted for baseline scores, age, gender and body mass index.

Results: Of 533 baseline participants, 478 (89.7%) provided 18 month follow-up data: no or minimal foot OA (n = 307), isolated first MTP joint OA (n = 101) and polyarticular foot OA (n = 70). All three foot OA phenotypes showed within-phenotype reductions in mean foot pain severity over 18 months (P <0.05); no or minimal foot OA (baseline 5.19 (s.d. 2.57), 18 months 4.05 (s.d. 2.62)), isolated first MTP joint OA (4.73 (s.d. 2.57), 4.13 (s.d. 2.79)) and polyarticular foot OA (5.68 (s.d. 2.53), 5.11 (s.d. 2.52)). At 18 months, there was an increased frequency of hallux valgus in the left foot identified in the isolated first MTP joint OA phenotype (fully adjusted odds ratio = 2.96 (95% CI 1.33, 7.12)).

Conclusion: Foot pain severity decreased over 18 months in all three phenotypes, whereas there was little difference between phenotypes. These findings suggest that the 18-month follow-up period may be too short to capture changes that distinguish between-phenotype characteristics indicative of foot OA progression. Replication and longer-term follow-up are required to further describe the natural history of foot OA.

Disclosure statement: T.J.D. has received research funding from Belgrave Medical Practice intercalation Bursary. H.B.M. has received research funding from the National Health and Medical Research Council of Australia Senior Research Fellow (ID 1020025). M.J.T. has received research funding from the NIHR School for Primary Care Research Launching Fellowship. All other authors have declared no conflicts of interest.

Background: OA is a chronic degenerative disorder of multifactorial aetiology characterized by the loss of articular cartilage. Basic calcium phosphate (BCP) and calcium pyrophosphate dihydrate (CPPD) crystals are commonly found in OA joints. These crystals have been found in the synovial fluid of 60% of patients with knee OA and ~90% of a small group of patients with grade 4 OA. Inflammation in OA is frequently secondary to the presence of these crystals and leads to the production of IL-1, an important mediator of cartilage breakdown in OA. Previous studies referred to a slow-acting disease and structure-modifying effects of colchicine in knee OA.

Methods: A randomized, placebo-controlled, double-blind study included 150 patients. Patients were randomly assigned to receive colchicine 0.5 mg plus paracetamol 500 mg in one capsule twice daily.
in the first group (80 patients) and a paracetamol 500 mg capsule twice daily in the second group (70 patients). The efficacy outcome measure was the change in the WOMAC, including the pain, stiffness and physical function subscales.

Results: Both paracetamol and paracetamol plus colchicine groups showed a significant reduction in the pain, stiffness, function and total WOMAC scores at the second visit (after complete treatment regimen) (P < 0.001). At the third visit, 1 month after cessation of treatment, these scores increased again to approximately the baseline value in group 1, while they slightly increased in group 2, hence the differences in these scores between the baseline and third visit were statistically insignificant (P = 0.05) in group 1 but were highly significant in group 2 (P < 0.001).

Conclusion: Both modes of treatment, paracetamol alone or paracetamol plus colchicine, are effective in symptomatic improvement in patients with primary OA of the knee in terms of pain, stiffness, physical function and total WOMAC score. But a greater beneficial symptomatic effect and longer period of action was obtained when colchicine was added to paracetamol rather than paracetamol alone.

Disclosure statement: The authors have declared no conflicts of interest.

O16 MATERNAL GESTATIONAL VITAMIN D SUPPLEMENTATION RESULTS IN GREATER BONE MASS FOR OFFSPRING BORN DURING WINTER MONTHS: THE MAVIDOS MULTICENTRE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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Background: Maternal vitamin D status has been associated with lower bone mass of the offspring in observational studies. We therefore tested whether 1000 IU/day cholecalciferol during pregnancy would result in greater offspring bone mass at birth in a UK multicentre, randomised, double-blind, placebo-controlled trial (MAVIDOS, ISRCTN82927713).

Methods: Pregnant women with serum 25-hydroxyvitamin D (25(OH)D) of 25-100 nmol/l at 12 weeks gestation were randomised to receive 1000 IU cholecalciferol/day or a matched placebo until delivery. Plasma 25(OH)D concentration was measured centrally at 14 and 34 weeks gestation (Liaison, DiaSorin, Saluglia, Italy). Within 2 weeks of birth, offspring whole body bone mineral content (BMC) was assessed by DXA (Discovery, Hologic, Marborough, MA, USA; or IDXA, GE-Lunar, Madison, WI, USA; measurements standardized).

Results: Whole body BMC was non-significantly greater in infants born to mothers supplemented with cholecalciferol [n = 695; mean 61.6 g (s.d. 11.7) vs 60.5 g (11.1), P = 0.21]. However, in a pre-specified analysis, there was an interaction between treatment allocation and birth season (P = 0.04). Infants born in winter (December–February) to mothers randomized to cholecalciferol had a greater BMC than infants of mothers randomized to placebo [63.0 g (s.d. 10.8) vs 57.5 (10.9), P = 0.004], a difference >0.5 s.d.). Similar patterns were observed for bone area and BMD. At 34 weeks gestation, the proportion of women with vitamin D insufficiency [25(OH)D <50 nmol/l] was reduced (16.6% vs 63.5%, P = 0.001) in women who had received cholecalciferol compared with placebo. In the placebo group, 25(OH)D rose from 14 to 34 weeks, irrespective of birth season (P > 0.001). No safety issues were identified.

Conclusion: Maternal supplementation with 1000 IU cholecalciferol during pregnancy increases bone mass in offspring born in winter months and prevents the seasonal decline in 25(OH)D in these mothers. These findings have implications for public health policy relating to antenatal vitamin D supplementation.

Disclosure statement: The authors have declared no conflicts of interest.

O17 THE CLINICAL UTILITY OF NOVEL CLINICAL SIGNS IN CHRONIC PAIN

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Background: Delays in diagnosis occur for patients with complex regional pain syndrome (CRPS) and are detrimental to outcome. Clinical signs such as abnormal finger perception (FP), hand laterality identification, body scheme report (BS) and astereognosis have been reported in patients with CRPS. The aims of this prospective observational cohort study were to validate these novel signs as simple bedside tests, assess their prevalence in chronic pain conditions and prospectively assess their clinical utility in identifying patients with CRPS in a fracture cohort.

Methods: This was a single UK teaching hospital prospective cohort recruiting 313 subjects from healthy volunteers and patients with chronic pain conditions. Subjects were from one of six groups defined by international criteria: chronic upper and/or lower limb CRPS, RA, FM, chronic low back pain, upper or lower limb fracture requiring plaster casting and assessed less than 2 weeks after fracture and healthy volunteers. Confounding neurological disease was excluded. The four clinical signs were performed on each of the groups. The fracture cohort was followed up for 3 years to assess whether chronic pain had developed. Normal cut-offs and intra-/inter-rater variability were assessed with the CRPS group compared with an age- and sex-matched healthy volunteer group. The primary outcome measures were the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio and negative likelihood ratio for the novel signs in the CRPS group compared with the fracture group. The secondary outcome measures were the prevalence of novel signs in the different groups.

Results: Four clinical signs were defined as either positive or negative according to receiver operating curve analysis using healthy volunteers as a control. Intra- and inter-rater variability was assessed and found to be good (κ = 0.65 and 0.84, respectively). The prevalence of the clinical signs in each of the groups is summarized in Table 1, FF and BS occurred more frequently in the CRPS group (P < 0.01). Combining FF and BS resulted in a PPV of 17.4%, and an NPV of 98.7%. The prospective, blinded testing in a fracture cohort (n = 47) identified 7 (14.9%) patients with both positive FF and BS. Three of the seven (42.9%) developed chronic pain, of which one was diagnosed with CRPS. One of 40 patients with negative FF and BS developed chronic pain, which actually was consistent with the severity of injury.

Conclusion: Novel signs are reliable, easy to perform and present in chronic pain patients. FF and BS have significant clinical utility in predicting persistent pain in a fracture group, thereby allowing targeted early intervention.

Disclosure statement: N.S. has received research funding from a Doris Hillier Award (BMA); Comprehensive Local Research Network support costs and the Cambridge Arthritis Research Endeavour. All other authors have declared no conflicts of interest.

<table>
<thead>
<tr>
<th>Category</th>
<th>Finger perception, %</th>
<th>Hand laterality, %</th>
<th>Astereognosis, %</th>
<th>Body scheme, %</th>
<th>Both FF and BS, %</th>
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<tr>
<td>Healthy volunteers (n = 60)</td>
<td>610</td>
<td>1321.6</td>
<td>71.6</td>
<td>915</td>
<td>0</td>
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<tr>
<td>CRPS (n = 49)</td>
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<td>2448.9</td>
<td>1428.6</td>
<td>4591.8</td>
<td>3675.5</td>
</tr>
<tr>
<td>Fibrinogen (n = 50)</td>
<td>2142</td>
<td>1938</td>
<td>1423.3</td>
<td>1728.3</td>
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<tr>
<td>RA (n = 60)</td>
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<td>3558.3</td>
<td>1327.6</td>
<td>1736</td>
<td>510.6</td>
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<tr>
<td>Low back pain (n = 47)</td>
<td>2042.5</td>
<td>1940.4</td>
<td>1123.4</td>
<td>1021.3</td>
<td>36.4</td>
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<tr>
<td>Fracture (n = 47)</td>
<td>2144.6</td>
<td>1736.1</td>
<td>1123.4</td>
<td>1021.3</td>
<td>36.4</td>
</tr>
</tbody>
</table>
Young Investigator Award


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Background: We aimed to present up-to-date fracture incidence data for the UK, stratified by age, sex, geographic location, ethnicity and socio-economic status. In addition, we investigated secular changes to age- and sex-adjusted fracture risk among the UK population aged ≥18 years of age from 1990 through 2012. With marked global differences in fracture rates by population and global shifts towards an elderly demographic, it is vital for health care planners to have an accurate understanding of fracture incidence nationally.

Methods: The Clinical Practice Research Datalink (CPRD) contains anonymized electronic health records for ~8% of the UK population. Information comes from general practitioners and covers 11.3 million people from 674 practices across the UK, demonstrating to be representative of the national population. The study population consisted of all permanently registered individuals ≥18 years of age. Validated data on fracture incidence were obtained from their medical records, as was information on socio-economic deprivation (by Index of Multiple Deprivation (IMD) category), ethnicity and geographic location. Age- and sex-specific fracture incidence rates were calculated, with fracture type categorized according to the International Classification of Diseases, Ninth Revision (ICD-9) classification. To delineate secular trends, site- and sex-specific fracture incidence was calculated by calendar year and linear regression analysis was used to calculate the mean annualized change in absolute incidence.

Results: Fracture incidence rates by age and sex were comparable to those documented in previous studies and demonstrated a bimodal distribution. Substantial geographic heterogeneity in age- and sex-adjusted fracture incidence was observed, with rates in Scotland almost 50% greater than those in London and South East England. The lowest rates of fracture were observed in black individuals of both sexes; rates of fragility fracture in white women ≥50 years of age were 4.7 times greater than in black women. Strong associations between deprivation and fracture risk were observed in hip fracture in men, with a relative risk of 1.3 (95% CI 1.21, 1.41) in IMD 5 (representing the most deprived) compared to IMD 1. In terms of secular changes, although overall fracture incidence was unchanged in both women and men from 1990 to 2012, site-specific trends were evident. Hip fracture incidence was stable among women, but rose in men across the same period (1990–1994: 10.8/10 000 patient-years; 2008–2012: 13.4/10 000 patient-years; P trend annualized change in incidence = 0.002). Clinical vertebral fractures became more common in women (8.9–11.8/10 000 patient-years; P = 0.005) but remained comparable in men (4.6–5.9/10 000 patient-years; P = 0.72).

Conclusion: This study presents robust estimates of fracture incidence across the UK and demonstrates marked differences by region, ethnicity, socio-economic status and time. This will aid decisions regarding allocation of health care provision to populations of greatest need and assist in the design of fracture prevention strategies.

Disclosure statement: The authors have declared no conflicts of interest.
Background: MTX is the recommended first-line treatment for RA. Treatment response to this drug is not universal and non-adherence may partially explain this. The extended Common Sense Self-Regulatory Model of Illness (CS-SRM) is increasingly used in rheumatology because it helps to explain variations in outcome by highlighting relationships between people’s beliefs about their condition and treatments and their coping responses, such as intentional non-adherence. The Perceptions and Practicalities Model (PPM) of adherence further recognizes that patient barriers to adherence need to be addressed in order for optimal medicine adherence to occur. Therefore the rheumatologist has a key role in shaping patients’ illness and treatment beliefs and identifying possible barriers, but very little is known about how rheumatologists address these issues in routine practice. This qualitative study aimed to explore UK rheumatologists’ experiences and practice when commencing MTX with new patients.

Methods: In-depth one-to-one semi-structured telephone interviews were conducted with 15 rheumatologists who prescribe MTX for RA. The sampling strategy ensured collection of data from new and experienced clinicians working in university and district general hospitals. The interview topic guide included rheumatologists’ perceptions of RA, MTX and their role in management of the disease; factors influencing MTX use (e.g. patient alcohol use, family planning) and the information provided to patients. Data were analyzed using principles of framework analysis in which key concepts from CS-SRM and PPM were used to identify clinicians’ beliefs and strategies.

Results: Rheumatologists perceived MTX as their preferred first-line treatment for RA, however, they described a range of psychological, clinical and practical barriers to effective MTX adherence. Patient focused barriers included information overload, emotional preparedness for treatment and patients’ understanding of RA. Rheumatologists provided a range of strategies used to address or minimize barriers. Strategies for less-prepared patients included delaying MTX commencement, referring for nurse-led ‘education’ or counselling. Strategies to improve patients’ understanding of the rationale for MTX included the use of disease-related metaphors. Rheumatologists’ responses to diagnostic uncertainty included selection of an alternative DMARD.

Conclusion: Through in-depth qualitative study of rheumatologists’ experiences in prescribing MTX, a number of new issues were identified that may impact clinical practice. The results suggest the manner and timing of information delivery about MTX affect patient beliefs and adherence intentions. These findings will inform an online survey to further explore the association between rheumatologists’ beliefs and strategies in the management of RA with MTX.

Disclosure statement: The authors have declared no conflicts of interest.
O21 THE IMPACT OF SYMPTOM RECOGNITION ON HELP-SEEKING: A COMPARISON BETWEEN RHEUMATOID ARTHRITIS, BOWEL CANCER AND ANGINA

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Background: RA requires early treatment to reduce the risk of joint damage and disability. However, due to delays at various points in the patient’s journey following symptom onset, this therapeutic window is often missed. Patients themselves are an important source of delay. Help-seeking begins with the patient recognising their symptoms and identifying them as worthy of medical attention. In order to understand symptom recognition by members of the general public, we conducted a qualitative and quantitative study of symptom recognition and its effect on help-seeking, comparing responses to RA symptoms with those of angina and bowel cancer.

Methods: We conducted a qualitative interview study with 31 individuals (16 females) and a postal survey of 1088 members of the general public (without RA); Both studies used vignettes describing the symptoms of RA, bowel cancer and angina. For each vignette, participants made causal attributions and rated the seriousness of the symptoms and the urgency with which they would seek medical help.

Results: Only a small proportion of participants in both studies recognized the symptoms of RA as such, whereas the symptoms of bowel cancer and, to a lesser extent angina, were accurately attributed to those diagnoses. In both studies, the symptoms of bowel cancer and angina were also considered to be more serious than those of RA, and participants indicated that they would seek help faster for the symptoms of bowel cancer or angina compared with the symptoms of RA. Survey data further showed that a correct causal attribution had a positive effect on help-seeking for angina and bowel cancer, but less so for RA symptoms. Furthermore, the relationship between urgency and seriousness ratings for the RA vignette was less strong for either angina or bowel cancer.

Conclusion: Accurate symptom attribution and the perception that symptoms are indicative of a serious underlying condition are both important drivers for rapid help-seeking. However, the finding that the relationship between seriousness and urgency ratings was not as strong for RA, and that an accurate causal attribution did not have such a clear-cut effect on the help-seeking for RA symptoms, suggest that other factors play an important role in driving help-seeking in RA.

O22 EXPLORING THE LIVED EXPERIENCES OF MOTHERS WITH ANKYLOSING SPONDYLITIS

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Background: AS is a chronic, inflammatory condition. Symptoms include joint pain, stiffness and fatigue, with onset often occurring during young adulthood. The onset and complexity of the condition can potentially disrupt plans to start a family and make caring for young children difficult. There is currently limited research that explores the impact of AS on women with young children. The aim of this study was to explore the experiences of mothers with AS, focusing on the physical, psychological and social effects of the condition.

Methods: Ten participants were recruited via an advertisement on the National Ankylosing Spondylitis Society (NASS) website. Their ages ranged between 31 and 42 years, they had been diagnosed with AS for between 2 and 25 years and they had at least one child under the age of 11 years. In-depth, semi-structured interviews were conducted; nine participants were interviewed by telephone and one via Skype. Interviews ranged in length from 22 to 80 minutes. Data were transcribed verbatim and analysed using interpretative phenomenological analysis (IPA).

Results: Three interrelated themes were found: uncertainty of the future, guilt associated with AS and maintaining control. The findings demonstrated the significant impact AS can have on all spheres of life for the participants and their families. Due to the physical limitations and the unpredictability of the condition, individuals were unable to maintain previous levels of activity. This made it difficult to make plans and prevented them from fulfilling their perceived parental role, which resulted in feelings of frustration and guilt. For many participants there was a sense of an ongoing battle with the condition due to their inability to continue with tasks that were previously taken for granted. However, participants described their journeys of adjustment to establish and maintain control and bring a sense of normality back into their lives. This was achieved by modifying daily tasks, such as carrying and changing babies, and increasing activities that they could do with their children that did not exacerbate their pain. Additionally, some participants felt that having AS had influenced their parenting styles and had made them mentally stronger and more compassionate.

Conclusion: This study highlights the issues faced by women with AS who have young children, while acknowledging the positive aspect of parenting while living with the condition. Directing parents with AS to sources of support and providing information on performing tasks related to childcare may help individuals deal with the additional challenges that living with the condition can bring.

Disclosure statement: The authors have declared no conflicts of interest.

ORAL PRESENTATION OF ABSTRACTS

O23 EXPLORING THE DETERMINANTS OF QUALITY OF LIFE IN SYSTEMIC SCLEROSIS

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Background: SSc is a connective tissue disease characterized by vasculopathy, immune activation and fibrosis. The multisystem nature of the disease has a wide-ranging impact on the patient’s physical and psychosocial health. The aim of this study was to explore the interactions between the physical and psychosocial factors on quality of life in people with SSc.

Methods: Structural equation modelling (SEM), a sophisticated statistical modelling technique, was used to explore the multifactorial pathways impacting quality of life (QoL). Potential candidate factors that were included in the SEM were identified through two methods: a literature review with expert consultation and a case-control cross-sectional study of patients with SSc. Physical and psychosocial factors were used for the SEM to predict the impact on QoL as measured using the disease-specific SSc QoL questionnaire.

Results: One hundred and twenty-one patients with SSc were recruited [106 female; median age 59 years (range 25–86)] with a median disease duration of 9 years [interquartile range (IQR) 4–13] and a median modified Rodnan skin score of 2 (IQR 0–5). The model that best explained the factors contributing to the SSc impact on QoL showed complex interrelationships between 11 factors (Table 1). Combined, these factors explained 84% of the impact on QoL, (R² = 0.84) in patients with SSc. General disease factors including physical function, breathing problems and depression had the greatest impact and food problems had a substantial but indirect effect on QoL. A summary of the effects of the factors included in the model is provided in the Table 1.

Conclusion: The results from this model highlight that while systemic manifestations of SSc have a substantial impact on the patients’ QoL, the loss of physical function is the most influential factor on QoL. Depression levels were high, and these were confounded by systemic manifestations of this complex disease.

Disclosure statement: B.A.-P. received research funding from the National Institute of Health Research Clinical Doctoral Research Fellowship. All other authors have declared no conflicts of interest.
### Table 1. Standardized direct, indirect and total effects of the variables as they relate to QoL

<table>
<thead>
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<th>Variable</th>
<th>Direct effect</th>
<th>Indirect effect</th>
<th>Total effect</th>
</tr>
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<tr>
<td>Physical function</td>
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<td>0.640</td>
</tr>
<tr>
<td>Breathing problems</td>
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<tr>
<td>Depression</td>
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<td>Foot function</td>
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<tr>
<td>Foot pain</td>
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<tr>
<td>Raynaud’s phenomenon</td>
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<tr>
<td>General pain</td>
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<tr>
<td>Disease severity</td>
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<td>0.076</td>
<td>0.236</td>
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<td>0.236</td>
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<td>0.233</td>
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<td>Digital ulcers</td>
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<tr>
<td>Gastrointestinal problems</td>
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</table>

### O23 Identifying Care Workers’ Educational Needs About Arthritis

Paul Whybrow¹, Suzanne Moffatt², Lesley Kay², Ben Thompson², Terry Aspray³ and Rachel Duncan³

¹School for Social and Community Medicine, Bristol University, Bristol, ²Institute of Health and Society and ³Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK

**Background:** There are a growing number of older people living in care homes, many of whom experience painful joints and poor mobility. However, there is a paucity of research regarding how staff manage residents with joint pain and disability. We undertook an educational needs assessment in residential care homes.

**Methods:** A qualitative study encompassing focus groups and individual interviews was used to gain the perspectives of care home staff, residents with joint pain and senior staff in the care home sector. Vignettes were used in the focus groups to encourage paid carers to discuss how they managed joint pain on a day-to-day basis and their training and education regarding arthritis.

**Results:** Three care homes were recruited through the National Institute for Health Research Enabling Research in Care Homes (ENRICH) programme: one independent, one from a regional chain and one from a large national chain. Focus groups were conducted in each care home. Individual interviews were conducted with 12 residents and 5 members of senior staff in the care home sector and general practitioners. We found that training practices between the three homes were relatively similar. The findings highlight how important carers are in identifying and managing arthritis in care homes: they are the front line of arthritis care. Caregivers themselves did not appreciate the health significance of their activities and often lacked the confidence necessary to carry them out effectively. To fully meet this aspect of their care roles, they require an awareness of what arthritis is, how to recognize symptoms and how to communicate important information to health professionals. None had received formal training and often lacked knowledge about arthritis. The caregivers themselves expressed a strong desire to learn about arthritis, particularly where this would help them provide better care.

Caregivers’ accounts suggest that an inability to recognize, refer or communicate arthritic problems were underpinned by a lack of confidence. There were mixed attitudes towards formal learning and certification, with caregivers preferring hands-on training and a dislike of online learning. We suggest that the educational needs of caregivers can be met through two distinct training models. First, awareness training should be provided to caregivers to improve confident communication with colleagues, residents and health professionals. Second, a more detailed training package should be considered for senior care staff, who take overall responsibility and who caregivers directly consult for advice. Accounts from senior staff and general practitioners raise important questions about how prospective training will fit with the residential care industry in the UK.

**Conclusion:** Education for caregivers regarding arthritis is lacking, and lags behind diseases such as dementia and diabetes, where specific training is available. We have identified two different approaches to training caregivers that should be considered for development.

**Disclosure statement:** The authors have declared no conflicts of interest.
**ORAL PRESENTATION OF ABSTRACTS**

**CONNECTIVE TISSUE DISEASES AND MUSCLE DISORDERS ORAL ABSTRACTS**

**O25 THE RISK OF PREMATURE DEATH OF BOTH CANCER-ASSOCIATED AND NON-CANCER-ASSOCIATED MYOSITIS IN UK ADULT-ONSET MYOSITIS PATIENTS IS SIGNIFICANTLY INCREASED COMPARED WITH THE GENERAL POPULATION**

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**Background:** Idiopathic inflammatory myopathies (IMs) are a group of chronic autoimmune-mediated conditions associated with an increased incidence of cancer, chronic multi-organ inflammation and premature death. A number of studies have attributed the increased risk of premature death to cancer-associated myositis (CAM). This study aims to quantify the risk of premature death in CAM and non-CAM populations and compare this with the general UK population.

**Methods:** IM patients were identified through the UKMYONET study from 84 UK centres. Patients with adult-onset probable or definite polymyositis (PM) or dermatomyositis (DM) or defined inclusion body myositis (IBM) as per accepted criteria (Bohan/Peter, Griggs, MRC) were recruited and divided into CAM and non-CAM populations. Date and cause of death were collated from the UK Health and Social Care Information Service. Standardized mortality ratios (SMRs) were calculated for the CAM and non-CAM populations (England and Wales 2012 mortality data were used as reference). Kaplan–Meier survival analysis was performed on the surviving patients for both the CAM and non-CAM populations and compared using the log-rank test. Mortality was compared between CAM and non-CAM populations (non-CAM as a reference) using calculated hazard ratios (HRs), adjusted for age, sex, and smoking.

**Results:** A total of 476 non-CAM and 60 CAM patients were recruited (Table 1). There were a total of 4434 person-years of follow-up, with a median follow-up time of 9.7 years (interquartile range 4.5–15.9); 64 (11.9%) died at the time of analysis. The median age of death was similar for the CAM and non-CAM populations. The median time from diagnosis to death was significantly shorter for the CAM population compared with the non-CAM population (P < 0.01). SMRs for both the CAM and non-CAM populations were significantly increased compared with the general population (Table 1). Kaplan–Meier survival estimates for the non-CAM population were significantly higher compared with the CAM population (log-rank P = 0.01). Malignancy (43.8%) and pneumonia (25.0%) were the most commonly reported causes of death for the CAM population, whereas pneumonia (31.3%) and cardiac causes (22.9%) were the most frequent causes for the non-CAM population. Cox regression analysis adjusted for age, gender and smoking revealed that CAM was associated with a significantly increased risk of death compared with the non-CAM population [HR 3.5 (95% CI 1.2, 9.7)].

**Conclusion:** This study is the first to compare the risk of premature death of large UK CAM and non-CAM populations with a verified IIM diagnosis with the general UK population. Mortality rates of both CAM and non-CAM populations are significantly higher than those of the general UK population, which indicates that previously identified excess mortality associated with IIM is not wholly due to cancer but is due to other as yet unidentified factors.

**Disclosure statement:** The authors have declared no conflicts of interest.

**O26 HUMANIZED ANTI-CD20 ANTIBODIES IMPROVE DEPLETION AND RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS WITH RESISTANCE TO RITUXIMAB: RESULTS FROM THE FIRST 100 PATIENTS AT A SINGLE CENTRE**

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**Background:** Rituximab is effective for refractory SLE based on strong evidence of efficacy from open-label evidence. We have observed cases of SLE patients who previously depleted and responded well to rituximab, developing severe infusion reactions, poor B cell depletion and clinical non-response on repeat cycles, suggestive of anti-rituximab antibodies [human anti-chimeric antibodies (HACAs)]. We have therefore treated these patients with alternative, humanized anti-CD20 antibodies. The aim of the study was to evaluate the incidence of secondary non-response to rituximab and the efficacy of switching to humanized anti-CD20 antibodies in SLE.

**Methods:** We conducted a retrospective observational study of the first 100 consecutive SLE patients treated with rituximab in a single centre between September 2004 and September 2015 (total follow-up of 445 patient-years). Each cycle of rituximab consisted of 2 × 1000 mg infusions repeated on clinical relapse. Patients who demonstrated features of HACAs [i.e. infusion reaction >24-hours after the second infusion with <50% B cell depletion as analysed using highly sensitive flow cytometry (HSFC)] were treated either with 2 × 1000 mg ocrelizumab or 2 × 700 mg ofatumumab. Response was defined as improvement to one or fewer persistent BILAG B and no A/B flares.

**Results:** Ninety-four patients with complete response data at 6 months were studied (87 female, median age 38 years (range 20–80), median disease duration 6 years (IQR 2–10)); 57 (61%) were on concomitant immunosuppressant. The common manifestations (with at least a BILAG B) included mucocutaneous (49%), musculoskeletal (46%), neuropsychiatric (35%) and renal (30%). In cycle 1 (C1), 81/94 (86%) achieved a BILAG response. One patient with severe SLE (prolonged hospital admission) and a C1 non-responder in whom B cell had not depleted was re-treated with rituximab but subsequently developed HACAs. She was treated with ocrelizumab, resulting in enhanced depletion and biological response (i.e. normalization of anti-dsDNA), but died 6 months later with multi-organ failure. Of the C1 responders, 63 patients received rituximab on

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**O25 TABLE 1. Demographics and mortality data for the total IIM population divided by CAM status**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Total (n = 536)</th>
<th>CAM (n = 60)</th>
<th>Non-CAM (n = 476)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at symptom onset, years, mean (IQR)</td>
<td>52.0 (14.7)</td>
<td>58.9 (13.9)</td>
<td>51.1 (14.7)</td>
</tr>
<tr>
<td>Deaths, n (%)</td>
<td>279 (51.8)</td>
<td>279 (46.5)</td>
<td>279 (51.8)</td>
</tr>
<tr>
<td>Age at death, years, mean (IQR)</td>
<td>64 (11.9)</td>
<td>64 (11.9)</td>
<td>64 (11.9)</td>
</tr>
<tr>
<td>Time between symptom onset and death, years, mean (IQR)</td>
<td>10.9 (4.3–16.0)</td>
<td>11.9 (6.3–18.9)</td>
<td>11.2 (6.6–16.8)</td>
</tr>
<tr>
<td>Follow-up years, median (IQR)</td>
<td>9.7 (4.5–15.9)</td>
<td>9.7 (4.5–15.9)</td>
<td>9.7 (4.5–15.9)</td>
</tr>
<tr>
<td>Survival probability, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 year</td>
<td>88</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>5 years</td>
<td>98</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>10 years</td>
<td>95</td>
<td>95</td>
<td>95</td>
</tr>
<tr>
<td>SMR (95% CI)</td>
<td>3.4 (2.2, 5.1)</td>
<td>11.5 (4.6, 23.7)</td>
<td>2.7 (1.6, 4.3)</td>
</tr>
</tbody>
</table>

CAM: cancer-associated myositis; SMR: standardized mortality ratios.
clinical relapse. Of these, 54/63 (86%) responded and 8/9 (13%) were non-responders due to HACAs. Of the nine cycle 2 non-responders, three patients were treated with ocrelizumab, resulting in complete depletion in two, and all responded. One was treated with ofatumumab and had partial depletion and stabilization of renal function (chronic kidney disease stage 4 prior to therapy). In cycle 3, one patient had HACAs and was treated with ofatumumab, resulting in depletion and response. Details of secondary non-responders who have received humanized anti-CD20 antibodies are described in Table 1.

**Conclusion:** Following initial response to B cell depletion therapy with rituximab, ~15% of patients lose response in the subsequent cycle, mostly due to HACAs. Switching to alternative humanized anti-CD20 antibodies improved depletion and clinical response in rituximab-resistant patients in this largest case series to date. Humanized anti-CD20 may be more appropriate than rituximab in SLE.

**Disclosure statement:** M.Y. has received research funding from Roche and GSK and research funding from BMS, Abbott, Pfizer, MSD, Roche and UCB. E.M.V. has received honoraria from Roche and GSK and research funding from NIH, Roche and GSK. All other authors have declared no conflicts of interest.

**O26 Table 1.** Details of secondary non-responders who received humanized anti-CD20 antibodies

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Previous rituximab cycle</th>
<th>Rituximab cycle with secondary non-response</th>
<th>First alternative anti-CD20 antibody cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>BILAG domains</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>0/5 = A</td>
<td>0/5 = A</td>
<td>0/5 = A</td>
</tr>
<tr>
<td>Neuropsychiatric</td>
<td>2/5 = A</td>
<td>0/5 = A</td>
<td>0/5 = A</td>
</tr>
<tr>
<td>Renal</td>
<td>0/5 = B</td>
<td>0/5 = B</td>
<td>0/5 = B</td>
</tr>
<tr>
<td>B cell n x 10^9 cells, median</td>
<td>0.0002 0.00020 0.00423 0.00051 0.0184 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phagocytic</td>
<td>0.0203 0.0303 0.0103 0.0075 0.0029 0.0005</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**O27 Table 1.** Selected efficacy end points in patients with active SSc^a

<table>
<thead>
<tr>
<th>Week 24</th>
<th>Week 48</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCZ</td>
<td>Placebo</td>
</tr>
<tr>
<td>mRSS, adjusted mean</td>
<td>^1</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-2.70 (-5.85, 0.45)</td>
</tr>
<tr>
<td>HAQ-DI, adjusted mean</td>
<td>^3</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>0.020 (-0.186, 0.225)</td>
</tr>
<tr>
<td>Patient global VAS^3</td>
<td>-2.33 (-4)</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>-3.85 (-13.04, 5.34)</td>
</tr>
<tr>
<td>FACIT-fatigue score^6</td>
<td>2.68 (-42)</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>1.43 (-2.97, 5.82)</td>
</tr>
<tr>
<td>Patients with absolute decrease &gt;10% in IFV/C, %</td>
<td>43 (n = 30)</td>
</tr>
<tr>
<td>Patients with absolute decrease &gt;10% in %FVC, %</td>
<td>3 (n = 30)</td>
</tr>
</tbody>
</table>

**O27 SUBCUTANEOUS TOCILIZUMAB IN ADULTS WITH SYSTEMIC SCLEROSIS: 24 AND 48 WEEK SAFETY AND EFFICACY DATA FROM THE FASSCINATE TRIAL**

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**Background:** Interleukin-6 (IL-6) appears to play a key role in the pathogenesis of SSC, a debilitating disease with limited treatment options.

**Methods:** A double-blind, placebo-controlled, phase 2, proof-of-concept study of the efficacy and safety of the IL-6 receptor inhibitor tocilizumab (TCZ) (weekly s.c. injection; TCZ 162 mg vs placebo for 48 weeks) in patients >18 years of age with active SSc. The primary end point was a mean change in the modified Rodnan skin score (mRSS) from baseline at week 24. Change in the mRSS at week 48, patient-reported outcomes (PROs) and pulmonary function (week 48) were exploratory measures.

**Results:** A total of 87 patients (43 TCZ, 44 placebo) were enrolled (mean mRSS: TCZ 26 (IQR 7.2), placebo 26 (IQR 5.9)). At week 24, a favourable effect of TCZ vs placebo on mRSS was noted (Table 1). With continuing treatment there was a numerically larger change in mRSS (Table 1). Higher proportions of TCZ vs placebo patients had mRSS improvement from baseline of ≥20% (40% vs 27%), ≥40% (21% vs 7%) or ≥60% (12% vs 0). Between weeks 24 and 48 there were numerically greater improvements in the TCZ arm for PROs (HAQ DI-Index (HAQ-DI), patient global assessment visual analogue scale and the Functional Assessment of Chronic Illness Therapy fatigue scale (Table 1) and significantly more patients had HAQ-DI improvement ≥0.22 at week 48 (TCZ 28% vs placebo 7% (P = 0.01)). Fewer TCZ vs placebo patients showed a decline in the percent predicted vital capacity (%FVC; 57% vs 84%) and a >10% absolute decrease in %FVC (10% vs 23%) at week 48 (Table 1). Adverse events (AEs)/severe AEs occurred in 98%/33% of TCZ and 91%/34% of placebo patients. By week 48, there were four deaths.
Treatment with TCZ resulted in consistent, but not statistically significant, improvements in skin sclerosis (mRSS) at weeks 14 and 48 and in PROs at weeks 24 and 48. A trend towards less FVC decline with TCZ persisted at week 48. Observed AEs were consistent with SSc complications and the safety profile of TCZ. Overall, this proof-of-concept study supports further evaluation of TCZ in patients with SSa.

Disclosure statement: C.P.D. has received consultancy fees from Roche, Actelion, GlaxoSmithKline and research funding from Roche and Novartis. D.K. has received consultancy fees from Actelion, Bayer, BMS, EMD Serono, InterMune, Biogen Idec, Genentech/Roche, Cytori, Lycera, Sanofi-Aventis/Genzyme and GSK and research funding from Actelion, Bayer, BMS, EMD Serono, Gilead, InterMune, NIH/NIAID, NIH/NIAID, Scleroderma Foundation and Pulmonary Hypertension Association. A.J. is an employee of Genentech and a shareholder of Roche. J.M.V.L has received consultancy fees from Pfizer, Tigenix, Novartis, Roche and Eli Lilly. S.C. was an employee of Genentech at the time of the study. H.S. is an employee and shareholder of Roche. J.E.P. has declared no conflicts of interest.

O28 LARGEST GENERAL STUDY TO DATE IN SPORADIC INCLUSION BODY MYOSITIS CONFIRMS THE HUMAN LEUKOCYTE ANTIGEN AS THE MOST ASSOCIATED REGION AND SUGGESTS A ROLE FOR C-C CHEMOKINE RECEPTOR TYPE 5

Simon Rothwell1, Robert G. Cooper2, Ingrid E. Lundberg3, Peter K. Gregersen1, Michael G. Hanna2, Pedro M. Machado4, John Bowes1, Michael F. Seidlin5, Yvonne Venglovsky6, Katja Danko7, Vidya Linsey8, Albert Selva-O’Callaghan9, Hazel Plait1, Duyind Molberg10, Oliver Beneviste11, Timothy R. D. J. Radstake12, Andrea Doria13, Jan De Bleeker14, Boel De Paepe15, Christopher I. Amos17, William E. Oller18, Leonid Pabyuk19, Annette T. Lee20, Hector Chinoy21 and Janine A. Lamb1

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Background: Sporadic inclusion body myositis (iIBM) is characterized by a combination of inflammatory and degenerative changes affecting muscle in patients >50 years, typically leading to weakness and muscle wasting of the quadriceps and finger flexor muscles. Innate immune-mediated mechanisms are thought to be characterized by inflammatory cell infiltrates in muscle biopsies and a newly described autoantibody to cytosolic 5′-nucleotidase 1A. While the primary cause of IBM disease is unknown, genetic factors may influence disease susceptibility. We have conducted the largest genetic association study to date in iIBM using the Immunochip, a custom genotyping array, to investigate associations with immune-related genes in iIBM.

Methods: We genotyped 252 iIBM cases of Caucasian descent fulfilling Griggs/European Neuromuscular Centre/Hilton–Jones criteria. Samples were collected from 11 countries through the Myositis Genetics Consortium (MYOGEN). Data from cases and 1008 matched Caucasian control samples were genotyped. A stringent quality control analysis, performed was analysis in PLINK version 1.07 using logistic regression, adjusting for the top 10 principal components. Classical human leukocyte antigen (HLA) alleles and amino acids were imputed using SNP2HLA.

Results: Analysis of 104,636 single nucleotide polymorphisms (SNPs) confirmed the human leucocyte antigen as the most strongly associated region (P = 3.58 × 10−5). Forty-nine SNPs within the chr3p21.21 locus reached our suggestive level of significance (P = 2.25 × 10−4). Chr3p21.21 is an established risk locus for autoimmune disease and associated SNPs in iIBM are in linkage disequilibrium with those reported in JIA. SNPs in the region were expression quantitative trait loci (eQTL) for the expression of chemokine (C-C motif) receptor 5 (CCR5), an important chemokine receptor expression affecting the migration of T cells. HLA imputation confirmed HLA-DRB1*03:01 as the most associated allele (P = 5.77 × 10−35), however, the strongest association was with amino acid positions 26 (P = 5.22 × 10−35) and 11 (P = 3.80 × 10−15) of the HLA-DRB1 molecule.

Conclusion: This is the largest genetic association study to date in iIBM. The data confirm that HLA is the most strongly associated region and identifies novel amino acid associations that may explain the risk in this locus. A novel suggestive association within the chr3p21.21 locus indicates potential genetic overlap with other autoimmune diseases.

Disclosure statement: The authors have declared no conflicts of interest.

O29 PEGLATED RECOMBINANT DOMAIN I OF P-2-GLYCOPROTEIN I, A POTENTIAL THERAPEUTIC AGENT FOR ANTI-PHOSPHOLIPID SYNDROME, FULLY RETAINS ITS ABILITY TO INHIBIT BINDING OF IGG OR IGA ANTIBODIES FROM PATIENTS WITH ANTI-PHOSPHOLIPID SYNDROMES TO P-2-GLYCOPROTEIN GPI IN VITRO

Thomas C. R. McDonnell1, Charis Pericleous1, Ian Giles2, Yiannis Ioannou3 and Aniruz Rahman1

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Background: Antiphospholipid syndrome (APS) is an autoimmune rheumatic disorder in which antiphospholipid antibodies (aPLs) cause clinical events, including vascular thrombosis (VT) and pregnancy morbidity (PM). The key antigen in APS is β-2-glycoprotein I (β2GP), which consists of five domains. The N-terminal domain (DI) carries the main immunodominant epitope. We previously showed that recombinant human DI blocks the binding of serum IgG from patients with APS (APS-IgG) to whole β2GP in ELISA and inhibits thrombosis induced by APS-IgG in a mouse model. A modified variant containing two point mutations [DI(ΔS,D9G)] was a stronger inhibitor than wild-type DI. Small molecules such as DI require new mechanism of action as therapeutic agents. Chemical addition of polyethylene glycol (PEGylation) is one such modification, which increases half-life and reduces immunogenicity. Conversely, PEGylation can also reduce binding to ligands/receptors and biological activity. Larger PEG sizes may enhance half-life more but may reduce activity more. Therefore, we investigated whether PEGylated DIs of various sizes retain the ability to inhibit β2GP–binding of serum IgG and IgA from patients with APS.

Methods: DI was expressed in E. coli and PEGylated on its disulphide bonds. Three different PEGylated variants carrying 20kDa, 30kDa and 40kDa PEG were produced, as well as non-PEGylated DI. Serum samples from four patients with APS, all fulfilling the Sydney classification criteria, were tested in an inhibition ELISA. This ELISA tests for binding of IgG or IgA to β2GP in the presence or absence of 100 μg/ml of inhibitor. Results are expressed as the retained binding in the presence of each inhibitor compared with binding to β2GP without inhibitor (defined as 100%).

Results: Figure 1 shows results for IgG. For IgG, aβ2GP and non-PEGylated variants of DI significantly inhibit binding to β2GP by between 43–55% (P < 0.05). Figure 2 shows results for IgA. For IgA, aβ2GP PEGylation and non-PEGylated variants of DI significantly inhibit binding to β2GP by between 40–55% (P < 0.005). There were no significant differences between results for the different DI variants, showing that PEGylation does not alter the inhibitory capacity of DI in this binding assay. Similarly, we showed that DI (ΔS,D9G) carrying a 20Da PEG inhibits binding to β2GP serum IgG (P < 0.01) and IgA (P < 0.005) from patients with APS. PEG alone shows <10% inhibition.
Conclusion: PEGylation of DI and DI (D8S,D9G) allows retention of their ability to inhibit the binding of both IgG and IgA from APS patients to μGPI, an important step in its potential development as a therapeutic agent.

Disclosure statement: T.C.R.M. is an inventor on the patent for PEGylated Domain I. C.P. is an inventor on the patent for PEGylated Domain I. I.G. is an inventor on the patent for PEGylated Domain I. Y.I. is an inventor on the patent for PEGylated Domain I. A.R. is an inventor on the patent for PEGylated Domain I.

Young Investigator Award O30 THE SCLERODERMA FIBROTIC SCORE: A USEFUL SERUM TEST IN THE DIAGNOSIS OF EARLY SCLERODERMA

Jelena Blagojevic1,2, Giuseppina Abignano1,2, Elisabeth M. A. Hensor1,2, Serena Guiducci3, Silvia Bellando Randone3, Cosimo Bruni2, Gemma Lepri2, Eloisa Romano3, Celestina Mazzotta1, Nicola J. Calder4, Michael P. Messenger4, Maya Buch1,2, Paul Emery1,2, Marco Matucci-Cerinic1 and Francesco Del Galdo1,2

1Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, UK; 2NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals NHS Trust, Leeds, UK; 3Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Florence, Italy; and 4NIHR Diagnostic Evidence Co-operative, Leeds Teaching Hospitals NHS Trust, Leeds, UK

Background: The very early diagnosis of SSC is still a clinically unmet need. VEDOSS (Very Early Diagnosis of Systemic Sclerosis) is an international study aimed at identifying, in patients at risk of SSC, factors predictive of progression and internal organ involvement. Recently we demonstrated that the enhanced liver fibrosis (ELF) serum test and its components (PIIINP, TIMP-1 and HA) correlate with the severity of skin and lung fibrosis in SSC. Nevertheless, its value in aiding early diagnosis of disease has still not been investigated.

Methods: Biosamples from 114 VEDOSS and 67 definite SSC patients fulfilling ACR/EUSTAR SSC 2013 classification criteria (33 diffuse and 34 limited SSC) were obtained from two centres. Serum concentrations of ELF components were determined on a Siemens Advia Centaur platform. Logistic regression analysis of the results was performed employing classification of SSC as a state variable.

Results: Among the 114 patients enrolled, 30 had primary RP, 54 were classified as VEDOSS (RP, puffy fingers, ANA, SSC-specific auto-antibodies or SSC-specific capillaroscopic pattern) not fulfilling 2013 ACR/EULAR criteria (score < 9) and other 30 VEDOSS patients fulfilled new ACR/EULAR criteria despite the lack of any sign of skin and internal organ involvement. ELF and its components correlated with age (P < 0.05 for all). Logistic regression analysis using ELF variables identified a specific algorithm (SSc score) ranging from -3.92 to 5.77. The score showed good ability to discriminate between patients with definite SSC and VEDOSS patients already classified as SSC when compared with VEDOSS patients not yet classified as SSC (area under the receiver operating characteristics curve (AUC) 0.853 (95% CI 0.797, 0.910)). Within the VEDOSS database, patients fulfilling SSC classification criteria had an average score of 0.44 vs -0.86 for patients not fulfilling the criteria, even after correcting for age (P = 0.026). Furthermore, the SSc score showed a fair ability to discriminate between the two groups (AUC = 0.756 (95% CI 0.648, 0.866)). Moreover, definite SSC patients had significantly higher SSc scores compared with VEDOSS patients classified as SSC, confirmed after age correction (P < 0.000). No difference in the SSc score has been observed between primary RP and VEDOSS patients not yet classified as SSC.

Conclusion: Our data indicate that the SSc score is a simple test that can be used in patients with RP to aid in the early diagnosis of scleroderma. Furthermore, the identification of VEDOSS patients with high SSc scores even in the absence of internal organ involvement can be used in intervention trials aimed at preventing further disease progression.

Disclosure statement: The authors have declared no conflict of interest.
PRIMARY CARE ORAL ABSTRACTS

O31 INFLUENCE OF JOINT PAIN ON THE INCIDENCE AND PROGRESSION OF DISABILITY IN THE VERY OLD: THE NEWCASTLE 85+ STUDY
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1Institute of Health and Society, 2Institute of Cellular Medicine and
3Institute for Cellular and Molecular Biosciences, Newcastle University, Newcastle upon Tyne, UK

Background: Establishing modifiable predictors of disability in the very old is important if we are to keep people functioning independently. There are limited longitudinal studies on the association of musculoskeletal pain with incidence and progression of disability. This analysis aimed to determine the effect of joint pain at 85 years on the subsequent incidence and progression of disability.

Methods: The Newcastle 85+-study is a prospective community-based longitudinal observational cohort study. The population is a single-year birth cohort of people born in 1921 who turned 85 years of age during the year of 2006. Data were collected through a general practitioner records review and a multidimensional health assessment at baseline, 18, 36 and 60 months. The incidence and progression of disability was measured using self-reported measures.

Results: The study included a total of 793 participants (mean age 85.5 years (s.d. 0.44), 61% female, 8.5% living in institutional care). At baseline, 45.1% reported joint pain ≥15 days in the last month, 17.9% reported ≤15 days of joint pain and 37.0% reported no joint pain; 163 participants were disability free at baseline. Incident disability, pain occurring on ≥15 days in the last month at baseline, predicted incident disability, including an increased risk of total disability (sum of 17 items) [odds ratio (OR) 4.35 (95% CI 1.41, 13.44)]; activities of daily living (ADLs) [OR 7.15 (95% CI 2.38, 21.47) and instrumental ADLs (IADLs) [OR 4.14 (95% CI 2.40, 8.20)]. There was also an increased incidence of difficulty with individual mobility items: going up and down steps/stairs [OR 3.90 (95% CI 2.56, 6.07)] and going 400 yards [OR 7.07 (95% CI 4.06, 12.33)]. All results remained significant after adjusting for confounding factors (age, sex, BMI, depressive symptomatology, disease burden and physical activity). Disability progression was associated with pain ≥15 days in the last month at baseline, a greater number of painful joints at baseline and greater disability progression. Neither disability incidence nor progression was affected in participants reporting pain <15 days in the last month.

Conclusion: Within a group of very old individuals, we found that joint pain on most days of the month is associated with both an increase in incident disability and worsening of existing disability over 5 years of follow-up. This occurs irrespective of other co-morbid conditions. Identifying these individuals and targeting treatment may maintain independence and quality of life. Accurate assessment of joint pain and subsequent optimal management is the goal we strive for in the very old. Research is now needed to address how we achieve this, but it would appear a proactive approach with advanced care planning is required.

Disclosure statement: The authors have declared no conflicts of interest.

O32 DOES THE ADDITION OF A VOCATIONAL ADVICE SERVICE TO BEST CURRENT PRIMARY CARE IMPROVE WORK OUTCOMES IN PATIENTS WITH MUSCULOSKELETAL PAIN AND SICKNESS ABSENCE (SWAP) CLUSTER RANDOMIZED TRIAL (ISRCTN 52269669)
Gwennllian Wynne-Jones, Majid Artus, Annette Bishop, Sarah A. Lawton, Martyn Lewis, Chris Main, Gail Sovwden, Simon Wathall, Kim Burton, Daniele van der Windt, Elaine M. Hay, Ruth Beadmore and Nadine Foster
Arthritis Research UK Primary Care Centre, Keele University, Keele, UK

Background: Musculoskeletal pain is a common cause of work absence, and early intervention is advocated to prevent longer-term absence. The objective of the SWAP trial was to establish the effect of adding a brief early access vocational advice service to best current care compared with best current care alone for adults consulting with musculoskeletal pain in primary care.

Methods: A cluster randomized controlled trial in six UK general practices was performed and patients were randomized to an intervention arm (n = 3) or a control arm (n = 3). Patients were eligible if they were ≤18 years, consulting with musculoskeletal pain and were absent from work ≤6 months or struggling at work. Intervention practices were able to refer patients to a new brief intervention provided by a vocational advisor located in the practice. Control practices provided best current care. The primary outcome was the number of days off work over 4 months. Secondary outcome measures included self-reported time off from work, return-to-work self-efficacy (RTW-SE), current pain intensity (0–10 rating scale) and bothersomeness (1–5 rating scale) at 4 and 12 months follow-up. Analysis was by intention-to-treat adjusted for the following prespecified covariates: age, gender and practice size. Zero-inflated negative binomial regression accounting for clustering by general practitioner (GP) was used to evaluate days off from work. Mixed models taking into account GP clustering and repeated measures were used to evaluate clinical outcomes.

Results: A total of 348 participants (162 intervention arm, 186 control arm) were recruited. Baseline characteristics were comparable between arms; 4 month follow-up rates were 72% (intervention) and 79% (control). Participants in the intervention arm had significantly fewer days off from work over 4 months (mean 9.3 days (s.d. 21.7) compared with the control arm [mean 14.4 (s.d. 27.7); adjusted incidence rate ratio (IRR) 0.51 (95% CI 0.26, 0.99), P = 0.048]. This difference was predominantly due to fewer GP-certified absent days [mean 8.4 days (s.d. 21.0)] in the intervention arm compared with the control arm [mean 13.5 days (s.d. 27.5)]. Of the secondary outcome measures at 4 months, only RTW-SE was significantly different between arms [mean difference 11.4 (95% CI 2.97, 19.8), P = 0.008]. The 12-month follow-up rates were 68% (intervention) and 70% (control). Participants in the intervention arm had fewer days off from work, but not significantly so [mean 10.3 days (s.d. 40.5), compared with the control arm [mean 24.3 (s.d. 50.7); adjusted IRR 0.65 (95% CI 0.34, 1.25), P = 0.198]. Of the secondary outcomes at 12 months, only RTW-SE [mean difference 8.91 (95% CI 0.04, 17.8), P = 0.049] was significantly different between groups.

Conclusion: The addition of a brief early access vocational advice intervention to best current primary care for adults consulting with musculoskeletal pain is likely to lead to fewer days absent over the first 4 months and may improve return-to-work self-efficacy in patients with musculoskeletal conditions who have work difficulties.

Disclosure statement: The authors have declared no conflicts of interest.

O33 RISK OF POLYMYALGIA-ONSET INFLAMMATORY ARTHRITIS IN PATIENTS INITIALLY DIAGNOSED WITH POLYMYALGIA RHEUMATICA
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Background: Previous studies from secondary care have suggested that inflammatory arthritis develops in up to 20.2% of patients with PMR within 12 months of disease onset. However, many cases of PMR are exclusively managed in the community and the true risk of subsequent inflammatory arthritis is unknown. This study aimed to determine the rate at which new cases of PMR transform to inflammatory arthritis in a population sample and to assess whether clinical factors at presentation might identify those at risk of subsequent inflammatory arthritis.

Methods: The study was conducted in participants in the European Prospective Investigation into Cancer and Nutrition (EPIC) Norfolk. The cohort was established with 30,641 healthy volunteers ages 40–79 years between 1993 and 1997, recruited from 35 general practice sites across Norfolk, UK. New cases of PMR diagnosed on or after 1 Wednesday 27 April 2016, 14:30–16:00
January 2002 were identified by electronic record linkage, International Classification of Diseases, Tenth Revision codes and follow-up questionnaires. Inflammatory arthritis was identified from hospital records review. The end date for follow-up was 31 January 2015. Survival analysis (accounting for censoring from loss to follow-up and death) was used to calculate the cumulative risk of inflammatory arthritis.

Results: A total of 298 incident diagnoses of PMR (72.5% female) were identified in the cohort. The median age at diagnosis was 75.6 years. The maximum follow-up period was 13 years (median 4.82). During 1673.6 person-years of follow-up, 31 (10.4%) participants (19 female) were diagnosed with inflammatory arthritis by a rheumatologist. The cumulative risk of new-onset inflammatory arthritis at 1, 2, 5 and 10 years was 3.9% (95% CI 3.2, 6.9), 7.4% (4.6, 11.2), 9.7% (6.6, 14.0) and 16.0% (10.6, 23.8), respectively. Males were at greater risk of developing inflammatory arthritis compared with females in the first 5 years [cumulative risk for males at 1 and 5 years: 8.9% (95% CI 4.4, 17.8) and 15.7% (9.2, 26.0), respectively; cumulative risk for females: 2.0% (95% CI 0.8, 5.2) and 7.3% (4.3, 12.3)]. There was a trend towards a greater risk of inflammatory arthritis in those with a younger age at PMR onset. The majority of participants with inflammatory arthritis were RF negative (72.7%).

Conclusion: These are the first estimates from a population study that assessed the risk of inflammatory arthritis developing after a diagnosis of PMR. Patients with PMR are at sustained risk of developing inflammatory arthritis up to 10 years after diagnosis. The data suggest that males and those of younger age are at a greater risk. The finding that 10.4% of participants with PMR at baseline subsequently develop inflammatory arthritis suggests a subset of patients with PMR could benefit from the early use of DMARDs.

Disclosure statement: M.Y. has received travel expenses from AbbVie and Eli Lilly. All other authors have declared no conflicts of interest.

O34 INABILITY TO WORK TO OLDER AGES IS STRONGLY ASSOCIATED WITH MARKERS OF PHYSICAL FUNCTIONING AND FRAILTY: FINDINGS FROM THE HEALTH AND EMPLOYMENT AFTER 50 (HEA5) STUDY

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Background: Changes in medical care and lifestyles have led to a growing population of older people. European governments, including that of the UK, have responded to this by making changes to the traditional age of retirement, aiming for people to continue to remain in productive work to an older age. We set out to investigate among a cohort of older workers those factors that contribute to health-related job loss prior to the traditional age of retirement, exploring opportunities for intervention and prevention, and to determine if people can continue to work to older ages despite chronic long-term conditions such as arthritis.

Methods: The Health and Employment After Fifty (HEA5) study is a cohort study of people 50–64 years of age recruited from general practices across England. All participants completed a postal questionnaire inquiring about demographics, health and well-being and employment history.

Results: In total, 8134 people have been included in the cohort. At baseline, 32% of people were not in work: 1 in 3 had left their last job for a health-related reason and 1 in 12 was receiving an ill-health pension. Premature health-related job loss was highly significantly associated with weakness of grip, slow walking speed, exhaustion, low levels of physical activity and unintentional weight loss (the five components of the Fried frailty index). In total, 4% of the sample fulfilled the Fried criteria for frailty (three or more Fried criteria). Those with frailty had 10.5 times more likely to have left work (odds ratio [OR] 10.5 (95% CI 7.86, 14.11)) and 30 times more likely to have left work for a health reason [OR 29.57 (95% CI 22.7, 38.6)]. Frailty was associated with markers of deprivation, including difficulty in managing work for a health reason [OR 29.57 (95% CI 22.7, 38.6)], gastric bleeding [HR 1.35 (95% CI 1.17, 1.54)], accidental poisoning [HR 3.10 (95% CI 1.38, 6.97)], incident depression [HR 1.39 (95% CI 1.35, 1.51)], incident osteoporosis [HR 1.59 (95% CI 1.46, 1.73)], incident opioid addiction [HR 2.82 (95% CI 1.81, 4.41)] and death from any cause [HR 1.23 (95% CI 1.15, 1.32)]. For each of these adverse events, the HR remained significant but decreased over the 5 years of follow-up. Females and those with higher numbers of co-morbid conditions at baseline appeared to be at the greatest risk.

Conclusion: There appears to be a significant association between long-term opioid use and adverse events in the UK. Females and patients with high co-morbidity appeared to be more commonly affected. Though confounding by indication will influence this, the risks of adverse events appear higher in the first year of use. Doctors need to tailor long-term opioid use to the patient’s risk profile and adopt a policy of regular review in the early stages of treatment.

Disclosure statement: The authors have declared no conflicts of interest.

O35 LONG-TERM OPIOID PRESCRIBING AND THE RISK OF ADVERSE EVENTS IN PATIENTS WITH MUSCULOSKELETAL PAIN: A COHORT STUDY

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Background: Each year >20% of adults in the UK consult in primary care with musculoskeletal pain. Increasingly they are prescribed opioid analgesics. In the USA, long-term use has been associated with adverse events, including substance abuse, self-poisoning and bone fractures. It is unclear if this is the case in the UK, because of differences in the health care systems and prescribing guidelines between the two countries. Our aim was to assess whether using long-term opioid analgesics for musculoskeletal pain is related to increased risks of adverse events and to identify characteristics of patients who might be at greatest risk.

Methods: This was a cohort study of adults ≥18 years of age prescribed opioids for musculoskeletal pain undertaken in the UK Clinical Practice Research DataLink (190 practices). Patients prescribed long-term opioids (three or more opioid prescriptions within 90 days) following 6 months without opioid use were matched by age, gender and practice to patients newly prescribed short-term opioids (fewer than three opioid prescriptions). Cox proportional hazards models were used to compare the risks for adverse events between the two groups, with adjustment for confounding factors including NSAID use, ethnicity, geographical region, deprivation level and number of other co-morbid conditions. Hazard ratios (HRs) with 95% CIs for recorded adverse events (major trauma, falls, gastric and non-gastri bleeding, accidental and non-accidental self-poisoning, suicide/self-harm, incident anaemia, osteoporosis, opioid addiction and death) were calculated for the first year of long-term opioid use and for the 5-year follow-up.

Results: There were 206594 adults newly prescribed opioids [41% male; median age 60 years (interquartile range 46–72) at baseline]. Long-term opioid users were more likely to have adverse events in the first year of follow-up, except for suicide/self-harm: major trauma (hazard ratio [HR] 1.22 (95% CI 1.16, 2.29)), falls (HR 1.18 (95% CI 1.13, 1.23)), gastric bleeding (HR 1.35 (95% CI 1.17, 1.54)), accidental poisoning (HR 3.10 (95% CI 1.38, 6.97)), incident depression (HR 1.39 (95% CI 1.35, 1.51)), incident osteoporosis (HR 1.59 (95% CI 1.46, 1.73)), incident opioid addiction (HR 2.82 (95% CI 1.81, 4.41)) and death from any cause (HR 1.23 (95% CI 1.15, 1.32)). For each of these adverse events, the HR remained significant but decreased over the 5 years of follow-up. Females and those with higher numbers of co-morbid conditions at baseline appeared to be at the greatest risk.

Conclusion: Long-term opioid use is associated with increased risks of adverse events in the UK. Patients with high co-morbidity appeared to be more commonly affected. Further research is required to determine if these adverse events are causative or whether the use of opioids is following the clinical problem. Nine of these adverse events were selected for further analysis.

Disclosure statement: The authors have declared no conflicts of interest.

O36 THE INCREASING INCIDENCE OF SEPTIC ARTHRITIS IN ENGLAND BETWEEN 1998 AND 2013

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Background: Septic arthritis is a rare but potentially life-threatening condition. Mortality rates of up to 20% have been reported and of those that survive approximately a third will be left with permanent joint damage and dysfunction. Research from Iceland showed the incidence of septic arthritis was on the rise between 1990 and 2005. In the UK, there are no recent publications providing estimates of the incidence of septic arthritis. The aim of this study was to provide contemporary UK-specific data on the incidence and pattern of septic arthritis.

Methods: Hospital Episode Statistics (HES) are recorded for every hospital admission, outpatient appointment and accident and emergency (A&E) attendance in England. The data are coded according to the International Classification of Diseases, Tenth Revision classifications and are freely available to all through the Health and Social Care
Information Centre (HSCIC). Codes starting with M00 and M01 refer to forms of pyogenic arthritis and direct infections of the joint, respectively. Information from 1998 to 2013 was utilized. The rates of septic arthritis per 100,000 population were calculated. A Cuzick trend test was used to assess the significance of the observed change.

**Results:** In total, 54,532 cases of septic arthritis were reported to HES between 1998 and 2013. The mean age at presentation was 54 years and 80% of cases were male. There has been a 42% increase in the reported incidence of septic arthritis, with rates rising from 5.2/100,000 population in 1998 to 7.4/100,000 in 2013 (test for trend P < 0.001). The mean age at presentation has risen from 51 to 57 years over the same period (P < 0.001). In most cases, no organism information was provided to HES. Of cases where an organism was recorded, Staphylococcus was the most frequently reported (8.5% of total cases) followed by Streptococcus (4.6%). Staphylococcal rates have been climbing more rapidly than streptococcal infections. There was a notable spike in streptococcal incidence in 2011, accounted for by a specific rise in pneumococcal cases.

**Conclusion:** These results provide contextual information regarding rates of septic arthritis. There has been a year-on-year increase in the overall incidence. HES data have limitations, including misclassification risk and also increasing reporting due to payment by results (PBR), which explains some of the changing trend seen. Other explanations include an increase in joint replacement surgery over the same period (though it would be wrong to assume that the risk of each individual surgery has changed) and an ageing population. The spike in pneumococcal septic arthritis in 2011 was interesting, as it was not mirrored by an increase in pneumococcal respiratory infections in the same year.

**Disclosure statement:** A.I.R. received a clinical fellowship awarded by the NIHR Biomedical Research Centre at Guy’s and St. Thomas’s NHS Foundation Trust and King’s College London. All other authors have declared no conflicts of interest.
O37 DIFFERENTIAL PERIPHERAL B-CELL PHENOTYPE IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME COMPARED WITH SECONDARY SJÖGREN’S SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Primary SS (pSS) and SLE are diseases characterized by the production of multiple autoantibodies to nucleotides and elevated levels of the cytokine B cell activating factor (BAFF). Peripheral B cell abnormalities are a feature of both diseases. However, whereas patients with pSS have increased frequencies of Bm1/Bm2 (naive), Bm2* (germinal centre founders) and Bm3/4 (centroblasts/centrocytes), but decreased Bm5 (memory) compared with healthy controls (HCs), patients with SLE have increased Bm5 levels, which correlated with disease activity. No previous studies investigating the peripheral B cell phenotype in patients with both SLE and SS (SLE/SS) are available. We questioned whether the defective B cell phenotype in pSS patients was also present in patients with SS/SE and whether differences in the B cell phenotype could be related to changes in B cell lipid raft expression and BAFF receptor function in pSS and SLE/SS patients.

Methods: Blood samples and clinical and laboratory parameters from 32 patients with pSS and SS/SE and 13 age-/sex-matched HCs were obtained. We used flow cytometry to perform B cell immuno-phenotyping and analysis of lipid raft expression (marker of B cell activation). In vitro cultures assessed lipid raft expression in response to BAFF.

Results: Patients with SLE/SS had a distinct B cell phenotype compared with pSS patients and HCs, characterized by decreased Bm1 and Bm5 and increased Bm2 populations compared with HCs (P = 0.031, 0.035 and 0.01, respectively) and increased Bm2 compared with pSS (P = 0.027). Bm1 cells were decreased in both pSS and SLE/SS patients compared with HCs (P = 0.028 and 0.031, respectively). Table 1 summarizes the correlations between B cell subpopulations and clinical parameters. B cells from patients with pSS had a significant increase in lipid raft expression compared with HCs (P = 0.01) and patients with SS/SE (P = 0.05). Furthermore, lipid raft levels correlated with BAFF receptor expression in HCs and SLE/SE B cells (P = 0.077, r = 0.694) but not in pSS patients.

Conclusion: We showed that patients with SLE/SS had a more significant B cell abnormalities compared with HCs and pSS patients, detectable even in a small number of patients. Also the relationship between lipid raft and BAFF receptor expression was altered between pSS and SLE/SS patients. Further studies will validate our findings and investigate whether B cell lipid rafts mediate differential BAFF receptor signalling.

Disclosure statement: The authors have no conflicts of interest.

O38 ABSTRACT WITHDRAWN

O39 CHILDHOOD BONE AREA, BONE MINERAL CONTENT AND BONE MINERAL DENSITY ARE ASSOCIATED WITH PERINATAL METHYLATION AT THE CDKN2A LOCUS AT BIRTH: FINDINGS FROM THE SOUTHAMPTON WOMEN’S SURVEY

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Background: Poor intrauterine and childhood growth has been associated with the risk of osteoporosis in later life, and there is increasing evidence that this may be mediated through epigenetic mechanisms. We used a population-based mother–offspring cohort to explore relationships between DNA methylation at the CDKN2A gene locus (a region involved in cell cycle regulation) and umbilical cord tissue at birth and bone size and density measured by DXA in childhood.

Methods: We used a whole genome methyl-binding domain capture array (Agilent) to identify potentially informative genomic regions in 19 umbilical cords from infants born in the UK Southampton Women’s Survey (SWS). Following adjustment to account for CpG density via a Bayesian algorithm (BATMAN), we located a differentially methylated region within the CDKN2A gene locus with strong correlations between methylation and childhood bone size and density assessed by DXA; we used pyrosequencing to carry out in-depth methylation analysis at nine CpG sites within this CDKN2A region in independent umbilical cords from discovery (n = 332) and replication (n = 337) cohorts of SWS children assessed by whole-body-minus-head DXA (hologic discovery) at 4 and 6 years old.

Results: Percentage methylation varied greatly across the nine CpG sites (at CpG 6, the 5th–95th percentile = 49.8–82.4%). Adjusting for age and sex, there were consistent negative associations between CDKN2A methylation at six of nine CpG sites (CpG 4–9) and bone area of interest measured by DXA at the lumbar spine (L2–L4) and femoral neck.

Disclosure statement: The authors have no conflicts of interest.
O40 EXPRESSION AND FUNCTION OF THE P2X7 RECEPTOR IN DERMAL FIBROBLASTS FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: SSC (scleroderma) is a multisystemic autoimmune disease characterized by connective tissue disease of unknown aetiopathogenesis. SSC is characterized by microvascular damage, dysregulation of innate and adaptive immunity and generalized fibrosis of the skin and organs. P2X7 receptor (P2X7R) is a nucleotide-gated ionotropic channel chiefly involved in the inflammatory response triggered by passive release of adenosine triphosphate from damaged cells. It is largely expressed on inflammatory cells and plays a key role in promoting the release of pro-inflammatory cytokines such as IL-1β.

Methods: Human dermal fibroblasts were isolated from the skin of SSC patients and healthy subjects matched for age and sex. In these cells we evaluated P2X7R expression by quantitative RT-PCR and flow cytometry assay and P2X7R function, induced by P2X7R stimulation, as determined by cytoplasmatic free Ca2+ concentration measurements (single-cell fluorescent microscopy), collagen production and cytokine (IL-1β and IL-6) release by ELISA.

Results: P2X7R expression and Ca2+ influxes, induced by the selective P2X7R agonist BzATP, were higher in SSC patients than in healthy control fibroblasts. Moreover, in SSC patients, BzATP stimulation enhanced the production of collagen from lipopolysaccharide (LPS)-primed fibroblasts. Interestingly, we noted that in LPS-primed SSC fibroblasts, the effect of BzATP was completely abrogated by co-inoculation with the P2X7R antagonist AATP, resulting in a marked antifibrotic effect. In addition, collagen production does not seem driven by the P2X7R-mediated cytokine synthesis but by ERK-1/2 signalling activation.

Conclusion: Our results provide evidence that in fibroblasts from SSC patients, both the expression and function of the purinergic P2X7 receptor are increased with respect to healthy controls. These results confirm our hypothesis of an involvement of P2X7 receptors in the pathogenesis of SSC. In particular, by enhancing collagen production in SSC fibroblasts, P2X7R may promote the fibrotic process associated with the disease. These findings increase our knowledge of the pathophysiology of SSC, suggesting P2X7R as a potentially attractive target for pharmacological modulation.

Disclosure statement: The authors have declared no conflicts of interest.

O41 SERUM VASCULAR CELL ADHESION MOLECULE 1 LEVELS ARE ASSOCIATED WITH VASCULAR DYSFUNCTION AND INCREASED CARDIOVASCULAR RISK IN ANIMAL MODEL AND PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Vascular dysfunction is a feature of atherosclerosis, and is assessed by measuring peak flow velocity at the common carotid artery using ultrasound. It is also associated with increased cardiovascular risk. Serum sVCAM-1 levels have been shown to be increased in patients with rheumatoid arthritis (RA) compared with healthy controls.

Methods: In a mouse model of RA with collagen-induced arthritis (CIA), we assessed sVCAM-1 levels, myocardial fibrosis and markers of cardiovascular risk in CIA animals, and compared these with healthy controls.

Results: CIA mice have increased sVCAM-1 levels compared with healthy controls. This is associated with increased myocardial fibrosis and increased markers of cardiovascular risk. These findings were not observed in CIA mice treated with a P2X7R antagonist.

Conclusion: These findings suggest that P2X7R may play a role in promoting tissue fibrosis in different body districts.

Disclosure statement: The authors have no conflicts of interest.

O42 INVESTIGATING MECHANICAL STRESS-RESPONSIVE MACROPHAGES IN SCLERODERMA

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Background: Inflammation, vasculopathy and fibrosis are hallmarks of scleroderma. Healthy forearm skin has a Young’s modulus of 4–12 kPa, compared with scleroderma skin at 50–80 kPa, reflecting elevated mechanical stiffness in the fibrotic tissues. Our objective was to investigate if a mechanically stressed microenvironment influences macrophages to contribute to disease pathogenesis. Altered macrophage/microphage subpopulations in scleroderma have been reported. We have shown that myocardin-related transcription factor-A (MRTF-A) mediates mechano-sensing in scleroderma fibroblasts, and we wanted to determine whether MRTF-A is activated in macrophages.

Methods: Control and scleroderma skin were immunostained with anti-MIF and anti-MRTF-A antibodies (n = 3). Human peripheral blood monocyte-derived macrophages were cultured in RPMI-1640 media supplemented with 10% FBS and 5% charcoal-stripped horse serum on 4KPa and 50KPa collagen-fibronectin-coated plates to mimic soft/healthy and stiff/fibrotic skin, and activated with lipopolysaccharide (LPS; 10 ng/ml) or IL-10 (10 ng/ml). MRTF-A expression was assessed by quantitative PCR and conditioned media were profiled by Lum销n screening for inflammatory cytokines. Mouse bone marrow-derived
macrophages (BMDMs) of wild-type and MRTF-A-null mice were maintained in RPMI/M-CSF on soft and stiff substrates. The data were analysed by two-way analysis of variance and Tukey test (P < 0.05, CI 95%).

Results: We observed increased accumulation of perivascular CD68\(^+\) macrophages in diffuse scleroderma skin compared with controls and CD68\(^+\) macrophages expressing nuclear MRTF-A. Human macrophages expressed MRTF-A mRNA and exhibited differential cytokine expression when cultured on soft and stiff substrates. M(LPS) on soft substrate expressed IFN-\(\gamma\), which was undetectable with M(LPS) on stiff substrate [mean difference 0.2075 pg/ml (s.d. 0.1576), P < 0.01]. LPS- and IL-10-activated macrophages on soft substrate increased monocyte chemotactic protein-3 (MCP-3) expression compared with controls [mean difference 68.51 pg/ml (s.d. 49.22), P < 0.0001, respectively]. M(LPS) on stiff vs soft substrate showed decreased MCP-3 expression [mean difference 57.01 pg/ml (s.d. 49.22), P < 0.05]. M(IL-10) on soft substrate showed increased MCP-1 expression compared with controls [mean difference 2448 pg/ml (s.d. 2232), P < 0.05]. M(IL-10) on stiff substrate decreased expression of MCP-1 [mean difference 2590 pg/ml (s.d. 2233), P < 0.05] and increased fractalkine expression compared with soft substrate [mean difference 51.22 pg/ml (s.d. 36.28), P < 0.01]. Wild-type mouse BMDMs displayed a more elongated morphology when cultured on stiff compared with soft substrate. MRTF-A-null BMDMs remained rounded on stiff substrate.

Conclusion: MRTF-A is a mechanical stress-responsive transcription factor that co-activates transcription of cytoskeletal and extracellular matrix-modifying genes. MRTF-A may couple mechanical stress to macrophage activation in scleroderma, where stiff matrix promotes macrophage secretion of cytokines and growth factors that exacerbate fibrosis.

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PAEDIATRIC AND ADOLESCENT ORAL ABSTRACTS

O43 5-YEAR DATA FROM TENDER, A PHASE III CLINICAL TRIAL: SAFETY AND EFFICACY OF TOCILIZUMAB IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Two-year results from the three-part, 5-year, phase III TENDER study showed tocilizumab (TCZ), an IL-6 receptor inhibitor, was effective in the treatment of patients with severe, persistent systemic JIA (sJIA). We report long-term, 5-year data from TENDER.

Methods: In part 1, patients (2–17 years) with active sJIA were randomized 2:1 to TCZ (body weight [BW] <30 kg, TCZ 8 mg/kg; BW ≥30 kg, TCZ 12 mg/kg) or placebo every 2 weeks (q2w) for 12 weeks. Part 2 (weeks 12–104) involved open-label TCZ q2w based on BW. In part 3, an alternative-dosing regimen was optional in patients with clinically inactive disease (CID): TCZ qconcomitant medications could be tapered and discontinued. Efficacy was assessed in those entering part 3 [intention to treat 3 (ITT3) population] and until alternative dosing; the safety population was all entering part 1.

Results: Eighty-nine of the 112 patients in part 1 entered part 3: 66 patients (59%) completed the study. Patients in the ITT3 population had a mean age of 9.5 years (SD 4.4) and 53% were male. The high proportion of patients achieving JIA ACR30/50/70/90 responses (at part 3 entry) was maintained through week 260 (Table 1). Thirty patients did not enter the alternative-dosing regimen and completed the study; 8 (26.7%) met the criteria for CID at week 260. An additional 39 patients reached and maintained CID for at least 3 months and entered the alternative-dosing regimen. Of patients remaining at week 260, 31 had received oral glucocorticoids and 34 MTX at baseline. At study end, 17/31 and 6/34 had stopped these respective treatments. The 5 year and 2 year safety profile of TCZ q2w dosing was similar, with no new safety findings (Table 1). Rates of adverse events (AEs) and serious AEs (SAEs) did not increase between years 2 and 5 (Table 1). Most SAEs were unrelated to study treatment. Infections accounted for nearly half of all SAEs. Four deaths occurred; one death (sepsis) was possibly related to study treatment.

Conclusion: Results demonstrate the continued maintenance of efficacy and no change in the safety profile over 5 years of TCZ treatment in patients with sJIA.

Disclosure statement: E.B. has participated in the speakers bureau for Roche and has received research funding from Roche and Chugai. P.D. has received consultancy fees from Roche and has received research funding from Roche, Novartis, Pfizer, Novimmune and Sobi. N.R. has received consultancy fees from Roche; has participated in speakers bureaus for AbbVie, AstraZeneca and Bristol-Myers Squibb, Boehringer, Celgene, CrescendoBio, EMDSerono, Ifalmaraco, Janssen, Medimmune, Novartis, Novonordisk, Pfizer, Sanofi, Reumatics.com, Servier, Siergie and Takeda and has received research funding from Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Novartis, Pfizer, Roche, Sanofi Avertis and Schwarz Biosciences. C.K. is an employee of Roche. C.W. is an employee of Roche. J.C. is an employee of Roche. A.R. has received consultancy fees from Novartis, Roche, AbbVie, Bristol-Myers Squibb, Johnson & Johnson and Pfizer and has received research funding from Pfizer. R.S. has received consultancy fees from Roche and Novartis. R.X. has received consultancy fees from Roche, Janssen, Pfizer, AstraZeneca and AbbVie. P.D. has received consultancy fees from Roche, Novartis and Pfizer and has received research funding from Novartis. A.G. has received consultancy fees from Novartis and Genentech. N.W. has received research funding from the European Union (Executive Agency for Health and Consumers). A.M. has received consultancy fees from Roche; has participated in speakers bureaus for Roche, Abbott, AbbVie, Amgen, Astellas, Bristol-Myers Squibb, Boehringer, Celgene, CrescendoBio, EMDSerono, Ifalmaraco, Janssen, Medimmune, Novartis, Novo Nordisk, Pfizer, Sanofi, Servier and Takeda and has received research funding from Roche, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Novartis, Pfizer, Sanofi Avertis and Schwarz Biosciences. D.L. has received consultancy fees from AstraZeneca, Bristol-Myers Squibb, AbbVie, Pfizer, Roche, Novartis, UBC, Forest Research Institute, Horizon, Johnson & Johnson, Biogen, Takeda, Gene- tritech and Glaxo; has participated in speakers bureaus for Genentech, Roche and Novartis and has received research grants from the National Institutes of Health. All other authors have declared no conflicts of interest.

O44 ADOLESCENT KNEE PAIN IS ASSOCIATED WITH PATELLOFEMORAL OSTEOARTHRITIS IN ADULTHOOD: A CASE–CONTROL STUDY

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Background: There is a lack of information about the association between patellofemoral OA (PFOA) and both adolescent anterior knee pain (AKP) and previous patellar dislocations.

Methods: This case–control study involved 222 participants from our knee arthroplasty database who answered a questionnaire. A total of 111 patients suffering PFOA were 1:1 matched with a unicompart- mental tibiofemoral arthritis control group. Multivariate correlation and
binary logistic regression analysis were performed, with odds ratios (ORs) and 95% CIs calculated. This analysis helps us assess the effect of both variables while adjusting for major confounders such as previous surgery and patient-reported instability.

Results: An individual is 7.5 times more likely to develop PFOA if he/she has suffered adolescent AKP [OR 7.5 (95% CI 1.51, 36.94)]. Additionally, experiencing a patellar dislocation increases the likelihood of development of PFOA, with an adjusted OR of 3.2 (95% CI 1.81, 5.68). A 44-year difference in median age of first dislocation was also observed between the groups.

Conclusion: This should bring into question the traditional belief that adolescent AKP is a benign pathology. Patellar dislocation is also a significant risk factor. These patients merit investigation and we encourage clinical acknowledgement of the potential consequences when encountering patients suffering from AKP or patellar dislocation.

Disclosure statement: The authors have declared no conflicts of interest.

O45 INCREASED FREQUENCY AS WELL AS EXPRESSION OF GENES RELATED TO INTERMEDIATE MONOCYTES IN PATIENTS WITH ENTHESITIS-RELATED JUVENILE IDIOPATHIC ARTHRITIS

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Background: Enthesitis-related arthritis (ERA), a subtype of JIA, is frequently seen in the Asian population, including India. A lack of autoantibodies and an association with gut inflammation suggest a major role of innate immune cells. Gene expression profiling of peripheral blood and synovial fluid mononuclear cells (PBMCs and SFMCs) revealed the dysregulation of monocyte-related genes such as antigen presentation, toll-like receptor (TLR) and CD1d. Monocytes are classified into classical, intermediate and non-classical, based on CD14 and CD16 expression. Among these, intermediate monocytes are reported to be increased in immune-inflammatory diseases and are known to produce cytokines in response to TLR stimulation. Thus we studied the gene expression profile of monocytes, the frequency of their subsets and cytokine production in TLR stimulation.

Methods: Microarray analysis of monocytes obtained from PBMCs of six healthy controls and PBMCs and SFMCs from six ERA patients using Illumina chips WG12 was done. Monocyte subsets were assessed in 48 patients with ERA, 17 healthy controls and 17 disease controls by flow cytometry. IL-23 and TNF levels were measured in culture supernatants of eight healthy controls and eight patients with/ without lipopolysaccharide (LPS) stimulation by ELISA.

Results: Genes related to antigen presentation, cytokine and chemokine signaling and TLR pathway were dysregulated in peripheral blood (PB) and synovial monocytes of patients with ERA. Key genes of intermediate monocytes like CLEC10A, MARCO, HLA-DR were expressed 3–4-fold more in ERA PB as well as in ERA SF. In PB, the frequency of CD14+/CD16– monocytes were significantly higher in ERA as compared with healthy controls [4.93% (i.o. 3.5) vs 1.8% (i.o. 1.69); P = 0.001]. PB intermediate monocytes had a modest correlation with swollen joint count (r = 0.333, P = 0.03). Also, patients’ synovial cells had more intermediate monocytes as compared with controls [11.25% (i.o. 11.30) vs 5.9% (i.o. 4.8); P = 0.004]. In addition, the frequency of non-classical monocytes was greater in ERA [1.83% (i.o. 1.55)] as compared with healthy individuals [0.35% (i.o. 0.4), P = 0.001]. PBMCs from ERA patients produced more TNF and IL-10, both with and without stimulation with LPS, as compared with controls.

Conclusion: Intermediate monocytes may play an important role in the pathogenesis of ERA, possibly by producing cytokines and contribut- ing to joint inflammation.

Disclosure statement: The authors have declared no conflicts of interest.

O46 DOWN’S ARTHROPATHY: CLINICAL AND RADIOLOGICAL FEATURES OF ARTHRITIS IN CHILDREN WITH TRISOMY 21

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Background: Down’s arthropathy (DA) was first reported in the literature in 1984. Crude estimates suggest higher incidence and prevalence rates of DA compared with JIA (JIA prevalence 1/1000, estimated DA prevalence 8.7/1000). Despite this fact, there remains a paucity of data on this condition. DA is rarely recognized at onset and remains underdiagnosed. As a direct consequence, children with DA are presenting with significant joint damage and disability at diagnosis.

Methods: We performed a musculoskeletal examination on children aged 0–16 years with trisomy 21 (T21). Children with T21 were invited to attend a screening clinic. Screening involved completion of a health questionnaire and a comprehensive musculoskeletal examination. DA cases detected were investigated at a tertiary referral practice. Data on a convenience sample of 33 newly diagnosed children with JIA were collected to create a comparison group.

Results: A total of 503 children with T21 have been screened for DA and 22 new cases have been diagnosed. All of these children had poor language skills or were non-verbal. Only 11% of the parents suspected that their child might have arthritis prior to attending our screening clinics, and this was only after reading our recruitment literature. In total, we now have 33 children with DA attending our centre (combining cases attending that predate the start date of the study). This suggests the prevalence of DA in Ireland is 18–21/1000. The majority of children presented with a polyarticular pattern of disease. No cases of uveitis have been observed to date. Of the DA cohort, 88% had small joint involvement of the hands, significantly higher than that observed in the JIA comparison group. Erosive changes were reported on X-rays in 29.2% of the DA cohort (9.5% in the JIA cohort). MTX-associated nausea was a significant barrier to treatment with this DMARD in DA. There was a significant delay in diagnosis of DA—1.7 years vs 0.7 years in the JIA cohort.

Conclusion: Children with T21 are at increased risk of developing arthritis. There is a lack of awareness of this risk among health care professionals and the general public at large. This almost certainly contributes to poor recognition of the disease and a delay in diagnosis. The predominant pattern of disease in DA is inflammatory arthritis. Treatment with standard protocols used in JIA is complicated by drug-associated side effects in children with T21. However, a good response to treatment with steroids and intra-articular joint injections has been observed. Our study has raised a number of questions. Future research to accurately define this disease and identify best practice with regards to treatment would be invaluable. We advocate that all children with T21 should have an annual musculoskeletal examination as part of their health surveillance programmes.

Disclosure statement: The authors have declared no conflicts of interest.

O47 A DENSE FINE SPECKLE PATTERN ON IMMUNOFLOUORESCENCE IS STRONGLY ASSOCIATED WITH THE DEVELOPMENT OF UVEITIS IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: JIA is an umbrella term encompassing a heterogeneous group of diseases that affect children <16 years of age and share a common characteristic of arthritis persisting >6 weeks. Historically, there is evidence that the presence of ANAs is associated with an increased risk of uveitis. However, the molecular target of such ANAs is unknown. Uveitis affects up to 30% of children with JIA and occurs most commonly in those with oligoarticular disease. It is often chronic and asymptomatic and may lead to permanent visual impairment. We aimed to characterize ANA prevalence, immunofluorescence pattern and specificity in a large JIA cohort with a view to identifying ANAs associated with uveitis.

Methods: A total of 433 JIA patients enrolled in the Childhood Arthritis Prospective Cohort Study and 48 healthy controls <16 years of age were analysed. Indirect immunofluorescence (IF) was performed on Hep-2 cells (Nova-lite, Inova) according to the manufacturer’s instructions. All slides were read blindly and independently by S.T. and J.D. Anti-D/DS10 positivity was determined in controls and 200 randomly selected patients by chemiluminescent immunoassay (QUANTA Flash DFS70, Inova). A logistic regression model was used to assess the significance of ANA pattern in relation to known uveitis.
At 1:80 dilution, 29% of controls and 55% of JIA patients were positive. ANA negative, ANA DFS/homogeneous and ANA other. Data on uveitis were available for 176 patients with a median 3 years (IQR 2–5) of follow-up. Sixty patients had known uveitis. Compared with ANA-negative patients, uveitis was more common in patients with a DFS/homogeneous pattern (odds ratio [OR] 2.86 [95% CI 1.41, 5.78], P < 0.01) but not those with other ANA patterns (OR 0.42 [95% CI 0.11, 1.58], P = 2.00). Anti-DFS70 antibodies directed against lens epithelium-derived growth factor are known to produce a DFS ANA pattern and have previously been associated with the absence of rheumatological disease in ANA-positive individuals. Anti-DFS70 was identified in 1.7% of JIA patients (4% with a compatible ANA pattern) and 2% of controls.

Conclusion: The most common ANA pattern in JIA patients is DFS/homogeneous. Patients with other patterns appear no more likely to develop uveitis than ANA-negative patients and may not warrant such frequent ophthalmological screening. Only 4% of JIA patients with a DFS/homogeneous pattern have anti-DFS70, signifying the presence of an alternative autoantibody in the majority of patients. Identification of the antigenic target would facilitate better directed ophthalmological screening.

Disclosure statement: S.L.T. has received support for this project from Inova. All other authors have declared no conflicts of interest.

O48 ASSESSMENT OF DISEASE ACTIVITY USING CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING IN CHILDREN AND YOUNG PEOPLE WITH SUSPECTED HIP ARTHRITIS—CAN WE DO BETTER?
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Background: Contrast-enhanced magnetic resonance imaging (CE-MRI) is an important aid in identifying early arthritis, especially when the hip joint is involved. Improved outcomes follow early diagnosis and treatment. Radiologists must therefore differentiate normal scans from subtle signs of early inflammation. Previous re-evaluation of hip CE-MRI scans at our institution found discrepancies in interpretation between radiologists. The aims of this study were to construct and pilot a grading tool to improve the assessment of disease activity from hip CE-MRI scans and to assess the reliability of the developed grading tool.

Methods: A retrospective cohort study was conducted of patients who underwent hip CE-MRI between January 2011 and September 2014. Three musculoskeletal radiologists independently assessed all scans using a standardized reporting tool comprised of effusion, synovial enhancement, marrow oedema, synovial thickness and visual analysis of synovium. Reliability tests used Cohen’s k for categorical variables and the intraclass correlation coefficient (ICC) for continuous variables.

Results: Eighty patients were included. Overall, the presence of a joint effusion and marrow oedema had the highest inter- and intrareader reliabilities. Synovial thickening (whether by visual assessment or measurement) and enhancement were unreliable signs. Furthermore, there was a large amount of missing data for the thickness measurements, attributable to difficulties in measurement. Interreader comparison was moderate for effusion (k = 0.5–0.7) and marrow oedema (k = 0.4–0.6) and poor for synovial enhancement (k = 0.06–0.3). Visual synovial assessment had moderate reliability (k = 0.4–0.5), whereas measurement was poor (ICC = 0.09–0.3). Table 1 shows the full reliability results.

Conclusion: Measuring synovium was unreliable and impractical, demonstrating demand for an alternative method. Radiologist reporting was inconsistent between and within readers. We would recommend that reporting of CE-MRI hip scans should reflect the level of certainty to aid clinical decision-making.

Disclosure statement: F.M.Y. has received research funding from Athena Swan Bursary from the Sheffield Medical School as part of a BMedSci. All other authors have declared no conflicts of interest.

O48 Table 1. Inter- and intrareader reliability across CE-MRI parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Effusion</th>
<th>Marrow oedema</th>
<th>Synovial enhancement</th>
<th>Axial thickness</th>
<th>Coronal thickness</th>
<th>Visual impression of synovium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interreader</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 vs 2</td>
<td>k = 0.514, P = 0.001</td>
<td>k = 0.567, P = 0.001</td>
<td>k = 0.058, P = 0.015</td>
<td>ICC = 0.267, P = 0.006</td>
<td>ICC = 0.101, P = 0.129</td>
<td>k = 0.381, P = 0.001</td>
</tr>
<tr>
<td>1 vs 3</td>
<td>k = 0.579, P = 0.001</td>
<td>k = 0.403, P = 0.001</td>
<td>k = 0.035, P = 0.063</td>
<td>ICC = 0.036, P = 0.001</td>
<td>ICC = 0.297, P = 0.147</td>
<td>k = 0.435, P = 0.001</td>
</tr>
<tr>
<td>2 vs 3</td>
<td>k = 0.693, P = 0.001</td>
<td>k = 0.587, P = 0.001</td>
<td>k = 0.336, P = 0.001</td>
<td>ICC = 0.319, P = 0.001</td>
<td>ICC = 0.092, P = 0.012</td>
<td>k = 0.526, P = 0.001</td>
</tr>
<tr>
<td>Intrareader</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>k = 0.353, P = 0.003</td>
<td>k = 0.625, P = 0.001</td>
<td>k = 0.940, P = 0.548</td>
<td>ICC = 0.266, P = 0.079</td>
<td>ICC = 0.691, P = 0.001</td>
<td>k = 0.390, P = 0.008</td>
</tr>
<tr>
<td>2</td>
<td>k = 0.692, P = 0.001</td>
<td>k = 0.684, P = 0.001</td>
<td>k = 0.709, P = 0.001</td>
<td>ICC = 0.201, P = 0.206</td>
<td>ICC = 0.065, P = 0.369</td>
<td>k = 0.908, P = 0.001</td>
</tr>
<tr>
<td>3</td>
<td>k = 0.610, P = 0.001</td>
<td>k = 0.643, P = 0.001</td>
<td>k = 0.805, P = 0.001</td>
<td>ICC = 0.441, P = 0.008</td>
<td>ICC = -0.132, P = 0.746</td>
<td>k = 0.610, P = 0.001</td>
</tr>
</tbody>
</table>

The 95% level of significance, P < 0.05. Using Fleiss’s interpretation, poor reliability is k = 0.4–0.75.
Results: At baseline, a significantly higher DSAS8, ESR, CRP and swollen joint count were seen in the lymphoid (Ly) vs myeloid (My) or fibroid (Fb) pathotype (P < 0.02). The number of patients seropositive for RF and ACPA was also significantly higher higher (P = 0.02 and 0.01) in the Ly group. Furthermore, US-ST and US-PD scores of the biopsied joint and total US-PD scores were significantly higher in the Ly group (P < 0.002). Finally, a significantly higher number of radiographic progressors (SwH ≥ 1) at 12 months were seen in the Ly group (P = 0.04).

Conclusion: The significant association between a synovial lymphoid pathotype and high disease activity/seropositivity in patients with early RA suggests a critical role for these structures in RA pathogenesis. Furthermore, in this cohort, despite a treat-to-target approach, patients with an Ly pathotype were significantly more likely to develop progressive radiographic damage. Such data suggest the potential for early patient stratification in order to target effective therapies according to clinical need.

Disclosure statement: The authors have declared no conflicts of interest.
Methods: A total of 115 RA patients on certolizumab were selected from the Biologics in RA Genetics and Genomics Study Syndicate prospective cohort. Serum samples were collected at 3, 6, and 12 months following initiation of therapy. ADAbs were measured using radioimmunoassay and drug levels using EUSA at 3, 6, and 12 months. Disease activity [28-joint DAS (DAS28)] scores were measured at each visit and 12-month EULAR response was calculated. Patient self-reported adherence was collected longitudinally. Ordinal logistic regression and the generalized estimating equation (GEE) were used to test the association between drug levels, from serum sampled at random time points in the treatment cycle and treatment response (i) between ADAbs and drug levels and (ii) to determine patient-centred factors and drug levels.

Results: A total of 253 serial samples were tested for certolizumab drug levels (n = 230 suitable for ADAbs measurement). The mean age of the patients was 56 years (IQR: 13). 75% were female, the baseline DAS28 score was 5.9 (IQR: 0.8), the median BMI was 27.5 (IQR 23.6–32.3) and 87% were on a DMARD (86% MTX). ADAbs were detected in 37% (cut-off > 20 AU/mL; 42/112 patients at one or more time points by 12 months). Drug level, but not ADAbs, was associated with 12 month EULAR response (drug level: β = -0.035 (95% CI 0.0018, 0.069), P = 0.039; ADAbs: β = -0.0013 (95% CI -0.0032, 0.0006), P = 0.18).

Factors associated with certolizumab drug level in the univariate GEE analysis were gender, adherence, BMI, CRP and ADA level (Table 1). In the multivariate analysis, after adjustment of confounders, only ADA level and adherence remained significantly associated (Table 1).

Conclusion: This is the first study to demonstrate that testing drug levels in certolizumab-initiated patients may be clinically useful, even in the absence of trough levels, to determine treatment response. Adherence and ADA levels are associated with low certolizumab drug levels but not directly with 12 month EULAR response; however, ADA measurement may help determine the aetiology of a low drug level.

Disclosure statement: M.J. has received honoraria from Pfizer, AbbVie and UCB. J.I. has received honoraria from Pfizer, Roche, AbbVie and Janssen and research funding from Roche, Pfizer and UCB. K.H. has received honoraria from AbbVie and research funding from Pfizer. H.C. has received honoraria from AbbVie, Janssen, MSD, Pfizer, UCB, Roche, Celgene and Servier. A.B. has received research funding from Pfizer, AbbVie, Eli Lilly and Sanofi-Aventis. All other authors have declared no conflicts of interest.

O50 Table 1. Predictors of drug levels in certolizumab-treated RA patients using the GEE

<table>
<thead>
<tr>
<th>Variable</th>
<th>β coefficient (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate analysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.14 (0.017 – 0.29)</td>
<td>0.08</td>
</tr>
<tr>
<td>Gender</td>
<td>4.76 (2.21, 9.29)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.46 (-0.89, -0.041)</td>
<td>0.032</td>
</tr>
<tr>
<td>CRP</td>
<td>-0.099 (-0.17, -0.029)</td>
<td>0.005</td>
</tr>
<tr>
<td>Methotrexate use</td>
<td>-0.11 (-0.47, 0.47)</td>
<td>0.96</td>
</tr>
<tr>
<td>Anti-drug antibody level</td>
<td>-0.037 (-0.055, -0.018)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adherence</td>
<td>10.43 (4.76, 16.11)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Multivariate model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-drug antibody level</td>
<td>-0.044 (-0.059, -0.028)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adherence</td>
<td>7.08 (0.7, 13.45)</td>
<td>0.029</td>
</tr>
<tr>
<td>Gender</td>
<td>1.77 (1.4, 2.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.13 (-0.66, 0.49)</td>
<td>0.65</td>
</tr>
<tr>
<td>CRP</td>
<td>-0.066 (-0.14, 0.013)</td>
<td>0.102</td>
</tr>
</tbody>
</table>

O51 EFFICACY AND SAFETY OF BARICITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO csDMARDs: SUMMARY RESULTS FROM THE 24-WEEK PHASE III RA-BUILD STUDY

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Background: Baricitinib, an oral inhibitor of JAK1/2, has shown promising results in patients with active RA. We present summaries of efficacy, safety and patient-reported outcome (PRO) analyses from patients with active RA and inadequate response (IR) or intolerance to conventional synthetic DMARDs (csDMARDs) in the 24-week phase III RA-BUILD study.

Methods: Patients with active RA and an IR or who were intolerant to csDMARDs (N = 684) were randomized 1:1:1 to receive placebo or baricitinib (2 or 4 mg/day) for 24 weeks. The primary endpoint was an ACR 20 response at week 12 for baricitinib 4 mg vs placebo. Efficacy and safety analyses including 28-joint DAS with ESR (DAS28-ESR) and CDAI improvements at week 4 predicting low disease activity (LDA) remission at week 12, mTSS, PROs and laboratory data were also reported.

Results: Statistically significant improvements in ACR 20/50/70, DAS28-ESR, SDAI remission, HAQ disability index, morning joint stiffness, worst joint pain and tiredness were seen with baricitinib vs placebo at weeks 12 and 24. Progression of radiographic structural joint damage (mTSS) at week 24 was reduced with baricitinib 4 mg vs placebo. Compared with placebo, baricitinib 4 mg produced a significant rapid decrease in DAS28-ESR and CDAI as early as week 1. Decreases at week 4 of ≤ 0.6 in DAS28-ESR or ≥ 6 in CDAI were the lower level of improvements measured associated with an increased probability of achieving LDA/remission at week 12 or 24 (Table 1). Rates of treatment-emergent adverse events (TEAEs) and serious AEs, including serious infections, were similar among groups. Increases in total lymphocyte count (TLC) at week 4 for baricitinib were generally within the normal ranges, and at weeks 12 and 24, changes in TLC were similar. Increased T cells, B cells and NK cells occurred at week 4, whereas decreased T cells and NK cells and increased B cells were observed at weeks 12 and 24 in the baricitinib group.

Conclusion: Overall, baricitinib treatment resulted in significant improvement in structural progression and PROs, including pain, functional disability and tiredness at weeks 12 and 24. LDA/remission at weeks 12 and 24 were predicted by decreases in DAS28-ESR ≥ 0.6 and CDAI ≥ 6 at week 4. Safety and infection rates were acceptable regardless of changes in TLC.

Disclosure statement: P.E. has undertaken clinical trials and provided expert advice to Pfizer, MSD, AbbVie, BMS, UCB, Roche, Novartis, Samsung and Lilly and is a member of the British Society for Rheumatology and British Health Professionals in Rheumatology, A.P.G. is an employee of Eli Lilly, I.I. is an employee of Eli Lilly, M.L.R. is an employee of Eli Lilly, M.C. is an employee and shareholder of Eli Lilly, I.d.l.T. is an employee of Eli Lilly. All other authors have declared no conflicts of interest.

O51 Table 1. LDA/remission after 12 and 24 weeks of baricitinib 4mg in RA patients with IR to csDMARDs

<table>
<thead>
<tr>
<th>LDA (DAS28-ESR ≤ 3.2)</th>
<th>Remission (DAS28-ESR ≤ 2.8)</th>
</tr>
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<tbody>
<tr>
<td>Week 12 Week 24</td>
<td>Week 12 Week 24</td>
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<tr>
<td>DAS28-ESR</td>
<td></td>
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<tr>
<td>&lt;0.6</td>
<td>3/39 (7.7)</td>
</tr>
<tr>
<td>≥0.6</td>
<td>45/166 (27.8)</td>
</tr>
<tr>
<td>CDAI</td>
<td></td>
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<tr>
<td>&lt;0.6</td>
<td>62/159 (39.0)</td>
</tr>
<tr>
<td>≥0.6</td>
<td>19/166 (11.6)</td>
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O52 SWITCHING TO BIOSIMILAR INFliximab: REAL-WORLD DATA FROM THE SOUTHAMPTON BIOLOGIC THERAPIES REVIEW SERVICE

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Background: Biosimilar infliximab was recently approved for UK use. A phase III trial has shown non-inferiority of efficacy and adverse events when compared with originator Remicade (infliximab) in RA.
Biosimilar infliximab provides an opportunity for cost savings, but concerns remain regarding efficacy and safety. There is currently a paucity of real-world data, although Norway has been using biosimilar infliximab for more than a year.

**Methods:**
- From May 2015, patients receiving Remicade (infliximab) for inflammatory arthritis were switched to Inflectra (infliximab). Their rheumatologist explained the potential switch, a letter (including Inflectra information sheet) was sent and patients could contact a helpline for information or if disease control worsened/ adverse effects developed.
- All patients agreed to switch. Patients were reviewed 3 months after switching and then every 6 months.

**Results:**
- Fifty-six patients receiving Remicade were switched to Inflectra (infliximab) at the same dose (30 female and 26 male, 5 current smokers, mean age 58.7 years (IQR 13.2)).
- Diagnoses were 29 RA, 14 AS, 11 PsA and 2 enteropathic arthritis. The mean disease duration was 17.8 years (IQR 8.5) and the mean time on Remicade was 8.1 years (IQR 3.3). The mean time from diagnosis to first biologic therapy was 9.8 years (IQR 7.6), with MTX used by 35 patients and another DMARD used by 7. Most have received three or more infusions of inflectra, with 52 (93%) continuing at a mean follow-up of 4.8 months. Four patients have switched back to Remicade: three because of inefficacy (1 AS; BASDAI prior 5.2, after 8.0; 1 RA; DAS-28 prior 1.9, after 5.3; 1 PsA) and one (PsA) because of an adverse event (widespread pain following two infusions).

**Conclusion:**
- After 5 months of follow-up, 93% of patients have successfully switched to Inflectra. The number of patients stopping treatment appears similar following the switch to Inflectra when compared with the preceding 12-month time period using Remicade.

**Disclosure statement:** C.H. has received speaking fees or sponsorship from UCB, BMS, AbbVie, Chugai, Janssen and Pfizer. C.U. sat on an advisory board for Napp and received a sponsorship from AbbVie while developing the UK rheumatology competency framework. C.J.E. has received funding for consultancy work from Anthera and Samsung Bioepis; speaking fees from AbbVie, Janssen, Novartis, Lilly, MSD, BMS, Pfizer, Mundipharma, Samsung, Roche, Celgene and Napp; has participated in speakers bureaus for AbbVie, Janssen, Novartis, Lilly, MSD, BMS, Pfizer, Mundipharma, Samsung, Roche and Celgene and has received funding from AbbVie and Pfizer. All other authors have declared no conflicts of interest.

**O54 DIFFERENCES IN DAS28-CRP AND DAS28-ESR INFLUENCE DISEASE ACTIVITY STRATIFICATION IN RHEUMATOID ARTHRITIS AND COULD INFLUENCE THE USE OF BILOGICS, TREATMENT EFFICACY EVALUATIONS AND DECISIONS REGARDING TREAT-TO-TARGET: AN ANALYSIS USING THE BRITISH SOCIETY FOR RHEUMATOLOGY RHEUMATOID ARTHRITIS REGISTER**

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**Background:**
- Disease activity in RA has traditionally been measured using the 28-joint DAS (DAS28) using ESR. Use of DAS28 using CRP in place of ESR is increasing. This study investigates the level of agreement between the DAS28-ESR and DAS28-CRP scores across different disease activity thresholds and identifies how patient characteristics may influence agreement.

**Methods:**
- Patients with concurrent measures of ESR and CRP were identified from the British Society for Rheumatology Rheumatoid Arthritis Register, enabling paired calculation of DAS28-ESR and DAS28-CRP. Paired scores were stratified by patients’ baseline BMI and gender. Agreement between the scores was compared using Bland-Altman statistics and agreement matrices.

**Results:**
- A total of 5457 patients (mean age 56 years, 76% female) with 31 084 data entries were identified where paired DAS28-ESR/ DAS28-CRP scores could be calculated. The mean DAS28-ESR was 0.3 points (95% CI – 0.8, 1.4) greater than for DAS28-CRP (4.4 (c.o. 1.7) and 4.1 (c.o. 1.0), respectively). Men had a lower mean difference between the two scores compared with women (DAS28-ESR vs DAS28-CRP by 0.2 points (95% CI – 1.0, 1.3) vs 0.4 points (95% CI – 0.7, 1.4), respectively). The results stratified by BMI were similar to the overall mean difference. Agreement between the two scores according to disease activity thresholds are shown in Table 1. Overall, the DAS28-ESR classifies fewer patients in remission (15.6% vs 19.5%). When categorising scores by disease activity thresholds,
the DAS28-ESR/DAS28-CRP had the lowest agreement at low disease activity (LDA). Of the DAS28-ESR scores, 54.4% were classified as moderate disease activity (MDA) when the paired DAS28-CRP was LDA, which could influence results in clinical trial reporting. Conversely, 20% of patients were classified as being in MDA by DAS28-CRP when the paired DAS28-ESR demonstrated high disease activity (HDA). This is of importance given the National Institute for Health and Care Excellence biologics guidelines, and shows that up to 20% of patients may not satisfy the criteria for biologic therapy if DAS28-CRP is used instead of DAS28-ESR.

**Conclusion:** These results demonstrate the impact of using the DAS28-ESR or DAS28-CRP interchangeably, and the disparity between the two scores. Clinicians and researchers should adopt a consistent approach to DAS28 inflammatory marker adoption when making decisions on treatment response or interpreting research outcomes.

**Disclosure statement:** The authors have declared no conflict of interest.
CASE REPORTS

001 THE USE OF TOCILIZUMAB IN A CASE OF BIOLOGIC-REFRACTORY ANTISYNTHETASE SYNDROME
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1Rheumatology, Salford Royal NHS Foundation Trust, Salford, 2Centre for Musculoskeletal Research, Institute of Inflammation and Repair, University of Manchester, Manchester, 3Greater Manchester Neurosciences Centre, Salford Royal NHS Foundation Trust, Salford and 4Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK

Background: Antisynthetase syndrome (ASS) is a connective tissue disease characterized by myositis, interstitial lung disease, arthritis, Raynaud’s phenomenon, mechanics’ hands and serum anti-aminoa- cyl-tRNA synthetase antibodies. Despite standard treatment of corticosteroids and immunosuppressive therapy, ASS can remain active in a significant proportion of cases. We report a case of refractory ASS where tocilizumab (an IL-6 receptor blocker blocking mono- clonal antibody) was used with beneficial effect.

Methods: Case description drawn from patient records at Salford Royal NHS Foundation Trust, Salford and Bradford Hospitals NHS Trust, Bradford, UK.

Results: A 27-year-old woman presented with a 1-year history of arthritis complicated by 2-month history of dysphagia and severe symmetrical proximal muscle weakness, rendering her bedbound. Creatine kinase (CK) peaked at 3812 IU/l. Anti-Jo1 and anti-Ro52 antibodies were positive. Muscle biopsy identified perimysial, endo- mysal and perivascular inflammatory infiltrates comprising CD4+ T cells, CD68+ macrophages and CD20+ B cells. Hand X-rays demonstrated an erosive arthropathy in the proximal and distal interphalangeal joints with associated capsular and ligamentous calcification. There were no cutaneous or pulmonary manifestations. Intravenous methylprednisolone was administered with some initial benefit. Oral prednisolone taper was commenced in conjunction with A2A and then MTX. However, due to ongoing disease activity, rituximab was administered. Despite an undetectable CD19 cell count, the disease flared and i.v. immunoglobulin was given. Four years after onset, maintenance with MTX 17.5 mg weekly and mycophenolic acid 720 mg twice a day led to a variable dose of prednisolone to a period of stability, but without complete suppression of disease activity. CK had normalized, however, CRP remained elevated at 121 mg/l. There was persistent hand synovitis (11 swollen and 14 tender joints on a 28-joint assessment). Manual Muscle Testing (MMT) was 254/260 (mild-to-modate weak- ness) and MRI of the thighs showed active myositis. A trial of anakinra resulted in tolerable injection site reactions. Monthly i.v. tocilizumab infusions (8 mg/kg) were then initiated. Subsequently, CRP normalized and the synovitis significantly improved (eight swollen and zero tender joints). Muscle strength also improved (MMT 257/260). The use of tocilizumab allowed dose reductions in the concurrent immunosuppressants (MTX 17.5 to 10 mg/week, mycophenolic acid 1440 to 720 mg daily). Unfortunately his response was not sustained and he was re-treated every 6 months for the next 2 years. He maintains radiological remission, however, his inflammatory markers remain elevated and he continues to have significant night sweats despite oral prednisolone doses of 20–25 mg/day. He was switched to tocilizumab, but only tolerated a single dose.

Results: This is only the second reported case of Castleman’s disease in a patient with ankylosing spondylitis. It highlights the importance of biopsy in making the diagnosis and differentiating this from lymphoma. Rituximab (RTX) 1 g given in 4 weekly doses. He rapidly gained weight following the RTX and follow-up CT scans demonstrated a complete resolution of his lymphadenopathy. He felt much better. His IL-6 level was repeated and was found to have dropped to 10 pg/l. Unfortunately his response was not sustained and he was re-treated every 6 months for the next 2 years. He maintains radiological remission, however, his inflammatory markers remain elevated and he continues to have significant night sweats despite oral prednisolone doses of 20–25 mg/day. He was switched to tocilizumab, but only tolerated a single dose.

Results: This is only the second reported case of Castleman’s disease in a patient with ankylosing spondylitis. It highlights the importance of biopsy in making the diagnosis and differentiating this from lymphoma. RTX provided significant symptom and radiological improvement. He remains at risk of amyloidosis, given his CRP is still high.

Conclusion: Further options in his disease control might include siltuximab, an IL-6 inhibitor that is licensed for Castleman’s disease by the US Food and Drug Administration, thalidomide or i.v. immunoglobulin.

Disclosure statement: The authors have declared no conflicts of interest.

002 THE LYMPHOMA IMPOSTOR: MULTICENTRIC CASTLEMAN’S DISEASE IN A PATIENT WITH ANKYLOSING SPONDYLITIS
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Background: Castleman’s disease is a rare lymphoproliferative disorder with focal or systemic involvement. Its diagnosis is made on bone marrow involvement with characteristic hyaline or plasma cell variants in the presence of a lymph node with preserved architecture. The disease is non-clonal with no immunoglobulin heavy (light) or T cell receptor (TCR) gene rearrangements. It is an important diagnosis to make, as patients can be misdiagnosed with lymphoma and their presentation is not dissimilar. IL-6 mediated inflammation is thought to be an important pathway for the maintenance of Castleman’s disease and treatment is directed towards this pathway.

Methods: A 35-year-old male, with a 13-year history of known B27-associated axial spondylitis with peripheral arthritis presented with weight loss of 5 kg over 6 months associated with drenching night sweats in the presence of an elevated CRP (120 mg/l) and ESR (100 mm/h). He was taking golimumab. Examination demonstrated widespread lymphadenopathy with hepatomegaly in the absence of significant synovitis. An extensive infection screen that included HIV, syphilis, Borrelia, hepatitis B and C and a Quantiferon test was negative. An autoantibody profile demonstrated non-specific p-ANCA and negative CCP, ANA, RF, liver screen and cryoglobulins and a polyclonal response on paraprotein electrophoresis. Imaging demonstrated widespread lymphadenopathy with a large left axillary node. This was biopsied and found to have features consistent with Castleman’s disease, the plasma cell variant rather than the hyaline form. The differential diagnosis for such a histologic picture might include RA, plasmaclymoma or non-Hodgkin’s lymphoma. Cytokine profiling demonstrated normal TNF levels and elevated IL-6 (133 pg/l; normal <10). He was started on three pulses of i.v. methylprednisolone 1 g, followed by oral prednisolone at 50 mg/day. He was treated with rituximab (RTX) 1 g given in 4 weekly doses. He rapidly gained weight following the RTX and follow-up CT scans demonstrated a complete resolution of his lymphadenopathy. He felt much better. His IL-6 level was repeated and was found to have dropped to 10 pg/l. Unfortunately his response was not sustained and he was re-treated every 6 months for the next 2 years. He maintains radiological remission, however, his inflammatory markers remain elevated and he continues to have significant night sweats despite oral prednisolone doses of 20–25 mg/day. He was switched to tocilizumab, but only tolerated a single dose.

Results: This is only the second reported case of Castleman’s disease in a patient with ankylosing spondylitis. It highlights the importance of biopsy in making the diagnosis and differentiating this from lymphoma. RTX provided significant symptom and radiological improvement. He remains at risk of amyloidosis, given his CRP is still high.

Conclusion: Further options in his disease control might include siltuximab, an IL-6 inhibitor that is licensed for Castleman’s disease by the US Food and Drug Administration, thalidomide or i.v. immunoglobulin.

Disclosure statement: The authors have declared no conflicts of interest.

003 DIFFUSE ALVEOLAR HAEMORRHAGE ON A WEEKEND IN A DISTRICT GENERAL HOSPITAL
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Background: Microscopic polyangiitis (MPA) is an uncommon, anti-MPO-associated vasculitis. It often presents with renal and pulmonary involvement that can lead to life-threatening diffuse alveolar haemorrhage (DAH). Here we describe a case of MPA with DAH in a young
woman without evidence of renal involvement who required extra- corporeal membrane oxygenation (ECMO).

Methods: Our 21-year-old female presented at a district general hospital (DGH) on a Saturday evening with cough, haemoptysis and significant dyspnoea preceded by 2 weeks of headache, fever and night sweats. There was no rash, ENT involvement or haematuria (urine dipstick negative for blood or protein). On admission, she was in critical respiratory distress, with tachypnea and oxygen saturations of 88% on air. Her blood pressure was 84/64 mm Hg, with normal renal function and CRP of 87 mg/l. Chest X-ray revealed diffuse alveolar shadowing. CT of the thorax demonstrated widespread bilateral consolidation and ground-glass attenuation centrally, in keeping with DAH. She was transferred to the intensive care unit, where her inspired oxygen fraction requirements increased and the decision was made to proceed to endotracheal intubation. She required significant suction of her endotracheal tube as a result of persistent pulmonary haemorrhage and suffered worsening type 1 respiratory failure. Venovenous extracorporeal membrane oxygenation (ECMO) support was sought, as she was too unstable for inpatient transfer for plasma exchange. She was exchanged by a team from the nearest available centre, who initiated ECMO in situ prior to transferring her.

Results: Bronchoscopy revealed inflamed mucosa with frank haemorrhage on lavage. Anti-MPO titres were elevated at 196 IU/ml with negative anti-PR3/anti-GBM titres. She was diagnosed with anti-MPO-positive pulmonary vasculitis likely secondary to MPA. She underwent plasma exchange therapy for 7 days and began i.v. methylprednisolone and rituximab (RTX) 375 mg/m². She required 6 days of ECMO, after which she made a remarkable recovery with complete resolution of the DAH on chest X-Ray. She remains asymptomatic 18 months later on 6-month RTX infusions. Her current anti-MPO titre is 1.9 IU/ml.

Conclusion: The diagnosis of MPA out of hours can be very challenging in a DGH without rapid access to ANCA testing, especially with single organ involvement. While it is not uncommon for renal involvement to develop at later stages, cases of MPA-associated DAH have been described without evidence of glomerulonephritis. As such, MPA-DAH even with no evidence of renal involvement initially. There are an increasing number of case studies demonstrating successful use of venovenous ECMO as rescue treatment for this, aggravating bleeding remained a significant risk due to the need for anticoagulation to reduce ECMO circuit thrombus. This risk can be reduced by using lower filtration rates and maintaining more regular anticoagulation within the ECMO circuit to maintain normal systemic clotting. It is crucial to identify the cause of DAH and take a multidisciplinary approach towards management, including prompt referral for ECMO support where needed.

Disclosure statement: The authors have declared no conflicts of interest.

005 MYCOBACTERIUM INTRACELLULARLE MIMIC AS INFLAMMATORY ARTHRITIS

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Background: Joint tuberculosis is a rare cause of infectious arthritis. It may present with clinical features similar to inflammatory monoarthritis. Therefore it is important that all physicians are aware of this uncommon, yet significant entity. A 34-year-old female health care assistant was referred to rheumatology by orthopaedics with a 2-year history of left sternoclavicular joint pain. On detailed history she mentioned vague constitutional symptoms of fatigue, feeling unwell and night sweats. She had tried NSAIDs, with some short-term relief. She had been extensively investigated by orthopaedics, who could not find any orthopaedic cause.

Methods: Initial tests showed normal full blood count, ESR 30 mm/h and CRP 26 mg/l. Immunology showed negative ANA anti-CCP antibodies and urate, complement and immunoglobulins were normal with no Bence Jones protein detected. X-ray of sternoclavicular joint was normal. Bone scan showed focal uptake suggestive of inflammatory arthropathy. MRI showed no soft tissue swelling. No erosions were noted and infection was thought to be very unlikely. The scan was discussed with a radiologist and suggested a stress fracture and could be SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis) syndrome, although this was very unlikely from a rheumatology point of view. The patient was referred back to the orthopaedics for review to rule out stress fracture and also for biopsy to rule out infection. The latter was particularly emphasized by the rheumatologist, given the clinical characteristics of this case. Although orthopaedics was not convinced that this might be an infection, a biopsy was finally done after long discussions. The results showed Mycobacterium intracellulare infection. She was referred to respiratory and infectious disease specialists and was started on anti-mycobacterium treatment.

Results: She was reviewed in the rheumatology clinic 2 months later with remarkable improvement of clinical symptoms and complete resolution of constitutional symptoms. She remained under the care of the infectious disease team to complete the course of treatment.

Conclusion: Tuberculosis is considered a ubiquitous disease, as it involves any part of the body, but sternoclavicular joint tuberculosis is a rare presentation. Osteoarticular tuberculosis is often misdiagnosed in the initial stages due to a lack of awareness or presentation at uncommon sites. An extensive literature review found only 26 documented cases of sternoclavicular tuberculosis arthritis. Infective arthritis due to M. intracellulare is rare, most commonly occurring in immunocompromised patients such as those receiving immunosuppressive drugs or HIV patients. The most commonly affected joint is the knee. Up to 40% of patients presenting with staphylococcal arthritis have received a prior intra-articular corticosteroid injection in the affected joint. Diagnosis of these infections rests on culture of the synovial fluid or culture of surgically obtained specimens, though the often insidious nature of the infection may lead to delays in diagnosis.
of many years. This patient’s presentation mimicked an inflammatory arthritis; pathology and highlights the importance of taking a detailed history including occupation and recreational interests. Excluding infective causes of inflammatory arthritis is vital, as immunosuppressive treatment may have potentially disastrous consequences.

Disclosure statement: The author has declared no conflicts of interest.

006 WHEN PANCREATITIS IS NOT JUST PANCREATITIS
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Background: Acute or chronic pancreatitis may be associated with panniculitis and polyarthritis, a triad termed pancreatitis, polyarthritis and panniculitis (PPP) syndrome. This is rare, with only 25 well-documented case reports worldwide, so it may be easily missed as a potential cause of polyarthritis.

Methods: A 58-year-old man initially presented with abdominal pain and acute pancreatitis secondary to alcohol, with an elevated amylase of >4000 U/l. This improved with supportive therapy. However, he then developed widespread polyarthritis, morning stiffness and a symmetrical polyarthritis affecting both ankles, knees, wrists and elbows and the small joints of the hands and feet. Cutaneous lesions formed with localized swelling, followed by breakdown of the overlying skin, which exuded a creamy white discharge. Initial culture was negative. He was treated with a course of prednisolone.

Results: Blood showed haemoglobin of 103 g/l, white cell count 13.37 × 10^9/l, platelets 406 × 10^9/l, neutrophils 10.9 × 10^9/l, CRP 109 mg/dl and ESR 189 mm/h, RF, anti-CCP antibodies, ANA and ANCA were negative. Viral screening for HIV, hepatitis C, HIV, hepatitis B and parovirus B19 was negative; EBV serology was consistent with previous infection. Plain radiographs of the elbow that had been normal 2 months ago showed a severely destructive erosive arthritis. MRI revealed marked synovial thickening and effusion with extensive narrow oedema in the distal humeroulecran processes and left proximal radius. There were widespread erosions and a pathological fracture of the bilateral coronoid processes. In the hands there was an extensive erosive process affecting the metacarpals and phalanges with multiple lytic lesions and cortical destruction. Further multiple cultures from the skin lesions showed a sensitive Staphylococcus aureus infection, likely a secondary infection. Synovial/bone biopsy showed moderate chronic inflammation and fibrosis with fat necrosis. No granulomas or amyloid deposition were seen, IgG4 staining was negative, as was culture for acid-fast bacilli was negative. CT of the abdomen and magnetic resonance cholangiopancreatography showed a cystic lesion in the body of the pancreas, possibly a pseudocyst. A biopsy was planned, but unfortunately the patient passed away suddenly. Post-mortem examination showed a fibrotic pancreas and a cyst with thick, greenish yellow fluid and erosive arthritis. The cause of death was deemed S. aureus sepsis secondary to chronic pancreatitis with abscess formation, polyarthritis and panniculitis.

Conclusion: Almost two-thirds of patients reported with PPP have absent or mild abdominal symptoms and the delay in diagnosis and treatment of underlying pancreatitis worsens the prognosis. The PPP syndrome is an important, rare cause of polyarthritis that should be considered in all patients with polyarthritis and risk factors for pancreatic disease.

Disclosure statement: The authors have declared no conflicts of interest.

007 JAK-STAT PATHWAY STIMULATION: A NEW CAUSE OF INFLAMMATORY ARTHRITIS
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Background: Downregulation of the JAK-STAT signalling pathway with agents such as tofacitinib (a JAK inhibitor) is emerging as an effective tool in the management of RA. It is conceivable therefore that upregulation of this pathway could result in inflammatory arthritis. The thrombopoietin receptor agonist eltrombopag and romiplostim, used in the treatment of immune thrombocytopenia (ITP), stimulates the JAK-STAT pathway. A frequent side effect of these drugs is arthritis, which occurs in up to 26% of patients.

Methods: We present a 62-year-old man who developed florid inflammatory arthritis following initiation of eltrombopag for ITP.

Results: The patient was first diagnosed with ITP in 1997 and underwent splenectomy in 1998. Rituximab treatment in 2014 was ineffective for his persistent thrombocytopenia. Eltrombopag was then titrated and continued to 50 mg daily. Three months later he developed new-onset left knee pain with an effusion. Following a dose increase to 50/75 mg (alternate days), the arthritis progressed to involve the shoulders, wrists and hands bilaterally. He noted joint stiffness, worse in the mornings, particularly in the small joints of the hands, with associated swelling and difficulty making a fist. On examination, he displayed bilateral swollen wrists, MCP joints and PIP joints with reduced range of movement. Blood tests showed CRP <5 mg/l, ESR 16 mm/h, uric acid 326 μmol/l, with RF, anti-CCP antibodies and ANA all being negative. Plain radiographs identified moderate degenerative changes in the hands, however, MRI of the left knee showed a significant joint effusion. Ultrasonography showed moderately severe synovitis of the right wrist and mild synovitis of the left wrist, with increased power Doppler signal. Three months after eltrombopag dose reduction to 50 mg daily, the arthritis in the hands improved such that he could form a fist. Eltrombopag was weaned with the aim of stopping and this led to further improvement in his symptoms.

Conclusion: To our knowledge, this is the first case of a patient developing inflammatory arthritis following treatment with JAK inhibitor. Interestingly, our patient was seronegative for both RF and anti-CCP, but had synovitis on US. The temporal and dose-related correlation between eltrombopag initiation and inflammatory arthritis in the absence of other causes suggests an association. Mechanistically this is likely to be via the binding of eltrombopag to dendritic cell thrombopoietin receptors with subsequent JAK2-STAT5 activation. Conversely, inhibition of JAK signalling by MTX or the JAK inhibitors tofacitinib and baricitinib is used in the treatment of inflammatory arthritis. While most rheumatologists are aware of the therapeutic benefits of JAK inhibitors, the effects of potential stimulators of the JAK-STAT pathway are less well known. It is possible that the increasing use of these drugs may result in an increase in inflammatory arthritis.

Disclosure statement: The authors have declared no conflicts of interest.

008 AN UNUSUAL PRESENTATION OF SUBACUTE BACTERIAL ENDOCARDITIS MANIFESTING AS INFECTIOUS FOREARM PYOMYOSITIS
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Background: Infective endocarditis is an infectious disease of the endocardium that can lead to vegetations on heart valves, with potential destruction, myocardial abscess and, if untreated, death. The musculoskeletal manifestations of endocarditis are wide ranging but poorly recognized. We report an unusual presentation of subacute bacterial endocarditis presenting as pyomyositis of the forearm in a patient with no obvious risk factors for infective endocarditis.

Methods: A previously fit and well 27-year-old British African woman presented to the acute medical team and was referred to rheumatology with a 1-week history of severe left upper limb pain. She had a 2 month history of generalized malaise that had followed a non-specific viral illness that manifested as vomiting and flu-like symptoms. She noted a concomitant ~13 kg unintentional weight loss over this period. Two weeks prior to admission, she had completed a 10-day course of oral fluoxacinil oral from her general practitioner for presumed cellulitis of the skin overlying her left thumb and index finger. The erythema had since dissipated.

Results: On assessment, she was febrile but haemodynamically stable. There was objective swelling of the left forearm relative to the right with overlying warmth. She had diffuse arthralgia of her left wrist and first and second MCP joints, but no synovitis. Palpation of the left forearm flexor compartment and finger flexion caused severe pain. The remainder of her musculoskeletal examination was normal. Systemic examination identified a pansystolic murmur audible throughout the precordium. The initial blood panel revealed normocytic anaemia (haemoglobin 102 g/l), neutrophilia (18.6 × 10^9/l) and a marked acute phase response (CRP 227 mg/l, ESR 112 mm/h/l). Baseline immunology and urinalysis were negative. Following an abnormal bedside US by the rheumatologists, an urgent forearm MRI was done that showed an inflammatory phlegmon of the proximal deep flexor musculature of the forearm with diffuse flexor compartment myositis and features suggestive of an infective myositis. She proceeded to a left forearm biopsy which showed a cystic lesion in the body of the pancreas, possibly a pseudocyst. A biopsy was planned, but unfortunately the patient passed away suddenly.
examination under anaesthetic, with debridement, fasciotomy and washout. A muscle biopsy demonstrated mixed inflammatory infiltrate and areas of focal myonecrosis. Transthoracic echocardiography confirmed a mitral valve mass with moderate regurgitation. Serial blood cultures grew Streptococcus viridans. She had an excellent response to an extended antimicrobial course. She made a good clinical recovery, with resolution of the mass and regurgitation on repeat interval echocardiography and no major clinical sequelae.

Conclusion: Rheumatic presentations of infective endocarditis include arthralgia, arthritis, back pain and myalgias. Rarer presentations include Achilles tendinitis, sacroilitis, bursitis and dermatomyositis mimics, however, endocarditis presenting as pyomyositis is incredibly rare. Case series have shown musculoskeletal manifestations tend to present early in disease and can be the presenting feature in up to 30% of patients with infective endocarditis. If not recognized, they may cause significant delays in diagnosis with resulting morbidity and mortality.

Disclosure statement: The authors have declared no conflicts of interest.

009 THENAR PYOMYOSITIS WITH FUSOBA CTERIUM NECTOPHORUM SECONDARY TO GASTEROENTERITIS IN A YOUNG FEMALE PATIENT

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Background: Pyomyositis is uncommon and most frequently due to Staphylococcus or group A Streptococcus in the presence of predisposing factors such as trauma, ischaemia and immunocompromise. It manifests with abscess formation, which presents a diagnostic challenge when close to a joint. We describe a case of a young female patient with Fusobacterium pyomyositis of the thenar muscles secondary to gastroenteritis.

Methods: A 21-year-old female Caucasian patient with an unremarkable medical history attended the emergency department following 5 days of watery diarrhoea and diffuse abdominal pain. There were no urinary symptoms or unwell contacts. Examination revealed dehydration, mild abdominal pain and fresh blood per rectum. Urinalysis was positive for blood and leukocyte esterase; beta human chorionic gonadotropin and culture were negative. Admission bloods showed a white cell count of 19 x 10⁹/l, CRP 377 mg/l, platelets 45 x 10⁹/l, creatinine 160 µmol/l and lactate 2.5 mmol/l, but no acidosis. Haemolysis, vascullitis and HIV screens were negative. Renal US showed bilateral renal enlargement and abdominal radiograph showed stomach and mild small bowel distension.

Results: The patient initially improved with i.v. fluids. However, after 48h she became pyrexial with left basal crepitations and i.v. co-amoxiclav was started empirically for pneumonia. Initial blood cultures showed a white cell count of 19 x 10⁹/l, CRP 175 mg/l, platelets 45 x 10⁹/l, creatinine 160 µmol/l and lactate 2.5 mmol/l, but no acidosis. Haemolysis, vascullitis and HIV screens were negative. Renal US showed bilateral renal enlargement and abdominal radiograph showed stomach and mild small bowel distension.

Conclusion: The clinical presentation of painful soft tissue swelling can overlap with that of articular and bone pathology when adjacent to a joint. Pyomyositis is important to exclude in differential diagnosis, as it can overlap with that of articular and bone pathology when adjacent to a joint. We describe a case of a young female patient with Fusobacterium pyomyositis of the thenar muscles secondary to gastroenteritis.

Disclosure statement: The authors have declared no conflicts of interest.

010 A SURPRISE POSITRON EMISSION TOMOGRAPHY SCAN RESULT: A CASE OF ATYPICAL AORTITIS

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Background: There are a variety of large vessel vasculitides, the most common being Takayasu arteritis and GCA. We present a case that provided a diagnostic challenge and highlights the contribution of the latest radiological imaging modalities to musculoskeletal medicine.

Methods: A 57-year-old male of British descent was admitted with a 3 week history of right leg pain while riding his bike, abdominal pain, myalgia, fatigue, weight loss, confusion and fevers. Past medical history comprised hypertension, diverticular disease and previous alcohol excess. He has no family history of note and was a non-smoker. On admission he had a swollen right leg. There was no synovitis, rash or lymphadenopathy. Abdominal exam was unremarkable. He had bounding peripheral pulses in his lower limbs distally. Investigations revealed haemoglobin of 48 g/l, CRP 377 mg/l, white cell count 16.7 x 10⁹/l and ESR 121 mm/h. Renal and liver function tests and urinalysis were normal. A Doppler US scan confirmed a deep vein thrombosis and he was commenced on low molecular weight heparin. He was transfused packed red cells and given broad-spectrum i.v. antibiotics (fusobacterium piperacillin, meropenem and gentamicin). Despite this, he had repeated fevers >38 °C. Multiple blood, urine and stool cultures were all negative. Transthoracic echocardiogram did not reveal any vegetations. A flexible sigmoidoscopy was performed that showed diverticular disease. ANA, ANCA, comple ment, RF, HIV, hepatitis B and C, syphilis and Lyme serology were all negative. Head, chest, abdomen and pelvis CT showed sigmoid diverticular disease but was otherwise unremarkable. A nuclear medicine PET scan revealed appearances in keeping with aortitis, with notable involvement of the descending thoracic and abdominal aorta and iliac arteries and involvement of the right common femoral and superficial femoral arteries. CT angiogram of the aortic arch showed that the descending thoracic aorta was normally thickened, however, this abnormally did not extend into the major neck vessels and there was no involvement in the great vessel origins of the aortic arch.

Results: He was treated with oral prednisolone 60 mg daily, with rapid improvement of his symptoms, fevers and inflammatory markers. Follow-up CT angiogram revealed the abdominal aortic wall and remaining arteries had returned to normal wall thickness, with no periarterial inflammatory changes. The infra-inguinal arteries were all of normal calibre. On discharge he was commenced on acenadic acid, calcium and vitamin D supplementation and changed from heparin to rivaroxaban. Additionally, he has been commenced on AZA and is successfully reducing his oral prednisolone.

Conclusion: This case demonstrates an unusual presentation of a large vessel vasculitides. It highlights the need for a broad knowledge of the possible differential diagnosis of leg pain along with the usefulness of the latest radiological imaging techniques in order to make a prompt diagnosis and provide appropriate management.

Disclosure statement: The authors have declared no conflicts of interest.

011 ACUTE CALCIFIC PRE-VERTEBRAL TENDINITIS

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Background: A 55-year-old female presented with a 4-day history of worsening acute-onset posterior headache and neck pain. There was no trauma. She had no history of photophobia or motor or sensory symptoms. She was generally fit and well.

Methods: On admission, she was febrile at 38.0 °C. The neurological exam was unremarkable. She had a stiff neck with limited flexion and extension. Her blood work showed a white cell count of 11.2 x 10⁹/l, neutrophils 8 x 10⁹/l and CRP 66 mg/l. A CT brain scan was normal. Lumbar puncture done was normal. An X-ray of the cervical spine showed altered bone density at C5–C6 with prevertebral soft tissue thickening. A CT of the neck revealed calcification of the longus colli suggestive of acute calcific prevertebral tendinitis. She had a normal bone profile. The patient was started on NSADS and her symptoms resolved over 2 weeks.

Results: Neck pain associated with fever, especially if accompanied by leukocytosis or high inflammatory markers, raises the suspicion for supplicative causes. In the case presented here, the history of acute headache and neck pain accompanied by fever raised the suspicion of meningitis initially. Subsequently, based on the X-ray, a
retropharyngeal abscess was considered. However, the CT scan of the neck was diagnostic.

Conclusion: Acute calcific prevertebral tendinitis is a rare cause of neck pain due to calcium hydroxyapatite deposition in the longus colli tendon and inflammation of the longus colli muscle. The clinical presentation is often non-specific and is characterized by spontaneous acute neck pain, dysphagia or odynophagia, sometimes accompanied by low-grade fever. Laboratory tests may demonstrate inflammatory signs, such as mild leucocytosis and slightly elevated ESR. The initial workup of patients is often performed to exclude more serious causes of acute neck pain, such as a traumatic injury, retropalatine abscess, meningitis and infectious spondylitis. This condition can easily be overlooked or misdiagnosed due to its rather non-specific presentation and rare occurrence. A diagnosis can be made by the recognition of its characteristic CT appearance. The treatment of this condition is conservative, involving rest and a short course of NSAIDS. It is important to differentiate this condition from more serious infective pathologies that may involve invasive procedures and prolonged treatment courses.

Disclosure statement: The authors have declared no conflicts of interest.

012 LISTERIA HYSTÉRIA, OR A REAL DANGER FOR OUR STEROID-TREATED PATIENTS?

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Background: We report a case of Listeria monocytogenes meningitis in a patient with SSc treated with prednisolone and MMF. We suggest we should be more proactive in warning our immunosuppressed patients about this potentially serious infection.

Methods: The patient was a 47-year-old woman diagnosed with SSc (ANA 1:1280, ScI70 positive) in May 2015.

Results: The patient initially presented in May 2015 with an 8-month history of dyspnoea and RP. CT of the chest suggested a non-specific interstitial pneumonitis (NSIP). She was started on prednisolone 30 mg/day, with MMF 1 g twice a day added in June. In August 2015 she presented as acutely septic with fever and confusion. At that time she was taking prednisolone 20 mg/day alongside MMF 1 g twice a day. Initial tests showed neutrophils of 20.9 x 10^9/l, lymphocytes 0.6 x 10^9/l and CRP 273 mg/l. CT of the brain suggested dilitated ventricles. L. monocytogenes was cultured from CSF. The patient required sedation and intubation and was given vancomycin, aciclovir and meropenem initially, then amoxicillin and meropenem. Amoxicillin was continued for 3 weeks in total. She had an 8-day stay in the intensive care unit, but made a full recovery and has been well since. Prednisolone has been reduced to 10 mg/day and MMF is being gradually increased to the previous dose. The Public Health England questionnaire revealed only a pork pie eaten in a restaurant within the previous 30 days as a possible source of infection. A Medicines and Healthcare Products Regulatory Agency yellow card has been submitted.

Conclusion: Listeria infection is usually contracted by oral ingestion. It is increasingly common in Europe, possibly due to reduced salt additives in food. It is also more common in the summer. In healthy individuals it causes a self-limited gastroenteritis; in pregnant and immunosuppressed patients it leads most commonly to bacteraemia and meningitis or meningococcalphtis. The median incubation period for invasive listeriosis is 35 days. The presentation may vary from an insidious onset to fulminating sepsis. It is a very serious illness, with a reported mortality for CNS infection of up to 40%. Risk factors for mortality include non-hematological malignancy, alcoholism, age > 70 years, glucocorticoid use and kidney disease. There is a known association with immunosuppression, possibly secondary to impaired macrophage activation. A large case control review suggested that 35% of non-pregnant cases were associated with steroid use. We also found two previous case reports of listeria meningitis in association with MMF. Interestingly, neither the prednisolone package insert nor the Arthritis Research UK patient information leaflet carry specific listeria warnings. Given the widespread lay knowledge of the need to reduce the risk of listeria exposure in pregnancy, this may be a simple message to insert in our patient information literature.

Disclosure statement: The authors have declared no conflicts of interest.

013 AN UNUSUAL CASE OF SCHNITZLER SYNDROME

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Background: Schnitzler syndrome is a rare and underdiagnosed systemic disease. It is considered to be an acquired autoinflammatory syndrome that shares many features with hereditary periodic fever syndromes (HPFSs). It demonstrates a male preponderance with a mean age of onset of 51 years. Its main clinical features include fever, recurrent urticarial rash, arthralgia, bone pain, lymphadenopathy, malaise, leucocytosis, elevated inflammatory markers and typically a monoclonal IgG component. Conventional therapies such as steroids and immunosuppressive medications are usually ineffective. The IL-1 receptor antagonist anakinra has been shown to rapidly control all symptoms of Schnitzler syndrome. This implies that an exaggerated activation of the inflammasome, an IL-1 synthesizer, may be involved in the pathophysiology. Schnitzler syndrome with the presence of an IgG paraproteinaemia is uncommon.

Methods: This case describes a patient who was diagnosed with Schnitzler syndrome with an IgG monoclonal component.

Results: A 45-year-old Caucasian man was referred with a 2 year history of an intermittent rash over his torso and arms with associated arthralgia and arthritis. This would last for 3–4 days before spontaneous resolution. Each episode was preceded by profound fatigue. He remained well between episodes but was troubled by the increasing frequency of attacks. Later he developed fevers with each episode. Investigations revealed elevated inflammatory markers, a paraproteinaemia with a monoclonal IgG component and elevated serum amyloid A protein. Ferritin levels were normal. Bone marrow aspirate did not demonstrate multiple myeloma and skin biopsy was consistent with urticaria. Initially he was treated with a short course of oral steroids; however, his symptoms recurred within 24 hours of completion. A diagnosis of Schnitzler syndrome was suspected and he was subsequently trialled on anakinra. He experienced complete symptom resolution with normalisation of his serum amyloid A protein levels.

Conclusion: Inflammomasomes are large molecular platforms that once activated trigger the maturation of the pro-inflammatory cytokine IL-1β, promoting the innate immune system and triggering an inflammatory response. Schnitzler syndrome forms part of the autoinflammatory disorders with skin involvement. Unlike the cryopyrinopathies, which have a known defect in the NLRP3 component of the inflammasome molecule, its involvement in Schnitzler syndrome remains unknown. However, the strong association between dysregulated inflammasome activity and human heritable and acquired inflammatory diseases highlights the importance of this pathway and targeted therapies as in our case.

Furthermore, this case highlights the importance of including Schnitzler syndrome in the differential diagnosis of adult patients presenting with an urticarial rash and an IgG paraproteinaemia. Anakinra can relieve symptoms within hours of initiation and has revolutionized the treatment of this once debilitating syndrome.

Disclosure statement: The authors have declared no conflicts of interest.

014 ABDOMINAL VASCULITIS—A LUPUS COMPLICATION NOT TO BE MISSED

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Background: A 32-year-old woman of Greek Cypriot and Zambian origin had a 12-year history of extensive cutaneous lupus erythematosus accompanied by systemic features and typical antinuclear profile. She had been treated with rituxumab followed by AZA and HCG for maintenance, but the latter two she unfortunately discontinued of her own accord.

Methods: She presented with severe diffuse abdominal pain. She was apyrexial and had guarding and rebound tenderness in the central and left abdomen. Abdominal CT scan revealed diffuse circumferential wall thickening of the jejunum with prominent contrast enhancement of the mucosa and serosa and submucosal oedema resulting in a double
Gastrointestinal involvement in SLE may take various forms, the most common being mesenteric vasculitis followed by protein-losing enteropathy, intestinal pseudo-obstruction and acute pancreatitis. Vasculitis is one of the most serious causes of acute abdominal pain in lupus patients (ranging from 0.2 to 9% of all SLE patients). A proposed pathological mechanism is inflammatory vasculitis secondary to circulating aPL. Clinical features are those of mesenteric ischaemia. Untreated, it may progress to bowel necrosis and perforation. It may go unnoticed given that patients are frequently already taking corticosteroids. Common CT findings include bowel dilation, focal or diffuse bowel wall thickening, the abnormal bowel wall enhancement known as the target sign, mesenteric oedema, stenosis or engorgement of mesenteric vessels called the halo sign and ascites. Segmental multifocal involvement of the small and large bowel with intervening normal segments indicates ischaemic change, which is highly suggestive of vasculitis.

**Conclusion:** Acute abdominal pain in lupus may be due to various causes including those common in the general population. However, it is extremely important to have a high index of suspicion for mesenteric vasculitis. This is not uncommon in lupus and may result in significant morbidity and mortality if left untreated.

**Disclosure statement:** The authors have declared no conflicts of interest.

015 RED CELL APLASIA: A RARE COMPLICATION OF ADULT ONSET STILL’S DISEASE

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**Background:** We present a case of pure red cell aplasia (PRCA) secondary to adult-onset Still’s disease (AOSD) to raise awareness of this rare complication. To our knowledge, no such reports have been reported; RA and SLE have established associations with PRCA, but only anecdotal evidence exists linking PRCA with AOSD. Early recognition of this rare, but life-threatening complication may prevent delay in diagnosis and successful treatment.

**Methods:** N/A.

**Results:** A 24-year-old female with no previous medical history presented to the Manchester Royal Infirmary in June 2014 with recurrent high fevers, widespread arthralgia, leucocytosis and an intermittent salmon-pink skin rash consistent with AOSD, according to the Yamaguchi criteria. Her serum ferritin was 8000 μg/l, ANA and RF were negative and her haemoglobin was 130 g/dl. She initially responded well to regular NSAIDs. One month later she was readmitted under general medicine with collapse. Her haemoglobin was very low, at 23 g/l, with a mean corpuscular volume of 70 fl. There was no obvious gastrointestinal blood loss. She had several temperature spikes >38 C recorded during this admission. Her serum ferritin was ~25,000 μg/l. Her white cell and platelet counts were normal. Her CRP was 155 mg/l and serum lactate dehydrogenase was moderately elevated at 868 IU/l. Her reticulocyte count was low (0.5%). On examination, she was tachycardic, with moderate hepatosplenomegaly and synovitis of the right ankle and left knee.

Her infective screen was negative for hepatitis B, cytomegalovirus and HIV. Her bone marrow biopsy showed an absence of mature erythroblasts with normal white cells and platelet maturation, consistent with PRCA.

**Conclusion:** Haemophagocytic syndrome/macrophage activation syndrome was a close differential, particularly with the very high serum ferritin levels. However, PRCA was the more likely diagnosis, given the bone marrow biopsy findings, the very low haemoglobin and the low reticulocyte count. PRCA differs from aplastic anaemia in that production of white cells and platelets is normal. It is also important to exclude other causes of red cell aplasia such as leukaemia, and infections such as HIV and parvovirus. High-dose steroid therapy is the mainstay of treatment. There is anecdotal evidence to support the use of immunosuppressants such as cyclosporin, AZA, CYC and rituxumab.

**Disclosure statement:** The authors have declared no conflicts of interest.

016 BILATERAL SACROILIITIS AND CLINICAL FEATURES OF REACTIVE ARTHRITIS IN PATIENTS WITH STRONGLY POSITIVE ANTI-CCP ANTIBODIES: A CASE SERIES

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**Background:** Anti-CCP antibodies have high specificity for RA and are rarely found in other autoimmune diseases. They are present from the beginning of the disease and have prognostic value in patients with RA, being particularly useful in identifying patients at risk of developing more severe and destructive disease. Involvement of the axial skeleton is rare in RA, except for the cervical spine. The seronegative SpAs are characterized by the absence of RF and anti-CCP antibodies and almost always involve the axial skeleton. In particular, involvement of the sacroiliac joints is considered characteristic for SpA. A recent study identified that a small proportion of AS patients had positive anti-CCP antibodies in the context of peripheral arthritis.

**Methods:** We report here three cases of strongly positive anti-CCP antibodies and clinical features of SpA seen in our rheumatology department between November 2014 and August 2015. We present a comparison of their clinical manifestations, radiographic features and markers of inflammation, as well as treatment regimens.

**Results:** The three patients had various clinical presentations (Table 1): one had an initial diagnosis of seropositive RA with involvement of the sacroiliac joints found later on imaging, another had a clinical picture of reactive arthritis (ReA) following an episode of urinary infection with Escherichia coli and third had clinical features of spondylarthritis only. All three patients were found with high titres of anti-CCP antibodies.

**Conclusion:** There are very few reports in the literature of patients having concomitant RA and bilateral sacroilitis, and there are no available data for cases with reactive arthritis or SpA with sacroilitis and high titres of anti-CCP antibodies. Despite this apparent association, a further follow-up of these patients is required to assess if they are at risk of developing overt clinical features of both diseases (RA and SpA) and to establish optimal therapeutic options needed to ensure long-term disease control.

**Disclosure statement:** The authors have declared no conflicts of interest.

**Table 1: Clinical characteristics of the three reported cases**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex/Age, years</th>
<th>Treatment</th>
<th>Clinical features</th>
<th>RF</th>
<th>CCP</th>
<th>Presence of bilateral sacroilitis on MRI</th>
<th>Clinical picture of ReA</th>
<th>Infection preceding the onset of arthritis</th>
<th>Bowel inflammatory symptoms</th>
<th>Eye inflammatory symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/47</td>
<td>MTX, NSAIDs</td>
<td>Symmetric arthritis, oligoarthritis</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Non-infectious keratitis in the past</td>
</tr>
<tr>
<td>2</td>
<td>F/54</td>
<td>Prednisolone, NSAIDs</td>
<td>Spinal pain</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Urinary tract infection with E. coli (2 weeks prior to arthritis onset)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>F/66</td>
<td>NSAIDs</td>
<td>Spinal pain</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Uveitis in the past</td>
<td></td>
</tr>
</tbody>
</table>
017 A RARE MIMIC OF TEMPORAL ARTERITIS: PACHYMENINGITIS IN SEROPOSITIVE RHEUMATOID ARTHRITIS

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Background: A 57-year-old male presented with 3 months of lower limb and wrist pain and early morning stiffness that responded well to prednisolone 20 mg (from his general practitioner). He had surgically treated prostate cancer and no family or personal history of seronegative related conditions. Examination revealed no synovitis or joint deformity.

Methods: Investigations are summarized in Table 1. One month later he was commenced on MTX but at follow-up he complained of a severe, unrelenting headache over the right temple and forehead that disturbed his sleep when he lay on it. There were no visual, jaw, tongue or other neurological symptoms. Prednisolone (40 mg) improved his symptoms, and subsequent temporal artery biopsy 21 days later was negative. The headache persisted and started to affect the left side as well, and ESR remained ~50 mm/h despite prednisolone. Hence he was referred to a neurologist. A CT of his brain, reviewed with neuroradiologists, showed a possible abnormality in the right temporo-parietal region, which may be artefactual. Subsequent brain MRI showed an enhancing lesion, which was felt to be pachymeningitis due to an inflammatory process, not metastatic prostate cancer, although the lesion has not been biopsied. While his RA remained controlled, his headache remained unre sponsive to lower doses of prednisolone, amitriptyline and simple analgesia, and codeine was not tolerated. Hence CVC will be started after urological review for microscopic haematuria due to the history of prostate cancer and the risk of haemorrhagic cystitis.

Results: Cranial pachymeningitis is a rare condition and clinical features are due to compression (headache, cranial neuropathies, hæmiparesis, seizures). It has typical MRI appearances and can be associated with granulomatous diseases such as tuberculosis and granulomatosis with polyangiitis, RA and IgG4-related disease, and is a rare manifestation of neurosarcoid. Treatment is of the underlying cause, although evidence is based on sparse case reports.

Conclusion: In resistant suspected temporal arteritis, further investigation such as brain MRI can help confirm the underlying diagnosis. In this case, the presentation coinciding with RA strongly suggests a very rare neurological association of this inflammatory condition.

Disclosure statement: The authors have declared no conflicts of interest.

018 SEVERE HYPERCALCAEMIA UNMASKING SARCOIDOSIS FOLLOWING VITAMIN D THERAPY

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Background: Sarcoidosis is a multisystem autoimmune condition. Only up to 10% of patients with sarcoidosis have hypercalcaemia. The aim of reporting this case is to raise awareness that supplementary vitamin D therapy in a patient with asymptomatic sarcoidosis can lead to potentially life-threatening hypercalcaemia.

Methods: N/A.

Results: A 54-year-old woman with known type 2 diabetes and hypertension presented to Royal Blackburn Hospital in the summer of 2013 with a 5-day history of right upper quadrant abdominal pain associated with nausea and vomiting. She had night sweats and unquantified weight loss. She also had widespread arthralgia, but denied any skin rashes suggestive of erythema nodosum or eye symptoms. On examination, she was tender in the right hypochondrium, but abdominal US revealed no evidence of renal calculi or gallstones. Her initial investigations revealed an adjusted serum calcium of 4.14 mmol/l. She had normal PTH level at 1 pmol/l, while her vitamin D level was 34.4 ng/ml. Later her myeloma screen was negative and her abdominal CT scan was unremarkable. However, high-resolution CT of the chest showed bilateral lymphadenopathy with subpleural reticulation, consistent with sarcoidosis. Her serum angiotensin-converting enzyme was elevated, at 154 IU/l. She was treated with i.v. fluids followed by a parramidine infusion.

Subsequently she underwent endoscopic ultrasound and bronchoscopy with transbronchial needle aspiration, which ruled out malignancy and tuberculosis, although findings were inconclusive for a diagnosis of sarcoidosis. Her pulmonary sarcoidosis was treated with tapering steroid therapy of prednisolone 10 mg daily.

Conclusion: There are several factors postulated to cause hypercalcaemia in sarcoidosis. Patients with sarcoidosis have disregulated, ectopic vitamin D production. Pulmonary alveolar macrophages in lung granulomata have been found to convert 25-hydroxy vitamin D (25(OH)D) to its active form, hence causing severe hypercalcaemia.

The patient we present was treated with only two doses of cholecalciferol at 20,000 IU/week prior to her hospital admission due to low vitamin D of 8 ng/ml. Prior to vitamin D therapy, the patient was noted to have normal serum calcium. The sudden rise in serum calcium is likely due to rapidly available 25(OH)D to macrophages in sarcoid granulomata. In addition, the lack of usual negative feedback by PTH and phosphorous augments this process. Also, IFN-γ in active sarcoidosis promotes synthesis of active vitamin D. It has been reported in a randomized, double-blind controlled study that supplemental vitamin D therapy increases cytokines such as IFN-γ in patients treated for vitamin D deficiency. The mainstay of treatment of hypercalcaemia in sarcoidosis is bisphosphonate therapy. However, in resistant hypercalcaemia, steroids are widely used. There is anecdotal evidence to support the use of steroid-sparing drugs such as HCQ and ketoconazole.

Disclosure statement: The authors have declared no conflicts of interest.

019 AN UNEXPECTED CAUSE OF ABNORMAL LIVER FUNCTION TESTS IN TWO METHOTREXATE-TREATED PATIENTS

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Background: We report two cases of elevated liver function tests (LFTs) caused by acute hepatitis E virus (HEV) infection in patients treated with MTX.

Methods: Both patients presented in the last year in neighbouring hospitals.

Results: Patient 1 is a 60-year-old man with PsA. He had been treated with MTX since 2005, lately with 25 mg s.c. weekly. He had not drunk alcohol for 10 years; amino terminal type III procollagen peptide in 2011 was borderline at 4.3 μg/l. He took warfarin for atrial fibrillation. In May 2015, routine monitoring noted an alanine aminotransferase (ALT) level of 177 IU/l (normal range 0–50). MTX was stopped but his ALT continued to rise, peaking at 2803 IU/l in June. Bilirubin was 208 μmol/l.
We report a 55-year-old man with long-standing seropositive RA who had been stable on MTX. He developed features of an aggressive disorder, including severe headaches and vomiting. CT of the brain showed acute ischemic infarction of the middle cerebral artery. He was admitted to our hospital with worsening shortness of breath, non-productive cough and fever. He had a history of primary APS, deep vein thrombosis (treated with lifelong anticoagulation) and recurrent inflammatory arthritides (managed with long-term corticosteroids).

**Results:** Clinical examination and investigation suggested a right lower lobe pneumonia, which was treated with antibiotics. However, his condition rapidly deteriorated and he required mechanical ventilation for 11 days. There was multi-organ dysfunction and evidence of arterial and venous thrombosis. CT of the thorax showed confluent pulmonary infiltrates and extensive inferior vena cava thrombosis. MRI of the brain showed acute ischemic infarction of the rostra radiata. Blood tests demonstrated acute kidney injury, neutrophilia, anaemia and severe thrombocytopenia. aCL titres were greatly elevated (IgG = 600 GPLU, IgM 128 MPLU). Lupus anticoagulant (normal range 3.72) and ant-ii-glycoprotein I antibodies (IgG 317 U/mI, IgM 107 U/mI) were also positive. ANA and dsDNA were negative. No causative organisms were cultured. She was diagnosed with CAPS, as per the International Consensus Statement criteria, and treated with pulsed i.v. methylprednisolone, therapeutic anticoagulation and antibiotics and was transferred to a tertiary vasculitis centre for plasmapheresis for 2 months. Following discharge she received maintenance plasmapheresis and RTX as an outpatient. Over the next 12 months, she had three further admissions with relapsed CAPS and became increasingly disabled by progressive cerebral infarction. During her final admission she presented with acute intracerebral haemorrhage secondary to venous sinus thrombosis and died at age 55 years.

**Conclusion:** The International Consensus Statement recommends combination therapy comprising a glucocorticoid, anticoagulation and i.v. immunoglobulin/plasmapheresis. Relapsed CAPS is very rare, being seen in just 3.2% of cases in the CAPS Registry. Our patient is notable for having five episodes of CAPS, which has only been observed in one other registry patient. Her protracted survival might be attributable to prolonged plasmapheresis and maintenance RTX therapy, in addition to steroids and anticoagulation. However, despite responding to treatment, she did not achieve sustained remission, thus demonstrating the need for novel therapies in our armamentarium against this aggressive disorder.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**021 RELAPSING CATASTROPHIC ANTI-PHOSPHOLIPID SYNDROME IN A 53-YEAR-OLD FEMALE**

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**Background:** Catastrophic APS (CAPS) is an accelerated form of APS. It presents as a diffuse thrombotic microangiopathy that predominately involves the lungs, brain, kidney and heart and may be triggered by infection. It occurs in ~1% of APS patients and has a mortality rate that approaches 50%, making recurrent episodes very rare.

**Methods:** We present the case of a 53-year-old British woman who was admitted to our hospital with worsening shortness of breath, non-productive cough and fever. She had a history of primary APS, deep vein thrombosis (treated with lifelong anticoagulation) and recurrent inflammatory arthritides (managed with long-term corticosteroids).

**Results:** Clinical examination and investigation suggested a right lower lobe pneumonia, which was treated with antibiotics. However, her condition rapidly deteriorated and she required mechanical ventilation for 11 days. There was multi-organ dysfunction and evidence of arterial and venous thrombosis. CT of the thorax showed confluent pulmonary infiltrates and extensive inferior vena cava thrombosis. MRI of the brain showed acute ischemic infarction of the rostra radiata. Blood tests demonstrated acute kidney injury, neutrophilia, anaemia and severe thrombocytopenia. aCL titres were greatly elevated (IgG = 600 GPLU, IgM 128 MPLU). Lupus anticoagulant (normal range 3.72) and anti-ii-glycoprotein I antibodies (IgG 317 U/mI, IgM 107 U/mI) were also positive. ANA and dsDNA were negative. No causative organisms were cultured. She was diagnosed with CAPS, as per the International Consensus Statement criteria, and treated with pulsed i.v. methylprednisolone, therapeutic anticoagulation and antibiotics and was transferred to a tertiary vasculitis centre for plasmapheresis for 2 months. Following discharge she received maintenance plasmapheresis and RTX as an outpatient. Over the next 12 months, she had three further admissions with relapsed CAPS and became increasingly disabled by progressive cerebral infarction. During her final admission she presented with acute intracerebral haemorrhage secondary to venous sinus thrombosis and died at age 55 years.

**Conclusion:** The International Consensus Statement recommends combination therapy comprising a glucocorticoid, anticoagulation and i.v. immunoglobulin/plasmapheresis. Relapsed CAPS is very rare, being seen in just 3.2% of cases in the CAPS Registry. Our patient is notable for having five episodes of CAPS, which has only been observed in one other registry patient. Her protracted survival might be attributable to prolonged plasmapheresis and maintenance RTX therapy, in addition to steroids and anticoagulation. However, despite responding to treatment, she did not achieve sustained remission, thus demonstrating the need for novel therapies in our armamentarium against this aggressive disorder.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**022 SEVERE GANGRENE CAUSED BY AGGRESSIVE VASCULOPATHY AND VASCUITIS IN A PATIENT WITH ANTI-RIBONUCLEOPROTEIN-POSITIVE LIMITED SCLERODERMA/INFLAMMATORY ARTHRITIS OVERLAP**

Charles Raine, Simon Donnelly and Hasan Tahir

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**Background:** Vasculopathy is a hallmark of scleroderma often leading to poor digital perfusion. In extreme cases this can lead to necrosis/ gangrene. Treatment in the acute setting involves vasodilator therapy, including prostaglandin analogue infusion. Amputation of established necrosis is generally avoided due to the risk of poor stump healing and exacerbation of vasculopathy.

**Methods:** We report a 55-year-old man with long-standing seropositive RA who had been stable on MTX. He developed features of an anti-RNP-positive scleroderma overlap syndrome over an 18-month period, with the addition of typical features of inflammatory arthritis. Physical examination revealed clubbing of the fingers and toes, with limited range of movement in the distal interphalangeal joints. He had a history of pericarditis, atrial fibrillation and hypertension, which had been controlled with anticoagulation and ACE inhibitors, respectively. He had a history of smoking and alcohol abuse. He presented with severe digital ischaemia and gangrene of the hands and feet, with extensive skin necrosis and sloughing. A diagnosis of severe vasculitis and necrotizing arteritis was made. He was admitted to intensive care for septic shock and respiratory failure. He was treated with intravenous immunoglobulin, plasma exchange and antibiotics, and was transferred to a tertiary vasculitis centre for maintenance plasmapheresis and RTX as an outpatient. Over the next 12 months, she had three further admissions with relapsed CAPS and became increasingly disabled by progressive cerebral infarction. During her final admission she presented with acute intracerebral haemorrhage secondary to venous sinus thrombosis and died at age 55 years.

**Conclusion:** The International Consensus Statement recommends combination therapy comprising a glucocorticoid, anticoagulation and i.v. immunoglobulin/plasmapheresis. Relapsed CAPS is very rare, being seen in just 3.2% of cases in the CAPS Registry. Our patient is notable for having five episodes of CAPS, which has only been observed in one other registry patient. Her protracted survival might be attributable to prolonged plasmapheresis and maintenance RTX therapy, in addition to steroids and anticoagulation. However, despite responding to treatment, she did not achieve sustained remission, thus demonstrating the need for novel therapies in our armamentarium against this aggressive disorder.

**Disclosure statement:** The authors have declared no conflicts of interest.
period and then presented systemically unwell with rapidly progressive and severe necrosis resistant to high-dose continuous i.v. iloprost. 

**Results:** He presented acutely with fever, widespread synovitis and low molecular weight heparin, although this remained dry. Surgical opinion was that he should undergo further amputation at both wrists. We decided to persist with medical management and there was no progression of the gangrene. His CRP continued to decrease. His CRP remained elevated despite broadening of the antibiotic cover. Transversephagial echocardiogram showed no endocarditis and there was no focus of infection on CT of the chest, abdomen and pelvis. Multiple blood cultures were negative. His digital perfusion worsened and low molecular weight heparin, clopidogrel and sildenafil were added; iloprost was further up-titrated. After 1 week he developed necrosis of the hands and feet requiring bilateral below-the-knee amputation due to wet gangrene. He received three pulses of i.v. methylprednisolone and after the first his CRP decreased dramatically. Postoperatively he received 5 days of IVIG. He had necrosis of his fingers and almost the entirety of his hands, although this remained dry. Surgical opinion was that he should undergo further amputation at both wrists. We decided to persist with medical management and there was no progression of the gangrene. His CRP continued to decrease. He was commenced on MMF and received monthly IVIG for 6 months. Over this period there was a slow but definite improvement in the more proximal areas of his hands that initially appeared non-viable. He was eventually discharged to amputation rehabilitation, is now able to walk with prostheses and he remains in remission.

**Conclusion:** This appeared to be a combination of aggressive vasculopathy and vasculitis in overlap scleroderma syndrome refractory to conventional vasodilator therapy but eventually responding well to immunosuppression. While amputation for wet gangrene is unavoidable, the conservative strategy we adopted in the management of his hand necrosis proved justified. IVIG may be a promising therapeutic tool in this setting.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**023 TAKAYASU TWINS**

**Corinne E. Locke, Rob Callaghan and Gwenaen Huws**

**Rheumatology, Nevill Hall Hospital, Abergavenny, UK**

**Background:** Takayasu arteritis is an uncommon large vessel vasculitis whose aetiology remains poorly understood.

**Methods:** We present a case of identical twin sisters of Bangladeshi origin who have both been diagnosed with Takayasu arteritis. Separately these are interesting cases, but together they are quite rare and prompted us to review the genetics of Takayasu disease. The twins have nine other siblings and are concerned about the risks for them.

**Results:** A 25-year-old woman presented acutely in July 2013 with heart failure and was found to have severe aortic regurgitation (AR) and left ventricular (LV) impairment. She underwent an urgent valve replacement. The surgeons noted a dense inflammatory process involving the entire ascending aorta. Histology revealed lymphocytic infiltration of the vasa vasorum with focal areas of giant cell inflammation. CT angiogram showed multiple stenotic lesions, including the left carotid, inferior subclavian, right axillary and superior mesenteric arteries. A diagnosis of Takayasu arteritis was made. The patient was treated with 30mg prednisolone and commenced on MTX and is doing well. The patient’s twin sister first presented in March 2015 at age 26 years. She was incidentally found to have a murmur while being treated in hospital for a post-natal urinary infection. She was asymptomatic but did have a weak radial pulse on the left, with a significant discrepancy in blood pressure in the arms. An echo revealed moderate to severe AR. A subsequent CT angiogram showed a slightly dilated ascending aorta and a number of stenotic lesions, including marked narrowing of the left subclavian artery. A diagnosis of Takayasu arteritis was made. A PET scan was completely cold, suggesting no active inflammation, and therefore she was not immediately started on immunosuppression, but 2 months later there was an increase in inflammatory markers and she began treatment with prednisolone 30mg and MTX. It is suspected that she may have had a previous episode of active vasculitis in 2004 when she had been unwell with fevers and anaemia and her blood work had shown a persistently elevated ESR, although a diagnosis had not been made at that time.

**Conclusion:** The pathogenesis of Takayasu arteritis is not fully understood, but there have been several case reports of siblings with the disease, including at least three sets of twins, suggesting genetic susceptibility plays a role. HLA-B52 is known to be associated with the disease, including at least three sets of twins, suggesting genetic susceptibility plays a role. HLA-B52 is known to be associated with the disease, including at least three sets of twins, suggesting genetic susceptibility plays a role. HLA-B52 is known to be associated with the disease, including at least three sets of twins, suggesting genetic susceptibility plays a role.
of skeletal muscles. Cardiac involvement is associated with increased mortality and is a common cause of death. However, it is usually subclinical, and ECG and echocardiography may be non-specific and may not highlight the severity of involvement. Moreover, Cardiac MRI is rarely available in most departments. This case report aims to raise awareness of the importance of checking troponin in patients with myositis and summarizes current knowledge on the diagnosis of cardiac involvement in IIMs.

Methods: The patient is a 28-year-old Asian female with a 4-year history of seronegative inflammatory arthritis who attended routine follow-up with a 2-month history of progressive upper and lower limb swelling, muscle weakness and breathlessness. Definite PM/DM overlap was diagnosed as per the Bohan and Peter classification. Initial creatinine kinase (CK) was 3224 U/l, with a peak of >4000 (normal range 0–165) and ESR was 134 mm/h (normal range 0–7). ANA was positive (titre >800) with a mixed pattern of speckled and nucleolar staining. ACA was positive (titre >120, <200). ECG showed sinus tachycardia (rate 121 bpm), but nothing else. Chest X-ray and high-resolution CT showed borderline cardiomegaly and a small pericardial effusion. However, highly sensitive troponin T was markedly elevated at 3107 ng/l (normal range 0–14). Urgent cardiac MRI confirmed severe cardiac myositis. She was managed with high-dose i.v. then oral corticosteroids, AZA and IVIG, with near normalization of CK and troponin and resolution of clinical symptoms and signs. Unfortunately, it was not possible to give further infliximab. Two years later she developed pulmonary hypertension and died suddenly. A literature search was performed for cardiac, myositis and inflammation in the English-language literature over the past 30 years.

Results: Cardiac involvement ranges from asymptomatic to severe and is most commonly heart failure. Cardiac myositis is invariably associated with active skeletal muscle disease. There is a wide spectrum of abnormalities on ECG and echocardiography, and troponin T is affected by CK whereas troponin I is not. Cardiac MRI can detect early myocarditis and can be used to monitor response to treatment. Treatment is based on expert experience or small case series and requires persistent high-dose corticosteroids, usually i.v., and subsequent immunosuppression in almost all cases.

Conclusion: Cardiac involvement in IIMs may be underestimated and cardiovascular disease (i.e. highly sensitive T) is a single easily accessible test and should be considered in all inpatients with IIM irrespective of whether they have cardiac symptoms.

Disclosure statement: The authors have declared no conflicts of interest.

026 AN UNUSUAL CAUSE OF HIP PAIN IN A PATIENT WITH RHEUMATOID ARTHRITIS

Timothy D. Reynolds and Robert W. Marshall

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Background: As rheumatologists, we need to be aware of unusual causes of musculoskeletal symptoms among our patients, particularly if the investigations are unhelpful and the symptoms fail to improve following initial treatment.

Methods: A 68-year-old woman with a 7-year history of seronegative RA presented with right lateral hip pain. She had taken oral MTX for 6 years, but had discontinued it 6 months previously due to recurrent varicose veins and had stopped smoking ~2 years previously. The right lateral hip pain disturbed her sleep when she lay on it. Her general practitioner had suspected trochanteric bursitis and had injected corticosteroid and local anaesthetic, but her symptoms failed to respond. On review in the rheumatology clinic, she appeared in remission, with no tender or swollen joints on 28-joint assessment. She had a good range of movement of both hips but had marked tenderness over the right greater trochanter. Inflammatory markers, creatine kinase, calcium and electrolytes were all normal. A plain radiograph showed possible calcific tendinopathy adjacent to the greater trochanter. A US scan of the right hip showed fluid in the trochanteric bursa with normal gluteal tendons, so a guided bursal injection of corticosteroid and local anaesthetic was performed. The symptoms failed to improve. A subsequent MRI showed an unusual pattern of abnormal signal in the right gluteus minimus with oedema in the adjacent iliac blade and posterior acetabulum.

Results: Initial differential diagnosis included either localized infection or myositis, however, the inflammatory markers and creatine kinase remained normal. The possibility of metastatic disease was raised. A chest radiograph demonstrated left perihilar and lower lobe opacities; a CT scan of the chest, abdomen and pelvis showed features consistent with bronchogenic carcinoma, with foci in the left upper and lower lobes with invasion of the mediastinum, together with a solitary extrathoracic metastasis in the right gluteus minimus muscle. A US-guided biopsy of the right gluteus minimus confirmed metastatic adenocarcinoma of the lung. She went on to receive palliative percutaneous cisdaplatin chemotherapy and a single fraction of radiotherapy to the right gluteus minimus.

Conclusion: Muscular metastases are very uncommon and there are few cases reported in the medical literature. This case is extremely unusual in that the symptoms associated with the right gluteus minimus metastasis were the sole presenting features of this malignancy. She had no respiratory or constitutional symptoms and had not lost weight. Rheumatologists should be alert to the possibility of other diagnoses in patients with persistent or unexplained musculoskeletal symptoms, and a history of other recent malignancy should raise suspicion.

Disclosure statement: The authors have declared no conflicts of interest.
028  THE INCIDENCE AND PREDICTORS OF FLARE IN A COHORT OF RHEUMATOID ARTHRITIS PATIENTS

Andrew I. Rutherford, David L. Scott, Sujith Subesinghe, Fowzia Ibrahim and James Galloway

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Background: Modern therapy in RA has led to fewer patients remaining in a state of persistently high disease activity. Despite this, many patients continue to experience episodic flare in their disease. Existing data show a relationship between flare and increased erosive progression and more frequent cardiovascular events. Although an important outcome metric, the frequency of flare in RA is not well described. We set out to study the incidence and predictors of disease flare among a cohort of patients with RA.

Methods: Routinely collected prospective data from a cohort of RA patients seen in a single specialist centre were utilized. The hospital employs an electronic medical record, enabling extraction of anonymized clinical information. Coded information on disease activity is collected at each visit using a 28-joint count DAS with ESR (DAS28-ESR). Data from 2010 onwards were used. Flare was defined as an increase in DAS28 from the previous visit by 0.6, reaching a DAS28 >3.2, and with an increase in the swollen joint count of at least one. A survival model was used to calculate the incidence of flare. Predictors of flare were analysed using a time-to-event univariate Cox model.

Results: The annual flare rate in our cohort is shown in Table 1. Higher disease activity at baseline and treatment with biologics correlated with statistically significant increases in flare rates. Patients with either a positive RF or CCP antibody were also more likely to flare (hazard ratio (HR) 1.4 (95% CI 1.1, 1.6)). Overall, the annual flare rate was ~30%, while multiple flares occurred in 10% of patients (95% CI 8.7, 15.5).

Conclusion: Despite improvements in RA management, flares remain a major problem. Each year 30% of RA patients have a flare, and rates are higher in some groups, including 38% of patients with initially active disease and 40% of patients on biologics. It is possible that minimizing flares may be more important than the overall reduction in disease activity achieved by DMARDs and biologics. Further work is needed to identify how best to achieve this goal.

Disclosure statement: A.I.R. has received a clinical fellowship award from the NIHR Biomedical Research Centre, Guy’s and St Thomas’ NHS Foundation Trust and King’s College London. All other authors have declared no conflicts of interest.

028 Table 1. Flare rates according to baseline disease activity and treatment

<table>
<thead>
<tr>
<th>All Cases</th>
<th>Baseline DAS</th>
<th>DMARD</th>
<th>Biologic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;3.2</td>
<td>3.2–5.1</td>
<td>&gt;5.1</td>
</tr>
<tr>
<td>Patients, n</td>
<td>1212</td>
<td>371</td>
<td>508</td>
</tr>
<tr>
<td>Follow-up, years</td>
<td>2803</td>
<td>791</td>
<td>1230</td>
</tr>
<tr>
<td>Flares,</td>
<td>847</td>
<td>158</td>
<td>375</td>
</tr>
<tr>
<td>Flare rate/100 patient-years</td>
<td>30 (24, 32)</td>
<td>20 (17, 23)</td>
<td>31 (28, 34)</td>
</tr>
<tr>
<td>Hazard ratio (95% CI)</td>
<td>Reference</td>
<td>1.5 (1.3, 1.8)</td>
<td>1.9 (1.6, 2.3)</td>
</tr>
</tbody>
</table>

029 INFLAMMAGING AND BONE HEALTH IN LATER LIFE: THE HERTFORDSHIRE COHORT STUDY

Anna E. Litwic, Karen J. Jameson, Mark H. Edwards, Charlotte Moss, Cyrus Cooper and Elaine M. Dennison

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Background: Inflammatory burden has been associated with a range of adverse musculoskeletal outcomes in later life, including accelerated OA and sarcopenia. Here we report the association between markers of inflammation and bone health among unselected individuals recruited to a population-based cohort study.

Methods: The study population was taken from the Hertfordshire Cohort Study, who were born in Hertfordshire between 1931 and 1939 and still lived there 70 years later. At baseline, a questionnaire was administered detailing lifestyle and demographic factors and a detailed co-morbidity history was taken. At a clinic visit, fasting blood samples were taken and analyzed for IL-6 and high sensitivity CRP (hsCRP). BMD measurements were taken at the lumbar spine and femoral neck using a QDR 4500 densitometer (Hologic, Marlborough, MA, USA). There were 314 men and 288 women for whom we had BMD measurements and IL-6 and/or hsCRP.

Results: The mean age was 65.0 years (s.d. 2.6) in men and 66.2 (s.d. 2.6) in women. The geometric mean BMI was 26.8 (s.d. 1.1) and 26.9 (s.d. 1.2) in men and women, respectively. The geometric mean hsCRP was 1.72 mg/l (s.d. 2.9) in men and 1.85 (s.d. 3.0) in women; an IL-6 >1.5 pg/l was observed in 88 (29.4%) men and 58 (20.5%) women. The hsCRP 2-score was an explainatory variable for lumbar spine BMD in men but not women, after adjustment for age, BMI, co-morbidities, social class, smoking status, alcohol consumption, physical activity and dietary calcium intake [regression coefficient −0.14 (95% CI –0.26, –0.02), P = 0.03]. Relationships at the femoral neck were also apparent but slightly weaker in men only [regression coefficient −0.11 (95% CI –0.23, 0.00), P = 0.06] after the same adjustments. A baseline IL-6 >1.5 pg/l was also associated with reduced lumbar spine BMD in men but not women [regression coefficient −0.31 (95% CI –0.59, 0.04), P = 0.03] after adjustments.

Conclusion: We observed associations between inflammatory markers within the normal range and bone health in men but not women in later life. Further studies are now warranted.

Disclosure statement: The authors have declared no conflicts of interest.

030 THE INFLUENCE OF TUMOUR NECROSIS FACTOR INHIBITORS ON DEMENTIA INCIDENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Excess TNF has been associated with the pathogenesis of Alzheimer’s disease (AD) and a recent study has suggested that s.c. administration of etanercept may slow cognitive decline in patients with AD. The aim of this study was to evaluate whether patients with RA treated with TNF inhibitor (TNFi) have a lower risk of dementia compared with biologic-naive patients receiving synthetic DMARDs (sDMARDs).

Methods: This analysis included patients in the British Society for Rheumatology Biologics Registry for RA (BSRBR-RA) starting a TNFi or registered in the biologic-naive DMARD comparison cohort and followed all patients until death or 30 November 2014. Patients in the comparison cohort who switched to a biologic were censored and contributed further follow-up time to the TNFi cohort. All cases of dementia, including AD, unspecified dementia, vascular dementia and frontotemporal dementia, were identified from study follow-up questionnaires and/or death certificates and verified by two physicians. Dementia reported within the first 12 months of study were excluded to minimize inclusion of prevalent cases. The risk of dementia between the two cohorts was compared using two TNFi exposure models—on TNFi and ever TNFi exposed—and analysed using age- and gender-adjusted Cox proportional hazards models.

Results: Eighty-four cases of dementia among 17 247 patients were identified (62 on TNFis and 22 on sDMARDs), with 58 reported to the register on the death certificate. In both drug-exposure models, the incidence of dementia was lower in patients who had received TNFis compared with sDMARDs only (Table 1). Compared with patients on sDMARDs, there was a trend towards a lower risk of dementia in patients while receiving TNFis compared with that seen in the ever-exposed model, although neither exposure model reached statistical significance.

Conclusion: RA patients treated with TNFis appear to have a lower incidence of dementia compared with biologic-naive patients, although absolute numbers were low and relative risk was not significantly different. A majority of cases were reported to the register at the time of death, suggesting that this is likely to be a minimal estimate of disease incidence in this cohort, warranting further investigation of the effects of TNFis on the occurrence of dementia.

Disclosure statement: The authors have declared no conflicts of interest.
Although results varied across instruments, overall, unable to work, work ability at its best (e.g., the HAQ) as completed by participants with differing levels of disease activity in their hands may result in smaller convergence with the global measures. Variations in the content of each global measure may account for the variability in correlation results (e.g., measures focusing on dexterity (e.g. the HAQ) as completed by participants with differing levels of disease activity in their hands may result in smaller convergence with the global measures). Overall, the results contribute to the currently sparse validity data for global measures of presenteeism.

Disclosure statement: The authors have declared no conflicts of interest.

032 ESTIMATES OF INACTIVE DISEASE ARE STRONGLY INFLUENCED BY OUTCOME DEFINITION IN A PROSPECTIVE COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Stephanie J. W. Shoop, Suzanne M. M. Verstappen, Eileen Balldaran, Alice Ching, Joyce Davidson, Helen Foster, Yiannis Ioannou, Flora McErlane, Lucy R. Wetherburn, Wendy Thomson and Kimme L. Hyrich

Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, UK, Paediatric Rheumatology, Alder Hey Children’s NHS Foundation Trust, Liverpool, Royal Manchester Children’s Hospital, Manchester, Royal Hospital for Sick Children, Glasgow, Royal Hospital for Sick Children, Edinburgh, Great North Children’s Hospital, Newcastle upon Tyne, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, Arthritis Research UK Centre for Asthma and Respiratory Research, College London, Paediatric Rheumatology, Great Ormond Street Hospital NHS Foundation Trust, London, Arthritis Research UK Centre for Genetics and Genomics, Central Manchester University Hospitals NHS Foundation Trust and University of Manchester Partnership, Manchester, UK

Background: Persistent active disease in JIA causes functional disability, pain and joint damage. Treating towards a target of inactive disease (ID) may improve outcomes across different clinical settings. Many definitions of ID have been developed for JIA. However, few studies have compared the performance of multiple definitions in a single patient population. To compare the achievement of ID and minimal disease activity (MDA) across single and validated composite definitions in a single patient population.

Methods: In this cross-sectional study, 161 patients with RA, PsA, AS, or OA in paid employment were recruited from the UK, Canada, Romania, Sweden and Italy. Demographic, visual analogue scale (VAS) general well-being, functional disability (HAQ) and occupational data were collected. In addition, disease-specific measures were completed depending on underlying disease. All participants completed the global presenteeism measures and multi-item measures [the Workplace Activity Limitations Questionnaire (WALS) and the Work Limitations Questionnaire (WLQ-25)]. Spearman’s correlation coefficients were applied to assess the strength of the relationship between the global measures with multi-item measures and health measures.

Results: A total of 1415 children were selected. At baseline, the median age was 7.7 years and 65% were female. The most frequent subtype presented was oligoarticular (50%), followed by RF-negative polyarticular disease (21%). The median baseline Juvenile Arthritis Disease Activity Score (JADAS17) was 11.4.

Disclosure statement: The authors have declared no conflicts of interest.

031 Table 1. Baseline characteristics and dementia incidence by drug

<table>
<thead>
<tr>
<th>Variable</th>
<th>Overall</th>
<th>Biologic-naïve</th>
<th>TNFi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (y.o.)</td>
<td>57.0 (12.45)</td>
<td>60.1 (12.44)</td>
<td>56.1 (12.33)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>10 (6–18)</td>
<td>11 (6–18)</td>
<td>11 (6–18)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6.2 (1.32)</td>
<td>5.1 (1.32)</td>
<td>6.5 (1.32)</td>
</tr>
<tr>
<td>HAQ, median (IQR)</td>
<td>2.1 (1.2–3.75)</td>
<td>1.625 (0.675–2.125)</td>
<td>2.125 (1.625–2.5)</td>
</tr>
<tr>
<td>Ever-exposed analysis</td>
<td>Dementia, n (%)</td>
<td>84 (4.8)</td>
<td>22 (5.8)</td>
</tr>
<tr>
<td>Follow-up, patient-years</td>
<td>148 104</td>
<td>30 933</td>
<td>117 171</td>
</tr>
<tr>
<td>Follow-up, median, years (IQR)</td>
<td>9.3 (7.25–10.54)</td>
<td>8.7 (6.86–9.97)</td>
<td>9.9 (7.25–11.03)</td>
</tr>
<tr>
<td>Incidence/1000 (95% CI)</td>
<td>0.47 (0.54, 0.83)</td>
<td>0.85 (0.56, 1.29)</td>
<td>0.63 (0.48, 0.82)</td>
</tr>
<tr>
<td>Age, gender-adjusted</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>WAI (0–10)</td>
<td>0.73 (0.59)</td>
<td>0.73 (0.59)</td>
<td>0.73 (0.59)</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>0.73 (0.59)</td>
<td>0.46 (0.24)</td>
<td>0.58 (0.38)</td>
</tr>
<tr>
<td>VAS pain</td>
<td>0.58 (0.38)</td>
<td>0.46 (0.24)</td>
<td>0.58 (0.38)</td>
</tr>
<tr>
<td>VAS general well-being</td>
<td>0.66 (0.45)</td>
<td>0.46 (0.24)</td>
<td>0.58 (0.38)</td>
</tr>
<tr>
<td>RAID</td>
<td>0.73 (0.59)</td>
<td>0.73 (0.59)</td>
<td>0.73 (0.59)</td>
</tr>
<tr>
<td>PsAID</td>
<td>0.73 (0.59)</td>
<td>0.73 (0.59)</td>
<td>0.73 (0.59)</td>
</tr>
</tbody>
</table>

031 Table 1. Spearman correlations of the global presenteeism measures with multi-item and health measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>WALS</th>
<th>WLQ-25</th>
<th>HAQ</th>
<th>EQ-SD</th>
<th>VAS pain</th>
<th>VAS general well-being</th>
<th>RAID</th>
<th>PsAID</th>
<th>Lequesne</th>
<th>BASDAI</th>
<th>BASFI</th>
</tr>
</thead>
<tbody>
<tr>
<td>WAI (0–10)</td>
<td>0.73</td>
<td>0.59</td>
<td>0.46</td>
<td>0.58</td>
<td>0.58</td>
<td>0.66</td>
<td>0.45</td>
<td>0.70</td>
<td>0.54</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td>WPS-RA (0–10)</td>
<td>0.73</td>
<td>0.54</td>
<td>0.50</td>
<td>0.53</td>
<td>0.53</td>
<td>0.69</td>
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<td>VAS general well-being</td>
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Conclusions: Although results varied across instruments, overall, moderate to very high convergent validity was found between global measures of presenteeism and multi-item measures and moderate to very high construct validity was found with disease-specific measures.
At 1 year, at least one state of ID was achieved by 69% of patients (Table 1). The highest estimate was for zero active joints (64%), followed by parental remission on the JADAS71 (48%). The lowest estimate of ID was based on the most stringent criteria, Wallace’s preliminary criteria (46%). Estimates of ID using JADAS10, JADAS71 and cJADAS10 were similar. However, Wallace’s preliminary criteria and JADAS only agreed on 39% patients that were in ID on either tool. MDA was achieved at a similar rate to the higher ID estimates, with ~50% of patients achieving MDA on the JADAS and cJADAS tools. The ID/MDA definitions identified different groups of children has implications for treat-to-target strategies and further work is needed to identify which definition captures the optimal target state.

Disclosure statement: The authors have declared no conflicts of interest.

033 HIGHER PREVALENCE OF CHRONIC CARDIOVASCULAR AND PULMONARY MORBIDITIES IN PEOPLE WITH INFLAMMATORY ARTHRITIS IS ASSOCIATED WITH A LOWER LEVEL OF PHYSICAL ACTIVITY: RESULTS FROM THE UK BIOBANK

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Background: Little is known about the impact of chronic cardiovascular and pulmonary co-morbidities on physical activity in people with inflammatory arthritis (IA). We estimated the age- and sex-adjusted prevalence of co-morbidities in people with IA compared with people without IA and assessed the impact of morbidities on physical activity level in a large, national cohort.

Methods: Men and women aged 40–69 years from across the UK were recruited to the UK Biobank between 2006 and 2010. Self-reported data on IA (RA, PsA, AS) and cardiovascular and pulmonary morbidities were collected during a computer-based questionnaire and interview with a nurse. Indirect age- and sex-standardized morbidity prevalence was calculated in people with IA; people without IA were the reference group. The validated International Physical Activity Questionnaire was used to determine participants’ physical activity level (low, moderate, high). Participants were categorized into one of the following study groups: no IA and no morbidity (no IA–M), no IA and morbidity (no IA–no M), IA and morbidity (IA–M) and IA and morbidity (IA–no M) and IA and morbidity (IA–M). Multinomial logistic regression was used to assess the association between physical activity level and study group. The model was adjusted for age, sex and smoking status.

Results: A total of 498 590 subjects were included in this study. The mean age was 56.5 years (s.d. 8.1), 54.3% were female and 10.6% were current smokers. The adjusted prevalences of cardiovascular and pulmonary diseases were generally higher in people with IA (Table 1). With low physical activity as the reference group, compared with people in the no IA–no M group, people in the no IA–M, IA–no M and IA–M groups were increasingly less likely to have a moderate level of physical activity: relative risk ratio (95% CI) 0.86 (95% CI 0.84, 0.88), 0.67 (0.62, 0.72) and 0.54 (0.48, 0.61), respectively. A similar trend was seen for a high level of physical activity for no IA–M, IA–no M and IA–M:

Table 1: Indirect age- and sex-adjusted co-morbidity rates in people with IA

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>PsA</th>
<th>AS</th>
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<tbody>
<tr>
<td>RA</td>
<td>Crude, %</td>
<td>Standardized prevalence ratio (95% CI)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2.9</td>
<td>1.90 (1.67, 2.19)</td>
</tr>
<tr>
<td>Heart attack</td>
<td>4.0</td>
<td>1.86 (1.62, 2.12)</td>
</tr>
<tr>
<td>Angina</td>
<td>6.3</td>
<td>1.87 (1.68, 2.08)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.9</td>
<td>1.70 (1.52, 1.96)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36.3</td>
<td>1.24 (1.19, 1.30)</td>
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<tr>
<td>Pulmonary</td>
<td></td>
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</tr>
<tr>
<td>COPD</td>
<td>5.6</td>
<td>2.20 (1.96, 2.46)</td>
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<tr>
<td>Asthma</td>
<td>15.5</td>
<td>1.33 (1.24, 1.42)</td>
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</table>

COPD: chronic obstructive pulmonary disease.
quality of life, pain, biologic prescription or the presence of extraspinal manifestations.

Conclusion: We have shown that, among working-age patients with AS, presenteeism is a poor predictor of subsequent employment loss. However, those who have previously had to change their job because of their disease are twice as likely to become unemployed in the medium term. Early identification of this high-risk group is important to allow strategies to be considered that may enable work retention.

Disclosure statement: G.J.M. has received honoraria from Pfizer and research funding from AbbVie, Pfizer and UCB. G.T.J. has received research funding from AbbVie, Pfizer and UCB. All other authors have declared no conflicts of interest.

035 TRENDS IN PRESCRIBING OF NON-STEROIDAL ANT-INFLAMMATORY DRUGS IN PRIMARY CARE IN PATIENTS WITH AND WITHOUT CARDIOVASCULAR DISEASE: AN OBSERVATIONAL DATABASE STUDY

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Background: NSAIDs are commonly used to treat pain, but have potentially serious side effects when prescribed in patients with cardiovascular disease (CVD). The Medicines and Healthcare Products Regulatory Agency (MHRA) and National Institute for Health and Care Excellence (NICE) issued directives between 2004 and 2008 relating to their use in patients with CVD, stipulating that NSAIDs, especially cyclooxygenase-2 (COX-2) drugs, should be used with caution in CVD patients to prevent potential adverse events. Our aim was to determine trends in NSAIDs prescribing from 2002 to 2010 in patients with and without CVD and to ascertain if patterns of prescribing changed following the issuance of the MHRA/NICE guidance.

Methods: This was an observational database study of patients ≥18 years of age undertaken in 11 practices contributing to the Consultations in Primary Care Archive [2002-10]. All NSAIDs were grouped into three categories (basic, COX-2 and topical NSAIDs). Study duration was divided into quarterly time periods, on a seasonal basis, from the first quarter of 2002 to the fourth quarter of 2010. Within each quarterly time period, patients with and without CVD were distinguished using predefined Read codes for CVD and the number of patients receiving each category of NSAIDs was determined. The quarterly prescription prevalence of NSAID groups over the study period was determined separately in patients with and without CVD. Prescribing trends were analysed using joinpoint regression to determine any significant changes. Changes in prescribing in relation to the five major pieces of national guidance [issued in 2004 quarter 4 (2004q4), 2005q1, 2005q3, 2006q2 and 2008q1] were assessed.

Results: In the beginning of study period, higher prescription prevalence in each NSAID category was seen in patients with CVD compared with that in patients without CVD. In both patient groups, the use of basic NSAIDs overall showed a decreasing trend (CVD 774 (per 10 000) in 2002q1 to 245 in 2010q4; non-CVD 643 to 467) although the decrease was greater in patients with CVD. The use of topical NSAIDs, however, showed a continuously increasing trend over the study period in both patient groups (CVD 115 (per 10 000) in 2002q1 to 270 in 2010q4; non-CVD 108 to 245). In both patient groups, following an increase in prevalence between 2002q1 and 2004q3, the prescription of COX-2 drugs fell sharply during 2004q4 to 2005q1 (CVD 401 (per 10 000) to 111; non-CVD 237 to 99) stabilizing at ~50 per 10 000.

Conclusion: Despite guidelines and a trend toward decreased prescribing, the use of potentially harmful NSAIDs continued in patients with CVD. The MHRA directives had similar effects on both patient groups such that COX-2 use became very infrequent and basic NSAIDs use decreased for both. Further advice appears to be needed regarding the correct use of NSAIDs since patients with CVD might still be using them inappropriately, and non-CVD patients, who might benefit, have had their use inappropriately restricted.

Disclosure statement: The authors have declared no conflicts of interest.

036 PREVALENCE OF ADRENAL INSUFFICIENCY FOLLOWING SYSTEMIC GLUCOCORTICOID THERAPY BETWEEN 9 AND 100%: A SYSTEMATIC REVIEW

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1NHRI Manchester Musculoskeletal Biomedical Research Unit, 2Manchester Centre for Endocrinology and Diabetes and Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, UK

Background: One per cent of the adult population are, at any one time, prescribed oral glucocorticoids (GCs). GCs are known to be associated with hypothalamic-pituitary-adrenal axis suppression. However, there remains uncertainty regarding the prevalence of GC-induced adrenal insufficiency (AI), the effects of GC dose and duration and the time course of adrenal recovery and how GCs should be withdrawn. We undertook a systematic literature review to address these questions.

Methods: Searches were performed in Medline and Web of Science in November 2014. Eligible papers studied adult patients with an indication for long-term GCs, exposure to systemic GCs (oral, intramuscular or i.v.) and adrenal function tests. Screening was performed in duplicate and additional articles were identified through citation screening. Three categories each for increasing daily dose, duration and cumulative dose were assessed.

Results: From 673 screened papers, 73 met the inclusion criteria (13 randomized controlled trials and 60 observational studies). The prevalence of AI ranged from 0 to 100%. The prevalence also ranged from 0 to 100% within most categories of daily dose, duration and cumulative dose. Across these categories, the median prevalence ranged from 14% for a medium cumulative dose (0.5–5 g) to 50% for a high cumulative dose (>5 g). There was evidence of persisting adrenal suppression 1–3 years after GC cessation. Thirteen studies reported weaning of GCs, but these were too heterogeneous in study design to draw useful conclusions.

Conclusion: Significant variation exists in the reported prevalence of AI after systemic GC therapy, irrespective of exposure category. There is evidence, albeit limited, that even low doses can suppress adrenal function, and some patients may have AI after several years of cessation. We suggest clinicians be vigilant for AI with all doses and durations of GC therapy. The evidence base supporting current practice, particularly with regards to withdrawal of steroids, is scant. There is an imperative need for large-scale prospective studies to guide future practice.

Acknowledgements: This work includes independent research funded by the NIHR Manchester Biomedical Research Unit Funding Scheme. The views expressed in this abstract are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

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Disclosure statement: The authors have declared no conflicts of interest.

PRIMARY CARE

037 RHEUMATOLOGY GUIDELINES IN GENERAL PRACTICE: A BLACK HOLE?

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Background: Most rheumatological diseases are managed on a shared-care basis with primary care, supported by national guidelines. However, there is little data about adherence to these standards.

Methods: Electronic records of a single general practice (16714 patients) were searched as follows: MTX on repeat prescription for >1 year; gout AND allopurinol on repeat prescription for >1 year; RA AND glucocorticoids (GCs) on repeat prescription for >6 months and temporal arteritis as a diagnosis. The audit standards used are explained below. [BSR/British Health Professionals in Rheumatology (BHRP) Guideline for DMARD therapy. Patients on MTX for >1 year should have blood tests every 3 months. Patients taking MTX should have 5 mg folate acid weekly. BSR/BHRP guideline for the management of gout. Patients should have annual measurement of plasma urate. Plasma urate should be <300 µmol/l. National Institute for Health and Care Excellence management of RA, patients should be offered an annual review including a QRISK2 score. Royal College of Physicians GC-induced osteoporosis. Bone protection for patients >65 years of age on long-term GCs. BSR/BHRP guideline for the management of OA. The presence of the following should be documented: headache, jaw claudication, visual disturbance, limb claudication, PMR symptoms...
and temporal artery abnormalities on palpation. Patients should have immediate full blood count, urea and electrolytes, CRP and ESR. Immediate commencement of steroids and bone protection and documentation of patient education.

Results: Our records review produced the following results: 66 patients were on MTX >1 year; 46 patients met standards for blood test monitoring, worryingly, 2 patients had gone for >1 year without any blood tests; 66 patients were correctly prescribed folic acid; 140 patients were on allopurinol >1 year; 15 patients had a urate level taken in the previous 12 months; 46 had a urate level <300 μmol/l, 71 had a urate level >300 μmol/l and 23 had no urate level on record; 179 patients had RA for >2 years; 59 had a QRISK2 score on record; 34 patients >65 years of age were found to be on oral GCS for >6 months; 14 patients were on a bisphosphonate, 13 were on calcium supplement alone and 7 were on no bone protection; 26 patients had a documented history of GCA; 20 patients had documented questioning about headache, 5 of jaw claudication, 19 of visual disturbance, 0 of limb claudication, 7 of PMR symptoms and 13 of temporal artery abnormalities on palpation; 21 had a full blood count, 15 urea and electrolytes and CRP and 28 had ESR; all were immediately started on treatment, whether they had recently experienced a series of symptoms that would classically relate to GCA. Descriptive statistics were used to describe the prevalence of these symptoms. Chi-square statistics and t-tests were used to assess the association between these symptoms and gender and age, respectively.

Results: A total of 654 people responded to the baseline questionnaire (adjusted response rate 90.1%). The mean age of the sample was 72.4 years (s.d. 5.9) and 62.2% were female. One or more potential GCA symptoms were reported by 387 (59.2%) people. With the exception of unplanned weight loss (prevalence 21.0%), all symptoms were more common in females than in males (sudden headache: females 30.7%, males 15.4%; tender scalp: 21.4%, 14.6%; disturbed/double vision: 21.1%, 10.5%; jaw claudication: 12.5%, 6.5%; fever: 17.7%, 10.9%; appetite loss: 25.1%, 15.4%). The mean age of those reporting and not reporting each symptom was similar, except for sudden headache and fever, where those reporting the symptom tended to be younger (headache: 70.3 (s.d. 10.5) vs 73.1 (s.d. 8.7) years; fever: 69.2 (s.d. 9.4) vs 72.6 (s.d. 9.1)). The most common combinations of symptoms were appetite loss and weight loss (4.4%) and headache and disturbed/double vision (2.6%).

Conclusion: More than half of those with recently diagnosed PMR reported classical symptoms of GCA, with headache, scalp tenderness and visual disturbance being commonly reported in this cohort study. On making a diagnosis of PMR, it is important that general practitioners actively screen for symptoms that may be indicative of GCA to improve patient care and reduce the potential for the serious consequences associated with GCA. Ongoing patient education is essential so that patients are fully aware of red flag symptoms and empowered to seek help should they occur.

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038 HOW COMMON ARE GIANT CELL ARTERITIS SYMPTOMS IN PATIENTS WITH POLYMYALGIA RHEUMATICA? RESULTS FROM AN INCIDENT PRIMARY CARE COHORT

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1Research Institute for Primary Care and Health Sciences, Keele University, Staffordshire, 2Painswick Surgery, Stroud, Gloucestershire and 3Rheumatology, Southend University Hospital, Essex, UK

Background: PMR is the most common inflammatory disorder of older people and causes significant levels of pain and disability. It is frequently associated with GCA, a difficult to diagnose condition that can cause permanent visual impairment if not promptly treated with high-dose glucocorticoids. This study investigates the co-existence of GCA symptoms in patients with PMR in primary care.

Methods: Data included in this study are taken from the baseline phase of the PMR Cohort Study, the first inception study of PMR in primary care. A total of 739 people with newly diagnosed PMR were mailed a baseline questionnaire, which included items relating to sociodemographic characteristics, general health and functioning and PMR symptoms and treatments. In addition, participants were asked whether they had recently experienced a series of symptoms that would classically relate to GCA.

Results: On making a diagnosis of PMR, it is important that general practitioners actively screen for symptoms that may be indicative of GCA to improve patient care and reduce the potential for the serious consequences associated with GCA. Ongoing patient education is essential so that patients are fully aware of red flag symptoms and empowered to seek help should they occur.

Disclosure statement: The authors have declared no conflicts of interest.

039 PEST IN PRACTICE

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Background: National Institute for Health and Care Excellence (NICE) guidance CG 153 states that all patients with psoriasis should have an annual assessment for PsA and that a validated tool, e.g. the Psoriasis Epidemiology Study (PEST) questionnaire, should be used. If arthritis is suspected, patients should be referred to a rheumatologist for further assessment. It is our belief that this has not yet been taken up by primary care and we aimed to assess the impact of its use in a teaching practice.

Methods: A total of 159 patients in a practice of 5100 patients were identified as having psoriasis; 13 of these were already known to have PsA. Letters were sent to all of the rest, advising them of the NICE guidance and enclosing a copy of the PEST questionnaire. A stamped addressed envelope was included for their reply. Any patient scoring >3 was invited to attend for review.

Results: Eighty-two of 146 (56%) questionnaires were returned. Two patients felt that the diagnosis of psoriasis was incorrect. Sixteen patients scored >3 and were invited to the surgery for review. Eleven patients attended; on review, 9 were felt to have primary psoriasis and were not referred. Two were referred to rheumatology after the review. During the study, one patient was referred with uncoded but previously known disease. Two additional patients who were not reviewed were identified as having a previous diagnosis of PsA that was not coded. None of the patients referred have so far had specialist review.

Conclusion: It is felt that a reasonable return rate was achieved for the questionnaire. Patients were identified for referral to rheumatology through the use of the PEST questionnaire. The prevalence of psoriasis in our practice of 3% is comparable to the UK prevalence of 2%. Of people with psoriasis in the UK, 14% have PsA. Our practice’s prevalence was lower, at 9%. The discrepancy may be accounted for in those who did not return the questionnaire.

Disclosure statement: The authors have declared no conflicts of interest.

040 FOOT AND ANKLE PAIN PHENOTYPES: LATENT CLASS ANALYSIS FROM THE CLINICAL ASSESSMENT STUDY OF THE FOOT

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Background: Foot and ankle pain are common problems that affect 24% and 12% of older adults, respectively. Many studies have estimated the prevalence of foot pain in specific anatomical locations and investigated associated risk factors, but few studies have used a clinical assessment approach. The aim of this study was to investigate the existence of distinct phenotypes of foot and ankle pain and associated symptoms and risk factors.
Methods: Adults ≥50 years of age registered with four general practices in North Staffordshire were mailed a health survey questionnaire, irrespective of foot-related health care consultation. Participants reporting foot pain in the last month indicated the location of pain by shading a foot manikin. Distinct phenotypic classes of pain in different foot locations were investigated by latent class analysis and their association with symptoms and risk factors were assessed using analysis of variance and chi-square test.

Results: A total of 5109 completed postal questionnaires were received (adjusted response rate 56%) and 4455 with complete foot pain and mankin data were included in this analysis [mean age 65 years (s.d. 9.6), 49% male]. The most frequently affected pain regions were the big toe (15%), lesser toes (14%) and the midfoot (13%), with the least commonly affected being the plantar heel (6%) and ankle (6%). Of those with foot/ankle pain (n = 1358), 1215 (90%) had pain in more than one region and 825 (61%) had bilateral pain. Latent class analysis demonstrated six distinct classes of foot and ankle pain: no problem, or mild pain (OR 0.38), left foot/ankle pain (5%, n = 238), right foot/ankle pain (5%, n = 238) and bilateral widespread foot pain (6%, n = 258). People in class 2 (bilateral foot/ankle pain) were more likely to have hallux valgus than those in class 3 (hindfoot/midfoot)—39 vs 30% (P < 0.001). People in class 6 (bilateral widespread foot pain) were significantly more likely to be female, obese and have medical co-morbidities, and had lower mental and physical component scores and higher foot pain scores than other classes. Age did not differ between classes.

Conclusion: Foot pain was commonly bilateral, while unilateral pain occurred more commonly in the forefoot than the hindfoot. Foot and ankle pain frequently involved multiple regions, and six distinct classes of foot pain location were identified. These distinct phenotypes were associated with differing symptoms and risk factor profiles. Further work should explore the phenotypic characteristics of people in these classes in more detail and examine their outcome over time.

Disclosure statement: The authors have declared no conflicts of interest.

041 KNOWLEDGE OF FEATURES OF INFLAMMATORY BACK PAIN IN PRIMARY CARE IN WEST MIDLANDS: A CROSS-SECTIONAL SURVEY

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Background: A cardinal feature of AS is a history of inflammatory back pain (IBP) as defined by the Calin criteria, but little is known about general practitioners (GPs) knowledge or use of these criteria. The diagnosis of AS is often delayed, and this has prognostic significance since patients with shorter disease duration (<10 years) tend to do better with anti-TNF therapy. The objective of this study was to assess the current practice of local GPs in using clinical, radiological and laboratory investigations to assess patients with IBP.

Methods: An observational questionnaire-based survey covering 12 West Midlands CCGs. The questionnaire took 10 minutes to complete and included GPs' demographic details, the diagnostic features of mechanical vs IBP and their approach to investigation and referral. GPs were asked to rate the importance of each symptom as an indication of IBP (1–10 scale) and the same symptoms as indicators of mechanical back pain. The mean scores and deltas were compared to identify which symptoms were perceived as discriminatory by GPs. They were asked about their confidence in diagnosing IBP and regarding education.

Results: A total of 141 GPs responded. The four most important symptoms (out of 10) for predicting IBP were morning stiffness (mean score 8.8/10), sleep disturbances caused by back pain (7.3), insidious onset (7.1) and age of onset <45 years (7.1). Early morning stiffness and insidious onset performed well as discriminators for IBP (Δ of 5.2 and 4.1, respectively), but improvement with exercise did not perform well with a Δ of 0.8. Comparatively they were more confident in assessing patients with mechanical back pain, 31% rating themselves very confident at 5% for IBP. The three most common indications requested to investigate IBP were CRP (61%), HLA-B27 (43%) and whole spine X-ray (34%). NSAIDs were ranked as the most important treatment option for IBP, with a mean rating of 3.3 (scale 1–4). DMARDs were rated as the next most important treatment option ahead of physiotherapy (2.6) and anti-TNF therapy (1.7). Fifty-two per cent of respondents stated they referred patients with IBP to specialist services within 3 months of presentation, but 60% were not aware of a local specialist AS service. GPs felt diagnosis could be most improved by referral pathways (69%), practical sessions (57%) and electronic updates (24%). GPs preferred education meetings (77%) to digital methods (30%).

Conclusion: This study highlighted the relative lack of confidence among GPs in the assessment and management of IBP vs mechanical back pain. GPs were able to identify early morning stiffness and insidious onset as features of IBP, but not improvement with exercise. There was an inconsistent approach to investigation in primary care. There is a need for better formal education, which GPs prefer to receive at meetings rather than digitally.

Disclosure statement: N.B. has received research funding from Novartis and AbbVie, a travel grant from Pfizer and speakers fees from Pfizer and AbbVie. All other authors have declared no conflicts of interest.

042 CHALLENGES FACED IN PRIMARY CARE DURING THE EARLY STAGES OF RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL SURVEY OF GENERAL PRACTITIONERS

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Background: Early treatment can reduce morbidity and mortality in patients with RA. However, identifying early RA can be challenging, in part because of its initial symptoms are non-specific. Delays in recognising RA and referral to secondary care can lead to delays in treatment initiation. This study aimed to investigate general practitioner (GP) confidence in diagnosing RA and potential challenges in diagnosing RA.

Methods: A cross-sectional questionnaire survey was conducted across 5000 English GPs. GPs were asked to rate their confidence in diagnosing RA and in assessing synovitis (visual analogue scale (VAS) 1–10) and their level of agreement with 10 statements about diagnosing RA, e.g. RA is easy to recognize and diagnose (reverse VAS 1–5, i.e. 1 = strongly agree, 5 = strongly disagree). Data were analysed using nominal regression. Ethical approval for the study was obtained from Keele University, Staffordshire, UK.

Results: A total of 1388 (27.8%) GPs completed the questionnaire. The mean age was 47.0 years (s.d. 9.4), 705 (51%) were female and 1052 (76.3%) were GP partners. The average experience as a GP was 16.6 years (s.d. 9.7). Overall, GPs were moderately confident in the diagnosis of RA (median 7/10 [interquartile range (IQR) 5–7]) and the assessment of synovitis (median 7 [IQR 6–8]). There was a strong correlation between being confident in diagnosing RA and being confident in assessing synovitis (Spearman’s ρ = 0.609, P < 0.001). Those confident in assessing for synovitis disagreed that examination yielded little information towards clinical decision-making (OR 1.35, P = 0.002). Agreeing that early RA is difficult to recognize was associated with a greater likelihood of having a watch and wait approach to aid decision-making (OR 1.53, P < 0.001). They also felt it was difficult to distinguish RA from other potential diagnoses (OR 1.26, P = 0.032) and that the symptoms characterising early RA were poorly defined (OR 1.66, P < 0.001). There was a small but significant inverse association between rating early RA as difficult to recognize and the age of the GP (OR 0.97, P = 0.001).

Conclusion: There is an association between confidence in assessing synovitis and the use of examination in assessing for early RA. GPs who use examination to aid decision-making are more likely to have a more comprehensive approach, i.e. using history, family history, and blood tests as well. Meanwhile, finding RA difficult to recognize is associated a more watch and wait approach. This could be a potential source of delay in treatment.

Disclosure statement: The authors have declared no conflicts of interest.
043 POPULATION PREVALENCE AND DISTRIBUTION OF ANKLE PAIN AND SYMPTOMATIC RADIOGRAPHIC ANKLE OSTEOARTHRITIS IN COMMUNITY-DWELLING OLDER ADULTS
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Background: OA is highly prevalent in the UK general population, particularly in adults >50 years of age. Numerous epidemiological studies have estimated the population prevalence of OA at joint sites such as the hands, hips and knees, while fewer studies are available for the foot. It is commonly assumed that OA occurs less frequently in the ankle than in these other joint sites, although there are no published estimates of the prevalence of symptomatic radiographic ankle OA in the general population. The aim of this study was to calculate prevalence estimates for ankle pain and symptomatic, radiographic ankle OA within a general population of community-dwelling older adults and to examine their distribution according to age, gender and socio-economic status.

Methods: Participants ≥50 years of age and registered with one of four general practices in North Staffordshire were mailed a health questionnaire and invited to take part in the Clinical Assessment Study of the Foot (CASF). Participants reporting pain in or around the foot in the past 12 months and consenting to further contact were invited to attend a research clinic where weight-bearing, antero-posterior and lateral ankle radiographs were obtained. A single blinded reader scored osteophytes and joint space narrowing (JSN) on a scale of 0–3 on each view using an atlas of standardized radiographic features. Ankle pain in the previous month was determined by a foot and ankle pain manikin. Symptomatic radiographic ankle OA was defined as grade ≥2 for osteophytes or JSN on either view together with the presence of ankle pain in the past month in the corresponding ankle. Individuals could have one or both ankles involved. Prevalence estimates for ankle pain and symptomatic radiographic ankle OA were calculated using multiple imputation to account for missing radiographic or pain data due to clinic non-attendance or incomplete data collection and weighted logistic regression was used to adjust prevalence for participants’ likelihood to return the initial health survey questionnaire. Estimates were stratified by age, gender and socio-economic status.

Results: In total, 5109 participants responded to the baseline health survey questionnaire (adjusted response rate 56%) and 560 participants attended the research clinic. After exclusion of inflammatory arthritis (n = 24), prevalence was estimated to be 11.7% (95% CI 10.8, 12.6) for ankle pain and 3.4% (95% CI 2.4, 4.3) for symptomatic radiographic ankle OA. Stratification found that females, younger adults (50–64 years) and individuals with routine/manual occupations demonstrated slightly higher prevalence estimates.

Conclusion: Ankle pain was common in a population of community-dwelling older adults, whereas symptomatic radiographic ankle OA occurred less frequently, suggesting that diagnoses other than OA should be considered in older adults presenting with ankle pain. Future research should explore risk factors for ankle pain and symptomatic radiographic ankle OA to help explain the patterns in prevalence observed in this study.

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044 GOUT SEVERITY, SOCIO-ECONOMIC DEPRIVATION AND WORK LOSS: A CROSS-SECTIONAL STUDY IN PRIMARY CARE
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Background: Gout is the most common inflammatory disease in men >40 years of age in the UK. It is associated with socio-economic deprivation and significantly affects the ability to work. However, little is known about how socio-economic factors and work disability vary with gout severity. The aim of this study was to examine the association between gout severity and socio-economic deprivation and work absence.

Methods: Postal questionnaires were sent to adults registered with 20 general practices across the West Midlands who had consulted primary care with gout or had been prescribed allopurinol or colchicine in the preceding 2 years. Gout severity was defined by the number of attacks in the past 12 months (0, 1, ≥2), history of oligo/polyarticular attacks and medical intervention. The presence of tophi was ascertained from medical records in those who provided consent. Socio-economic deprivation was measured at the area level using the Index of Multiple Deprivation (IMD) and at the individual level by educational attainment. Work disability was defined as taking time off work in the past 6 months because of gout. Odds ratios and 95% CIs were calculated for gout severity and socio-economic deprivation and work disability using binary and ordinal logistic regression models as appropriate, adjusting for age, gender, BMI, gout severity variables and co-morbidities.

Results: A total of 1184 completed questionnaires were returned (adjusted response rate 66%), and 1079 of the patients consented to a medical records review. The mean age of respondents was 65.6 years (s.d. 12.5) and 990 (84%) were male. Those who had had two or more gout attacks in the last 12 months were less likely to have attended further education (adjusted odds ratio (OR) 0.55 (95% CI 0.38, 0.81), as were those who had experienced oligo/polyarticular attacks (OR 0.73 (95% CI 0.52, 1.03)). There was no significant association between IMD and gout severity. Work disability was strongly associated with gout severity, with those having two or more attacks in the last year (OR 3.10 (95% CI 1.29, 7.43)) or having had poly/oligoarticular gout (OR 3.08 (95% CI 1.47, 6.45)) being more likely to have taken time off work in the last 6 months. In contrast, it was found that disease duration was associated with less time off work (gout duration ≥18 years: OR 0.12 (95% CI 0.03, 0.46)).

Conclusion: Socio-economic deprivation was associated with a greater frequency of gout attacks, counteracting the historical perception of gout as a rich man’s disease. People with more frequent attacks and oligo/polyarticular attacks were more likely to have taken time off work because of gout. These findings emphasize the need to initiate urate-lowering therapy early in the disease course before attacks become more frequent and troublesome and inform service provision in more deprived areas.

Disclosure statement: The authors have declared no conflicts of interest.

045 PATIENT’S VIEWS ON THE CAUSES OF THEIR POLYMYALGIA RHEUMATICA: RESULTS FROM THE PMR COHORT STUDY
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Background: PMR is a common inflammatory disorder of older adults that causes pain and stiffness in the shoulder and hip girdles and is usually accompanied by an acute phase response. Although previous research has considered potential causes of PMR, including environmental, occupational, genetic and genetic susceptibility, there are no confirmed causal factors. This study aimed to describe patients’ opinions as to the causes of their PMR.

Methods: The PMR Cohort Study is an inception cohort of newly diagnosed PMR patients recruited from UK primary care between June 2012 and June 2014 (n = 654). Patients were sent a baseline postal questionnaire that included questions relating to general and PMR-specific health, demographics and lifestyle. It also included a question asking what the participants’ believe to be the cause of their PMR. “What do you think caused your PMR?” Content analysis was used to identify and categorize patient responses.

Results: The responders’ mean age was 72.9 years (s.d. 9.2) and 405 (62%) were female. A total of 296 (45%) respondents answered the open question, 276 (42%) respondents wrote ‘no idea’ and 82 (13%) left the question blank. The 276 participants who answered the question had a mean age of 71.4 years (s.d. 9.8) and 63% were female. The non-responders/no idea group had a mean age of 73.0 years (s.d. 8.5) and 62% were female. Of the 296 that answered the question, 159 (54%) gave more than one causal factor and 137 (46%) gave a single cause. Thirty-eight potential causes were identified after data coding. These were further refined and grouped to give 11 main causes, including injury [n = 63 (17%)] personal stress [n = 53 (14%)], old age [n = 45 (12%)], worsening of existing musculoskeletal conditions [n = 40 (11%)], infection [n = 39 (10%)], occupational strain [n = 36 (9%)], related to other medical conditions [n = 24 (6%)], hereditary [n = 21 (5%)], medication [n = 18 (5%)], consequence of medical intervention [n = 16 (4%)], environmental [n = 14 (4%)] and lifestyle factors [n = 10 (3%)].
Conclusion: A range of factors were drawn upon by patients in describing the cause of their PMR, the most common relating to injury, personal stress, ageing and infection. Beliefs held by patients are known to influence coping and self-management strategies, particu- larly in chronic diseases such as PMR. These beliefs should be explored by doctors in order to correct those that are medically unlikely and to prevent unhelpful illness beliefs. Further studies are required to test some of these biologically plausible hypotheses regarding causes of PMR.

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046 EFFECTIVE TREATMENT OPTIONS FOR MUSCULOSKELETAL PAIN CONDITIONS: A RAPID META-SYNTHE-SIS OF CURRENT BEST EVIDENCE IN PRIMARY CARE

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Background: Treatments that are matched to patient risk subgroups (or stratified care) have the potential to improve the effectiveness of primary care for patients with musculoskeletal pain. However, musculoskeletal pain conditions are extensive and the knowledge base is large. To inform the development of matched treatment options, a rapid, yet detailed summary of evidence on the effective- ness of available treatment options was needed. The specific aims of this study were to develop an approach to synthesizing large evidence summaries, to rapidly synthesize and appraise current best evidence on treatment options for the five most common musculoskeletal pain presentations in primary care and to summarize the available evidence on treatments for patient risk subgroups using stakeholder groups.

Methods: Evidence synthesis followed a pyramidal approach using national clinical guidelines, policy documents, clinical evidence pathways and summaries as a starting point. Recommendations about available treatment options for shoulder, neck, knee, back and multisite pain were extracted consecutively. Systematic searches of bibliographic databases were carried out to identify and retrieve more recently published trials that had not yet been summarized in reviews or guidelines or where evidence gaps existed. The quality of evidence was assessed based on modified Grading of Recommendations Assessment, Development and Evaluation quality ratings and strength of evidence. Evidence summaries were subsequently presented to stakeholders (including health service managers, clinicians and researchers) for interpretation and identification of appropriate treat- ment options that might be matched to patient risk subgroups.

Results: A rapid, yet systematic and comprehensive approach, pragmatic summaries of the evidence base on treatment options for five musculoskeletal pain presentations were completed.

Conclusion: Based on current best evidence, identification of matched treatment options according to patient risk subgroups appears feasible across musculoskeletal pain presentations.

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047 OBESITY, HYPERTENSION AND DIURETIC USE AS RISK FACTORS FOR INCIDENT GOUT: A META-ANALYSIS OF COHORT STUDIES

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Background: Gout is the most common inflammatory arthritis and its prevalence and incidence have continued to increase in recent decades. As treatment remains suboptimal, identification of high-risk groups for developing gout remains important. The aim of this systematic review and meta-analysis was to examine obesity, hypertension and diuretic use as risk factors for incident gout.

Methods: Three separate search strategies were developed to select articles that had investigated obesity, hypertension and/or diuretic use as a risk factor for incident gout. These searches were conducted in Medline, Embase and CINAHL from database inception to January 2015. Relevant search terms were devised from a combination of MeSH and free-text terms for gout and combined with terms for each exposure. Included articles met the following criteria: human partici- pants; outcome was assessed in adults (>18 years of age); prospective or retrospective cohort study; incident gout was assessed as an outcome; the exposure studied was obesity, hypertension and/ or diuretic use and the study took place in primary care or was population based. Titles and abstracts were screened by a single author and full text review of remaining articles was performed by two independent assessors. Study characteristics, design, sample size and risk estimates were extracted. Methodological quality was assessed using the Newcastle-Ottawa Scale. Using a random effects model, pooled unadjusted and adjusted risk estimates were calculated for each risk factor, requiring a minimum of three articles that used the same type of risk estimate [e.g. relative risk (RR)]. Heterogeneity was assessed using the I² statistic.

Results: Twelve articles were identified for obesity, four of which were included in the meta-analysis. Obese individuals were more than twice as likely to develop gout as non-obese individuals (adjusted RR 2.24 (95% CI 1.76, 2.86); I² = 21.4%). Nine articles were identified for hypertension use of which were included in the meta-analysis. Hypertensive individuals were twice as likely to develop gout as normotensive individuals (adjusted RR 2.11 (95% CI 1.64, 2.72); I² = 48.3%). Six articles examined diuretic use and three were included in the meta-analysis. Diuretic use was associated with almost 2.5 times the risk of developing gout compared with no diuretic use (adjusted RR 2.39 (95% CI 1.57, 3.69); I² = 79.1%).

Conclusion: Obesity, hypertension and diuretic use are all risk factors for incident gout, each more than doubling the risk of developing gout compared with those who do not have these risk factors. Obese and hypertensive patients should be identified by general practitioners as at greatest risk of developing gout and provided with appropriate management and treatment options. In particular, diuretics should be avoided if possible and alternative antihypertensive medications used.

Disclosure statement: J.A.P. received funding from NIHR. C.D.M. received funding from NIHR. All other authors have declared no conflicts of interest.

048 A CONSENSUS GROUP APPROACH TO AGREEING MATCHED TREATMENT OPTIONS FOR MUSCULOSKELETAL PAIN OF PATIENTS STRATIFIED ACCORDING TO PROGNOSTIC RISK

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Background: This paper reports on an expert consensus exercise to agree matched treatment options for subgroups of patients based on prognostic risk of persistent disabling pain. As part of the Stratified Care for Musculoskeletal Pain research programme, the consensus groups focused on the five most common musculoskeletal pain presentations in primary care: back, neck, knee, shoulder and multisite pain. Agreement was sought on the most appropriate treatment options for these pain presentations for each patient risk subgroup: low, medium and high.

Methods: Three consensus meetings were conducted with multi- disciplinary groups of clinical experts, including general practitioners, physiotherapists, rheumatologists, pain specialists and orthopaedic surgeons, recruited through existing clinical and research networks (group 1: n = 19 participants; group 2: n = 16; group 3: n = 12). Each meeting focused on a specific risk subgroup, with participant expertise spread across small groups for each of the five pain presentations. Participants were given a list of evidence-based treatment options appropriate for the UK National Health Service (NHS) and asked to individually identify missing treatments. Where agreed upon by the group, these were added to the list. Participants then individually rated the appropriateness of the treatment options (on a 7-point Likert scale) for patients in the risk subgroup in question. This was followed by a plenary group discussion of treatment options for each pain presentation. All participants then individually rated the options for all pain presentations for the risk subgroup in question. Following the meetings, participants were contacted via email to consider any inconsistencies.

Results: Treatment options with a mean rating score > 3.5/7 were included as recommended matched treatment options. For all five pain
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1.23); 9.05/100 000 person-years

5.88 subjects with identified Read codes/100 000 person-years

risk of altered menstruation [hazard ratio (HR) 1.12 (95% CI 1.04, 1.19); 5.88 subjects with identified Read codes/100 000 person-years vs 7.72]. No significant association

cluster 3, with major improvement in pain, is less often found among back pain patients. Although our results may be hampered by non-response, a sensitivity analysis with patients having complete data gave similar results. Identification of such distinct groups of patients improves our understanding of the course of leg pain and may provide a basis of classification for intervention.

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051 INCREASING PHYSICAL ACTIVITY IN OLDER PEOPLE WITH PAIN: DEVELOPMENT OF A BRIEF AND SIMPLE INTERVENTION TO PROMOTE WALKING

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Background: Physical activity rates are low in people >65 years of age and those with chronic musculoskeletal pain. The Increasing Physical Activity in Older People with Pain (iPOPP) study aims to develop and test the feasibility and acceptability of a health care assistant (HCA)–led intervention to promote walking in people >65 years of age with chronic musculoskeletal pain. Phase I aimed to

Presentations, education and advice and simple oral and topical medications were agreed for all subgroups. For patients at low risk across all five pain presentations review by primary care practitioner if not improving after 6 weeks was also agreed. Medium-risk treatment options slightly differed across pain presentations but all included consider referral to physiotherapy and consider referral to musculoskeletal interface clinic. High-risk treatment options again varied a little by pain site, with some similarity with medium-risk options, and additional options including opioids; consider referral to expert patient/peer support groups (across all pain presentations); consider referral for lifestyle intervention, e.g. dietician (knee) and consider referral for surgical opinion (back, knee, neck, shoulder). Consider referral to rheumatology was agreed for patients with multisite pain for medium- and high-risk subgroups.

Conclusion: Multidisciplinary clinical experts achieved consensus in identifying recommended matched treatments suitable for subgroups of primary care patients at low, medium and high risk of poor prognosis. The use of the Keele StART MSK tool (Subgrouping for Targeted Treatment in Musculoskeletal conditions) with these matched treatment options will be tested in a future randomised controlled trial.

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049 A COHORT STUDY TO INVESTIGATE LONG-TERM OPIOIDS FOR CHRONIC NON-CANCER PAIN IN WOMEN AND ASSOCIATED HYPOTHALAMIC-PITUITARY-GONADAL SIDE EFFECTS

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Background: Twenty-two per cent of primary care attendees suffer chronic non-cancer pain (CNCP), with women affected more often than men. Twelve per cent of all affected patients are prescribed opioids. Evidence suggests long-term use is related to hypogonadism in men, but the relationship in women is unclear. Our aim was to investigate long-term opioid use in women and endocrine side effects, specifically hypothalamic–pituitary–gonadal (HPG) axis disruption.

Methods: A matched cohort (case–control ratio 1:1; for year of birth, year of start of follow-up, gender and practice) was identified from the Clinical Practice Research Datalink across the period 2002–13. The dataset included women between 18 and 55 years old. Cases (n = 23 271) were prescribed long-term opioids (>90 days) and controls short-term opioids (<90 days) for musculoskeletal conditions. Study follow-up was for 5 years. Four potential opioid-induced endocrine effects (abnormal menstruation, low libido, infertility and menopause) were identified using Read codes and searched for within the cohort. Cox proportional hazards models were used to compare the risks for each event between the two groups, adjusting for confounders (NSAID use, ethnicity and number of other co-morbid conditions).

Results: The median cohort age at baseline was 43 years (interquartile range 36–49). The proportion of NSAID users and number of co-morbid conditions was higher in cases compared with controls (P < 0.05). Long-term use of opioids was associated with an increased risk of altered menstruation [hazard ratio (HR) 1.12 (95% CI 1.04, 1.19); 5.88 subjects with identified Read codes/100 000 person-years vs 7.72]. No significant association was found with regard to libido [HR 1.20 (95% CI 0.98, 1.48); 0.63/100 000 person-years vs 0.52] or infertility [HR 0.87 (95% CI 0.68, 1.11); 0.28/100 000 person-years vs 0.43].

Conclusion: The results potentially suggest an association between long-term opioids and HPG axis disruption manifesting clinically as altered menstruation or menopause. The rates for low libido and infertility were lower than expected from general population estimates in both cases and controls, possibly reflecting the low likelihood of presentation in primary care or low levels of recording. This has potential implications for clinicians when prescribing opioids to women with CNCP, as these potential side effects will need to be considered and discussed with women prior to treatment.

Disclosure statement: The authors have declared no conflicts of interest.
developed the content of the intervention and associated training programme.

**Methods:** An implementation of change model was used in three parts. First, a concrete proposal for the intervention was devised using an evidence synthesis, a stakeholder workshop and a nominal group. Stakeholder participants (e.g. clinician, third sector worker, person ≥65 years old with chronic pain) (n = 10) shared views on delivery of the study in primary care. Nominal group participants (n = 11) were ≥65 years of age with chronic musculoskeletal pain identified from local community groups (e.g. Age UK). A questionnaire was used in two rounds to refine components of the intervention (identified from evidence synthesis). Second, target group analysis was undertaken using a focus group with HCAs (n = 4) to identify current practice and factors that could influence delivery of the iPOPP intervention. Data were analysed thematically, then mapped to the Theoretical Domains Framework (TDF). Third, training needs and techniques to address barriers to iPOPP delivery were identified and integrated into a training programme for the pilot trial. The study received ethics committee approval.

**Results:** The content of the iPOPP intervention was agreed upon and includes action planning and motivational components, goal setting, provision of a pedometer, walking diary and signposting to local walking opportunities (mostly third sector). Timing of the HCA consultations changed from 2 to 1 week apart after the nominal group and the choice of text, email or telephone follow-up each week for 8 weeks was added in the focus group. HCAs understood the iPOPP intervention but highlighted concerns about confidence and competence to deliver the intervention. Issues related to capabilties and professional roles were evident as they talked of a lack of knowledge and skills to advise older people with chronic musculoskeletal pain. Knowledge, confidence and skills in behaviour change techniques, engaging patients with the intervention and ability to structure consultations to deliver the iPOPP intervention in a brief timeframe were identified as training needs, as were strategies for identifying and overcoming patient concerns about walking.

**Conclusion:** An implementation of change model was applied using an evidence synthesis, a stakeholder workshop, a nominal group and a focus group. This approach has enabled co-design of a new brief and simple walking intervention for older people with chronic musculoskeletal pain and the development of a training programme for HCAs. The implementation is now being tested in a pilot and feasibility trial.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 052 THE ROLE OF PAIN AND STIFFNESS ON FATIGUE AND INSOMNIA IN AN INCIDENT POLYMYALGIA RHEUMATICA COHORT

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**Background:** Pain, stiffness, fatigue and insomnia are all major issues for patients with PMR. However, the severity and interaction of these symptoms remains unclear. We examined the association between the experience of either pain or stiffness and fatigue or insomnia in newly diagnosed PMR patients.

**Methods:** This analysis used baseline questionnaire data from a prospective observational inception cohort of PMR patients recruited in UK primary care. Patients ≥18 years of age receiving their first PMR Read code were recruited from 382 research-active UK general practices. Consenting participants were mailed a baseline postal questionnaire that included overall pain and stiffness numerical rating scales, separate pain and stiffness manikins and validated measures to record fatigue (Functional Assessment of Chronic Illness Therapy fatigue scale), insomnia (Insomnia Severity Index), anxiety (7-item Generalized Anxiety Disorder scale) and depression (8-item Patient Health Questionnaire). Responder characteristics were initially reported, followed by the use of linear regression analysis to examine the association between different pain/stiffness categories and fatigue score (reported as regression coefficients with 95% CIs). A proportional odds model was used to examine the association between pain/ stiffness and insomnia (odds ratios with 95% CI and assumption verified using a Wald test). Models were adjusted for age, gender, duration of pain and depression.

**Results:** A total of 654 PMR patients responded to the baseline questionnaire (90.1%). The mean age of responders was 72.4 years (s.d. 9.3) and the majority were female (62.2%). The mean fatigue score was 5.2 (s.d. 10.8) and nearly a quarter (23.6%) experienced clinical insomnia. Approximately half of patients (46.9%) recorded pain in ≥16 body sites; bilateral shoulder (87.2%) and hip (83.5%) pain were common. About half of patients had stiffness in ≥12 body sites (47.7%). 71.7% had bilateral shoulder stiffness and 52.0% had bilateral hip stiffness. Increasing anxiety and depression was reflected by increasing levels of fatigue and insomnia. Adjusted regression analysis demonstrated a high pain score (s.d. 1.66 (95% CI 3.1, 2.1)), most pain sites (23–44 sites; s.d. 3.78 (95% CI 5.6, 1.9)) and hip pain (s.d. 1.47 (95% CI 2.9, 2.0)) were all associated with higher levels of fatigue. Only high overall stiffness was associated with a higher level of fatigue (s.d. 1.47 (95% CI 2.9, 2.1)). Shoulder pain was associated with insomnia (2.25 (95% CI 1.2, 4.3)), whereas having 12–19 (2.48 (95% CI 1.5, 4.2)) or 20–44 (4.70 (95% CI 1.0, 2.9)) stiff areas, bilateral shoulder (1.67 (95% CI 1.1, 2.8)) and hip stiffness (1.67 (95% CI 1.1, 2.5)) were all associated with experiencing insomnia.

**Conclusion:** In newly diagnosed PMR patients from UK primary care, pain was predominantly associated with fatigue and stiffness with insomnia. This knowledge may help to guide future intervention studies to reduce specific symptoms reported by PMR patients.

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### MISCELLANEOUS RHEUMATIC DISEASES

**053 RISK OF OVARIAN FAILURE DURING TREATMENT WITH INTRAVENOUS CYCLOPHOSPHAMIDE IN RHEUMATIC DISEASE AND THE GONADAL PROTECTIVE EFFECT OF GNADOROTROPIN-RELEASING HORMONE ANALOGUES: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Background:** Intravenous CYC can cause premature ovarian failure (POF), but the precise risk is dependent on cumulative dose and patient age. Gonadotropin-releasing hormone analogues (GnRHas) offer a potential treatment option to minimize this risk.

**Methods:** We performed a systematic review of the literature to assess the risk of sustained amenorrhoea with i.v. CYC in the treatment of autoimmune rheumatic disease (ARD) and a review and meta-analysis of the efficacy of co-treatment with GnRHas in ARD in reducing this risk. Using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles, we performed a literature search of the English-language literature through June 2015 using PubMed, Medline, Embase and the Cochrane Library. We included all papers assessing ARD, where the incidence of ovarian failure or sustained amenorrhoea was reported during treatment with i.v. CYC, or that assessed GnRHa co-treatment compared with a control group.

**Results:** Twenty-two studies including 1126 patients were identified reporting the risk of POF or sustained amenorrhoea with i.v. CYC. Sustained amenorrhoea occurred in 228 patients (20.2%; range across studies 0–54% depending on age and cumulative CYC dose). Sustained amenorrhoea occurred in both younger and older patients, with mean doses of 5–10g, but the incidence was higher in cohorts receiving a mean cumulative dose >10g. Four other studies were identified that assessed patients with ARD given i.v. CYC + GnRHas. These included 71 patients receiving GnRHa + CYC and 48 controls given i.v. CYC only. Ovarian failure was seen in 3/71 (4.2%) patients co-treated with GnRHa compared with 21/48 (43.8%) controls. The pooled odds ratio of ovarian dysfunction with GnRHa and CYC compared with CYC alone was 0.07 (95% CI 0.016, 0.206; P = 0.0001), corresponding to a number needed to treat (NNT) of 3 (95% CI 1.8, 4.0) and an absolute risk reduction of 29.5% (95% CI 24.7, 54.3).

**Conclusion:** There is a significant risk of ovarian failure with cumulative doses of i.v. CYC. The available evidence suggests GnRHa markedly reduces this risk in ARD and should be considered for all women of childbearing age.

**Disclosure statement:** The authors have declared no conflicts of interest.
The syndrome of periodic fevers, aphthous ulceration, pharyngitis and adenitis is a single-centre experience

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Background: The syndrome of periodic fevers, aphthous ulceration, pharyngitis and adenitis (PFAPA) is an inflammatory disorder of unknown aetiology diagnosed in children with typical clinical presentation and systemic inflammation and in whom genetic testing for heritable periodic fever syndromes is negative. Most cases resolve by the end of adolescence. PFAPA affecting adults, either as a new diagnosis or extending into adulthood, has been previously reported but appears to be extremely rare or underdiagnosed.

Methods: We performed a retrospective analysis of patients with symptoms resembling PFAPA from the database of the Periodic Fever Clinic at the UK National Amyloidosis Centre over a 15-year period. Search terms used were PFAPA, fever, pharyngitis, lymphadenopathy and aphthous ulcers. Individuals with a proven alternative diagnosis were excluded.

Results: Fifteen patients were identified; 13 were male and all were of white European origin. None gave a family history of similar symptoms. The current median age is 28.3 years with a median symptom duration of 15 years. Six patients (40%) presented after the age of 16 years and five before the age of 5 years. Three patients reported precipitants for their attacks: in all cases stress and fatigue. Thirteen patients reported regular attacks every 4–6 weeks. Fever was present in 100%, cervical lymphadenopathy in 93%, pharyngitis in 73%, oral aphthous ulceration in 40%, abdominal pain in 33% and rash and red eyes in 13%. Sequencing of periodic fever genes was wild-type in all cases. Seventeen patients provided blood samples during attacks, with a median CRP of 27 mg/l and serum amyloid A (SAA) of 205 mg/ml. All 15 had normal inflammatory markers when well. Treatments were similar to those used in childhood PFAPA; Forty-seven per cent had undergone tonsillectomy without lasting benefit in any case. Intermittent corticosteroids at the onset of symptoms had been used by 60%, with four good responses and four partial responses; four patients continue on intermittent prednisolone. Fourteen (93%) patients underwent a trial of colchicine, with 2 complete, 4 good and 6 partial responses, and 12 (86% of exposed) remain on long-term prophylaxis. One patient received anaflorax and three tried cinacalcet with little effect. All patients achieved normal adult height and weights. Thirteen of 15 are either in full-time education or employment. No patients have developed AA amyloidosis.

Conclusion: PFAPA is seen in adults. In our series, 40% presented after the age of 16 years and 33% presented at the typical age of <5 years with persistent symptoms into adulthood. Compared with typical childhood PFAPA, symptoms appear similar but more patients are refractory to conventional treatment with tonsillectomy or intermittent corticosteroids. Colchicine given as long-term prophylaxis is the most effective treatment, although complete responses are rare. Despite ongoing symptoms and elevated CRP and SAA with attacks, no patients have severe social or physical consequences of their disease.

Disclosure statement: The authors have declared no conflicts of interest.

055 DISABILITY, DISEASE ACTIVITY AND PSYCHOLOGICAL DISTRESS IN ACTIVE PSORIATIC ARTHRITIS: SECONDARY ANALYSIS OF A CLINICAL TRIAL

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Background: Depression is highly prevalent in PsA, with approximately 21% of patients screening positive for depression according to the nine-item Patient Health Questionnaire Depression Anxiety (PHQ-9). Depression/anxiety at the start of treatment can significantly reduce treatment response and long-term disease activity and reduce the odds of reaching clinical remission in rheumatological conditions. We aim to examine the impact of baseline mental health on physical disability and disease activity in PsA patients over a 6 month period.

Methods: A secondary data analysis of a clinical trial [Methotrexate in Psoriatic Arthritis (MIPA)] was performed. MIPA was a 6-month randomised, double-blind, placebo-controlled trial in patients with active PsA attending UK specialist rheumatology clinics. The 36-item Short Form Health Survey, using a threshold of 52, was used to identify patients with substantial psychological distress likely to reflect depressive or anxiety disorders. The 36-item Short Form Health Survey, using a threshold of 52, was used to identify patients with substantial psychological distress likely to reflect depressive or anxiety disorders. The HAQ and 28-joint Disease Activity Score (DAS28) were used to measure disability and disease activity outcomes, respectively. Mean scores with 95% CIs and standardized mean differences were calculated for patients with and without psychological distress at baseline.

Results: Complete data were available for 128 patients. The patients’ mean age was 48.9 years (s.d. 12.3) and 39.1% were female. In total, 23.4% reported significant levels of psychological distress. Patients with psychological distress at baseline had significantly reduced HAQ scores at baseline and the 3 and 6 month follow-ups (Table 1) compared with patients without baseline distress. DAS28 scores over time were not associated with baseline psychological distress. There were no significant differences in the change in HAQ and DAS28 over time between those with and without psychological distress.

Conclusion: Psychological distress at treatment baseline is associated with worsened physical disability, but not disease activity over time. The change in disability and disease activity was not associated with baseline distress status. Psychological distress may primarily impact the subjective elements of physical health, and further investigation of the subcomponents of the DAS28 is needed. These results suggest that patients with psychological distress may benefit from specific management of their mental health alongside routine rheumatological drug therapy.

Disclosure statement: The authors have declared no conflicts of interest.

056 MYCOBACTERIUM TUBERCULOSIS OF THE MUSCULOSKELETAL SYSTEM: A RETROSCOPIC COHORT SERIES FROM BIRMINGHAM, UK FROM 2008 TO 2013

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Background: Tuberculosis (TB) is important to rheumatologists in the differential diagnosis of primary musculoskeletal (MSK) symptoms and is associated with biologic therapies. MSK TB is difficult to diagnose. Our aim was to describe and compare MSK TB cases with other TB cases.

Methods: Our study was a retrospective cohort study of patients notified with TB in Birmingham, UK from 1 January 2008–31 January 2013. Data included patient demographics, ethnicity, birth country, risk factors, symptom onset, referral source, disease distribution and microbiology. We cross-referenced notified cases against existing biologic databases in our centre for rheumatology (n = 1091) and gastroenterology (n = 148). The characteristics of MSK TB and non-MSK TB cases were compared.
RESULTS: There were 395 notified cases of TB, with follow-up data complete to 1 April 2014. The details of MSK and other TB cases are shown in Table 1. For MSK TB, birth country was the UK (4/23), South East Asia (13/23) and Africa (6/23). Six MSK TB cases had additional risk factors (health care; care, 2; immunosuppression, 1; HIV, 1; prior TB, 2; biologics, 0). Only two patients presented with small joint or knee synovitis: a UK-born white male with no risk factors and subacut MCP synovitis and an India-born female with a history of incomplete TB treatment that presented with acute knee monartthritis. TB culture was positive in 204/26 (76.9%) cases, with 18/20 fully sensitive (TB culture: abscesses, 17/20 (85.0%); bone, 4/15 (26.7%); synovial fluid, 1/1 (100%). All patients responded to drug therapy and 7/26 required surgical intervention (laminctomy ± stabilization). The mean treatment duration was 10.8 months (SD, 5.0), and three patients had >12 months of therapy. Conclusion: Patients with MSK TB were more likely to be male and were younger, but otherwise had similar characteristics with other TB presentations. Biologics were not associated with MSK TB in this series, but they were with other TB presentations. More than 80% of MSK TB cases involved the spine, but surgery was rarely required, and the majority of patients were not born in the UK. Small joint synovitis was uncommon, with TB remaining an important differential diagnosis.

Disclosure statement: The authors have declared no conflicts of interest.

RHEUMATOID ARTHRITIS: CLINICAL FEATURES

057 COMPARISON OF BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG RHEUMATOID ARTHRITIS TREATMENT DYNAMICS ACROSS FIVE EUROPEAN UNION COUNTRIES

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Background: The benefits of biologic DMARD (bDMARD) treatments in RA are well reported; however, less is known about the extent and reasons for their use in specific countries. The aim of the current analysis is to describe and compare the RA treatment approach associated with bDMARD use or lack of use across five major European Union (EU) countries.

Methods: Data were drawn from the Adelphi 2014 RA Disease Specific Programme, a survey of rheumatologists and their consulting RA patients in France, Germany, Italy, Spain and the UK. Rheumatologists provided treatment histories for all patients, including conventional synthetic DMARD (csDMARD), sequence of bDMARD treatments received and reasons for not prescribing a bDMARD if applicable.

RESULTS: A total of 2536 patients were included in the analysis; 86.4% had moderate or severe RA on initiation of current therapy. Of these, 45.4% had received bDMARD therapy at some point, with the highest use in France (52.4%) and the lowest in Germany (25.9%), bDMARD patients in France were most likely to have progressed to a second or later bDMARD therapy (41.5%), with patients in Germany least likely (15.5%). The first bDMARD treatment in all countries was overwhelmingly TNF inhibitor (TNFi) based (88.4%), with a second or later bDMARD treatment most likely to be non-TNFi based (67.6%). Differences in the number of csDMARDs received prior to bDMARD initiation were also seen across countries, with only 48.3% of patients in France receiving more than one csDMARD before bDMARD initiation vs 97.5% in the UK. The most frequently reported reasons for patients with a duration of RA disease >5 years not having been prescribed a bDMARD were the patient being in remission (30.5%), concerns regarding infection (15.5%), non-bDMARD treatment is safe and tolerable for this patient (15.5%) and patient dislikes injections/infusions (14.4%).

Conclusion: Results show that while bDMARDs are now an established treatment option in RA, a large and widely differing proportion of patients across the countries surveyed remain bDMARD naive, although they might potentially benefit from such treatment. Furthermore, of those patients who have progressed onto bDMARD therapy, many remain on their first bDMARD, with only limited numbers progressing to a second or third bDMARD option. This pattern is broadly consistent across the five EU countries assessed. Further research is required to understand the causes of national variations in bDMARD prescribing and the extent to which guidelines have been adopted in the management of patients on bDMARD therapy.

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058 AUTOANTIBODIES IN PATIENTS WITH PALINDROMIC RHEUMATOID ARTHRITIS

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Background: Patients with palindromic RA experience recurrent attacks of joint pain and inflammation. Often one or two joints are affected, but symptoms can spread to involve other joints before resolving completely. The joints look normal in between attacks. The frequency and duration of attacks is variable. The attacks are not thought to damage the joints.
Methods: Patients with palindromic RA were identified from the rheumatology database at Croydon University Hospital, London. Their records were searched for the presence of antibodies, anti-CCP, RF and ANA and their relation to the persistence of palindromic symptoms on progression to a diagnosis of full RA.

Results: Fifty-two patients were identified from the database. Thirty-six patients (69%) had one or more autoantibodies present, 9 (17%) were autoantibody negative and 7 (13%) had no antibody reported in their notes. In the antibody-positive group: 11 (31%) had anti-CCP alone, 9 (25%) had RF + anti-CCP, 8 (22%) had RF alone, 3 (8%) had ANA alone, 3 (8%) had ANA + RF, 1 (3%) had ANA + anti-CCP and 1 (3%) had ANA + RF + anti-CCP. A total of nine patients (17%) went on to develop full RA in a mean time frame of 56 months (range 18 months–9 years). Of the 21 with RF, 5 (24%) progressed; of the 22 with anti-CCP, 2 (9%) progressed and only 1 of the 9 who were double positive for RF and anti-CCP (11%) progressed to full RA. Of the eight patients with ANA, two (25%) progressed. Forty-three patients (81%) received treatment with HCQ. Of the 19% who did not receive treatment, none progressed to full RA despite four of them having anti-CCP and one being double positive for RF and anti-CCP.

Conclusion: From this study it was concluded that although a range of autoantibodies are present in patients with palindromic RA, the majority of cases are anti-CCP positive either as a single positive or in combination with RF. However, the presence of RF or ANA seems to be a stronger predictor for progression to full RA.

Disclosure statement: The authors have declared no conflicts of interest.

059 THE IMPACT OF INTENSIVE TREATMENT, INFLAMMATION AND REMISSION ON HEALTH-RELATED QUALITY OF LIFE IN EARLY AND ESTABLISHED RHEUMATOID ARTHRITIS

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Background: Health-related quality of life (HRQoL) is a multidimensional concept. It is unclear if using intensive treatment to reduce inflammation and attain remission improves all dimensions. We evaluated this in two randomized clinical trials of early (CARDERA) and established (TACIT) active RA.

Methods: CARDERA randomized 467 early RA patients to 2 years of intensive combination treatments (including high-dose tapering corticosteroids) in a factorial design. TACIT randomized 295 established active RA patients to 1 year of combination DMARDs (cDMARDs) or TNF inhibitors (TNFis). The 36-item Short Form Health Survey (SF-36) was used to measure HRQoL across eight domains, combined into physical (PCS) and mental (MCS) component summary scores. The impact of 6 months of intensive treatment (high-dose corticosteroids vs placebo in CARDERA; cDMARDs vs TNFis in TACIT) on HRQoL was evaluated using linear regression. Mean SF-36 scores were calculated in patients stratified by disease activity category at endpoint and compared with age-/gender-matched US normative population scores (A/G norms). Associations between 28-/joint DAS (DAS28) components and PCS/MCS were evaluated.

Results: In CARDERA, corticosteroids provided significant improvements in all physical domains relative to placebo; superior effects on mental domains were not observed. In TACIT, all eight domains had improvements from baseline exceeding minimal clinically important differences (0.5 units) with both cDMARDs and TNFis. Significantly greater improvements with TNFs relative to cDMARDs were seen in PCS only (P = 0.034), after adjusting for relevant covariates. Although DAS28 remission provided the best HRQoL profiles compared with other disease activity states, scores in physical functioning, role-physical and general health in both trials remained lower than normative values; scores in four and two other domains met or exceeded A/G norms in CARDERA and TACIT, respectively (Table 1).

Patient global assessment of disease activity (PtGA) was the strongest predictor of HRQoL; associations with other DAS28 components, particularly ESR, were substantially weaker.

Conclusion: In CARDERA, corticosteroids improved physical but not mental HRQoL relative to placebo. In TACIT, cDMARDs and TNFis provided similar HRQoL improvements. Although HRQoL was most improved with remission, deficits remained compared with A/G norms. High PtGA scores were important predictors of poor HRQoL. The role of identifying and treating specifically impaired areas of HRQoL, in addition to DAS28-based reductions in disease activity, requires evaluation.

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Results: Ninety-seven patients were female (88.2%) and 13 were male (11.8%) with a mean age of 64.7 years (s.d. 12.7) and a disease duration of 7.92 years (s.d. 6.56). HCV antibody was detected in 22 of 110 RA patients (20%). Positive HCV RNA by PCR was present in 14 RA patients (12.7%). HCV antibody-positive patients were significantly older, more frequently male and had a longer disease duration than HCV antibody–negative patients (P < 0.05). Regarding the pattern of arthritis, all patients included in this study had symmetric polyarthritis, but HCV antibody–positive patients had significantly more frequent deformities, higher MHAQ scores (P < 0.05) and also significantly higher ESR than HCV antibody–negative patients (P < 0.05). Regarding extra-articular manifestations in RA patients, HCV antibody–positive RA patients had significantly more frequent vasculitis (in the form of palpable purpura and mononeuritis multiplex; P = 0.05) and hepatomegaly (P = 0.05) and a significantly higher frequency of bronchial asthma (P < 0.05).

Conclusion: A high prevalence of HCV infection is present among Egyptian RA patients, reflecting the high prevalence of HCV infection in Egypt, so routine screening for HCV infection in Egyptian RA patients is recommended. Moreover, HCV infection in RA patients is associated with significant disability and co-morbidities in the form of bronchial asthma, hepatomegaly and vasculitis.

Disclosure statement: The authors have declared no conflicts of interest.

061 HOW COMMON IS CHRONIC KIDNEY DISEASE IN A COHORT OF PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS?

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Background: Prevalence estimates of chronic kidney disease (CKD) in RA vary from 5 to 50% depending on the population studied and CKD measure used. The aim of this study was to determine the prevalence of renal disease in an RA cohort and investigate what factors predicted the development of CKD in this population.

Methods: Data were collected from an established UK RA cohort (median disease duration 9 years). Consenting patients fulfilling the 1987 ACR criteria for RA were followed up annually, with data gathered on patient demographics (age, gender and BMI) and co-morbidities such as smoking status, hypertension, hypercholesterolaemia and diabetes. Data were also collected on RA characteristics, including RF status, disease duration, disease activity (28-joint DAS (DAS28), disability (HAQ) and inflammatory markers (ESR, CRP). Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) equation, with an eGFR > 60 ml/min/1.73 m² defined as CKD. Ethical approval was obtained.

Results: Data were available on 426 patients at baseline, of whom 73 (17.1%) had CKD. Those with CKD were likely to be older (median age 70 years [interquartile range (IQR) 63–74] vs 60 [53–67.5], P = 0.0001), female (80.8 vs 65.4%, P = 0.01) and be obese (38.4 vs 26.2%, P = 0.04). Patients with CKD were more likely to have other co-morbidities, specifically hypertension (74.6 vs 34.6%, P = 0.0001) and non-insulin-dependent diabetes mellitus (NIDDM) (12.3 vs 3.7%, P = 0.002). Patients with CKD were more likely to have a higher HAQ score (median HAQ 1.875 [IQR 1.375–2.125] vs 1.5 [0.875–2.0], P = 0.01) and increased ESR [median ESR 26 (IQR 14–40) vs 18 (10–34), P = 0.03], although the DAS28 score was similar in both groups. Patients without CKD at baseline were followed up at 3 years; data were available on 259 patients. Of these, 19 (7.3%) developed new CKD. No difference was seen in the demographics or RA characteristics of those developing CKD vs those not developing CKD, except baseline CRP, which was higher in those developing CKD (median CRP 21.7 [IQR 11.0–46.6] vs 9.78 [4.0–19.0], P = 0.005). Logistic regression analysis with adjustment for baseline eGFR showed that those developing CKD were more likely to have hypertension at baseline [odds ratio 4.3 (95% CI 1.3, 14.6), P = 0.02].

Conclusion: Prevalent CKD is common in patients with established RA and appears to be associated with patient demographics and co-morbidity (particularly hypertension) rather than RA-specific characteristics. This suggests RA patients should be screened for hypertension and aggressively managed to reduce the risk of CKD.

Disclosure statement: The authors have declared no conflicts of interest.

062 CHANGES IN BODY MASS INDEX IN RHEUMATOID ARTHRITIS: INCREASES AT DISEASE PRESENTATION OVER TIME AND WITH DISEASE DURATION IN TWO UK PROSPECTIVE STUDIES

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Background: Obesity is a risk factor for developing RA and also for worse RA outcomes. The objective of the present analysis was to determine BMI levels and obesity prevalence at presentation, changes in BMI over time and demographic and clinical variables associated with increased BMI.

Methods: Two consecutive UK multicentre observational studies were used: the Early RA Study and the Early RA Network. Between 1986 and 2012, 2701 patients were recruited from a total of 32 outpatient rheumatology clinics. Sociodemographic and standard clinical variables were recorded at baseline and then annually. Height and weight were recorded at each visit and converted to BMI. BMI data were available for at least one assessment for 2408 patients (89.2%). Mixed-effects models were used to determine longitudinal changes in BMI over time, while linear splines with a change point at 24 months allowed for non-linear change.

Results: Over the period of recruitment there was a considerable increase in BMI at baseline visit between patients, equivalent to 0.15 units per calendar year (95% CI 0.11, 0.18), which related to an increase in the prevalence of obesity from 13.3% in 1990 to 33.6% in 2010. In addition to this change across patients over time, a considerable within-person increase in BMI over the course of the disease was also observed. The rate of change in BMI by disease duration was non-linear, with a rapid increase during the first 2 years that reached a plateau by ~5 years. On average, BMI was 26.48 at baseline and increased by 0.49 units over the first 2 years of the disease (95% CI 0.40, 0.59), equivalent to an increase of 1.6 kg (3.5 lb) for an individual of height 178 cm (5’10”), 10 in. A larger increase in BMI over the 2 years from baseline was significantly related to younger age and higher baseline HAQ, ESR and swollen joint count, but not to sex, use of steroids, RF positivity, baseline tender joint count or living in a socially deprived area.

Conclusion: RA patients in the UK are becoming more obese at first presentation to a rheumatologist and rapidly gain weight in the first 2 years of disease. This could partly reflect the impact of the disease on mobility, supported in this analysis by the association of increases in BMI with higher HAQ, ESR and swollen joint count. Other explanations, such as the use of steroids, are possible but were not confirmed. Close weight monitoring may be important in the early management of RA in view of its impact on the course and outcomes of disease.

Disclosure statement: The authors have declared no conflicts of interest.

063 SURVIVAL IN RHEUMATOID LUNG DISEASE IS LONGER IN PATIENTS TREATED WITH RITUXIMAB THAN THOSE RECEIVING ANTI-TUMOUR NECROSIS FACTOR THERAPY

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Background: The evidence base to support treatment decisions in managing patients with RA and related interstitial lung disease (ILD) is very limited. In particular, guidance on which biologic therapy to use in patients with active articular disease does not exist.

Methods: We obtained data from the British Rheumatoid Interstitial Lung (BRILL) network on all patients with RA-ILD whose first biologic was rituximab (RTX). We assessed survival and compared this with patients with RA-ILD who had taken an anti-TNF agent as their first
biologic. Data were corrected for age, gender, disease duration, extent and subtype. Survival curves were plotted on a Kaplan–Meier chart and statistical differences were calculated at 5, 7 and 8 years using a Cox regression model.

Results: We identified 51 patients with RA-ILD who had received RTX as their first biologic agent and 100 who had received an anti-TNF drug first. There was no significant difference between the anti-TNF agents, so data in this group were combined. Survival was significantly better in the RTX group who had received RTX (P = 0.03) when compared with those who had been treated with anti-TNF therapy, and this difference was evident by 3 years and maintained at 5 and 7 years.

Conclusion: For those patients with RA-ILD who qualify for biologic therapy on the basis of their articular disease, the evidence from this large retrospective UK study suggests that survival is longer in those who first receive RTX than in those treated with anti-TNF therapy. This study cannot offer guidance on whether RTX can be proposed as a treatment for ILD, but it does suggest it should be the agent of first choice in managing articular disease in this clinical setting.

Disclosure statement: The authors have declared no conflicts of interest.

064 CAROTID INTIMA-MEDIA THICKNESS AND INTERLEUKIN-17 LEVEL IN RHEUMATOID ARTHRITIS PATIENTS

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Background: RA patients are at risk of cardiovascular disease (CVD). The objective of this study was to assess the carotid intima-media thickness (cIMT) in RA patients who have no traditional cardiovascular risk factors and a low disease activity state. This study was also aimed at determining the correlation between serum IL-17 with cIMT.

Methods: RA patients who were in low disease activity or remission (28-joint DAS <3.2) from the Rheumatology Clinic, National University of Malaysia Medical Centre were recruited. Patients with traditional cardiovascular risk factors were excluded. Carotid US was performed in RA patients and their age- and gender-matched healthy controls to determine the cIMT thickness. Serum IL-17 was measured using ELISA.

Results: A total of 22 RA patients were recruited. Patients with RA had significantly higher median cIMT (0.53 mm [interquartile range 0.13]) compared with controls [0.47 mm (IQR 0.14)] (P = 0.01). In RA patients, the cIMT had significant positive correlation with age (r = 0.84, P < 0.001), systolic blood pressure (r = 0.45, P = 0.04), waist circumference (r = 0.43, P = 0.04), total cholesterol (r = 0.54, P = 0.01), BMI (r = 0.45, P = 0.04) and serum IL-17 (r = 0.45, P = 0.03) but negative correlation with total high-density lipoprotein (r = 0.43, P = 0.05).

Conclusion: Patients with RA had significantly higher cIMT as compared with healthy controls despite minimal disease activity and lack of traditional cardiovascular risk factors, suggesting that the vascular injury due to previous inflammation may not be reversible. Serum IL-17 was also found to be correlated significantly with cIMT, suggesting that it may play a role in atherogenesis among RA patients.

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Disclosure statement: The authors have declared no conflicts of interest.

065 PERIPHERAL ARTERIAL DISEASE SCREENING USING THE ANKLE BRACHIAL PRESSURE INDEX TO IDENTIFY THE CAROTID-ARTERIAL DISEASE RISK IN RHEUMATOID ARTHRITIS

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Background: In the literature, the relationship between RA and peripheral arterial disease (PAD) is sparse. Most citations propose that PAD should be further investigated in RA patients. We identified those with PAD as an independent risk factor for PAD. Emphasis on early PAD screening among patients with a greater risk of cardiovascular disease (CVD) was suggested so as to provide the best medical therapy available to prevent co-morbidities and mortalities. The ankle-brachial pressure index (ABPI) was suggested to be a specific reliable indicator for such purpose.

Methods: The study was a single-centre, non-experimental, prospective, observational study involving 100 adult Maltese RA patients. This study was conducted at the only local general hospital in Malta over 13 months. The inclusion criteria included patients diagnosed by a rheumatologist excluding those with a history of known cardiovascular events, taking anti-platelet and/or anticoagulant medication, with diabetes mellitus, previous or current PAD symptoms, ulcerations on the foot or leg or who underwent a revascularisation procedure. The only co-morbidities included were hypertension and hyperlipidaemia. Data collection was done using a self-designed structured questionnaire and a vascular assessment. The result sheet was divided into three sections: (i) Demographic data: age, gender, BMI, history of RA, hypertension, hypercholesterolaemia and smoking status. (ii) Blood results: the most recent blood results that were routinely ordered by the rheumatologist were recorded, including CRP, ESR, RA factor, ACPA and blood cholesterol level. (iii) Vascular assessment: the Hunteigh Dopplex Assist was used to measure the waveforms and the resting ABPI while pedal pulses were taken manually.

Results: ABPI showed that the RA condition was being well controlled since 98% of the participants had normal ABPI while 2% showed mild obstruction of peripheral arteries. A significance was found between ABPI and total blood cholesterol (TBC) (P = 0.034) and ABPI and low-density lipoprotein (LDL) (P = 0.027). The statistics showed that as both cholesterol levels increased, the ABPI decreased, indicating atherosclerosis.

Conclusion: The results suggest that RA patients with high TBC and LDL values should be followed closely since the ABPI was shown to be significantly lower within the normal ABPI range. In studies, high levels of TBC and LDL were associated with increased CVD risk. No significance was found between the other CVD risk factors and ABPI. This study suggests that LDL should be considered in the SCORE model, which predicts the 10 year cardiovascular risk, as this was found to be significant even in early PAD screening. Also, further studies should be done in the management of LDL, as suggested by the European League Against Rheumatism, for management of CV risk in RA.

Disclosure statement: The authors have declared no conflicts of interest.

066 THE RELATIONSHIP BETWEEN ANXIETY AND DISEASE CHARACTERISTICS IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL OBSERVATIONAL STUDY

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1Psychological Medicine and 2Rheumatology, Kings College Medical School, London, UK

Background: Rates of affective disorder are two to three times higher in RA patients when compared with the general population. Both depression and anxiety have been linked with poor health outcomes in RA, including worse symptoms of pain and fatigue, poor compliance to medication, increased health care costs and even mortality risk. While there is established evidence for the association between depression (with or without anxiety) and RA outcomes, there is more limited evidence for the association of anxiety and RA outcomes. This study investigated whether anxiety was associated with RA outcomes and looked at the characteristics of RA that predispose to it.

Methods: The study had an observational, cross-sectional design. Data from patients with RA were obtained through the web-based patient reported outcome screening tool (IMPARTS) at King’s College London Hospital’s rheumatology department. Demographic data, disease activity (28-joint DAS (DAS28)), functional impairment (HAQ), depression (PHQ-2) and general anxiety disorder (GAD2) scores were collected from the IMPARTS database, which was linked to the electronic patient records. Pearson’s correlation values and multiple linear regression models were used to assess the association between the variables. The variables were chosen as a literature search confirmed a definite association with depression in RA patients.

Results: Data were available for 364 patients (Table 1). The prevalence of probable depressive disorder was 181 (23%), anxiety disorder 177 (22%) and both 117 (15%). Higher disease activity was found to be a significant predictor for both higher levels of depression and anxiety, with a 1 unit increase in DAS28 related to a 0.54 increase in PHQ2 (P < 0.001) and 0.34 increase in GAD2 (P < 0.001). High functional limitation was found to be a significant predictor for both higher levels of both depression and anxiety, with a 1 unit increase in HAQ related to a 0.13 increase in PHQ2 (P < 0.001) and 0.84 increase in GAD2 (P < 0.001). Neither age nor disease duration was found to be associated with either depression or anxiety.
Conclusion: The findings for depression and RA are in keeping with previous literature. This study showed that anxiety had a similar relationship with disease activity and functional limitation, albeit with weaker effect sizes. These findings are important, as recognition of anxiety in this group of RA patients is a first step in appropriate treatment. Further longitudinal studies are recommended to further investigate the directionality of the association.

Disclosure statement: The authors have declared no conflicts of interest.

067 DISABILITY AND PSYCHOLOGICAL DISTRESS IN ESTABLISHED RHEUMATOID ARTHRITIS: SECONDARY ANALYSIS OF A CLINICAL TRIAL

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Background: The impact of active RA on disability and quality of life and the improvements when patients are treated with DMARDs and biologics are well known. However, the added impact of psychological stress upon these key outcomes has received little attention. We have undertaken a secondary analysis of a randomized clinical trial in established RA patients to define how much disability and quality of life are influenced by psychological distress when established RA patients are treated with conventional DMARDs and biologics.

Methods: We analysed the TACIT trial, which compared treatment strategies using intensive DMARDs and biologics in patients with active established RA over 12 months. The trial enrolled 205 patients (mean age 57 years, mean disease duration 8 years, 74% female). We defined psychological distress as a 36-item Short Form Health Survey and (iv) anxiety and depression [Hospital Anxiety and Depression Scale (HADS)]—a common association affecting quality of life. and the improvements when patients are treated with DMARDs and biologics. To minimize disability and maximize quality of life, patients with RA who receive psychological treatment need additional treatments over and above intensive drug therapy with DMARDs and biologics.

Disclosure statement: The authors have declared no conflicts of interest.

Results: A total of 597 questionnaires were sent, 301 (50%) were completed and 129 patients were reviewed in the clinic. The mean HAQ score was 3.04 and the mean HAD score was 1.25. The HAD anxiety score was >11 in 41 (32%) patients, with a mean score of 8, and the HAD depression score was >11 in 46 (36%) patients, with a mean score of 9. Fifty-four of 129 patients (42%) had a QRISK2 >20%. There was 60% agreement in scores when comparing clinic and postal questionnaire information. Five per cent of patients assessed as low risk by questionnaire had a high risk QRISK2 score in the clinic. Nineteen patients (15%) had new hypertension and 32 (25%) had a previously unknown elevated cholesterol at the clinic review. Eighty-nine per cent of patients reported GI symptoms at least a monthly basis, with 17% reporting daily symptoms. No extra symptoms of concern were elicited at clinic review in any patient.

Conclusion: The psychological distress has major negative impacts on disability and quality of life in patients with established active RA. It appears to be independent of disease activity. There is no evidence that the effect of psychological distress on disability and quality of life is altered when patients receive intensive treatment with DMARDs and biologics. To minimize disability and maximize quality of life, patients with RA who receive psychological treatment need additional treatments over and above intensive drug therapy with DMARDs and biologics.

Disclosure statement: The authors have declared no conflicts of interest.

067 Table 1. Impact of psychological distress on HAQ and EuroQol scores

<table>
<thead>
<tr>
<th>Initial</th>
<th>Psychological distress (n = 107)</th>
<th>Psychological distress (n = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.77 (1.67, 1.87)</td>
<td>2.10 (1.95, 2.26)</td>
<td></td>
</tr>
<tr>
<td>4.16 (1.34, 1.58)</td>
<td>1.81 (1.62, 2.01)</td>
<td></td>
</tr>
<tr>
<td>1.38 (1.25, 1.51)</td>
<td>1.76 (1.56, 1.96)</td>
<td></td>
</tr>
<tr>
<td>0.32 (0.40, -0.23)</td>
<td>0.30 (0.47, -0.12)</td>
<td></td>
</tr>
<tr>
<td>0.39 (0.47, -0.31)</td>
<td>0.35 (0.54, -0.16)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean (95% CI).

068 OUTSIDE THE DISEASE ACTIVITY SCORE

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Background: Treat to target using the 28-joint DAS (DAS28) is now widely adopted to successfully improve disease outcomes in RA and is used to justify escalation to anti-TNF therapy. This approach may miss important disease-associated morbidities that impact upon quality of life. This, in turn, may be reflected in the patient global visual analogue scale (VAS) component, leading to unnecessary escalation of drug therapy, with associated cost and morbidity. We evaluated the utility and feasibility of preconsultation questionnaires to facilitate a holistic consultation.

Methods: Questionnaires were sent to all patients in our electronic database with a diagnosis of RA. Domains included (i) cardiovascular (CV) symptoms and risk factors—a common life-threatening association; (ii) gastrointestinal (GI) symptoms—may affect drug absorption and medication adherence; (iii) foot symptoms (score out of 10)—not included in the DAS28 and a source of morbidity; and (iv) anxiety and depression (Hospital Anxiety and Depression Scale (HADS))—a common association affecting quality of life. Patients were then reviewed clinically, with a full history and examination undertaken, and HAQ, DAS and QRISK2 scores were calculated for each patient. Questionnaire scores were compared with the clinical assessment.

Results: A total of 597 questionnaires were sent, 301 (50%) were completed and 129 patients were reviewed in the clinic. The mean HAQ score was 3.04 and the mean HAD score was 1.25. The HAD anxiety score was >11 in 41 (32%) patients, with a mean score of 8, and the HAD depression score was >11 in 46 (36%) patients, with a mean score of 9. Fifty-four of 129 patients (42%) had a QRISK2 >20%. There was 60% agreement in scores when comparing clinic and postal questionnaire information. Five per cent of patients assessed as low risk by questionnaire had a high risk QRISK2 score in the clinic. Nineteen patients (15%) had new hypertension and 32 (25%) had a previously unknown elevated cholesterol at the clinic review. Eighty-nine per cent of patients reported GI symptoms at least a monthly basis, with 17% reporting daily symptoms. No extra symptoms of concern were elicited at clinic review in any patient.

Conclusion: Treat to target using DAS28 may miss important disease-associated morbidity in RA. Preclinic screening by questionnaire is an efficient, effective and feasible way of identifying co-morbidities and directing treatment. Coexisting conditions can have an important bearing on treatment success, therefore a global health review is important when assessing RA patients for annual review.

Disclosure statement: The authors have declared no conflicts of interest.
RHEUMATOID ARTHRITIS: PATHOGENESIS

069 T FOLLICULAR HELPER–LIKE CELLS IN THE RHEUMATOID ARTHRITIS SYNOVIA ARE SELECTIVELY ASSOCIATED WITH INTERLEUKIN-21 PRODUCTION AND ECTOPTIC LYMPHOID STRUCTURES

Nikola Lepse, Alessandra Nerviani, Costantino Pitzalis and Michele Bombardieri
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Background: A subset of RA patients are characterized by the presence of ectopic lymphoid structures (ELSs) in the synovium. Synovial ELSs display germinal centres with the in situ selection of AC2A-producing autoreactive B cells. T follicular helper (Tfh) cells play a critical role in germinal centre reactions in secondary lymphoid organs via expression of co-stimulatory molecules (e.g. ICOS) and the release of IL-21, a potent B cell activator. Increased levels of IL-21 have been observed in RA synovium and considered a potential therapeutic target in RA. The aim of this study was to characterize Tfh-like and IL-21-producing T cells in the RA synovium and to assess their therapeutic potential.

Methods: RA synovial tissue was evaluated for the presence of Tfh-like cells (defined by co-expression of PD-1 and ICOS) by immuno-fluorescence microscopy. SF mononuclear cells were either directly stained for surface marker expression or stimulated for 4 h with leucocyte activation cocktail in the presence of brefeldin A to evaluate cytokine expression by flow cytometry. IL-21 receptor (IL-21R) expression on fibroblast-like synoviocytes (FLSs) was analysed by flow cytometry.

Results: The numbers of PD-1+ICOS+ cells were significantly higher in ELS-positive than ELS-negative synovial tissue [median 18.5 (IQR 9.9–57.0) vs 0.00 (1.4, P = 0.009)]. Consistent with the histological findings, increased percentages of CD4+PD-1+ICOS+ cells [63.63% (IQR 9.17, 21.72) vs 9.01 (4.8), and IL-21-producing CD4+ T cells were found in the SF of arthritis patients when compared with peripheral blood of healthy donors [median 19.53% (IQR 6.89–5.6) vs 5.43 (1.3)]. Furthermore, a sizeable subset of FLSs [55.85% (IQR 16.92)] expressed IL-21R, and IL-21R mRNA expression in FLSs could be significantly upregulated by Toll-like receptor stimulation.

Conclusion: Tfh-like cells are significantly more represented in ELS-positive than ELS-negative synovium. IL-21-producing CD4+ T cells in SF might have a direct pro-inflammatory effect on FLSs via IL-21/IL-21R signaling.

Disclosure statement: I.C.S. has received research funding from the NIHR (Clinical Lectureship) and Academy of Medical Sciences ( Starter Grant).

071 SYNOVIAL MAST CELLS CORRELATE WITH INFLAMMATION AND CELLULAR INfiltrATION AND ARE ASSOCIATED WITH ECTOPTIC LYMPHOID STRUCTURES IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: The analysis of synovial membrane has gained much attention in recent years as a biomarker for patient stratification in RA. Different degrees of cellular infiltration have been described, leading to the definition of specific histological patterns (pathotypes). Mast cells (MCs) are among the immune cells infiltrating the inflamed synovium, and many experimental observations suggest that they participate to the inflammatory response in RA. However, their contribution to the pathogenesis of RA is still controversial and, in particular, their presence in the synovial membrane has never been analysed systematically, nor their relation to synovial inflammation and pathotypes. The aim of this study was to evaluate the presence of MCs in the synovial membrane of early RA patients and assess the correlation with synovial inflammation and cellular infiltration.

Methods: Sections of paraffin-embedded synovial tissue obtained by US-guided synovial biopsy from DMARD-naïve patients with early (<12 months) RA (n = 79) were stained with haematoxylin and eosin to measure the degree of synovitis. Sequentially cut sections were stained by immunohistochemistry to evaluate the presence of infiltrating T cells (CD3+), B cells (CD20+), macrophages (CD68+), plasma cells (CD138+) and MCs (CD117+). Additionally, the interaction of MCs with B cell aggregates was assessed by double immunofluorescence in the tonsils of healthy donors (n = 3) and synovia from RA patients (n = 6).

Results: MCs showed a positive correlation with synovial inflammation (r = 0.54, P < 0.0001) and with infiltrating T cells (r = 0.52, P < 0.0001), B cells (r = 0.52, P < 0.0001), macrophages (lining: r = 0.45, P < 0.0002; sublining: r = 0.32, P = 0.0048) and plasma cells (r = 0.54, P < 0.0001). In particular, synovial MCs were significantly more represented in patients with ecotopic lymphoid structures (ELSs) (mean MCs/mm2 in ELS 15.58 vs ELS 42.96, P < 0.0001). Similarly, when patients were...
stratified according to MC numbers, the proportion of ELS in patients was significantly higher in RA patients with a high MC count (ELS- in patients with low MC count 36.8% vs high MC count 76.9%, P < 0.0001). Double immunofluorescent stainings showed MCs at the edges of germinal centres in organs (human tonsils). Accordingly, MCs were found in close proximity of B cell aggregates in ELS- synovial samples.

**Conclusion:** Our study indicates that MCs are part of the inflammatory infiltrate in the synovia of RA patients. More specifically, they are associated with the presence of ectopic lymphoid structures and have a spatial interaction with B cells in synovia, suggesting that their presence might contribute to the characterisation of synovial pathotypes. Additional studies are warranted in order to establish the functional relevance of MC interaction with B cells at the synovial level and their role in the pathogenesis of RA.

**Disclosure statement:** F.R. has received a fellowship from the People Programme (Marie Curie Actions) of the European Union’s Seventh Framework Programme (FP7/2007-2013) under REA grant agreement 608765. All other authors have declared no conflicts of interest.

**072 LACK OF C-REACTIVE PROTEIN RESPONSE IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: WHAT ARE THE IMMUNOLOGICAL CAUSES?**

Claire M. Bradforth, Lindsey Kidd, Victoria Howard, Cozana Curtin, Elizabeth C. Jury and Manson J. Jessica

**Background:** Musculoskeletal US clinics are used increasingly to assess joint erosions and disease activity in patients with RA. Using this technology, an atypical patient subgroup has been identified with active disease demonstrated by significant power Doppler but normal CRP levels. We questioned whether this presentation was associated with delayed diagnosis or relative undertreatment, risking worse disease outcome and disability. Furthermore, we hypothesized that understanding the underlying immune pathology in this atypical subset of patients could directly influence therapeutic targeting in patients whose needs are not currently met.

**Methods:** Twenty-seven RA patients with active synovitis were recruited, defined by at least one joint with power Doppler signal detected. Baseline US: 17 had normal CRP levels (<5mg/l), and 10 had high CRP levels (>5mg/l). Peripheral blood mononuclear cells (PBMCs) and serum as well as detailed clinical and disease activity scores were collected at the time of the scan. Blood was also collected from 18 age- and sex-matched healthy donors. To identify whether the disparity in CRP levels in the two patient groups was associated with a distinct immune profile, we used multicolour flow cytometry to perform in-depth PBMC immunophenotyping and serum cytokines were assessed using a 14-panel cytometric bead array.

**Results:** No significant differences were detected between the patient groups in terms of autoantibody levels, ESR and DAS28; however, the erosion accrual rate was elevated in patients with normal CRP compared to high CRP, suggesting that this group of patients acquired more disease-associated joint damage. Analysis of serum revealed increased levels of inflammatory cytokines in both normal CRP and high CRP patients, including IL-1β (P = 0.0364, P = 0.0233) and IL-6 (P = 0.0009, P = 0.0007), which is known to trigger CRP production. This suggested that normal CRP patients could have defects in downstream IL-6 signalling, or alternatively, the disease mechanism may not be IL-6 dependent in the normal CRP group. Since IL-6 is known to support T cell and T follicular helper cell activation and differentiation, we compared the T cell phenotype in the two patient groups. As predicted, the data suggest that the high CRP patients have an inflammatory profile that is typical of active RA, in particular CD4+ T cells were activated (P = 0.0054) and increased frequencies of central memory (P = 0.0380) and Th17 populations were seen compared with healthy controls. In contrast, T cells in the normal CRP group had a less inflammatory phenotype, as characterized by higher levels of regulatory T cells (P = 0.0036) and increased serum IL-10, despite synovitis on scans and high erosion accrual, suggesting increased immune modulation in these patients.

**Conclusion:** Overall, this supports altered immunological mechanisms in normal CRP compared with high CRP patients, which could have therapeutic implications.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**RHEUMATOID ARTHRITIS: TREATMENT**

**073 ABSTRACT WITHDRAWN**

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**074 A MULTICENTRE, OPEN-LABEL, LONG-TERM EXTENSION STUDY IN PATIENTS WITH MODERATE- TO SEVERE RHEUMATOID ARTHRITIS FROM THE SUMMACTA AND BREVACTA STUDIES: EVALUATION OF THE SAFETY AND EFFICACY OF SUBCUTANEOUS TOCILIZUMAB**

Alan Kivitz, Ewa Olech, Michael Borofsky, Jenny Devenport, Jürgen Perš, Thomas Wallace and Margaret Michalska

**Background:** Global phase III studies evaluated the safety and efficacy of s.c. tocilizumab (TCZ-SC). SUMMACTA was a 97-week study comparing TCZ-SC 162 mg weekly (qw) with i.v. TCZ (TCZ-IV) 8 mg/kg every 4 weeks. At week 24, patients were re-randomized to the initial formulation or switched formulations. BREVACTA was a 36-week study comparing TCZ-SC 162 mg qw with BREVACTA (BCZ-SC). SUMMACTA and BREVACTA were extensions of phase IIIb studies and investigated the efficacy and safety of TCZ-SC qw.

**Background:** The aims of this study were to continue the evaluation of the safety and efficacy of TCZ-SC qw in patients with active RA, and to assess the effects of switching to BREVACTA on clinical and laboratory measures.

**Methods:** Patients with at least one joint with power Doppler signal at baseline were randomized to: (1) TCZ-SC 162 mg qw in the first 12 months, and then switched to BREVACTA qw in the second year; or (2) BREVACTA qw throughout the 24-month extension. The primary endpoint was the proportion of patients achieving the European League Against Rheumatism (EULAR) response criteria (good responder and minimal responder) at week 24. Secondary endpoints included changes in the American College of Rheumatology (ACR) 20, ACR 50, and ACR 70 responses from baseline to week 24, and changes in the Disease Activity Score (DAS) 28 (ESR and C-reactive protein [CRP]) from baseline to week 24.

**Results:** A total of 268 patients were randomized to the first treatment group and 270 to the second. At week 24, there were no statistically significant differences between the two groups in terms of the primary endpoint or the secondary endpoints. The safety and tolerability of TCZ-SC qw was consistent with previous studies, with no new safety signals observed.

**Conclusion:** This study demonstrated that switching to BREVACTA from TCZ-SC qw did not affect the efficacy and safety profile of TCZ-SC qw in patients with active RA, and maintained the benefits seen in previous studies.

**Disclosure statement:** The authors have declared no conflicts of interest.
In this open-label, single-arm, US-based, phase IIIb long-term extension (LTE) study, patients who completed SUMMACTA and BREVACTA could enrol and continue to receive TCZ-SC q2w or qw, or switch from TCZ-IV to TCZ-SC qw. Non-biologic DMARDs were permitted in combination. The primary safety endpoint was the proportion of patients with serious adverse events (SAEs). Secondary endpoints included the proportion of patients with AEs of special interest and patients who discontinued, the incidence of laboratory abnormalities and efficacy assessments.

Results: Of the 217 patients (mean age 58.4 years, 76.5% female) treated in this LTE study, 23 patients (10.6%) had one or more SAES, a rate of 14.7/100 patient-years (Table 1). The most common SAES were infections [n = 7 (3.2%)]; eight patients had one or more serious or opportunistic infections or infections requiring i.v. anti-infectives. Thirty-four patients withdrew from TCZ-SC treatment, 13 (6.0%) due to AEs and 21 (9.7%) for non-safety reasons. Aminotransferase elevations were reported in 59 (27.2%) patients but were not associated with liver toxicity. Neutropenia [n = 11 (5.1%)] was transient. Injection site reactions occurred in six patients, who were non-serious and resolved without sequelae. No anaphylaxis or deaths were reported. The mean Clinical Disease Activity Index and 28-joint DAS scores decreased from baseline and remained stable.

Conclusion: The safety of TCZ-SC during this LTE study was consistent with that established during the core studies, with no new safety signals identified. Mean efficacy improvements were stable over time. Results demonstrate the durability of safety and efficacy responses with long-term exposure to TCZ-SC.

Disclosure statement: A.K. has received consulting fees from BMS, Genentech and UCB; has participated in the speakers bureau for BMS and has received research grants from AbbVie, Amgen, AstraZeneca, BMS, Celgene, Genentech, Janssen, Pfizer and UCB. E.O. has received consulting fees from Genentech and has participated in the speakers bureau for Genentech. J.D. is an employee of Genentech. J.P. is an employee of Genentech. M.M. is an employee of Genentech. All other authors have declared no conflicts of interest.

076 PNEUMOCOCCAL VACCINATION AND REVACCINATION IN PATIENTS TREATED WITH RITUXIMAB

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Background: Pneumococcal disease is a major cause of morbidity and mortality. Current British Society for Rheumatology (BSR)/British Health Professionals in Rheumatology (BHPR) guidelines recommend that pneumococcal polysaccharide vaccine (PPV) should be administered 4–6 weeks prior to rituximab (RTX) infusion and revaccination is delivered every 5 years. We audited PPV and influenza vaccination histories and evaluated patients’ recall of these vaccines in a cohort of patients treated with RTX attending our rheumatology day unit. The aim was to assess vaccination rates in this population with a view to reviewing our strategy for vaccination and identifying those patients who had not been vaccinated.

Methods: Questionnaires were received from 63 patients attending the day unit for RTX between 1 January and 1 June 2015. The questionnaire explored patients’ understanding of their vaccination history and sought consent for obtaining vaccination history from their general practitioner (GP) records. Fifty-four GP responses were received. Based on the information provided, recommendations were made for future vaccination.

Results: According to GP data, 15/54 (27.8%) had received PPV according to BSR guidelines, i.e. they had initial vaccination prior to RTX and received a booster at 5 years where necessary. Forty-four of 54 (81.5%) patients have received at least one PPV; 38/54 (70.4%) patients received an initial PPV prior to commencing RTX. At the time of our audit, 25/54 patients should have received their revaccination every 5 years. Of these, 8% were revaccinated within 5 years. 28% were revaccinated after 5 years (6–13 years after first vaccination) and 64% did not receive a booster. Initial influenza vaccination uptake rates [43/53 (81.1%)] were equivalent to initial PPV uptake rates. However, 38/53 (71.7%) patients were up-to-date with influenza vaccination.
compared with 28/54 (51.9%) being up-to-date with PPV. Patient recollection of vaccination history is demonstrated in Table 1.

**Conclusion:** Our previous strategy of informing GPs through correspondence and prompting patients to request PPV from their GP has not resulted in outcomes consistent with BSR guidance for vaccination and revaccination in this patient group. Equally, patient recall of vaccination history was not sufficient to guide revaccination; asking patients whether they are up-to-date with their vaccinations was not sufficient to identify those requiring further treatment. Revaccination rates with PPV are lower when compared with influenza revaccination, suggesting either a lack of knowledge of the vaccination guidelines or other barriers to following them. We are now providing further information for patients in a clinical setting and in patient literature. An infusion pro forma has been developed to remind staff to prompt patients to be aware of revaccination due dates. GP discharge letters have been amended to request a review of vaccination history in patients treated with RTX. We plan to re-audit following implementation of the recommendations with a view to extending them to other biologic treatment.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 077 IMMUNOGENICITY OF SUBCUTANEOUS AND INTRAVENOUS TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATOID ARTHRITIS

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**Background:** Tocilizumab iv. (TCZ-IV) and s.c. (TCZ-SC) formulations are indicated in adult RA based upon evidence from phase III and IV trials and open-label, long-term extensions. From these, we provide an overview of the immunogenicity profile of TCZ-SC and TCZ-IV as monotherapy or in combination with DMARDs.

**Methods:** In TCZ-IV studies, patients with RA were monitored for up to 5 years and for TCZ-SC up to 2 years. Blood samples were taken at baseline and regularly prior to TCZ dosing for anti-drug antibody (ADA) assessment. Samples were screened using a bridging ELISA method. Positive samples were analysed by a confirmation assay for specificity. Samples confirmed positive were characterized for neutralizing potential and IgE isotype (SC studies only). Safety and efficacy were evaluated in association with ADA development.

**Results:** The rate of ADA development was low and comparable for TCZ-SC and TCZ-IV (2.0 vs 1.2%, Table 1). ADA development was ≥ 0.2% and similar between patients who received TCZ monotherapy (1.3%) and TCZ + DMARDs (1.4%), regardless of formulation. No anaphylaxis or serious hypersensitivity reactions were observed in patients who received TCZ-SC monotherapy, TCZ-SC + DMARDs or TCZ-IV monotherapy and developed ADAs. In patients who had anaphylaxis, serious hypersensitivity or clinically significant hypersensitivity (n = 131), 7.6% developed ADAs. Of 63 patients who received TCZ-IV + DMARDs and developed ADAs, 5 had anaphylaxis, 1 had a serious hypersensitivity reaction and 4 had clinically significant hypersensitivity reactions. One patient on TCZ-IV monotherapy with ADAs had a clinically significant hypersensitivity reaction and 3 patients on TCZ-SC + DMARDs with ADAs had injection site reactions (ISRs); no ISRs occurred in patients on TCZ-SC monotherapy with ADAs. Among patients who developed ADAs with neutralizing potential, none experienced loss of efficacy, regardless of the formulation or concomitant DMARDs.

**Conclusion:** TCZ-SC and TCZ-IV have a low risk of immunogenicity potential, with no impact on safety or efficacy. For patients who received TCZ-SC, the proportion that developed anti-TCZ antibodies was comparable to that for TCZ-IV. TCZ had low and comparable immunogenicity when administered as a monotherapy or in combination with DMARDs.

**Disclosure statement:** M.C.G. has received consulting fees from Roche Pharmaceuticals, A.O. has received consulting fees from Chugai Pharmaceutical and has participated in the speakers bureau for Chugai Pharmaceutical. A.N. is an employee of Genentech Pharmaceutical. M.B. is an employee of Chugai Pharmaceutical. A.O. holds a patent and has received consulting fees from Crescendo Bioscience and was an employee of Genentech at the time of the study. S.L. is an employee of Roche Products. G.R.B. has received

### 077 Table 1. The immunogenicity profile of TCZ-SC and TCZ-IV in patients with RA

<table>
<thead>
<tr>
<th>TCZ-SC vs TCZ-IV</th>
<th>TCZ-SC all exposure (n = 1638)</th>
<th>TCZ-IV all exposure (n = 5875)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients screened, n</td>
<td>1636</td>
<td>5806</td>
</tr>
<tr>
<td>Anaphylaxis, n (%)</td>
<td>0</td>
<td>9 (0.2)</td>
</tr>
<tr>
<td>Clinically significant hypersensitivity, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>13 (0.8)</td>
<td>89 (1.5)</td>
</tr>
<tr>
<td>Serious hypersensitivity, n (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6 (0.4)</td>
<td>48 (0.8)</td>
</tr>
<tr>
<td>Injection site reactions, n (%)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>171 (10.4)</td>
<td>N/A</td>
</tr>
<tr>
<td>Total patients who developed ADAs, n (%)</td>
<td>33 (2.0)</td>
<td>69 (1.2)</td>
</tr>
<tr>
<td>Neutralization assay positive, n (%)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>25 (1.7)</td>
<td>54 (0.9)</td>
</tr>
<tr>
<td>IgE assay positive, n (%)</td>
<td>11 (0.7)</td>
<td>N/A</td>
</tr>
<tr>
<td>Anaphylaxis, n (%)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0</td>
<td>5 (0.1)</td>
</tr>
<tr>
<td>Clinically significant hypersensitivity, n (%)&lt;sup&gt;f&lt;/sup&gt;</td>
<td>0</td>
<td>10 (0.2)</td>
</tr>
<tr>
<td>Serious hypersensitivity, n (%)&lt;sup&gt;g&lt;/sup&gt;</td>
<td>0</td>
<td>6 (0.1)</td>
</tr>
<tr>
<td>Injection site reactions, n (%)&lt;sup&gt;h&lt;/sup&gt;</td>
<td>3 (0.2)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**TCZ monotherapy vs TCZ + DMARDs**

<table>
<thead>
<tr>
<th>TCZ-SC monotherapy (n = 172)</th>
<th>TCZ-SC + DMARDs (n = 1485)</th>
<th>TCZ-IV monotherapy (n = 753)</th>
<th>TCZ-IV + DMARDs (n = 5122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients screened, n</td>
<td>173</td>
<td>1463</td>
<td>745</td>
</tr>
<tr>
<td>Anaphylaxis, n (%)&lt;sup&gt;i&lt;/sup&gt;</td>
<td>0</td>
<td>1 (0.1)</td>
<td>8 (0.2)</td>
</tr>
<tr>
<td>Clinically significant hypersensitivity, n (%)&lt;sup&gt;j&lt;/sup&gt;</td>
<td>1 (0.6)</td>
<td>12 (0.8)</td>
<td>12 (1.6)</td>
</tr>
<tr>
<td>Serious hypersensitivity, n (%)&lt;sup&gt;k&lt;/sup&gt;</td>
<td>0</td>
<td>6 (0.4)</td>
<td>7 (0.9)</td>
</tr>
<tr>
<td>Injection site reactions, n (%)&lt;sup&gt;l&lt;/sup&gt;</td>
<td>30 (17.3)</td>
<td>141 (9.6)</td>
<td>N/A</td>
</tr>
<tr>
<td>Total patients who developed ADAs, n (%)</td>
<td>6 (3.5)</td>
<td>27 (1.8)</td>
<td>6 (0.8)</td>
</tr>
<tr>
<td>Neutralization assay positive, n (%)&lt;sup&gt;m&lt;/sup&gt;</td>
<td>N/A</td>
<td>25 (1.7)</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>IgE assay positive, n (%)&lt;sup&gt;n&lt;/sup&gt;</td>
<td>5 (2.9)</td>
<td>6 (0.4)</td>
<td>N/A</td>
</tr>
<tr>
<td>Anaphylaxis, n (%)&lt;sup&gt;o&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
<td>5 (0.1)</td>
</tr>
<tr>
<td>Clinically significant hypersensitivity, n (%)&lt;sup&gt;p&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Serious hypersensitivity, n (%)&lt;sup&gt;q&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
<td>6 (0.1)</td>
</tr>
<tr>
<td>Injection site reactions, n (%)&lt;sup&gt;r&lt;/sup&gt;</td>
<td>0</td>
<td>3 (0.2)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**ADA:** anti-drug antibody; IV: intravenous; mono: monotherapy; SC: subcutaneous; TCZ: tocilizumab.

<sup>a</sup>Anaphylactic reactions were defined using Sampson criteria.

<sup>b</sup>ISRs were AEs occurring at the local injection site.

<sup>c</sup>Serious hypersensitivity, clinically significant hypersensitivity reaction and serious hypersensitivity reaction were observed in patients who received TCZ-SC or TCZ-IV as monotherapy or in combination with DMARDs.

<sup>d</sup>Serious hypersensitivity events were defined as hypersensitivity events that were reported as serious AEs.

<sup>e</sup>ISRs were AEs occurring at the local injection site.

<sup>f</sup>In the MUSASHI study, hypersensitivity events were defined as adverse events (AEs), excluding ISRs that occurred during or within 24 h of an infusion or injection and which were judged as a hypersensitivity event by the clinical expert. In all other studies, hypersensitivity events were defined as all AEs, excluding ISRs, that occurred during or within 24 h of an infusion or injection and were not judged 'unrelated' to treatment by the investigator; those events may or may not be consistent with hypersensitivity clinically.

<sup>g</sup>This has led to withdrawal from treatment.

<sup>h</sup>Anaphylactic reactions were defined in the MUSASHI study, hypersensitivity events were defined as adverse events (AEs), excluding ISRs, that occurred during or within 24 h of an infusion or injection and were not judged ‘unrelated’ to treatment by the investigator; those events may or may not be consistent with hypersensitivity clinically.

<sup>i</sup>ISRs were AEs occurring at the local injection site.

<sup>j</sup>The neutralization assay was not performed in MUSASHI. The denominator used for this does not include the MUSASHI population.

<sup>k</sup>An IgE assay was not performed in the TCZ-IV studies.
consulting fees from Oche, Chugai, Pfizer, UCB and Bristol-Myers Squibb; has participated in speakers bureaus for Roche Products, Pfizer, Merck Sharp & Dohme, Abbott and Bristol-Myers Squibb and has received research funding from Roche, Abbott, Pfizer, UCB, Merck Sharp & Dohme and Bristol-Myers Squibb.

078 EFFICACY AND SAFETY OF BARICITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO TUMOUR NECROSIS FACTOR INHIBITORS: SUMMARY RESULTS FROM THE 24-WEEK PHASE III RA-BEACON STUDY

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Background: Baricitinib, an oral JAK1/JAK2 inhibitor, improved disease activity with an acceptable safety profile in the phase III RA-BEACON study of patients with moderately to severely active RA and inadequate response (IR) to TNF inhibitors (TNFis). A summary of efficacy and safety data up to week 24 in patients with IR/intolerance to one or more TNFis is presented.

Methods: A total of 527 patients with active RA despite previous use of one or more TNFis for ≥3 months were randomized 1:1:1:1 to receive placebo or baricitinib (2 or 4 mg four times a day). The primary endpoint was a 20% improvement in ACR criteria (ACR20) at week 12 (baricitinib 4 mg vs placebo). Subgroup efficacy by prior biologic use, safety and changes in total lymphocyte count (TLC), natural killer (NK) cells and B cells at week 12 and week 24. A decrease ≥0.6 in DAS28-CRP and ≥0.8 in CDAI was observed in 79% and 80% of patients on baricitinib 4 mg, respectively, and was associated with LDA/remission at week 12. More treatment-emergent adverse events occurred with baricitinib 2 and 4 mg vs placebo (71%, 77%, 64%), including infections (44%, 40%, 31%), although severe adverse events were similar. In patients on baricitinib 4 mg, no opportunistic infections were seen, but two patients had non-melanoma skin cancer. TLC changes in baricitinib groups were similar vs placebo at week 12 and week 24. There was an increase in T cells, B cells and NK cells at week 4, followed by decreases in T cells and NK cells and an increase in B cells at week 12 and week 24 for the baricitinib groups (all TLC changes within the normal range; NK cell decrease was not associated with increased infection).

Results: Fifty-seven per cent of patients had received two or more biologic DMARDs (bDMARDs) and 38% had received one or more non-TNF bDMARDs. ACR20 at week 12 was higher with baricitinib 4 mg vs placebo (55 vs 27%, P < 0.001), Improvements in ACR50/50/70, DAS28-CRP (Table 1) and CDAI, Simplified Disease Activity Index and HAQ Disability Index were observed at week 24. A decrease ≥0.6 in DAS28-CRP and ≥0.8 in CDAI at week 4 was observed in 79% and 80% of patients on baricitinib 4 mg, respectively, and was associated with LDA/remission at week 12 and week 24. More treatment-emergent adverse events occurred with baricitinib 2 and 4 mg vs placebo.

Conclusion: In RA patients, regardless of the number of prior biologics used, baricitinib showed rapid and sustained clinical improvements at week 4 through week 24 with an acceptable safety profile. Early clinical response at week 4 might predict later LDA/remission. The treatment benefit of baricitinib was accompanied by TLC changes that were unrelated to infections.

Disclosure statement: J.S.B. has received research funding and speakers fees from AbbVie and UCB. M.D. has received consulting fees from AbbVie, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB and Wyeth and has received research funding from AbbVie, BMS, Janssen and Merck. B.A.-F. is an employee and shareholder of Eli Lilly. A.B. is an employee of Eli Lilly. E.L. is an employee of Eli Lilly. M.C. is an employee and shareholder of Eli Lilly. J.S. is an employee of Eli Lilly. J.S. has received research funding from Eli Lilly and Pfizer and provided expert advice and/or been a speaker for Eli Lilly and Pfizer.

079 ABATACEPT PLUS METHOTREXATE CAN EFFECTIVELY AND SAFELY REGAIN THE TARGET OF REMISSION FOLLOWING RE-TREATMENT FOR FLARES AFTER Drug-Free WITHDRAWAL IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

Paul Emery1, Gerd Burmester2, Vivian Bykerk3, Bernard Combe4, Daniel E. Furst5, Michael Maldonado6 and Tom Huizinga7

1Rheumatic and Musculoskeletal Diseases, University of Leeds, Leeds, UK, 2Rheumatology and Clinical Immunology, Charité University Medicine Berlin, Berlin, Germany, 3Rheumatology, Hospital for Special Surgery, New York, NY, USA, 4Rheumatology, Montana University, Montpellier, France, 5Rheumatology, University of California, Los Angeles, Los Angeles, CA, 6Medical Affairs, Immunoscience, Bristol-Myers Squibb, Princeton, NJ, USA and 7Rheumatology, Leiden University Medical Center, Leiden, The Netherlands

Background: Assessing Very Early Rheumatoid arthritis Treatment (AVERT) was a phase IIib, randomized, active-controlled study to evaluate the efficacy and safety of abatacept in three phased periods: during treatment, following withdrawal of all therapies and during re-exposure. We present data from the withdrawal and re-exposure periods.

Methods: MTX-naive, anti-CCP2-positive patients with early RA [active synovitis in two or more joints for ≥8 weeks, 28-joint DAS with CRP (DAS28-CRP) ≥3.2 and onset of symptoms within ≤2 years] were initially randomized to 12 months of weekly s.c. abatacept.

078 Table 1. Efficacy response at weeks 12 and 24 in subgroups by prior bDMARD use (NRI)

Week 12 Week 24

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Baricitinib 2 mg</th>
<th>Baricitinib 4 mg</th>
<th>Placebo</th>
<th>Baricitinib 2 mg</th>
<th>Baricitinib 4 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 TNFi only</td>
<td>ACR20</td>
<td>22/69 (32)</td>
<td>32/61 (50)</td>
<td>40/63 (64)**</td>
<td>21/69 (30)</td>
<td>27/61 (44)</td>
</tr>
<tr>
<td></td>
<td>ACR50</td>
<td>8/69 (12)</td>
<td>15/61 (25)</td>
<td>25/63 (40)**</td>
<td>12/69 (17)</td>
<td>18/61 (29)</td>
</tr>
<tr>
<td></td>
<td>ACR70</td>
<td>1/69 (1)</td>
<td>12/61 (20)**</td>
<td>12/63 (19)**</td>
<td>2/69 (3)</td>
<td>9/61 (15)*</td>
</tr>
<tr>
<td>≥1 TNFi, no non-TNFi</td>
<td>DAS28-CRP ≥3.2</td>
<td>6/69 (12)</td>
<td>15/61 (25)</td>
<td>27/63 (43)**</td>
<td>10/69 (15)</td>
<td>12/61 (20)</td>
</tr>
<tr>
<td></td>
<td>ACR20</td>
<td>10/33 (30)</td>
<td>16/33 (50)</td>
<td>17/33 (51)</td>
<td>9/30 (30)</td>
<td>13/33 (40)</td>
</tr>
<tr>
<td></td>
<td>ACR50</td>
<td>1/30 (3)</td>
<td>8/33 (24)</td>
<td>7/33 (21)</td>
<td>4/30 (13)</td>
<td>10/33 (30)</td>
</tr>
<tr>
<td></td>
<td>ACR70</td>
<td>1/30 (3)</td>
<td>5/33 (15)</td>
<td>2/30 (6)</td>
<td>3/30 (10)</td>
<td>1/30 (3)</td>
</tr>
<tr>
<td>≥3 prior bDMARDs</td>
<td>DAS28-CRP ≥3.2</td>
<td>2/30 (7)</td>
<td>10/33 (30)</td>
<td>8/33 (24)</td>
<td>3/30 (10)</td>
<td>8/33 (24)</td>
</tr>
<tr>
<td></td>
<td>ACR70</td>
<td>0/47 (0)</td>
<td>3/47 (6)</td>
<td>5/45 (11*)</td>
<td>1/47 (2)</td>
<td>6/45 (12)</td>
</tr>
</tbody>
</table>

Data are presented as n/N (%). *P < 0.05, **P < 0.01, ***P < 0.001 vs placebo. Significant interaction between 1 TNFi and ≥1 TNFi. Significant interaction between bDMARDs. N = number of modified intent-to-treat analysis patients in the specified subgroup; n = number of patients in the specified category; NRI = non-responder imputation.

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125 mg + MTX, abatacept 125 mg monotherapy or MTX alone (withdrawal period). Patients with DAS28-CRP <3.2 at month 12 then entered a 12-month withdrawal period with no treatment. All patients with protocol-defined flare after month 15 could receive open-label abatacept + MTX (re-exposure period) for 6 months.

**Results:** Most patients could not remain treatment-free after complete withdrawal due to worsening disease activity (172/225 (76.4%) during the 12-month withdrawal period. Of those patients who completed the withdrawal period initially randomized to abatacept, no MTX, abatacept monotherapy and MTX alone, respectively, maintained DAS28-CRP < 2.6 free of all drugs, and 40.3, 25.9 and 15.0%, respectively, and only one serious infection was reported (MTX alone arm) (pneumonitis; 337.4 patient-years). In the re-exposure period, no patients discontinued due to AE and no serious infections were reported (292.2 patient-years). Overall infection rates were 8.1 and 16 (incidence rate/100 patient-years) in the withdrawal and re-exposure periods, respectively; rates for abatacept + MTX, abatacept monotherapy and MTX alone, respectively, were 116.6, 126.1 and 110.7 and 64.6, 66.5 and 72.8 in the first and second 6 months of the treatment period.

**Conclusion:** Re-treatment with abatacept + MTX can effectively recapture remission following flare after complete withdrawal of therapy. The likelihood of ever achieving an MCR was greater with abatacept + MTX treatment. There were fewer infection events in the combined withdrawal and re-exposure periods than in the initial treatment period; only one serious infection was reported in the combined withdrawal and treatment periods, suggesting re-treatment is well tolerated.

**Disclosure statement:** P.E. has received consulting fees from Abbott/ UCB, Pfizer, Roche Products, Eli Lilly, Novartis, Samsung, Takeda and UCB. G.B. has consulted from AbbVie, Bristol-Myers Squibb, Pfizer, Merck, MedImmune and UCB. C.P. has participated in speakers bureaus for AbbVie, Bristol-Myers Squibb, Pfizer, Merck, UCB and Roche and has received research funding from AbbVie, Pfizer, UCB and Roche. V.B. has consulted from Amgen, AbbVie, Bristol-Myers Squibb, UCB, Antares, Regeneron and Genentech and has received research funding from Genentech, Bristol-Myers Squibb, UCB and BPL. B.C. has consulted from Amgen, AbbVie, Bristol-Myers Squibb, Pfizer, Roche, Roche-Chugai and D.E.F. has received consulting fees from AbbVie, Actelion, Amgen, Bristol-Myers Squibb, Pfizer, Genentech, Novartis, Pfizer, Roche (Genentech and UCB) has participated in speakers bureaus for AbbVie, Actelion and UCB and has received research funding from AbbVie, Actelion, Amgen, Bristol-Myers Squibb, Genentech, Glaxo, NIH, Novartis, Pfizer, Roche/Genentech and UCB. M.M. is an employee and shareholder of Bristol-Myers Squibb. T.H. has consulted from AbbVie, UCB, Bristol-Myers Squibb, Pfizer, Roche and has received research funding from AbbVie, Pfizer, UCB and Roche. A.L. has received consulting fees from Amgen, AbbVie, Bristol-Myers Squibb, Pfizer, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience, Nycomed, Boehringer, Takeda, Zyus and Eli Lilly and has received research funding from Roche and Abbott.

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**080 BASELINE AUTOANTIBOIES PREFERENTIALLY IMPACT ABATACEPT EFFICACY IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE BIOLOGIC NAIVE:**

**6-MONTH RESULTS FROM A REAL-WORLD, INTERNATIONAL, PROSPECTIVE STUDY**

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**Background:** Neither RF nor anti-CCP antibody status appear to be associated with clinical response to treatment with anti-TNF agents, whereas anti-TNF-catabilaty may be associated with increased abatacept efficacy in patients with prior biologic failure and in biologic-naive patients. In this analysis, the efficacy of abatacept monotherapy after 6 months of follow-up in biologic-naive patients in the ACTION study was compared in RF/anti-CCP-positive vs negative patients.

**Methods:** ACTION is a 2-year, international, multicentre, prospective, observational study evaluating the retention and effectiveness of i.v. abatacept in patients with RA. Baseline characteristics and clinical outcomes were evaluated at 6 months and compared for anti-CCP/RF-positive and negative patients who were biologic naive using analysis of variance on ranks for quantitative variables and Fisher exact tests for qualitative variables. EULAR response was based on the 28-joint DAS (DAS28) with ESR or CRP and derived from individual core components, as were mean Clinical Disease Activity Index (CDAI) and Boolean remission.

**Results:** In 672 biologic-naive patients, RF status was reported in 577 patients [86%; 412 (71%) positive] and anti-CCP antibody status in 552 patients [82%; 364 (66%) positive]; 308/511 (60%) patients were double positive and 157/511 (25%) patients were double negative. Clinical outcomes at 6 months were more beneficial for patients who were RF or anti-CCP positive vs negative. A good/moderate EULAR response was observed in 84.6 vs 72.9% of patients who were RF positive and RF negative, respectively (P = 0.012) and in 85.2 vs 74.2% who were anti-CCP positive and anti-CCP negative, respectively (P = 0.018). The mean CDAI (calculated) was 10.9 (95% CI 9.8, 11.8) vs 15.3 (13.4, 17.2) for RF-positive and RF-negative patients, respectively (P < 0.001), and 10.9 (95% CI 9.8, 12.0) vs 14.3 (12.4, 16.2) for anti-CCP-positive and anti-CCP-negative patients (P = 0.005). Boolean remission was observed for 13.3% of RF-positive vs 4.0% of RF-negative patients (P = 0.008) and for 12.5% of anti-CCP-positive vs 6.3% of anti-CCP-negative patients (P = 0.096). Similarly, significant differences in clinical outcomes were observed for patients who were RF/anti-CCP single positive or double positive vs double negative; EULAR good/moderate response of 84.4 and 85.7 vs 71.8% (P = 0.011 and P = 0.008), respectively; mean CDAI (calculated) 11.1 (95% CI 10.2, 12.1) and 10.5 (9.3, 11.6) vs 14.5 (12.3, 16.7) (P = 0.003 and P = 0.001), respectively; Boolean remission in 12.3 and 13.8 vs 3.8% of patients (P = 0.025 and P = 0.013), respectively.

**Conclusion:** These are the first prospective real-world data showing the superior efficacy of abatacept in biologic-naive patients who are RF and/or anti-CCP positive vs negative, even when using stringent remission criteria. The association between autoantibody status and clinical outcomes with abatacept may be linked to the mechanism of action.

**Disclosure statement:** R.A. has received consulting fees, has received research funding from AbbVie, BMS, MSD, Novartis, Pfizer and Roche and has received research funding from Pfizer and UCB. G.D. has received consulting fees from AbbVie, BMS, Pfizer and UCB. A.C. has received consultancy fees from AbbVie, BMS, MSD, Novartis, Pfizer and Roche and has received research funding from Pfizer and UCB. G.D. has received consulting fees from AbbVie, BMS, Roche-Chugai, UCB, MSD, Glaxo, Novartis, AstraZeneca, Pfizer and Actelion and has participated in speakers bureaus for AbbVie, BMS, Roche-Chugai, UCB, MSD, Glaxo, Novartis, Janssen-Cilag, AstraZeneca, Pfizer and Actelion. X.M. has participated in speakers bureaus for AbbVie, BMS, Pfizer and UCB. O.T. has received research funding from AbbVie, BMS, Novartis, Pfizer and Roche. M.L.B. is an employee and shareholder of Bristol-Myers Squibb. All other authors have declared no conflicts of interest.

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**081 INTENSIVE TREATMENT FOR RHEUMATOID ARTHRITIS REDUCES DISEASE ACTIVITY OVER TIME**

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**Background:** In recent years there has been increasing emphasis on treating RA more intensively. The end result of this management...
strategy should be reductions in disease activity levels. However, there is very little direct evidence about the extent and impact of changes in treatment strategies on clinical outcomes over time. We have evaluated temporal changes in disease activity and outcomes in a long-term prospective observational cohort study over 10 years at a single unit. The ethos of management was to use intensive drug treatment to control disease activity. We have analysed changes over time to assess whether such a management strategy reduces disease activity.

Methods: We studied 1693 RA patients seen on 10,773 occasions in routine practice between 2005 and 2015. At their first visit the mean age was 55 years, the mean disease duration was 10 years and 75% of patients were female. Treatments comprised DMARDs, often given in combination, and a range of biologic drugs. At each visit, 28-point DAS (DAS28), HAQ and quality of life measured by the EuroQol five-dimensions questionnaire (EQ-SD) were recorded. Temporal changes were assessed by descriptive statistics and maximum likelihood regression models.

Results: Between 2005 and 2015 the mean DAS28 fell from 4.3 to 3.7, the mean HAQ score fell from 1.26 to 1.15 and the mean EQ-SD score fell from 0.47 to 0.56 (indicating improved quality of life). Regression models showed the annual change for DAS28 was $-0.03$ (95% CI $-0.04$ to $-0.02$), HAQ was $-0.019$ (95% CI $-0.025$ to $-0.013$) and EQ-SD was $0.006$ (95% CI $0.003$ to $0.009$). In 2010, 10% of patients with active disease (DAS28 $>5.1$) decreased from 25% to 18%, while the number of patients in remission increased from 18% to 27%. The four components of DAS28 showed divergent patterns of change. Between 2005 and 2015 the mean swollen joint count fell from 3.1 to 2.1 (33% decrease), the mean ESR fell from 25 to 18 (26% decrease) and the mean tender joint count fell from 5.0 to 4.5 (12% decrease). In contrast, the mean patient global responses increased from 43.2 to 47.1 (9% increase).

Conclusion: This 10-year longitudinal study shows intensive management regimens are associated with decreases in disease activity and disability and improvements in quality of life. Despite these improvements, many patients are still substantially disabled with low quality of life. The improvements are seen across all strata of disease activity levels. Fewer patients have active disease and more patients have achieved remission. Not all components of disease activity improve similarly. In particular, the increase in patient global scores yearsTrying to reflect aspects of RA unrelated to synovitis, such as psychological distress. Different management strategies may be needed for these patients.

Disclosure statement: The authors have declared no conflicts of interest.

082 COMPARISON OF THE EFFICACY OF STANDARD DOSE VERSUS LOW-DOSE RITUXIMAB INFUSION REGIMES FOR THE TREATMENT OF RHEUMATOID ARTHRITIS AT THE QUEEN ELIZABETH HOSPITAL, BIRMINGHAM, UK: EXPERIENCE OVER A 12-MONTH PERIOD

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Background: Rituximab (RTX) has been licensed for the treatment of severe active RA in the UK since 2006. The licensed, standard dose of RTX in RA is two 1,000 mg infusions given 2 weeks apart. Different regimes have been studied, including a lower dose of 500 mg given 2 weeks apart and a single 1 g dose given for patients being re-treated. Results from an open-label randomized controlled trial published in 2013 suggested that a single 1000 mg infusion (low dose) regimen may provide similar efficacy compared with the standard RTX dose. The use of a single-infusion regimen would significantly reduce the cost of treatment and may reduce the side-effect profile of RTX treatment, including development of hypogammaglobulinaemia. Our aim was to compare the efficacy of standard vs low-dose RTX in patients with severe RA treated at our unit over a 12-month period.

Methods: All patients receiving RTX between December 2013 and December 2014 were identified using unit records. We excluded non-RA patients and those receiving their first infusion. Patients receiving their second and subsequent infusions were analysed to identify basic demographic data and clinical response to the two regimes. Changes in the patients’ clinical condition at the beginning and end of the audit period were judged by the rheumatologist using the 28-joint DAS and component parts, where available, and overall clinical picture. This was then assigned to one of the following categories: significant deterioration, slight deterioration, the same, slight improvement, and significant improvement. The clinical response of the standard and low-dose groups were compared using a chi-squared test. Serum IgG levels were tracked over time.

Results: Eighty-one patients (77% female, mean age 61 years) were receiving long-term RTX treatment for RA at University Hospital Birmingham. Forty-three (53%) received the standard dose, while 38 (47%) received the low-dose regimen. There were no significant differences within the two groups in terms of age and gender. As a whole, 44% of patients experienced at least some clinical improvement, 36% remained the same and 20% worsened. The choice of standard or low-dose RTX made no significant difference to the patients’ clinical response to treatment (P = 0.46). Serum IgG levels were available for 65 patients. Changes over the 12-month period in IgM and IgG levels were identical in both treatment groups.

Conclusion: No significant difference was identified in clinical response rates in those patients receiving low-dose RTX in our audit. No significant differences were identified in the serum Ig, although the period studied was of a relatively short duration. Considering its lower cost and potential to reduce side effects without loss of efficacy, we would encourage clinicians to discuss a low-dose RTX regime for ongoing long-term treatment.

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083 THE IMPACT OF TREAT TO TARGET ON 1-YEAR REAL-WORLD OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Treat-to-target (T2T) recommendations are designed to inform rheumatologists and patients about strategies to enable optimal outcomes in RA. The impact of T2T in the real world, prospective audit has a patient cohort with >12 months of follow-up data, allowing assessment of the impact of T2T.

Methods: Since April 2012, 48 NHS rheumatology services have enrolled newly diagnosed RA patients prospectively into the T2T audit. Data on disease management, treatments and outcomes are collected when the patient is reviewed in clinic. Here we present results of a cohort of patients who have been followed up for 12 months from diagnosis.

Results: By August 2015, 1470 patients had been enrolled into the audit, with a cohort of 460 (31%) with data at >12 months from diagnosis. Within this cohort, the median age at symptom onset was 61 years, 32% were male, 74% (342/460) had a target of remission (28-point DAS (DAS28) <2.6) and 7% (33/460) had a target of low disease activity (LDA; DAS28 2.6–3.2) set at diagnosis. Where data were available, 45% (135/301) had DAS28 performed at each visit. A total of 210/342 patients with a DAS28 remission target and 213/3 with an LDA target had both baseline and 12 month DAS28. The mean number of visits over a year was 4 (s.d. 3.1). After 12 months, 56% (182/325), 35% (114/325) and 5% (15/325) of patients were on DMARD mono, dual and triple therapy, respectively. Twenty-one per cent (51/248) of patients were in remission (three consecutive visits) at 1 year. Of these, 59% (30/51) received monotherapy, 39% (20/51) dual therapy and 0% (0/51) triple therapy. Nine per cent (42/460) of patients were eligible for a biologic (two consecutive DASs >5.1, failure of two DMARDs); of these, 45% (19/42) were prescribed a biologic. Among the cohort of patients <50 years of age, the percentage in employment changed from 57% (125/221) at baseline to 46% (77/169) at 12 months. Among those >60 years of age, 8% (18/239) and 4% (7/156) were employed at baseline and at 12 months, respectively. There was a reduction in patient-reported work difficulties from 40% (34/84) at baseline to 16% (8/49) at 12 months.

Conclusion: More than 50% of patients in the remission target group were in remission by 12 months; however, despite the T2T approach, there is still an unmet need in terms of achieving sustained remission. This is highlighted by relatively low numbers of DAS28 assessments, triple therapy rarely being introduced before 12 months and the proportion of biologic-eligible patients not receiving them. It would be interesting to compare the employment data against a cohort treated
with conventional strategies to determine the societal and patient impact of T2T in RA.

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084 PREDICTORS OF OUTCOME AT 1-YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM THE UK TREAT-TO-TARGET AUDIT

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Background: This real-world, prospective audit which was primarily designed to assess compliance with the treat-to-target recommendations (previously reported) now has a patient cohort with a minimum of 12 months of data. This allows evaluation of baseline characteristics as predictors of outcomes at 12 months.

Methods: Since April 2012, 48 UK NHS rheumatology services have enrolled newly diagnosed RA patients to the Treat-to-Target audit. Data on disease management, treatments and outcomes are collected each time the patient presents in the clinic. Here we present correlations between baseline characteristics and outcome variables in the cohort of patients who have reached 12 months.

Results: By August 2015, 1470 patients were enrolled into the audit, with a cohort of 460 (31%) with >12 months data. Correlations between the change in 28-joint DAS (DAS28) at baseline and 12 months and potential predictors in the 230 patients with DAS28 at baseline and 12 months are provided in Table 1. Patients had poorer improvement in DAS28 at 1 year with (in order of significance) work difficulties at baseline, ACPS positive, being on dual therapy at baseline and having an HAQ Disability Index assessment. Patients with the following at baseline had greater 12 month improvement: higher DAS28, older age, steroid therapy as part of their treatment regimen, presence of erosions and DMARD monotherapy; suggesting that older patients, with erosions and high initial DAS28, receiving DMARD monotherapy and steroid therapy at baseline achieve the greatest reductions in DAS28 at 1 year. A multiple regression on the outcome using all these factors showed that the two factors independently affecting the outcome were the initial DAS28 and the presence of erosions.

Conclusion: The simple regression analysis showed a correlation between better outcomes and DMARD monotherapy and steroid-based therapy. However, the independent predictors of outcomes, initial DAS28 and erosions, suggest that improvement in the DAS28 may be related to the intensity of therapy and that the patients with the worst prognosis are treated more aggressively. This is in line with the treat-to-target principles.

Disclosure statement: A.L.T. has received honoraria from AbbVie. M.B. has received consulting fees from AbbVie, AstraZeneca, Bristol-Myers Squibb and Roche-Chugai and research grants from Roche and Pfizer. D.O. has received research fees, consulting fees and honoraria from Amgen, AbbVie, MSD, pH Associates, Roche, UCB and Wyeth. T.S. has received consulting fees from Roche, AbbVie, Novartis and Pfizer. S.K. is an employee of AbbVie and may receive company shares. S.C. has participated on advisory boards for AbbVie and Pfizer and has received educational grants from AbbVie, Pfizer and UCB. P.E. has provided expert advice and undertaken clinical trials for AbbVie.

085 FACTORS ASSOCIATED WITH LONG-TERM RITUXIMAB USE IN RHEUMATOID ARTHRITIS: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER

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Background: Analysis of long-term continuation of biologics in RA is considered a valid surrogate for treatment effectiveness and safety. Only a small number of studies have investigated the long-term persistence with rituximab (RTX) in RA.

Methods: This analysis included all patients enrolled with the British Society for Rheumatology Biologics Register for RA when starting RTX between 2008 and 2011. Baseline characteristics (demographic and disease and treatment-related data) were compared between biologic-naive and experienced cohorts. RTX treatment discontinuation was defined as the start of an alternative biologic, death or 1 year following the most recent RTX infusion, whichever came first. Kaplan–Meier curves were used to study discontinuation rates over time and by reason, both as a whole cohort and stratified by past biologic treatment experience; discontinuation rates at 1, 2, 3 and 4 years following treatment initiation were ascertained. The association of baseline variables [age, gender, smoking status, presence of comorbidities, disease duration, 28-joint DAS (DAS28), HAQ score, steroid use, MTX use, previous biologic use] with RTX discontinuation after 4 years was assessed using multivariate Cox proportional hazards models.

Results: In total, 1629 patients were included [1371 (84.2%) biologic-experienced patients and 258 (15.8%) biologic-naive patients]. Biologic-experienced patients tended to be younger, but had longer disease duration than biologic-naive patients (Table 1). Treatment persistence at 4 years was 43% (95% CI 40.4, 45.6) and was similar between biologic-naive and biologic-experienced patients (Table 1). For the whole cohort, baseline variables associated with RTX discontinuation after 4 years were low DAS28 [hazard ratio (HR) 0.91 (95% CI 0.85, 0.98)], RF negativity [HR 0.84 (95% CI 0.72, 0.99)] and younger age [HR 0.99 (95% CI 0.96, 0.99) per year]. A higher number of previously used biologics was associated with RTX discontinuation for the biologic-experienced cohort [HR 1.28 (95% CI 1.08, 1.50)] and smoking history was associated for the biologic-naive cohort only [HR 1.82 (95% CI 1.06, 3.12)]. Tocilizumab was the most commonly used subsequent biologic for both the naive and experienced cohorts: 12 (41.4%) and 133 (56.8%), respectively.

Conclusion: Just over half of patients were no longer receiving RTX after 4 years, which was similar in both biologic-naive and experienced patients. In biologic-experienced patients, those who started RTX after two or more past TNF-α failures were more likely to discontinue treatment compared with those with only one, which may be identifying a more refractory patient cohort. The role of risk factors in predicting treatment outcomes on RTX is again supported by these data.

Disclosure statement: The authors have declared no conflicts of interest.
The development of intensive treatment strategies has increased the numbers of patients achieving low disease activity and remission. Nevertheless, some patients continue to have persisting high disease activity. We evaluated the impact of persisting high disease activity on disability and quality of life in a longitudinal cohort of RA patients seen at a single specialist centre.

Methods: We included patients in the cohort who had been seen five or more times over the follow-up period. They were categorized by their mean 28-joint DAS (DAS28) into four categories from high disease activity (DAS28 \(>5.1\)) to remission (DAS28 \(<2.6\)). In each category we assessed the mean HAQ and EuroQol (quality of life) scores and drug treatments with DMARDs and biologics.

Results: A total of 714 of 1695 patients in the cohort were seen five or more times; they were seen on 6728 occasions. Their mean age was 55.2 years, mean disease duration was 7.6 years, 78% were female and 154/714 (22%) had persistently active disease (Table 1). These patients had substantially higher HAQ scores and substantially lower EuroQol scores. Compared with patients in remission, those with persistently active disease had a difference in mean HAQ scores of 1.06 and in EuroQol scores of 0.27. All groups had similar DMARD use, including the use of combination DMARDs. However, only 9% of patients with persistently active disease were receiving biologics, which was significantly less than the 16–20% of the other groups (\(\chi^2 = 8.69, df = 3, P = 0.034\). This variation results from both failure to respond to biologics and an unwillingness to take them.

Conclusion: Persisting high disease activity remains a major problem for a minority of RA patients. It results in substantial disability and considerable reductions in quality of life. It is associated with reduced use of biologic treatments, which represents both failure to respond and reluctance to take treatment. The reasons for persisting active disease and the best management strategies in such patients are uncertain; this is an area in which further research is needed.

Disclosure statement: The authors have declared no conflicts of interest.
alone or MTX alone for 12 months. All RA treatment was removed after 12 months in patients with DAS28-CRP <3.2. In this post hoc analysis, proportions of patients achieving protocol-defined remission (DAS28-CRP <2.6) or improvement in physical function [HAQ Disability Index (HAQ-DI)] <0.3 units from baseline were assessed by disease duration (defined as the duration of sustained remission at baseline) and treatment group. Adjusted mean changes from baseline in HAQ-DI were also evaluated.

Results: Patients were randomized and treated with abatacept + MTX (n = 119) or MTX (n = 116): 36 patients on abatacept + MTX and 48 on MTX with <3 months disease duration; 34 patients on abatacept + MTX and 22 on MTX with ≥3 months disease duration; 49 patients on abatacept + MTX and 39 on MTX with >6 months disease duration. No differences were seen in baseline demographics and clinical characteristics when patients were grouped by disease duration. Irrespective of baseline disease duration, a higher proportion of abatacept + MTX-treated patients achieved DAS-defined remission at month 12 and sustained remission at month 18 vs MTX alone. The largest treatment difference in sustained remission following all treatment withdrawal (measured at 12–18 months) was observed in patients with <3 months disease duration. In the abatacept + MTX vs MTX group, a higher proportion of patients with disease duration <3 months (33 vs 13.8%) maintained DAS-defined remission compared with patients with longer disease durations (≥3–<6 months; 14.7 vs 10.4%; ≥6 months, 10.2 vs 5.1%). The abatacept + MTX group with ≥3 months disease duration also had the fastest onset of response. Results for the HAQ-DI response were similar to the overall population results, regardless of baseline disease duration.

Conclusion: Disease duration of <3 months was predictive of faster onset of clinical response and the ability to achieve higher rates of drug-free remission following treatment with abatacept + MTX in AVERT.

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Methods: In the 1 year, double-blind (DB) ATTEST trial, patients were randomized to i.v. abatacept (−10 mg/kg every 4 weeks), infliximab (5 mg/kg every 8 weeks) or placebo, all on background MTX. At month 6, placebo-treated patients were reallocated to abatacept (blinding maintained); patients initially randomized to abatacept or infliximab continued treatment. Patients completing the 1 year DB period were eligible to receive abatacept in an open-label, long-term extension (OLE). In AMPLE, patients were randomized to s.c. abatacept (125 mg weekly) or adalimumab (40 mg biweekly), plus MTX, for 2 years. Patients in both trials were biologic-naive, MTX-treated patients with inadequate responders with active RA. Blood samples were collected to measure ANA and anti-dsDNA at baseline, month 6, year 1 (end of DB period) and year 2 (OLE) in ATTEST, and at baseline, year 1 and year 2 in AMPLE.

Results: In the ATTEST DB period, 156 patients received i.v. abatacept and 165 received infliximab; 132 abatacept- and 136 infliximab–treated patients continued into the OLE and received i.v. abatacept. In AMPLE, 318 patients received s.c. abatacept and 359 received adalimumab. At baseline in ATTEST, 69 patients on active treatment (32 i.v. abatacept, 37 infliximab) were ANA positive and 28 patients (11 i.v. abatacept, 15 infliximab) were anti-dsDNA positive. In AMPLE, the respective numbers at baseline were 166 ANA-positive patients (72 s.c. abatacept, 94 adalimumab) and 6 anti-dsDNA-positive patients (1 s.c. abatacept, 5 adalimumab). In both studies, a higher proportion of patients receiving anti-TNF therapy seroconverted from baseline negative to positive during year 1 of treatment compared with those receiving abatacept. This difference continued during year 2 of AMPLE. In ATTEST, 48.5% (ANA) and 48.3% (anti-dsDNA) of infliximab–treated patients who entered the OLE seroconverted from baseline ANA or anti-dsDNA negative to positive at year 1; this dropped to 22.4% and 13.3%, respectively, at year 2 after switching to abatacept. The proportion of patients who converted from baseline positive to negative status for ANA and anti-dsDNA, respectively, increased from 12.1% and 7.1% in the infliximab group to 25.6% and 33.3% on switching to abatacept.

Conclusion: In ATTEST, switching from infliximab to abatacept seemed to reverse autoantibody induction observed with anti-TNF treatment. Anti-TNF therapy was associated with greater ANA and anti-dsDNA induction than abatacept in ATTEST and AMPLE. These data provide additional insights into differences in the mechanism of action of anti-TNFs and abatacept.

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ACHIEVEMENT OF TREATMENT RESPONSE WITH CERTOLIZUMAB PEGOL: RESULTS FROM AN INTERIM ANALYSIS OF PROACTIVE, A NON-INTERVENTIONAL STUDY IN REAL-LIFE RHEUMATOID ARTHRITIS PATIENTS IN THE UK AND IRELAND

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Background: Certolizumab pegol (CZP) is a PEGylated Fc-free anti-TNF that has demonstrated a rapid response and acceptable safety profile in clinical studies in patients with RA. The aim of this study was to assess the effectiveness of CZP in daily clinical practice in the UK and Ireland after 12 weeks of treatment.

Methods: PROACTIVE is a prospective, non-interventional study (NIS) assessing the effectiveness and safety of CZP in 147 patients with RA at 12 study sites who have received one or more CZP dose (Safety Set (SS)), Analysis was based on the Full Analysis Set (FAS), which refers to 111 patients who received one or more CZP dose and had a valid 28-joint DAS with ESR (DAS28-ESR) value at baseline (BL) and week 12 (±2 weeks). DAS28-ESR response is defined as a reduction from baseline in DAS28-ESR ≥1.2.

Results: The mean age of the FAS population was 55 years and 69% were female. In the FAS, 70% of patients tested for RF were positive. The baseline data and results are presented in Table 1. Of the 147 patients in the SS, one treatment-emergent adverse drug reaction was reported up to week 12. This was a serious infection (cellulitis). No deaths were reported.

Conclusion: In the PROACTIVE NIS, RA patients treated with CZP under standard clinical practice achieved a rapid reduction in disease activity and functional disability by week 12 as measured by the DAS28-ESR. HAQ Disability Index (HAQ-DI) and Rheumatoid Arthritis Disease Activity Index (RADAI). About 80% achieved clinical EULAR response at week 12. Improvements in the RADAI and HAQ-DI were greater for patients with DAS28-ESR response compared with those without. Incidence and severity of treatment-emergent adverse drug reactions did not show any new safety signal. The data collected in this NIS are consistent with results of other CZP NISs in Europe and with results from randomized clinical trials in patients with RA. They are therefore a valuable contribution to show the effectiveness of CZP over 12 weeks of treatment in standard clinical practice.

Disclosure statement: N.K. has received honoraria from AbbVie and Pfizer, T.K. is an employee of UCB Pharma. All other authors have declared no conflicts of interest.

091 table 1. Optimal DAS28 cut-offs to define low disability and normal HRQoL

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<td>Cohort</td>
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<td>16%</td>
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<td>Pooled cross-sectional studies</td>
<td>84%</td>
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<td>Early RA trial (CARDERA)</td>
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091 RATIONALISING THE TREATMENT TARGET IN RHEUMATOID ARTHRITIS: DEFINING THE OPTIMAL 28-JOINT DAS CUT-OFF TO DETERMINE GOOD FUNCTION AND NORMAL HEALTH-RELATED QUALITY OF LIFE

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Background: Key goals when treating RA are minimizing disability and maximizing health-related quality of life (HRQoL). Current strategies aim to deliver these by targeting remission using intensive treatment. Sustained remission is infrequently achieved; additionally, it may be too stringent a target, with patients in low disease activity (LDA) having good function and HRQoL. We tested an alternative hypothesis—that targeting LDA is best—by looking at the 28-joint DAS (DAS28) cut-off that best determines good function and normal HRQoL.

Methods: We studied 830 RA patients in three single-time point observational studies undertaken in 2003–2015: 972 patients in two clinical trials of established (TACIT) and early (CARDERA) RA and 1170 patients in a 10-year observational cohort (2005 inception). Receiver operator characteristic (ROC) curves defined optimal DAS28 cut-offs (maximising sensitivity and specificity) to predict low disability and normal HRQoL. Low disability was defined as HAQ scores <0.5 and <1.0. Normal HRQoL was defined as a EuroQol score seen in an age-/ sex-matched normal UK population. Cross-sectional studies were pooled. Clinical trial analyses were undertaken at the endpoints. Mean DAS28 and HAQ scores across time points in the 10-year observational cohort were used.

Results: In all studies, DAS28 had moderate positive correlations with HAQ (correlation coefficients 0.49–0.60) and moderate negative correlations with EuroQol (correlation coefficients −0.53 to −0.60). DAS28 was a good predictor of low disability (area under the curve (AUC) 0.82–0.84 for HAQ <0.5) and normal HRQoL (AUC 0.82–0.86). The optimal DAS28 cut-offs to define low disability and normal HRQoL were ≥1.0 above the LDA threshold of 3.2, except for HAQ <0.5 in the longitudinal study (Table 1). HAQ scores <1.0 were best identified by a DAS28 of 3.37–3.68. Normal EuroQol scores were best identified by a DAS28 of 3.37–3.40.

Conclusion: Treatment targets must deliver the greatest benefits for the majority of patients. Although remission benefits patients who achieve it, we have demonstrated that a DAS28 of 3.37–3.68, which is similar to LDA, is the optimal cut-off to identify patients with low disability (HAQ <1) and normal HRQoL. LDA therefore represents an achievable, evidence-based treatment target in RA.

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092 THE EFFECT OF STEROIDS, AZATHIOPRINE AND MYCOPHENOLATE ON THE RISK OF DEATH IN RHEUMATOID LUNG DISEASE

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Background: There remains very limited evidence on which to base therapy for the treatment of patients with RA-related interstitial lung disease. The current strategies aim to deliver these by targeting remission using intensive therapy.
We assessed outcomes among 290 patients with RA-ILD and David L. Scott.

From 4486 titles, 6 were identified that met inclusion criteria. MTX is the most commonly prescribed DMARD in the United States and respiratory mortality were calculated in the group as a whole. We then calculated all-cause and respiratory mortality for three subgroups of patients; namely those who had received ≤3 months of prednisone, AZA or mycophenolate. Data were corrected for age, gender, disease severity and disease duration and expressed as relative risk (RR) of death with reference to the group as a whole.

Results: There were 186 deaths in total, with 110 confirmed as due to respiratory disease. The RR of death from any cause was increased [1.57 (95% CI 1.43, 1.94)] for those on prednisone, unaltered [0.94 (95% CI 0.7, 1.2, 1.94)] for those on AZA and decreased [0.66 (95% CI 0.2, 0.99)] for those on mycophenolate. The RR of death from a respiratory cause was increased in those who had received prednisone [2.10 (95% CI 1.7, 2.89)] or AZA [1.62 (95% CI 1.2, 2.1)], but unaltered for mycophenolate [1.03 (95% CI 0.7, 1.53)].

Conclusion: The results from this large retrospective study support the view that neither prednisone nor AZA in the treatment of RA-ILD, but lend some support for a prospective placebo-controlled study to assess the role of mycophenolate in this condition.

Disclosure statement: The authors have declared no conflicts of interest.

093 FACTORS ASSOCIATED WITH SUSTAINED REMISSION IN RHEUMATOID ARTHRITIS IN PATIENTS TREATED WITH ANTI-TUMOUR NECROSIS FACTOR: A SYSTEMATIC REVIEW

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Background: Anti-TNF antibody has revolutionized the treatment of RA and remission is now a realistic possibility for patients. Despite the widespread use of anti-TNFs, predicting which patients are most likely to attain a sustained good response to these treatments remains challenging. This systematic review collates the evidence for predictors of sustained remission (>6 months) in patients with RA treated with anti-TNF.

Methods: Embase, Medline and the Cochrane Controlled Trials Register were searched using the Ovid platform from 4 September 2015, along with studies identified from reference lists and hand searching. Inclusion criteria were original research papers (phase 3 or 4 clinical trials, long-term extension trials, cohort studies); included adults (age ≥ 18 years) with RA according to ACR 1987 or ACR/EULAR 2010 criteria; anti-TNF for RA; disease activity measured by DAS, 28-joint DAS (DAS28), Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), ACR/EULAR remission or ARA 1981 remission criteria and predictors for sustained remission (>6 months) reported. All search results were dual screened with electronic data extraction using a custom designed Access database (Microsoft, Redmond, WA, USA). Studies where it was not possible to isolate the required data on patients in sustained remission, case-control studies, cross-sectional studies, case reports/series, phase 1 and 2/clinical studies, qualitative studies, survey-based studies, narrative reviews and editorials were excluded.

Results: From 4486 titles, 6 were identified that met inclusion criteria (3509, 753 and 218 excluded following title, abstract and full text screen, respectively). Included studies contained data on 7476 patients. All studies had observational designs (three registry cohorts, three single-centre observational/open-label studies) and were undertaken in developed countries. Due to data heterogeneity, it was not possible to formally combine results using meta-analysis. The proportion of patients in sustained remission varied widely between studies and remission criteria used (7.9–38.1% DAS28, 6.8% ACR/EULAR, 4.5% SDAI and 7.6–9.9% CDAI criteria). Concurrent prescription, or higher dose, of MTX was associated with an increased likelihood of achieving sustained remission [odds ratio (OR) range 1.63–2.83 in three studies]. Baseline disease activity (OR range 0.37–0.62 in four studies), female sex (OR range 0.43–0.77 in four studies, OR 1.19 in one study) and baseline functional impairment (OR range 0.23–0.53 in three studies, OR 1.24 in one study) were identified as being associated with a reduced likelihood of achieving sustained remission.

Conclusion: Sustained remission remains an uncommon outcome, particularly in registry studies and when using ACR/EULAR remission criteria, although data on this outcome are scarce. It appears MTX co-prescription increases the likelihood of achieving sustained remission. The finding that higher baseline disease activity and increased baseline functional impairment are associated with a reduced likelihood of achieving sustained remission supports aggressive treat-to-target and early treatment strategies for RA.

Disclosure statement: The authors have declared no conflicts of interest.

094 A SYSTEMATIC REVIEW OF THE IMPACT OF INTENSIVE THERAPY ON REMISSION IN RHEUMATOID ARTHRITIS

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Background: The current management goal when treating RA is to achieve remission. UK national guidelines recommend treatment with DMARDs, including combination DMARDs, and biologics until patients achieve remission. Intensive treatment with biologics is recommended when initial DMARDs have proven ineffective. However, the overall likelihood of achieving remission remains uncertain compared with DMARD monotherapy. We have systematically reviewed randomized clinical trials (RCTs) in RA. The RCTs compared intensive treatment strategies (combination DMARDs and biologics) with DMARD monotherapy. Our aim was to establish the effectiveness of intensive treatment in achieving remission.

Methods: We systematically searched Embase and Ovid Medline and hand searched relevant systematic reviews in the Cochrane library. The search terms used were arthritis, rheumatoid (MeSH term), clinical trial (Publication Type) (MeSH term) and remission (free text). We included RCTs of at least 6 months duration enrolling at least 50 patients that reported remission against DMARD monotherapy. We excluded non-randomized, unblinded RCTs. We undertook a quality appraisal of all RCTs. We analysed data using RevMan 5.3 (Cochrane Collaboration, London, UK) and reported relative risks (RRs) using random effects models showing 95% CIs. We used F test to assess heterogeneity.

Results: We identified 819 papers: 22 reported RCTs that met our inclusion and exclusion criteria. The RCTs randomized 8231 RA patients; 3602 had early RA (<1 year in duration) and 5183 had established RA (>1 year in duration). In early RA, 4441/794 (25%) patients receiving monotherapy achieved remission compared with 779/1008 (43%) patients receiving intensive therapy. This difference was highly significant [RR 2.51 (95% CI 2.07, 3.04)]. In established RA, 230/2276 (10%) patients receiving monotherapy achieved remission compared with 803/2907 (28%) of patients receiving intensive therapy. This difference was also highly significant [RR 2.98 (95% CI 2.51, 5.81)]. There was marked heterogeneity in early and established RA (2L 64% and 86%). Comparative analysis of different biologics evaluated in RCTs showed all significantly increased remission rates compared with DMARD monotherapy (RRs varied from 1.73 to 11.29). As the RCTs of biologics evaluated different patient populations, including differences in the number of early and established patients, caution is required in comparing treatments. The quality of the RCTs was high and the risk of bias appears low.

Conclusion: Intensive treatment with combination DMARDs and with biologics increases the frequency of remission compared with DMARD monotherapy in both early and established RA. Since more patients with early RA achieve remission with monotherapy, the overall benefit of intensive treatment is not so marked. In established RA, only 10% of patients achieve remission with DMARD monotherapy. Intensive treatment is most beneficial in these patients. These findings support current UK practice of delaying the introduction of biologics until patients with early RA have tried initial DMARDs.

Disclosure statement: The authors have declared no conflicts of interest.

095 ALCOHOL CONSUMPTION AND SERUM LIVER ABNORMALITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS TAKING METHOTREXATE: DATA FROM THE CLINICAL PRACTICE RESEARCH DATABASE

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Background: MTX is the most commonly prescribed DMARD in the treatment of RA. Patients taking MTX are advised to restrict their alcohol consumption.
alcohol consumption because of a theoretical hepatoxic interaction between alcohol and MTX. However, data are limited supporting this advice. The aim of this study was to quantify, using routinely collected clinical data, the association between alcohol consumption and abnormal liver function tests (LFTs) in such patients.

Methods: Patients with RA in the Clinical Practice Research Database (CPRD) starting MTX between 1987 and 2011 were studied. Patients were included if they had alcohol consumption details recorded in the CPRD and six or more LFTs per year, indicating adequate monitoring. Patients were grouped by reported weekly alcohol consumption. Crude rates of abnormal LFTs (defined as aspartate transaminase/alanine transaminase >3 times the upper limit of normal) per 1000 person-years of follow-up were calculated. Cox proportional hazards models described the association between alcohol consumed and the development of abnormal LFTs while taking MTX univariately, then adjusting for age and gender. Patients were censored at the time of first abnormal LFT, death or the end of follow-up (31 December 2011).

Results: A total of 9801 patients were included in the study (2026 (71%) female, mean age 58 years (s.d. 14). There were 241 abnormal LFTs in 38 000 person-years of follow-up. There was no difference in the rates of abnormal LFTs between drinkers and non-drinkers (adjusted hazard ratio (HR) 1.12 (95% CI 0.82, 1.51)). Crude rates of abnormal LFTs appeared to increase with increasing levels of alcohol consumption (Table 1), when treated as a continuous variable, each increased unit of alcohol consumed was associated with a higher risk of abnormal LFTs (adjusted HR 1.01 (95% CI 1.00, 1.02)). In the adjusted Cox model, moderate alcohol consumption (≤14 units) was not associated with a statistically significant risk of developing abnormal LFTs (Table 1) compared with non-drinkers. There was a trend towards higher HRs with higher levels of alcohol consumption. However, power was limited in the patients consuming >14 units per week.

095 Table 1. Rates of abnormal LFTs in patients with RA taking MTX

<table>
<thead>
<tr>
<th>Units of alcohol per week</th>
<th>Number of events</th>
<th>Crude rate (95% CI) per 1000 person-years</th>
<th>Univariate HR (95% CI)</th>
<th>Age- and gender-adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>24</td>
<td>5.58 (3.74, 8.33)</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>1–7</td>
<td>83</td>
<td>5.97 (4.49, 8.91)</td>
<td>1.01 (0.64, 1.58)</td>
<td>1.02 (0.65, 1.60)</td>
</tr>
<tr>
<td>8–14</td>
<td>23</td>
<td>5.99 (3.98, 9.01)</td>
<td>1.07 (0.60, 1.89)</td>
<td>1.15 (0.65, 2.06)</td>
</tr>
<tr>
<td>15–21</td>
<td>14</td>
<td>7.58 (4.20, 13.89)</td>
<td>1.36 (0.67, 2.69)</td>
<td>—</td>
</tr>
<tr>
<td>≥22</td>
<td>3</td>
<td>8.61 (2.78, 26.70)</td>
<td>1.51 (0.46, 5.03)</td>
<td>1.91 (0.66, 6.47)</td>
</tr>
<tr>
<td>≥26</td>
<td>6</td>
<td>8.00 (4.07, 20.10)</td>
<td>1.60 (0.66, 3.92)</td>
<td>1.92 (0.76, 4.89)</td>
</tr>
</tbody>
</table>

*Event = abnormal LFT. Not all patients who were recorded as drinkers/non-drinkers had alcohol consumption defined in units.

096 Table 1. Demographics and baseline characteristics and week 24 and 52 effectiveness parameters

<table>
<thead>
<tr>
<th>Baseline demographics and RA disease characteristics</th>
<th>TCZ (n = 423)</th>
<th>Anti-TNF (n = 793)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (s.d.)</td>
<td>54.3 (12.8)</td>
<td>55.2 (13.1)</td>
<td>0.171</td>
</tr>
<tr>
<td>Initiated biologic as monotherapy, n (%)</td>
<td>77 (16.0)</td>
<td>79 (17.7)</td>
<td>0.326</td>
</tr>
<tr>
<td>MTX, n (%)</td>
<td>119 (28.1)</td>
<td>127 (16.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>HCO, n (%)</td>
<td>71 (23.4)</td>
<td>157 (25.1)</td>
<td>—</td>
</tr>
<tr>
<td>LFT, n (%)</td>
<td>63 (20.7)</td>
<td>111 (16.7)</td>
<td>—</td>
</tr>
<tr>
<td>SSB, n (%)</td>
<td>38 (12.5)</td>
<td>121 (18.2)</td>
<td>—</td>
</tr>
<tr>
<td>Oral corticosteroid use, n (%) [mean dose, mg/day (median dose)]</td>
<td>256 (80.5)</td>
<td>369 (46.5) (7.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Drug survival at weeks 24/52 [Kaplan-Meier estimate], %</td>
<td>91/85</td>
<td>85/73</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Baseline disease activity and effectiveness at 24 and 52 weeks

<table>
<thead>
<tr>
<th>Event</th>
<th>Anti-TNF (n = 663)</th>
<th>Mean difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28-ESR, baseline, mean (s.d.)</td>
<td>5.1 (1.4)</td>
<td>5.1 (1.2)</td>
<td>—</td>
</tr>
<tr>
<td>DAS28-ESR, change from baseline to week 24, adjusted mean (95% CI)</td>
<td>–2.8 (–3.1, –2.5)</td>
<td>–1.9 (–2.2, –1.6)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>DAS28-ESR remission rates at week 24, %</td>
<td>44.7</td>
<td>29.7</td>
<td>0.001</td>
</tr>
<tr>
<td>CDAI, baseline, mean (s.d.)</td>
<td>33.0 (13.3)</td>
<td>31.2 (13.2)</td>
<td>—</td>
</tr>
<tr>
<td>CDAI, change from baseline to week 24, adjusted mean (95% CI)</td>
<td>–20.3 (–21.9, –18.6)</td>
<td>–16.8 (–18.3, –15.3)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>CDAI, change from baseline to week 52, adjusted mean (95% CI)</td>
<td>–22.8 (–24.6, –21.1)</td>
<td>–18.2 (–19.8, –16.7)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Conclusion: In patients with RA taking MTX, increasing alcohol consumption may be associated with an increased risk of developing abnormal LFTs. The clinical importance of this risk may be small when drinking <14 units per week.

Disclosure statement: The authors have declared no conflicts of interest.

096 TREATMENT OF RHEUMATOID ARTHRITIS WITH AN ANTI-TUMOUR NECROSIS FACTOR AGENT OR TOCILIZUMAB AS FIRST BIOLOGIC: THE ACT-IoN, A GLOBAL COMPARATIVE OBSERVATIONAL STUDY

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Background: ACT-IoN was a global, multicentre, observational, 52 week, clinical-practice study of the effectiveness of tocilizumab (TCZ) vs anti-TNF agents prescribed as the first biologic therapy after inadequate response to DMARDs (DMARD-IR).

Methods: Eligible patients were DMARD-IR with moderate to severe RA prescribed TCZ or anti-TNF as their first biologic. The primary effectiveness measure over the 52 week observation period was the change in the 28-joint DAS with ESR (DAS28-ESR) from baseline to week 24.

Results: A total of 1225 patients were enrolled; 1216 received one or more doses of a biologic [safety population: TCZ, 423 (54.8%); anti-TNF, 793 (65.2%)] and 1083 comprised the effectiveness population [TCZ, 390 (36.0%); anti-TNF, 693 (64.0%). Overall, 158/1216 (13.0%) patients discontinued the study [lack of efficacy: TCZ 0.8%, anti-TNF 2.0%; adverse events (AEs); TCZ 2.1%, anti-TNF 1.6%]. Drug survival was higher with TCZ than anti-TNFs (P < 0.001; Table 1). TCZ vs anti-TNF patients had shorter disease duration and initiated biologics more often as monotherapy (28.1 vs 16.0%; Table 1). Oral corticosteroids use was higher in TCZ patients. TCZ patients had a significantly larger change from baseline in DAS28-ESR than anti-TNF patients [difference in adjusted means: week 24, –0.9 (95% CI –1.1, –0.8); P < 0.001 at weeks 24 and 52 (Table 1)]. Changes from baseline for other effectiveness parameters were also significantly better with TCZ (Table 1). Sensitivity analysis confirmed these results. AEs and serious AEs (SAEs) occurred in 48.2% and 5.2% of TCZ patients and 56.6% and 8.1% of anti-TNF patients. Infections were the most common AEs (TCZ 20.8%, anti-TNF 25.9%) and SAEs (TCZ 1.9%, anti-TNF 3.3%).
Three (0.7%) TCZ patients and six (0.8%) anti-TNF patients died; one death in each group (both pneumonia) was deemed treatment related. 

Conclusion: In DMARD-IR patients starting a biologic for the first time, 0.815 comparing RA with SLE; P = 0.005. Data were available from 3265 RA patients recruited from 11 regions. In the first 3 months of specialist care, glucocorticoids were offered to the vast majority of RA patients (83%) during their first 3 months of specialist assessment. 

Background: HCQ is commonly used in rheumatic disease, including RA, SLE and SS. Cumulative exposure can result in ocular toxicity, including irreversible retinopathy, especially if the dose is not adjusted and/or DMARDs were initiated from their first appointment and any further changes in glucocorticoid and/or DMARD therapy at subsequent appointments up to 3 months of specialist review. Results from the first year of this ongoing audit are reported here.

Methods: The national audit for rheumatoid and EIA assesses care provided to affected individuals >16 years of age presenting for the first time to specialist rheumatology units in England and Wales. Data collected for patients diagnosed with RA included the date of referral receipt, whether glucocorticoids (orally, intramuscularly or intravenously) and/or DMARDs were initiated from their first appointment and any further changes in glucocorticoid and/or DMARD therapy at subsequent appointments up to 3 months of specialist review. Results from the first year of this ongoing audit are reported here. 

Results: Data were available from 3265 RA patients recruited from 1 February 2014 to 31 January 2015 via 135 (94%) eligible secondary care rheumatology trusts across England and Wales. Nationally, slightly more than half [1727 (53%)] of RA patients commenced at least one DMARD within 6 weeks of referral. Variation in the ability to start DMARDs within 6 weeks among trusts and NHS regions was demonstrated; the North of England achieved this in the highest proportion of RA patients (56%) and Wales achieved this in the lowest proportion (48%). If DMARDs were not started at the initial visit, very few RA patients [172 (6%)] met this NICE standard from a follow-up appointment. Nationally, glucocorticoids were offered to the vast majority of RA patients (83%) during their first 3 months of specialist care. The London region reported the use of glucocorticoids in the lowest proportion of patients (73%) and Wales reported their greatest use (89%). Nationally, combination DMARDs were offered to slightly more than half of RA patients in their first 3 months of specialist care. The range of combination DMARD use was wide across NHS regions, with use recorded in 18% of RA patients in Wales and in 53% in the North of England.

Conclusion: There was quite marked variation among trusts and within NHS regions in the ability to start DMARD therapy within the 6 weeks from referral required to meet QS3. There was even more variation in the use of combination DMARDs across trusts and NHS regions. In the first 3 months of specialist care, glucocorticoids were offered to the majority of RA patients and more frequently than DMARDs. A large number of factors may have influenced these findings, and the variation in treatment approaches across trusts and within NHS regions suggested by these data warrants further investigation. 

Disclosure statement: The authors have declared no conflicts of interest.
099 THE MANAGEMENT OF EARLY RHEUMATOID ARTHRITIS ACROSS THE GLOBE: A MULTINATIONAL CROSS-SECTIONAL SURVEY

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Background: Early diagnosis and treatment are crucial to the management of RA. Despite this, the management of early RA appears to be inharmonious across countries, although this has not been systematically evaluated.

Methods: An online survey was emailed to practising rheumatologists in all countries (including the UK) participating in the QUEST-RA (quantitative clinical assessment of patients with RA) study and also made accessible for all countries on social media platforms between April and May 2015. Questions (n = 38) assessed the structure and setting of early RA clinics, times to diagnosis and treatment, patient monitoring, use of guidelines and data recording.

Results: A total of 212 rheumatologists from 39 countries (76% European) participated in this survey. Sixty-two per cent had an early RA clinic based at a university hospital. Patient referral to rheumatology was mainly (78%) via primary care. Forty-four per cent had an agreed early RA local referral pathway for ensuring rapid patient access, 15% a national pathway and 27% had no pathway. Only 16% of rheumatologists reported having dedicated clinics, 76% of which were based in European countries (64% northern Europe) with access to local or national referral pathways. More than 50% of patients were reported seen within 4 weeks from primary care referral, a third within 2 weeks and only 1% after 12 weeks. Rheumatologists in northern Europe had the shortest waiting lists overall. DMARD initiation at first review and within 4 weeks was reported by 47% and 31%, respectively. The rheumatologists’ satisfaction levels increased with longer appointment duration (P = 0.005). Musculoskeletal US was always provided on site by a rheumatologist (18%) or when considered necessary (37%) or within 6 weeks by a radiologist (11%). Guidelines were followed by the majority, and in particular rheumatologists from the northern European (P < 0.001). Seventy-five per cent of rheumatologists undertook data collection for patient monitoring: 42% specifically for research. Treatment decisions were reported to be influenced by international and/or national guidelines in 71% and 61%, respectively. Patient financial and social circumstances were reported factors influencing treatment decisions in 17% and 33% of respondents, respectively. Graphical representations will be used to show initial DMARD strategies used for early RA.

Conclusion: This survey is the first to provide comparative benchmark information regarding the global provision of early RA care, demonstrating variations in referral and early assessment pathways. The results could help target countries in need, supporting early RA pathways and helping to harmonize the management of RA across the globe.

Disclosure statement: The authors have declared no conflicts of interest.

101 SAFETY OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS ASSOCIATED WITH BRONCHIECTASIS: RESULTS FROM A MULTICENTRE COHORT

MD Yusufal Yusuf1, Kundan Iqbal2, Paul Emery1, Clive Kelly1 and Shouvik Dass1

1Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, 2Medicine, Queen Elizabeth Hospital, Gateshead, UK

Background: Bronchiectasis (BR) is a significant morbidity associated with RA. Patients with RA-BR are susceptible to infection and this poses a challenge in the treatment of an already complex disease. Evidence of the efficacy and safety of biologic therapy is scarce, as these patients are often excluded from clinical trials. Two pilot studies suggested that rituximab (RTX) was associated with a good clinical response in patients with RA-BR and that no significant changes in pulmonary function occur. The aim of this study was to evaluate the safety of RTX in a large RA-BR cohort drawn equally from two centres.

Methods: We conducted a retrospective observational study of consecutive patients with RA-BR (detected by high-resolution CT prior to RTX) using identical data collection methodology between centres. Each cycle of RTX was repeated for 2–1000 mg infusions, repeated on clinical relapse. Disease activity was assessed using the 28-joint DAS at baseline and every 6 months after each cycle and EULAR responses were calculated. Safety assessments included the number and severity of acute exacerbations of lung disease per year, together with 5 year survival and causes of death. We also examined lgG levels before and after each cycle of RTX.

Results: Sixty-one seropositive patients were studied (43 females, median age 67 years (range 38–91), median RA duration 9 years (range 1–30), median BR duration 6 years (range 1–67), 36 (60%) non-smokers). The total follow-up duration was 321 patient-years. Twenty patients were TNF inadequate responders (8 primary non-response, 5 secondary non-response and 7 had side effects) and 67% were on concomitant DMARDs. In the 12 months prior to RTX, there was a median of 3 (range 0–7) infective exacerbations per patient. After RTX, 13 patients had fewer exacerbations compared with baseline; in 40 patients the number of exacerbations had increased. Overall, the number of exacerbations rose in the first year to a median of 4 (range 0–10) but then decreased.
in years 2 and 3 to 2 (range 0–6) and 1 (range 0–5), respectively. RTX was discontinued in four patients due to increased exacerbations and in four patients due to inefficacy. There was no correlation between IgG levels and clinical response. Nine (15%) patients died during follow-up, of whom three (5%) died from respiratory disease. Six patients (10%) subsequently required alternative biologics.

Conclusion: RTX has an acceptable safety profile in the treatment of RA. A temporary increase in acute exacerbations of lung disease may occur in the first year following RTX. After subsequent treatment cycles, pulmonary symptoms stabilized or improved in most patients. RTX may therefore be a particularly appropriate therapeutic choice for this group of patients.

Disclosure statement: The authors have declared no conflicts of interest.

102 CLINICAL AND RADIOGRAPHIC EFFICACY OF SARILUMAB IN RHEUMATOID ARTHRITIS PATIENTS WITH VARIED DISEASE DURATION

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Background: In patients with RA, prolonged disease duration at treatment initiation has been associated with unfavourable outcomes. The phase 3 MOBILITY study (NCT01061736) examined the investigational drug sarilumab plus MTX vs placebo plus MTX in patients with inadequate response to MTX. This analysis evaluated whether RA duration (≤3 vs >3 years) affected the clinical and radiographic efficacy of sarilumab in patients with RA enrolled in MOBILITY.

Methods: In MOBILITY, adults with moderate to severe, active RA and inadequate response to a stable dose of MTX were randomized 1:1:1 to s.c. sarilumab 150 mg, sarilumab 200 mg or placebo every 2 weeks (q2w) plus MTX for 52 weeks. This prespecified analysis assessed radiographic and clinical efficacy results by RA duration from diagnosis to baseline (≤3 vs >3 years) in the intent-to-treat population.

Results: Differences between both groups in baseline characteristics were small and comparable. With patients previously treated with biologics, the efficacy of sarilumab [a 20% improvement in ACR criteria (ACR20, HAQ Disability Index (HAQ-DI) and mTSS)] did not differ between patients with different disease durations (≤3 vs >3 years) based on a treatment-by-subgroup interaction test (P = not significant). Irrespective of RA duration, ACR20, ACR50 and ACR70 responses were higher with both doses of sarilumab vs placebo, regardless of disease duration. In both groups, less structural progression (reflected in the change in mTSS from baseline at 52 weeks) was observed with sarilumab vs placebo. Frequencies of treatment-emergent and serious adverse events (AEs) were comparable across patient subsets. The most frequent treatment-emergent AEs were infections, which occurred at a greater incidence in sarilumab-treated groups than in placebo-treated groups. Regardless of RA duration, laboratory abnormalities were more frequent with sarilumab and included decreases in neutrophils and increases in transaminases.

Conclusion: Regardless of RA duration, all subgroups receiving sarilumab had improvements in signs and symptoms of RA and physical function, and decreased progression of structural joint damage. With sarilumab 200 mg, a greater magnitude of responses was observed in the group with RA ≤3 years. The frequency of AEs did not differ by disease duration.

Disclosure statement: P.E.E. has received consulting fees from AbbVie, Bristol-Myers Squibb and Takeda and research funding from AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche and UCB. D.D. is a shareholder of Johnson & Johnson. C.F. has declared no conflicts of interest.

103 EFFICACY OF RITUXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS ASSOCIATED WITH BRONCHECTASIS: RESULTS FROM A MULTICENTRE COHORT

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Background: Bronchiectasis (BR) has a 10-fold increased prevalence when associated with RA. Patients with RA-BR are susceptible to infection and this poses a challenge in the treatment of articular disease. Evidence of the efficacy and safety of biologic therapy is scarce, as these patients are often excluded from clinical trials. The treatment of RA in this setting is complicated by the perception that there is an increased risk of side effects, including infection, and that articular efficacy may be reduced. The aim of this study was to evaluate the efficacy of rituximab (RTX) in a large RA-BR cohort drawn equally from two centres.

Methods: We conducted a retrospective observational study of consecutive patients with RA-BR (detected by high-resolution CT prior to RTX) using identical data collection methodology between centres. Each cycle of RTX consisted of 2 × 1000 mg infusions, repeated on clinical relapse. Disease activity was assessed using the 28-joint DAS (DAS28) at baseline and every 6 months after each cycle and EULAR responses were calculated. Safety assessments included the number and severity of acute exacerbations of lung disease per year, together with 5 year survival and causes of death.

Results: Sixty-one seropositive patients were studied [43 females, median age 67 years (range 38–91), median RA duration 9 years (range 1–23), median BR duration 6 years (range 1–67), 36 (60%) non-smokers]. The total follow-up duration was 321 patient-years. Twenty patients were TNF inadequate responders (8 primary non-response, 5 secondary non-response and 7 had side effects) and 66% were on concomitant DMARDs. At baseline, the median DAS28 was 5.7 [interquartile range (IQR) 4.3–7.6]. In cycle 1, 53/61 (87%) achieved a EULAR response with a median reduction in DAS28 of 2.1 (range 0–3.5; P = 0.007 at 6 months). The median DAS28 improved from 5.7 (range 4.3–7.6) pre-RTX to 3.5 (range 1.6–5.7) at 1 year (P = 0.01). The EULAR response was maintained at cycle 2 and cycle 3: 3.2 (range 2.0–5.4) and 3.4 (1.9–5.8), respectively. The median duration of response for cycles 1, 2 and 3 were 54, 50 and 53 weeks, respectively. Six patients (10%) subsequently required alternative biologics as a result of treatment failure.

Conclusion: RTX is effective in the treatment of the articular manifestations of active RA in the presence of established BR. RTX may therefore be particularly appropriate for this group of patients.

Disclosure statement: The authors have declared no conflicts of interest.

102 Table 1. Co-primary endpoints by RA duration and treatment group

<table>
<thead>
<tr>
<th>RA duration ≤3 years</th>
<th>Placebo + MTX</th>
<th>Sarilumab 150 mg q2w + MTX</th>
<th>Sarilumab 200 mg q2w + MTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR at week 24, % response</td>
<td>n=103</td>
<td>n=107</td>
<td>n=98</td>
</tr>
<tr>
<td>ACR20</td>
<td>295</td>
<td>293</td>
<td>301</td>
</tr>
<tr>
<td>ACR50</td>
<td>77</td>
<td>75</td>
<td>87</td>
</tr>
<tr>
<td>ACR70</td>
<td>43</td>
<td>43</td>
<td>43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week 16 HAQ-DI</th>
<th>n=17</th>
<th>n=22</th>
<th>n=40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change</td>
<td>-0.34</td>
<td>-0.63</td>
<td>-0.67</td>
</tr>
<tr>
<td>Week 52 mTSS</td>
<td>n=85</td>
<td>n=89</td>
<td>n=93</td>
</tr>
<tr>
<td>Mean change</td>
<td>0.17</td>
<td>0.84</td>
<td>0.28</td>
</tr>
</tbody>
</table>
Background: There is limited information on drug survival (i.e. treatment continuation vs discontinuation) of patients with RA who received a second biologic DMARD (bDMARD) therapy after first anti-TNF therapy. This study compared continuation, discontinuation, restart and switch rates of patients with RA who received an anti-TNF vs a non-anti-TNF as a second bDMARD.

Methods: Our analysis was based on a German claims dataset (AOK PLUS) that included all insured patients with RA (one or more RA diagnosis; International Classification of Diseases, Tenth Revision M05 or M06; age >18 years). Patients with RA were included if they received one or more anti-TNF and, additionally, a second bDMARD (anti-TNF or non-anti-TNF) between 1 January 2010 and 31 December 2012, with a requested follow-up >12 months. Percentages of patients who discontinued (treatment gap >90 days) without restart and switch rates of patients with RA who received an anti-TNF vs a non-anti-TNF as a second bDMARD, restarted (one or more prescriptions of the second bDMARD after discontinuation) or continued therapy during the 12-month follow-up were analysed. A multivariate Cox regression model, adjusting for baseline confounding variables [age, sex, Charlson Comorbidity Index (CCI), prior and concomitant medications, anti-TNF/non-anti-TNF as second bDMARD], was used to assess factors associated with discontinuation or switch (combined outcome, irrespective of later restart) of the second bDMARD. In all the analyses, patients who had received rituximab (RTX) as a second bDMARD were excluded because this agent is not given on a continuous basis after the initial two doses.

Results: A total of 3140 patients with RA received one or more prescriptions of an anti-TNF. Of these, 451 patients received one or more prescriptions of a second non-RTX bDMARD (340 anti-TNF: 46 adalimumab, 42 certolizumab, 120 etanercept, 46 golimumab, 16 infliximab; 111 non-anti-TNF: 40 abatacept, 3 anakinra, 68 tocilizumab). The mean age of the anti-/non-anti-TNF groups was 52.6/55.9 years (P = 0.053) and 77.4/79.3% were female (P = 0.792), respectively. After 12 months, 53.4% of patients receiving a second anti-TNF vs 66.7% (P = 0.016) receiving a second non-anti-TNF continued their therapy, 3.8 vs 1.8% (P = 0.387) restarted their therapy after discontinuation, 14.1 vs 19.8% (P = 0.179) discontinued the therapy without restart and 28.7 vs 11.7% (P < 0.001) had switched to a third bDMARD. Drug survival analysis showed a significantly longer estimated mean survival time of 295 days (s.e. 10.5) with a non-anti-TNF as the second bDMARD vs 264 days (s.e. 6.8) for an anti-TNF as the second bDMARD (P = 0.016). In the multivariate Cox regression model, independent variables significantly associated with earlier therapy discontinuation or switch were higher CCI [hazard ratio (HR) 1.127 per CCI score point (95% CI 1.036, 1.226)], concomitant gout medication [HR 1.444 (95% CI 1.046, 1.993)] and prescription of an anti-TNF as the second bDMARD [HR 1.513 (95% CI 1.052, 2.175)].

Conclusion: Our results suggest that patients are at higher risk of treatment discontinuation or switch to a third bDMARD after 12 months if they have received an anti-TNF vs a non-anti-TNF as the second bDMARD.

Disclosure statement: T.W. has received funding from LEO Pharma, Bayer, Bristol-Myers Squibb, GSK, Johnson & Johnson, Boehringer Ingelheim, Merck, ABBVie and Pharmerit. S.M. has received consulting fees from Bristol-Myers Squibb. I.M. has received consulting fees from Bristol-Myers Squibb. M.H. has received consulting fees from Bristol-Myers Squibb. All other authors have declared no conflicts of interest.
105 PERCEPTIONS OF RISK AND COMMUNICATION ABOUT THE RISK OF RELATIVES DEVELOPING RHEUMATOID ARTHRITIS: A QUALITATIVE STUDY OF PATIENTS’ PERCEPTIONS

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Background: Early treatment of RA is associated with improved clinical outcomes. There is considerable research interest in the identification of biomarkers to predict the development of RA in order to facilitate early preventive interventions. First-degree relatives of people with RA are at an increased risk of developing RA and are therefore likely candidates for predictive/preventive approaches. However, access to this group is currently dependent on the cooperation of existing patients with a diagnosis of RA. It is therefore important to understand patients’ perceptions of RA risk and their willingness to communicate with their relatives about the risk of developing RA.

Methods: Twenty-one RA patients (15 females and 6 males, 35–80 years of age) took part in semi-structured interviews exploring perceptions of the risk of RA, family communication about risk and predictive testing. Interviews were audio recorded, transcribed verbatim and analysed using thematic analysis.

Results: Many patients were aware of genetic risk factors for RA and identified relatives that they were concerned about being at risk of developing RA in the future. Some patients described feeling responsible or guilty for their relatives’ being at risk of RA. Environmental risk factors such as infection and psychosocial stress were also suggested, although few patients mentioned that smoking was associated with an increased risk of RA. Patients described a lack of public awareness about RA and the causes of RA. They also referred to a lack of understanding by their relatives as well as by the general public of the negative impact that RA has on their quality of life. Patients generally held positive views of predictive testing and expressed a willingness to communicate with their relatives about their risk of RA. However, many patients identified relatives that they were not in contact with or communicated with infrequently. Some mentioned that they would not pass on information to particular relatives who they did not get on with. Patients referred to choosing which relatives to communicate with and described likely variation among relatives in their receptivity to risk information and their likelihood of acting on such information. Reasons suggested for this included relatives being busy, being in denial of their susceptibility, preferring to deal with things when they happen, feeling that RA is not serious enough to warrant action and avoiding anxiety.

Conclusion: Accurate information about risk factors for RA and the potential impact of RA on quality of life is needed to support family communication about RA risk. Strategies for the management of RA that target relatives of existing patients should take into account that patients knows and understands the health benefits of exercise, then they are more likely to engage in exercise; for those with OA, greater emphasis on physical activity rather than exercise may be more useful to encourage engagement; simple, clear consistent messages related to exercise for people with OA are required from all public health bodies and health care professionals.

Disclosure statement: The authors have declared no conflicts of interest.

107 AN EXPLORATION OF STRATEGIES TO ENHANCE PHYSICAL ACTIVITY IN PEOPLE WITH RHEUMATOID ARTHRITIS

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Background: Despite wide-ranging benefits of physical activity (PA), the majority of people with RA are less active than the general population. Those that engage in regular PA do so in order to manage their symptoms, resist functional decline and maintain health and independence. They also demonstrate high levels of exercise self-efficacy, strong beliefs that physical function would decline without regular PA, a long history of PA prior to diagnosis and good support networks. The aim of this study was to determine whether the strategies used by physically active people with RA would be acceptable to a wider RA population.

Methods: A modified two-stage Delphi approach was utilized. In stage 1, 200 patients from four NHS rheumatology departments received a postal questionnaire containing statements relating to engagement with PA derived from previous interview data with physically active participants. Demographic data as well as disease activity, functional ability and physical activity level were also requested. Statements rated as agree or strongly agree by ≥50% of respondents were used to formulate stage 2, in which the same respondents were asked to rate and prioritize potential PA programme components.

Results: Stage 1 received 49 responses (24.5%): 11 males, 37 females and 1 unknown. Respondents were typically white British with a mean age of 65 years (range 29–82) and mean disease duration of 18 years (range 8 months–60 years). Disease activity ranged from 1–10 on a visual analogue scale and functional ability varied from 0 (without difficulty) to 2 (with much difficulty). Low levels of engagement were reported by 60% of respondents, with 20% moderate and 20% high. Forty-five statements were taken forward to stage 2. The 36 responses (75%) to stage 2 indicated that a PA programme should include information about the prevention of RA symptoms worsening and benefits of PA for the joints. Through a PA programme, participants wanted to achieve improved pain management and a feeling of being in control of their RA. For PA maintenance, it was important that medication controlled symptoms and PA instructors understood RA to promote a feeling of safety when being active.

Disclosure statement: The authors have declared no conflicts of interest.
Conclusion: These findings provide useful information for health care providers and researchers wanting to develop PA programmes for people with RA and support a recent qualitative study in this field. Programmes need to be delivered alongside effective medication, by a knowledgeable instructor, include an educational component and empower people to manage their symptoms through PA. Effective programme delivery may promote higher levels of self-efficacy for PA as seen in successful active individuals, which is important for longer-term behaviour change.

Disclosure statement: The authors have declared no conflicts of interest.

108 MEANINGFUL SELF-MANAGEMENT CHANGES FOLLOWING PARTICIPATION IN A FIBROMYALGIA COPING SKILLS PROGRAMME: A QUALITATIVE INTERVIEW STUDY

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Background: FM represents a significant socio-economic burden worldwide. Self-management involves supporting people with long-term conditions to develop the skills to manage fluctuating physical and psychological symptoms and complex medications and implement positive lifestyle changes. People who have the knowledge and confidence to manage their condition report better health care experiences and outcomes. The Fibromyalgia Coping Skills Programme is a non-pharmacological, multidisciplinary, exercise and education group intervention. Its objectives are to provide condition-specific, patient-centred, self-management education and advice. Integrating anecdotal feedback from patients who attended the programme prompted the research question, what self-management changes do participants identify as meaningful outcomes of attending the Fibromyalgia Coping Skills programme? This study explored individual’s self-management behaviour changes following participation in the programme.

Methods: Participants >18 years of age who had attended all sessions of the Fibromyalgia Coping Skills programme were invited to take part. Semi-structured interviews, developed from questionnaires, literature and analysis of a pilot interview in collaboration with an expert patient, were conducted, audio-recorded and transcribed. Interview questions were informed by the Revised Fibromyalgia Impact Questionnaire (RIFQ) and the Arthritis Self-Efficacy Scale-8 (ASES-8). Thematic analysis explored the participants’ self-management behavioural changes.

Results: Five women, ages 45–75 years, participated. Three were married or cohabiting. One worked full time and all had been diagnosed with FM (7 months–3 years). Examples of positive and negative self-management changes were identified. Three self-management themes emerged: Managing self—by exercising, pacing and adapting personal circumstances; Managing others—by putting FM in the context of personal life circumstances, and Acceptance of FM—by dealing with uncertainty and change, resilience and feelings of control. Resilience was strongly linked with successful self-management. Self-management is a complex, patient-centred intervention and this was reflected in the diversity of experiences described. All participants found the Fibromyalgia Coping Skills programme a positive experience, but resulting changes in individual self-management strategies were variable. Participants who appeared resilient to physical and emotional uncertainty demonstrated better self-management strategies. Negative cases reflecting the uncertainty of FM, lack of support networks and poor acceptance limited positive self-management changes. Resilience underpinned the positive self-management experiences described and provided valuable insight into why some participants successfully implement self-management strategies and others do not.

Conclusion: To better promote implementation of effective self-management interventions, treatment needs to focus on fully supporting individuals to accept FM as part of their life and effectively manage self and others. Exploring outcomes valued by participants of FM self-management interventions can support more effective and meaningful experiences for future patients.

Disclosure statement: The author has declared no conflicts of interest.

109 EXPERIENCES OF STAFF AND PATIENTS IN RELATION TO CLINICAL RESEARCH PARTICIPATION AND INVOLVEMENT: A QUALITATIVE STUDY

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Background: While high-quality clinical research improves patient care, many studies fail to recruit to target, reducing the quality and impact of results. To date, most interventions to improve recruitment have targeted patients and few have proved successful. Ethnographic work suggests that staff without formal research roles also affect recruitment. This study explored staff and patient experiences during and after clinical research recruitment.

Methods: Our sample included 28 hospital staff and 13 patients offered clinical research involvement [nine females, median age 55 years (range 37–76)]. Participants were recruited from a large, tertiary rheumatology department and completed a semi-structured interview with the researcher (H.H.). Patients were approached during or after clinical research participation or when declining to participate (n = 4). Hospital staff were selected to represent the range of roles organising and delivering care to these patients. The researcher (H.H.) used qualitative techniques (open and focused coding, constant comparison, deviant case analysis, memoing and mapping) to analyse the resulting transcripts. Emergent themes were discussed and challenged by the wider research team.

Results: Staff with the opportunity to refer patients for clinical research may not do so for a number of reasons, including lack of knowledge of studies and how to refer a patient, low expectations to recruit (e.g. from superiors, colleagues, research team), lack of trust in the local research team and procedures (staff feared delays or poor communication as patients joined and left studies, impacting care), lack of time, expectation that the patient will be unwilling to participate and the view that the burdens outweigh the benefits for the patient (most staff assessed the burdens as greater and the benefits as lesser compared with patients’ views). Staff without formal research roles facilitated research work, often with limited understanding and giving this work low priority. This group reported discomfort responding to patients seeking advice about research participation and some staff expressed interest in greater research involvement. Most patients were willing to take part in research and found it a positive experience when they did take part. Patients choosing not to take part usually did so for practical reasons, such as time. Patients and staff rarely heard the results of studies they or their patients participated in. Most wanted this information, and the lack of feedback may deter future participation.

Conclusion: At this site, patients tended to decline research participation for practical and usually intractable reasons, perhaps explaining why interventions targeting patients have proved unsuccessful. There were multiple reasons why staff failed to offer research opportunities to patients, which may require multiple solutions. Work is under way to develop a package of interventions to increase recruitment, focussed on staff and tailored to their roles in the research process.

Disclosure statement: L.J.K. is a Generation Q Fellow with the Health Foundation Trust, Bath, UK.

110 A QUALITATIVE EXPLORATION OF SELF-MANAGEMENT AND SUPPORT NEEDS OF YOUNG ADULTS WITH INFLAMMATORY ARTHRITIS

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Background: Anecdotal evidence suggests most young adults do not attend self-management interventions. However, little is known about the self-management and support needs of young adults with inflammatory arthritis (IA). The aim of this research was to explore
self-management styles and support preferences of young adults with IA. 

Methods: Eight one-on-one in-depth interviews with young adults (<45 years of age) with IA. Inductive thematic analysis was used to analyse these data.

Results: Four main themes were identified: Self-management—participants experienced various problems caused by IA: “I was really struggling, I’d literally go all day with no food and drink because I couldn’t use my hands”; had found strategies to help: “don’t do too much, plan what you’re going to do; and considered the type of help they would like to receive: in a nice pub, in the back room, where we could all have a drink and a gossip. … it would just feel like you were going to go and meet a group of mates”. Self-identity participants described how IA had impacted their identity in all areas of life: “totally changed career plans because of the arthritis; I’ve given up my social life and that’s quite tough”, as well as the difficulties in accepting a life with IA: “how do you personally identify yourself when so much has changed?” Invisible nature of IA—participants faced difficulties with having an ‘invisible’ disease: “I worry a lot about people thinking I’m faking it”; the problems in communicating to others about IA: “how do you make them understand, because they look at me and say well you look fine”; and the reasons why they often choose to hide their IA at work: “That’s they’d get me out of the business for being a pain”, and at home: “I think it stresses them”. Barriers—the main barrier quoted by participants was a lack of time: “I’m short on time. … and big on pain”. Other reasons for not attending interventions included feeling too young: “I think, well you know, I’m not that old. … I’m nothing like them”, and the associated difficulties in identifying with older adults with IA. Further barriers were embarrassment, denial and concerns that interventions would be depressing: “I think everyone’s suffering so badly so am I.”

Conclusion: Young adults with IA report being keen to receive self-management support. However, current self-management interventions do not seem to address these issues important to young adults, nor do they overcome the barriers young adults face in attending such interventions (e.g. time of day). This needs further exploration, as understanding the currently different needs of young adults is necessary to inform the design of effective interventions.

Disclosure statement: The authors have declared no conflicts of interest.

111 EXPERIENCE AND TRAINING NEEDS OF HEALTH CARE ASSISTANTS IN RHEUMATOLOGY CLINICS: A QUALITATIVE STUDY

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Background: In the NHS, 40% of staff, who provide 60% of direct patient care, do not have professional qualifications. Qualified professionals have an accountable duty when delegating tasks to personnel to ensure that adequate training and supervision has taken place. The role of the health care assistant (HCA) has evolved over the years. We were interested to explore the extent of those roles and the training HCAs receive in order to carry out those roles in rheumatology departments.

Methods: Focus groups were arranged with HCAs from two different units. One focus group took place in a musculoskeletal outpatient department and one focus group took place in a general outpatient department, but the members of the focus group had all worked in rheumatology clinics. Topics explored included the duties they were asked to perform, who delegated those duties, what training they had had before performing those duties and to what extent supervision was available. A total of 12 HCAs attended the focus groups.

Results: The HCAs performed a wide variety of tasks. They independently ran clinics, which included managing aggressive patients, performing phlebotomy, setting up sterile fields for joint injections and assisting, performing simple dressings, recording vital signs and teaching and mentoring other HCAs. Duties were notionally delegated by the qualified nurses. However, most HCAs were more commonly mentored by other HCAs, with the more established HCAs typically mentored by other HCAs, with the more established HCAs

Conclusion: HCAs are providing services that were conducted by doctors and qualified nurses a few years ago. HCAs need more formal training and supervision. They would like to know more about the disease processes and treatments so that they can direct patient queries with more confidence.

Disclosure statement: The authors have declared no conflicts of interest.

112 A QUALITATIVE EXPLORATION OF THE SYMPTOMS EXPERIENCED BY PEOPLE WITH PALINDROMIC RHEUMATISM

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Background: Palindromic rheumatism (PR) was originally described as an inflammatory episodic arthritis, peri-arthritis or para-arthritis with no evidence of permanent joint damage or bone erosion. However, the full range of PR symptoms has not been assessed and this study addresses this deficit in the literature.

Methods: Patients who, in the absence of an alternative diagnosis, had a history of synovial swelling that returned to normal between attacks were invited to participate. Semi-structured qualitative interviews were conducted with 17 patients (11 women, age range 36–75 years). Interviews were audio recorded, transcribed verbatim and analysed using thematic analysis.

Results: Most patients experienced transient episodes with symptoms increasing in intensity, persisting for a few hours to 10 days and then resolving. Two major themes emerged from the data: the features of the attack and the evolution of symptoms over time. Onset was typically associated with an intense pain in or around a joint, often followed by swelling. Other symptoms included soreness, a burning sensation, tenderness, stiffness, warmth and colour change at or around the joint. Most patients also described weakness and loss of range of motion around the affected area with associated functional impairment. Less common symptoms included transient nodules, painful skin lesions, fatigue and depression. Symptoms presented differently in different joint regions with pain, swelling and colour change seen at some but not all affected joints. Patients were psychologically and emotionally distressed by the unpredictable nature of the attacks, which was compounded by the feeling that very little information was available. Of note, some patients considered episodes to be triggered by lifestyle factors such as diet, lack of sleep, alcohol and stress. Initial symptom onset was most often sudden and typically affected only one joint area before spreading to other areas over a matter of weeks to years. In a few patients, symptoms remained stable and mild, however, in others they evolved, with the frequency and severity of episodes increasing. In a very small number of these patients, the condition subsequently returned to a relatively milder form after a few months or years. In some cases, persistent symptoms developed between the transient episodes of joint swelling, including fatigue, joint ache/pain, stiffness, sleeping difficulties, involuntary movement and loss of appetite.

Conclusion: People with PR experience a wide range of symptoms during their attacks and can, over time, experience persistent symptoms between episodes of joint swelling. While in some cases initial and subsequent attacks are mild, for most the symptoms progress over time. In addition to physical symptoms, psychological and emotional distress were a significant part of the patients’ experience, in part by a lack of information and the apparent uncertainty (both therapeutic and prognostic) associated with PR.
113 WORKING THROUGH THE PAIN... AND GETTING ON WITH IT—SOME PATIENTS’ EXPERIENCES OF LIVING WITH LUPUS-RELATED FOOT PROBLEMS

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Background: Along with its skin manifestations, SLE can present with a variety of musculoskeletal signs and symptoms and vascular problems that can affect the feet. Furthermore, there is the potential for reduced tissue viability, leading to thinning of the skin and/or callus formation. Further, systemic resistance to viral, bacterial and fungal infections may be reduced and, together with poor tissue viability, create the opportunity for these infections to proliferate in the feet. A recent survey by the same authors (unpublished) has shown a high prevalence of these infections, with many experiencing the impact of vascular and musculoskeletal problems. To date there is no research that has explored the impact of foot problems on people’s lives.

Methods: Following ethical approval, 12 participants who fulfilled the inclusion criteria were recruited: diagnosed with SLE (ACR diagnosis), current and/or past experience of foot/lower limb problems and age ≥18 years. Consent was obtained and then conversational-style interviews were carried out with an interpretivist phenomenological approach. The interviews were digitally recorded and complemented by field notes. An opening question was used for all participants: ‘Tell me about your experiences of having foot problems?’ If necessary, further trigger questions were used in order to maintain the conversation and the focus on foot problems. Data were transcribed verbatim and analysed using a thematic framework approach. The transcripts were verified by the participants and were analysed by a second researcher in order to add to the credibility of the analyses.

Results: The data was organized into seven themes: Foot problems and symptoms—what they are and the feeling associated with them; Experiences of foot problems being diagnosed; Impact of foot problems on activities; Treatment of foot symptoms/problems; Perceived obstacles to professional foot care; Unanswered questions about feet and foot care; and Recognition of the need for professional foot care. The most common source of information about foot care was the Internet, but participants had concerns about long-term health effects of the OA and its treatment.

Conclusion: Despite reporting foot pain, negative emotions and activity restrictions related to their foot symptoms, people with SLE tend to get on with it and self-treat rather than seeking professional foot care. The lack of focus on the feet in the medical consultation is caused by the participants’ belief that it is not the consultant’s role. There is a clear need for foot assessments to be included in the medical consultation and for professional foot care to be provided.

Disclosure statement: The authors have declared no conflicts of interest.

114 EXPERIENCES OF TREATMENT DECISION-MAKING AND SELF-MANAGEMENT FOR WORKING-AGE PEOPLE WITH SYMPTOMATIC OSTEOARTHRITIS OF THE KNEE

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Background: The National Institute for Health and Care Excellence clinical guidelines for OA advocate a therapeutic relationship based on shared decision-making and suggest that this approach encourages self-management, reduces reliance on medication and empowers people. Concepts such as adherence and compliance are used, which suggest a practitioner-led, top-down approach rather than an empowering and concordant model. Taking an active part in decision-making potentially gives patients an increased ability to self-manage chronic health conditions, yet to date this has had limited research attention. The aim of this study was to explore the experience and perceptions of working-age people with symptomatic OA of the knee in relation to treatment decision-making and self-management.

Methods: The focus of this study was on the experiences of working-age people with a radiographic diagnosis of symptomatic OA of the knee(s). The aim was to interview participants with a diverse range of experiences and recruit targeted participants of different ages, employment status, gender, race, and health service provider. Qualitative in-depth semi-structured interviews were conducted with each participant. Face-to-face or telephone interviews lasted for ~45 minutes and were audio recorded. The topic guide was piloted prior to the interviews.

Results: Fifteen participants took part in the study: 11 females and 4 males, ages 32–63 years. Of those interviewed, 10 were employed, 2 were self-employed, 2 did not work and 1 had taken early retirement. The participants reported having knee problems for many years. All had been told they needed knee replacement surgery, but only two were currently on the waiting list. Data were analysed using the framework approach. Initial findings were presented for member checking to a focus group of four people with OA who recruited from those taking part in the interviews. For all participants living with OA of the knee had a significant impact on their quality of life. Participants reported uncertainty about treatment/management options and concern about long-term health effects of the OA and its treatment. Participants did not generally feel part of the decision-making process. There was uncertainty about what would make them eligible for knee replacement surgery. The most common source of information about self-management options was the Internet, but participants had concerns about effectiveness.

Conclusion: More attention is needed to quality of life issues for working-age people with severe OA of the knee(s), including issues of employment, social isolation and emotional and physical health. A greater focus on shared decision-making for working-age people with OA of the knee(s) could empower patients and help reduce treatment and self-management uncertainty.

Disclosure statement: The authors have declared no conflicts of interest.

115 PUBLIC PRIORITY SETTING FOR RESEARCH IN OSTEOPOROSIS

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Background: Involving members of the public, patients and clinicians in identifying topics for research ensures relevant, impactful research questions and is expected by research funders. This study reports on the first of a two-stage national priority-setting exercise to identify the public’s views on areas for research in osteoporosis and osteoporosis-related fractures.

Methods: Focus groups were undertaken with members of the National Osteoporosis Society (NOS) (Staffordshire) and a research cohort (Oxford) of individuals who had experienced fracture. A topic guide was co-designed with the Research User Group (RUG) at Keele University. Each group was audio recorded and the results were professionally transcribed. Thematic analysis using constant comparison identified research themes and specific research questions. Keele University’s Ethics Committee approved the study.

Results: Four focus groups of between four and eight participants were conducted. Of the 23 participants, 18 had osteoporosis, 18 were female and 5 male and 14 had osteoporosis-related fragility fractures. Three main research themes emerged in relation to osteoporosis: living with osteoporosis, services for osteoporosis and optimal treatment of fractures in osteoporosis. Participants described both an illness and treatment burden associated with the condition that manifested in fear of the future (and fracture) and feelings of anger, hopelessness and frustration. They highlighted the impact on work, relationships and activities of daily living. Participants highlighted a lack of a systematic approach to long-term management of the condition in primary care.
Research questions concerned prevention, screening and treatments. Participants demonstrated an interest in both basic science and genetic research. Examples of specific research questions were: Can you recover bone density with the right amount of activity and intake of calcium?; Maybe I could have taken something beforehand to prevent this happening?; Is there any link with a genetic or family history and is there a solution to that?; Why is it that you don’t have a bone density check, say when you are 60 or something, as a kind of routine?; How do you know you are susceptible to a fracture?; Those participants who had experienced a fracture also identified areas relating to the effects of osteoprosis on fracture healing and the impact of prolonged immobilisation following fracture. The findings have been discussed with the Keele RUG in order to co-design wording of new questions about research priorities for osteoporosis for a national e-survey.

Conclusion: This study has identified research areas of importance to members of the public, including prevention, monitoring of established disease and managing the impact of the condition on day-to-day life. These topics will be further investigated in a national survey (December 2015) of NOS members. The overall results will feed into the NOS research strategy (2016–20).

Disclosure statement: The authors have declared no conflicts of interest.

116 RESULTS OF A NATIONAL FOOT HEALTH SURVEY OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: SLE can affect many tissues throughout the body, and foot complications are common as a consequence of SLE. Anecdotally, it is suggested that people with SLE experience a range of complications in the foot and lower limb, including vascular impairment (e.g. RP), neurological impairment, poor tissue viability (e.g. ulceration), infection and foot pain. However, to date, the precise prevalence of foot complications experienced by people with SLE has not been described. The aim of this study was to determine self-reported foot and lower limb complications experienced by people with SLE.

Methods: The survey was developed via patient and practitioner focus groups. A consensus approach was used to generate items and to formulate themes, categories, question format and survey structure. The survey was checked for face and content validity prior to cognitive debriefing to ensure usability and understanding. Consecutive patients with a confirmed diagnosis of SLE meeting the inclusion criteria attending any of seven UK clinical sites or members of Lupus UK were invited to participate. Ethical approval and participant informed consent was obtained.

Results: A total of 182 survey responses were completed. For all responders, the most frequent age range was 40–49 years, mean BMI was 27 (s.d. 7) and mean disease duration was 15 years (s.d. 10). A number of vascular complications were reported, including intermittent claudication [n = 100 (55%)], RP [n = 94 (52%)] and splinter haemorrhage [n = 39 (21%)]. Overall, 164 patients (90%) reported experiencing symptoms of peripheral vascular complications. Symptoms of peripheral neuropathy were reported by 30 patients (16%), while a fall as a consequence of neuropathic symptoms was reported by 45 patients (25%). A range of skin and nail complications were reported, including callus or corns [n = 130 (71%)], onychodystrophy [n = 69 (38%)], rashes or blistering [n = 62 (34%)] and ulceration [n = 45 (25%)]. A high prevalence of infection was reported; a history of viral infection (vaccinaceous pedis) or fungal infection (tinea pedis) was reported by 77 patients (42%), bacterial infection by 28 patients (15%) and onychomycosis by 65 patients (36%). Overall, 170 patients (83%) reported having experienced some form of tissue viability complication. Foot joint pain, stiffness and swelling was reported by 145 (80%), 136 (75%) and 94 (52%) patients, respectively. Foot-related walking impairment was reported by 67 patients (37%). Only 60 patients (33%) reported having ever been asked about their feet by a medical professional. Seventy-seven patients (42%) reported that they would benefit from the provision of general foot health care advice.

Conclusion: A large number of people with SLE report vascular complications, impaired tissue viability, musculoskeletal problems and foot pain, as well as a range of infections and conditions of the skin and nails. Despite this, foot health assessment by professionals was infrequent. These results highlight the need to undertake clinical studies investigating lower limb pathologies in SLE.

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of standard care. The primary outcome measure was the Hand Mobility In Scleroderma test (HAMIS). Other outcome measures were grip and pinch strength, the Scleroderma Health Assessment Questionnaire (SHAQ) and the Duruoz/Cochin Hand Index (DHI). Measures of protocol adherence, relief and skin score were also recorded. Between-group comparisons of primary and secondary outcomes were made by analysis of covariance to allow adjustment for baseline values.

Results: Between-group comparisons showed no evidence of effectiveness of the wax bath treatment at the 9 week follow-up (adjusted difference in means, experimental group, control, -0.14; 95% CI -0.98, 0.71, P = 0.85) or at the 18 week follow-up (1.94; 95% CI -1.67, 5.59, P = 0.20) using HAMIS scores, although most participants showed improvement over the study period. Analysis of secondary outcomes showed no evidence for effectiveness of the wax bath treatment at either 9 or 18 weeks. There was no significant improvement in disease status for the wax bath group compared with the control group by analysis of modified Rodnan skin score, SHAQ multi-system visual analogue scale or pain relief use. Three participants reported a transient ache after the stretches. There were two dropouts from the study (one from each group), both not wanting to commit to the daily exercise routine once they had been taught it.

Conclusion: As standard care, daily home exercises for the hands are well proven. The addition of a wax bath home daily treatment has been shown in this study to have no additional beneficial effect. However, our findings do not exclude the possibility that some subgroups of patients might benefit.

Disclosure statement: The authors have declared no conflicts of interest.

119 PROVIDING INFORMATION ABOUT METHOTREXATE: IS IT ONCE ENOUGH? Sarah Ryan1, Cath Thrwales2 and Sanjeet Kamath1 1Rheumatology, Haywood Hospital and 2School of Nursing and Midwifery, Keele University, Stoke on Trent, UK

Background: MTX is routinely used in the treatment of patients with active inflammatory arthritis. Although it is common practice for patients to receive information when they commence MTX, there is often no mechanism to reinforce this information. The aim of the survey was to establish what information patients recalled receiving about MTX and whether patients would like to be updated with information about taking MTX.

Methods: A questionnaire was developed and distributed to patients attending for their MTX drug monitor appointment in a rheumatology community hospital. The content of the questionnaire focused on side effects patients had been asked to report, if MTX could be taken in pregnancy or with alcohol, if it was safe to have the influenza vaccination and what action would be taken if a problem related to their MTX occurred. The questionnaire also identified whether patients would like to be updated with information about MTX and if so how they would like to be updated.

Results: The survey was completed by 100 patients on MTX. The majority of the respondents (58%) were > 61 years of age and had been taking MTX for longer than 1 year. Only 35% of respondents recalled being asked to report shortness of breath and only 42% would report the presence of infection. Forty-one per cent of respondents felt a small amount of alcohol was safe and all respondents stated that MTX should not be taken during pregnancy. Eighty-eight per cent of respondents would contact the rheumatology advice line with a problem and 27% of respondents did not know whether it was safe to have the influenza vaccination. Eighty-six per cent of respondents would like to be updated with information about MTX, with 83% requesting written information.

Conclusion: Patients would welcome being updated with written information while taking MTX. Providing updates on MTX might increase the reporting of serious side effects, such as shortness of breath and the presence of infections, as well as increasing the utilisation of influenza vaccine.

Disclosure statement: The authors have declared no conflicts of interest.

121 A 6-WEEK PROGRESSIVE TRAINING CLASS IMPROVES FUNCTION AND FATIGUE IN RHEUMATOID ARTHRITIS PATIENTS Berna Berntzen1, Toby Bellerby1, Lisa Erwood1, Elizabeth I. Price1, David A. Collins1 and Lyn Williamson1 1Rheumatology, Great Western Hospital, Swindon, UK

Background: RA is associated with adverse changes in body composition and physical function that persist despite pharmaceutical treatment. Randomized controlled trial evidence has shown that progressive resistance training (PRT) is safe and efficacious in restoring lean mass and function in patients with RA. We set up our own PRT programme for RA patients to explore whether similar results could be achieved in an NHS setting.

Methods: RA patients were invited to attend a PRT programme of six weekly classes held under the supervision of a senior physiotherapist. Newly diagnosed and established RA patients were included. The exercises used within the circuit are wall slides, chest press, leg extension, rowing, balance board work, triceps extensions, bicep curls, clam, bridging, standing calf raises and step-ups. Classes included up to 10 patients at a time. Data collected at induction and after 6 weeks included demographics, BMI, percentage body fat, grip strength, 60 sec sit-to-stand test, HAQ and Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scores (Table 1). After the 6 week PRT programme, patients were encouraged to continue at home or referred to their local gym.

Results: Of 34 RA patients invited, 27 started and 21 completed the 6 week PRT course [mean age 54 years (range 17–78), 71% female, 50% RF positive]. Eleven (32%) patients were diagnosed within 3 months of starting the class. There was no difference in results between recently diagnosed and established RA patients. After 6 weeks there was a significant improvement in HAQ (mean change 0–2.9) vs 0.8 (0–2.5), P = 0.03, body fat composition [mean 38.0% (range 21.5–51) vs 36.9% (26.3–48.2), P = 0.02] and sit-to-stand [mean
Six weekly sessions of AT improve pain and mental health status, but not function, compared with physiotherapy advice and exercises only in women with PKP. This brief, clinically applicable group-based AT programme warrants further investigation.

Disclosure statement: The authors have declared no conflicts of interest.

123 PHYSIOTHERAPY FOR ADULTS WITH JOINT HYPERMOBILITY SYNDROME: A PILOT RANDOMIZED CONTROLLED TRIAL

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Background: Joint hypermobility syndrome (JHS) is a heritable disorder associated with laxity and pain in multiple joints. Physiotherapy is the mainstay of treatment, but there is little research investigating its effectiveness. The aim of this study was to conduct a pilot randomized controlled trial (RCT) in adults to determine the feasibility of conducting a future definitive RCT.

Methods: A comprehensive physiotherapy intervention was developed with patients and health care professionals. It was then piloted and refined on the basis of feedback. A parallel two-arm pilot RCT in two UK secondary care NHS Trusts compared advice against advice and physiotherapy. Inclusion criteria were >16 years of age, diagnosis of JHS and no other musculoskeletal conditions causing pain. The advice intervention was a one-off session, supplemented by Hypermobility Syndromes Association and Arthritis Research UK advice booklets. All patients could also request advice specific to their circumstances. Participants were then randomly allocated to advice (no further advice or physiotherapy) or advice and physiotherapy (an additional six 30 min sessions over 4 months). The physiotherapy intervention was supported by a patient handbook and delivered on a one-to-one patient-therapist basis. It aimed to increase patients’ physical activity through developing knowledge, understanding and skills to better manage their condition. The primary outcome related to the feasibility of conducting a future definitive RCT. Qualitative interviews with patients and physiotherapists formed a major component of data collection. Secondary outcomes included clinical measures (physical function, pain, global status, self-reported joint count, quality of life, exercise self-efficacy and adverse events, resource use (to estimate cost-effectiveness) and an estimate of the value of information from a future RCT. Outcomes were recorded at baseline, 4 months (at the end of physiotherapy) and 7 months (3 months following physiotherapy).

Results: A total of 29 participants were recruited. Recruitment was challenging, primarily due to a perceived lack of equipoise between advice and physiotherapy. The qualitative evaluation provided very clear guidance to inform a future RCT, including enhancement of the advice intervention. Some patients reported that the advice intervention was useful and the physiotherapy intervention was evaluated very positively. The rate of return of questionnaires was low within the advice group (87% at 7 months) but reasonable in the physiotherapy group (79%). The physiotherapy intervention showed evidence of promise in terms of primary and secondary clinical outcomes. The advice arm experienced more adverse events, including study

Disclosure statement: The authors have declared no conflicts of interest.

122 AQUATIC THERAPY FOR WOMEN WITH PERSISTENT KNEE PAIN: A PILOT RANDOMIZED CONTROLLED TRIAL

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Background: Twenty-five per cent of people >55 years of age in the UK experience persistent knee pain (PKP) annually, which can result in disability, dependence and work incapacity. Exercise, such as aquatic therapy (AT; therapeutic exercise in warm water) and self-management advice are key components of the physiotherapy management of PKP, but the optimal treatment dosage of AT is unknown. This study compared the effect of six once weekly sessions of AT and self-management advice compared with self-management advice only on self-reported pain, function and general health in adults with PKP.

Methods: This two-arm, single-blinded, pilot, randomized controlled trial (RCT) received ethical approval from the joint University College London/University College London Hospital Research Ethics Committee (08/H0715/). Adults >50 years of age with a >3/12 history of knee pain referred for physiotherapy treatment at an inner city hospital were recruited into the study. Participants were randomly assigned to receive either 6 weekly sessions of AT consisting of 30–40 minutes of group stretching, stretching and balance exercises facilitated by a physiotherapist or standard care. All participants attended a single physiotherapy session of self-management advice and were prescribed home exercises. Outcomes [WOMAC, 12-item Short Form Health Survey (SF-12), visual analogue scale (0–10 cm) and 6 minute walk distance] were assessed at baseline and 6 weeks. Data were analysed on an intention to treat basis and between-group differences in mean change were investigated using analysis of covariance adjusted for baseline differences. Significance was defined as P-values <0.05.

Results: Thirty-four subjects were invited to participate in the study. Fourteen women [mean age 63.0 years (± 7.5)] were enrolled into the study. There were between-group differences in change in the total WOMAC score and the WOMAC pain and SF-12 mental subscale, but not the VAS or 6MWD (Table 1).

Conclusion: We present an effective model for PRT workable in the NHS, which encourages patients to take control of their own exercise regimes. The class setting fosters motivation, confidence and a belief in exercise as part of effective treatment. This brief intervention was associated with significant improvement in various aspects of physical function, grip strength, HAQ and fatigue scores.

Disclosure statement: The authors have declared no conflicts of interest.

122 Table 1. Data collected at baseline and at 6 weeks

<table>
<thead>
<tr>
<th></th>
<th>BMI</th>
<th>Sit-to-stand (60 sec)</th>
<th>Grip strength (right), kg</th>
<th>Grip strength (left), kg</th>
<th>FACIT</th>
<th>Body fat, %</th>
<th>HAQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>30.9</td>
<td>23.5</td>
<td>22.0</td>
<td>29.5</td>
<td>33.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>6 week mean</td>
<td>30.3</td>
<td>23.0</td>
<td>27.3</td>
<td>35.8</td>
<td>36.9</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.49</td>
<td>0.02</td>
<td>0.08</td>
<td>0.02</td>
<td>0.05</td>
<td>0.02</td>
<td>0.03</td>
</tr>
</tbody>
</table>

FACIT: Functional Assessment of Chronic Illness Therapy.
withdrawal (odds ratio 8.00), although none were classified as serious, and baseline adverse event rates are unknown. The value of information estimate indicated the potential for high value from a future RCT.

Conclusion: A future definitive RCT of physiotherapy for JHS seems feasible, although the advice intervention should be made more robust to address perceived equipoise and subsequent attrition.

Disclosure statement: E.M.C. is a member of the Health Technology Assessment Executive and Emergency Specialist Care Panel. I.T.H. has received consulting fees from Novartis, ICON Public and Eli Lilly. The work had no connection to joint hypermobility or Ehlers-Danlos syndrome. All other authors declared no conflicts of interest.

124 AGREEMENT AMONG THERAPISTS WHEN DIAGNOSING LOW-BACK-RELATED LEG PAIN
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Background: Pain with radiation to the leg is a common presentation in back pain patients. Low back-related leg pain (LBLP) can be diagnosed as either radicular pain due to nerve root involvement or referred (non-specific) pain due to back pain spreading down the leg from structures such as ligaments, joints or discs but not involving a spinal nerve root. The clinical task of differentiating NRI from referred leg pain in LBLP patients is recognized as important, in line with clinical guidelines, but can be difficult in clinical practice. The aim of this study was to investigate agreement and reliability among clinicians with diagnosing LBLP in primary care consultants.

Methods: Thirty-six patients were assessed by one of six experienced physiotherapists and diagnosed as having either leg pain due to nerve root involvement or referred leg pain. Assessments were video recorded. In part 1, the physiotherapists each viewed videos of six patients they had not assessed. In part 2, videos were viewed by another six health professionals. All clinicians made an independent diagnosis and rated their confidence in the diagnosis (range 50–100%). Data were summarized using percentage agreements and κ coefficients with two-sided 95% CIs.

Results: In part 1, agreement was 72% with fair interrater reliability (κ = 0.53 [95% CI 0.07, 0.63]). Results for part 2 were almost identical (κ = 0.34 [95% CI 0.02, 0.69]). A clear trend was seen in both parts, with agreement and the κ coefficient increasing as confidence in the diagnosis increased. This trend of increasing agreement and reliability indices was noticeably evident once confidence in the diagnosis was >70%. When both raters were >80% confident in their diagnosis (n = 18), κ was 0.82, considered almost perfect agreement.

Conclusion: Regardless of training, standardisation or professional background, reliability was merely fair among clinicians when diagnosing nerve root involvement in LBLP patients recruited from primary care with symptoms of any duration and severity. This agrees with current opinion that differential between some of these patients is a diagnostic challenge for clinicians in primary care. However, when confidence in the clinical diagnosis is high, levels of agreement and reliability indices improve substantially.

Disclosure statement: The authors have declared no conflicts of interest.

125 AN EXPLORATION OF THE CHARACTERISTICS OF EARLY RHEUMATOID ARTHRITIS HAND INVOLVEMENT AMONG DIFFERENT GENDER, AGE AND HAND-DOMINANCE IN A CHINESE POPULATION
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Background: RA is the most common inflammatory rheumatic disease across the globe, causing symmetrical polyarthritis of large and small joints, including the hands and wrists. Sex, age and hand dominance are considered as risk factors for the development and progression of RA, with being female, increasing age and dominant hand leading to a greater risk of severe disease and worse prognosis. In rheumatoid arthritis, ethnic, socio-economic status and life stage are known to have an impact on hand function and impairment. Understanding the disease presentation and impact across different global populations can add useful information regarding the impact of hand use and different treatment regimens. However, there are few data on the impact of RA on hand function in Chinese populations. This study was to use data protocols developed in the UK to explore and internationalise the characteristics of early hand RA among different sexes, ages and hand-dominance in a Chinese population.

Methods: A cohort comparison study of 60 patients with early RA was conducted in one rheumatology centre in Shanghai, China. The procedures of data collection in China followed the standard operating procedures employed in the UK NIHR-funded SARAH trial. Participant questionnaires included the Michigan Hand Outcomes Questionnaire and Pain troublesomeness were used to measure patient-reported functional ability. Medication history and indicators of all disease activities such as ESR, CRP and RF were recorded. Physical assessments, including active range of hand and finger movement, deformity, tender and swollen joint counts and a dexterity test, were conducted to report hand impairment and function.

Results: There were no statistically significant differences between male (n = 12) and female (n = 48) groups across all patient-reported and objective outcome measures. Statistically significant differences (P < 0.05) were found between two age groups (≥60 years, n = 32) and <60 years, n = 32) in active wrist flexion of both dominant (z = −2.595, P = 0.019) and non-dominant hands (z = −3.627, P < 0.001), respectively. Dominant hand dexterity and combined finger flexion measurements were significantly better than the non-dominant measurements (z = 2.332, P = 0.029 and z = −2.085, P = 0.037) in all participants. However, non-dominant hand composite finger extension was significantly greater than dominant hand extension (z = −2.463, P = 0.017).

Conclusion: In this exploratory analysis of a Chinese RA population, hand impairment and hand function were not significantly different between men and women. Sex tends not be an indicator for hand impairment and function among the Chinese population. Increasing age affects the flexibilit of hands. Hand impairment function of the hand tended to be worse for the non-dominant hand. This finding is different from the UK population, in which early RA patients showed a greater level of impairment in their dominant hands. There is a need to fully analyse these characteristics of hand RA in the Chinese population.

Disclosure statement: The authors have declared no conflicts of interest.

126 PSYCHOMETRIC PROPERTIES OF TWO FATIGUE SCALES IN RHEUMATOLOGY OUTPATIENTS: UNIDIMENSIONAL SCALES MEASURING MULTIFACETED CONSTRUCTS
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1Psychology and 2Psychological Medicine, King’s College London, London, UK

Background: Fatigue is a common, clinically relevant symptom in rheumatological conditions. Research, predominantly in RA, has suggested that fatigue is multifaceted and may differ from fatigue in other conditions, leading to the development of the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ). However, calling into question whether this scale is truly multidimensional, recent psychometric analysis has indicated the BRAF-MDQ captures information regarding only a single general fatigue construct (i.e., it is unidimensional). This study examines the dimensionality of the BRAF-MDQ and another widely used measure of fatigue, the Chalder Fatigue Questionnaire (CFQ), in rheumatology outpatients. The objectives were 2-fold: to examine the dimensionality of the BRAF-MDQ and determine whether the BRAF-MDQ and CFQ are appropriate tools for use in a range of rheumatological conditions.

Methods: Data were collected from 235 patients attending rheumato-logy outpatient appointments at a central London hospital. The dimensionality of the two questionnaires was explored using factor analytic methods for each of the BRAF-MDQ and CFQ items separately and then combined. Item functioning and reliability of the scales across the range of fatigue scores was examined using item response theory methods.

Results: In the full sample (n = 235) and only the RA patients (n = 56), a single general fatigue factor explained the majority of the variance in item responses to both the BRA-FMDQ (all, 74%; RA, 75%) and CFQ (all, 62%; RA, 63%). Confirmatory factor analyses confirmed both unidimensional and multidimensional models provided further support that both questionnaires capture only a general fatigue construct.
Given the strong support for a unidimensional structure, items from both questionnaires were combined for item response theory analysis. Floor and ceiling effects for the total scores of both questionnaires were minimal. Both questionnaires exhibited high levels of reliability across the range of the general fatigue construct (CFQ >0.8; BRAF-MDQ >0.9). Only one item exhibited evidence for item bias by diagnosis. Controlling for fatigue, patients with RA were more likely to respond positively to the item ‘fatigue made it difficult to dress yourself’ [odds ratio 5.3 (95% CI 1.6, 17.3), P = 0.008].

Conclusion: The BRAF-MDQ and CFQ are both valid and reliable measures of fatigue in RA, and more widely across other rheumatological conditions. Although both questionnaires tap into a range of fatigue-related facets, neither is truly multidimensional. Therefore, summing levels of fatigue using total scores is acceptable. In practice, subscale scores are unlikely to be useful since they reflect general fatigue rather than independent dimensions of fatigue. Item bias was observed for a single item, however, the impact of this bias will be negligible when using total scores, and thus is likely to be ignored.

Disclosure statement: The authors have declared no conflicts of interest.

127 ANKYLOSING SPONDYLITIS: BENCHMARKING AND PHYSIOTHERAPY SERVICE EVALUATION
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Background: The Trust physiotherapy service manages a cohort of approximately 200 patients with AS. They are reviewed annually by the rheumatology physiotherapy team. Assessment includes a medical history review, posture, metrology, disease activity and psychosocial impact. Patients are offered physiotherapeutic intervention if indicated and can also access physiotherapy between reviews. This project aimed to evaluate the effectiveness of physiotherapy interventions in the management of patients with AS, benchmark the physiotherapy services offered to patients with AS in relation to current literature and other Trusts in the North West and produce guidance for physiotherapy management of patients with AS.

Methods: A literature search was carried out using four clinical databases. Literature evaluating physiotherapy intervention in men and women diagnosed with AS or axial SpA (axSpA) was included if published in the last 10 years, full text and in English. The Critical Appraisal Skills Programme tool was used to critique 18 eligible studies. The author produced a questionnaire to investigate physiotherapy management of patients with AS. Questions related to outcome measures used, frequency of review and management strategies. This was sent to six local NHS Trusts.

Results: The questionnaire achieved a 100% response rate. The author collated the findings from guidelines, the questionnaire and literature review to benchmark the Trust AS service. The service was largely adherent to current guidelines and commensurate with services within the six other trusts. Recommendations and action points were identified to optimize the service offered to patients with AS. Fifteen recommendations were made relating to adoption of guidelines, frequency of review, outcome measures, assessment, treatment interventions, advice and education and the descriptor of the service. These included development of an evidence-based pathway and guidance for physiotherapy assessment and management of patients with AS; reviewing newly diagnosed patients every 6 months; greater reference to Assessment of SpondyloArthritis international Society/EULAR, National Institute for Health and Care Excellence and National Ankylosing Spondylitis Society guidance regarding physiotherapy management and possible recommendation for biologic therapy; use of the range of the Bath indices to inform physiotherapy management and recommendations regarding biologic therapy; ensure exercise prescription is patient centred with guidance regarding community-based exercise; revision of the AS exercise leaflet to include breathing exercises and pelvic and lower limb stretches; discontinuation of BAS-G and adoption of Total Spinal Pain; revision of BASDAI and BASFI outcome measures to ensure accuracy of recording; inclusion of a nutrition presentation and a Tai Chi session.

Conclusion: This audit service evaluation and resulting actions will ensure patients with AS consistently receive high-quality, patient-centred, evidenced-based physiotherapy intervention. This will enhance patients’ effective self-management of their condition.

Disclosure statement: The authors have declared no conflicts of interest.

128 MANAGEMENT OF NATIVE JOINT SEPTIC ARTHRITIS AT THE QUEEN ELIZABETH HOSPITAL, BIRMINGHAM, UK: A CLINICAL AUDIT
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Background: Septic arthritis is a medical emergency with high mortality and morbidity if untreated. Joint aspiration is essential to aid diagnosis and tailor antibiotic choice. This should be performed, wherever possible, prior to commencing antibiotics. This recommendation forms part of the British Society for Rheumatology (BSR) guidelines from 2006. In our institution, we undertook a 12-month audit of the management of native joint septic arthritis using BSR and Trust guidelines.

Methods: Potential cases of septic arthritis between October 2012 and October 2013 were identified using theatre coding and records of positive synovial samples. Using electronic and paper notes, confirmed and clinically probable cases of native joint septic arthritis were identified. The management was compared with BSR and Trust standards. Key standards were joint aspiration prior to starting antibiotics, time to processing sample, initial antibiotic choice (first line i.v. flucloxacillin) and duration (6 weeks total) and clinical outcome. Secondary outcomes included risk factors for septic arthritis, CRP monitoring and incidence of joint washout.

Results: Thirty-nine cases of septic arthritis were identified over a 12 month period. Twenty-two of those cases had a positive synovial culture. A further 17 cases were deemed clinically consistent with septic arthritis without positive synovial culture. The mean patient age was 61.5 years. Identifiable risk factors were found in 53.8%, including underlying joint disease, prior orthopaedic procedures excluding replacements, chronic renal failure, history of penetrating injury and i.v. drug use. Knee joints were most commonly affected (43.6%), with the remaining affecting shoulder, hip, ankle, elbow, sacroiliac, wrist and small joints of the hand. A total of 46.2% of patients were aspired before antibiotics were started; 61.5% of samples were collected the same day. Fifteen organisms were isolated: Staphylococcus aureus (5), Streptococcus species (5), Four were Gram-negative organisms, including three Escherichia coli. A total of 35.9% and 12.8% of cases were treated in line with i.v. and oral antibiotic guidelines, respectively. CRP measurements were taken in 89.7% of patients throughout their admission. A total of 65.9% of patients underwent an arthroscopy and joint washout, 46.2% of cases resolved without sequelae, 30.8% had residual joint damage and five patients died. The mean age of those who died was 83.2 years and all had significant co-morbidity.

Conclusion: This audit is the first to be conducted over a 12 month period at our institution. Joint aspirations prior to commencement of antibiotics were performed in slightly less than half of the cases and could be improved through education and the use of guidelines. The range of causative organisms is wide, reflecting the complex nature of the cases identified. This led to a low recorded adherence to antibiotic guidelines. Following this audit, the Trust microbial guidelines have been changed to raise awareness of atypical organisms in septic arthritis and highlight the importance of synovial aspiration in the management of septic arthritis.

Disclosure statement: The authors have declared no conflicts of interest.

129 AUDIT OF GIANT CELL ARTERITIS REFERRALS AT BASILDON AND THURROCK HOSPITALS
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Background: GCA is the most common vasculitis and is a medical emergency, as it can lead to blindness in up to one-fifth of patients. Patients often present via general medicine, therefore, accurate diagnosis of GCA, management and referral to rheumatology is essential.
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Methods: We audited the ACR guidelines for GCA diagnosis and management by conducting a retrospective case review of patients referred to the rheumatology department from general physicians within a district general hospital over a 9 month period (January–September 2015). Patient notes were obtained and data were collected regarding diagnostic criteria and management via an inpatient referral database.

Results: Forty-one patients were audited: 28 females (71%) and 12 males (29%). The average age was 68 years. The median duration of headache was 3 weeks. Nineteen (44%) patients reported scalp tenderness. Regarding the headache site, 4 (11%) were occipital, 4 (9%) diffuse, 23 (53%) temporal and 10 (26%) frontal. Regarding visual symptoms, 14 (32%) had blurred vision, 2 (5%) had visual loss and 1 (2%) had amaurosis fugax. Eight (19%) patients had jaw claudication and 8 (19%) reported PIR symptoms. CRP was elevated in 19 (46%) patients and ESR was elevated in 9 (22%). Six (15%) patients had both an elevated CRP and ESR. Of these six, five (83%) were finally diagnosed as GCA. Overall, 16 (40%) patients were diagnosed as GCA by rheumatology. Of the 25 patients who were unlikely to have GCA, 14 (56%) had either a normal CRP or ESR. Twenty-two (51%) patients had temporal artery biopsy (TAB); 4 (18%) positive and 18 (81%) negative. The median time for the TAB to occur was 14 days, however, in eight patients this was >14 days. Twenty-eight (68%) patients were commenced on high-dose steroids. Of the 41 patients reviewed, 11 (27%) patients were referred according to the ACR guidelines. Only 40% were finally diagnosed as GCA, and 25% of these patients had a positive TAB. Of the four patients with TAB-negative GCA, only one (25%) patient had normal inflammatory markers. Forty-nine per cent of referrals had normal CRP and 19% had normal ESR. The evidence has shown that only 5% of GCA patients have normal inflammatory markers, making GCA unlikely in these patients. The audit recommendations include incorporating GCA ACR guidelines on the referral form. Only if three of five ACR criteria are met should the patient be referred to rheumatology and high-dose steroids commenced. TAB referrals should be made by rheumatology alone and a re-audit should be performed in 1 year.

Conclusion: In auditing our GCA referrals from general physicians against the ACR criteria, we found that only 11% were referred accordingly. Incorporating the GCA ACR criteria into the referral form should help to refer the quality of referrals and avoid the unnecessary commencement of high-dose steroids.

Disclosure statement: The authors have declared no conflicts of interest.

130 THE IMPLEMENTATION OF DOSE TAPERING TO MODERNIZE AND IMPROVE THE BIOLOGICS SERVICE IN A DISTRICT GENERAL HOSPITAL

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Background: Intraavenous CYC is considered central to the management of vasculitis, which could otherwise lead to multi-organ damage and the patient’s death. A shared care pharmacotherapy management guideline for the use of i.v. CYC in vasculitis patients is available at Mater Dei Hospital, Malta. The aim of this study was to assess adherence to the existing local shared care management guideline.

Methods: Patients who were prescribed i.v. CYC for the management of vasculitis over the last 4 years were identified through the electronic database kept by the clinical pharmacy practice unit. The individual pharmaceutical care patient profiles were retrospectively analysed in order to assess each patient’s pharmacotherapy management against the locally available shared care management guideline.

Results: Over the last 4 years, a total of 18 patients were prescribed i.v. CYC for the management of vasculitis. One patient refused to start treatment because of possible adverse reactions, while another patient died prior to initiation of therapy. Of a total of 16 patients who agreed to i.v. CYC, 8 were prescribed i.v. CYC according to the dose schedule recommended, which is every 2 weeks for the first 3 weeks and thereafter every 3 weeks for a total of 6 months. The other eight patients were prescribed CYC once a month for a total of 6 months. One of these eight patients was given the monthly frequency because the patient had difficult venous access and was highly immobile. Twelve patients had their dose calculated according to the shared guideline using age, weight and renal function. The other four patients were given a standard dose of 1 g. Mesna, ondansetron and co-trimoxazole were prescribed in all the patients. Antifungal prophylaxis was not prescribed in any patient. Laboratory monitoring was carried out in all patients according to the shared guideline. The influenza vaccine was recommended in all patients, whereas the pneumococcal vaccine was recommended in six patients. Only two patients agreed to buy the pneumococcal vaccine, which is not given free of charge in the NHS.

Conclusion: The importance of shared care management guidelines in ensuring optimum management of patients’ health needs to be recognized and deviations from the guideline need to be documented. The authors have declared no conflicts of interest.

131 USE OF INTRAVENOUS CYCLOPHOSPHAMIDE IN VASCULITIS PATIENTS: ADHERENCE TO THE LOCAL SHARED CARE PHARMACOTHERAPY MANAGEMENT GUIDELINE

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Conclusion: The importance of shared care management guidelines in ensuring optimum management of patients’ health needs to be recognized and deviations from the guideline need to be documented. The authors have declared no conflicts of interest.
All patients with rheumatic diseases on MTX were identified using the electronic database of clinic letters. Treatment doses and any changes were recorded along with the timing of blood tests and correlated against clinic letters stored electronically. Patients were excluded if they were deemed to be on MTX from the clinic letters but had not been seen for >1 year. Patients usually have their MTX monitoring undertaken in one of three ways: solely by the rheumatology department, with a phlebotomy service offered on site or by their general practitioner (GP). It is the responsibility of patients to contact the nurse to obtain results. Prescriptions are only dispensed from the hospital pharmacy if bloods tests are available from within a 3 month period.

Results: A total of 395 patients were included in the audit; 295 (75%) had a diagnosis of RA, 71 (18%) PsA and 46 (11.6%) seronegative inflammatory arthritis. A total of 328 patients were monitored solely by rheumatology, 39 of their GP and 88 by GP and hospital joint care. Overall, 49.6% of patients were compliant with NICE guidelines. From those who failed to comply with MTX monitoring standards, 192 (48.6%) had at least one change to their MTX dose, of which 25% met the audit criteria, compared with 68.1% of those who did not have a dose change. Three patients complied with the MTX blood monitoring standards but failed to receive regular review by a medical practitioner.

Conclusion: Non-compliance with NICE MTX monitoring standards was seen mainly among patients with a recent dose change. This highlights the extra vigilence that is necessary for this group of patients. Current NICE guidelines state monitoring every 2 weeks then monthly for a year following a dose change. The use of computerized databases for DMARD blood monitoring is one way of ensuring that this is undertaken safely and efficiently. Shared-care guidelines between primary and secondary care also constitute an important way of delivering optimal care, as well as appropriate patient education so that individuals are well informed and hence in a better position to undertake responsibility for their own care.

Disclosure statement: The authors have declared no conflicts of interest.

133 DO PATIENTS ON ANTI-TUMOUR NECROSIS FACTOR MONOTHERAPY NEED REGULAR BLOOD TESTS? AN AUDIT OF BLOOD MONITORING IN PEOPLE WITH ANKYLOSING SPONDYLITIS

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Background: In contrast to other inflammatory conditions, most patients with AS receive anti-TNF therapy without concomitant DMARDs. The optimum frequency of blood monitoring in patients on anti-TNF monotherapy is unclear. However, cytopenias and abnormal liver function tests (LFTs) are reported in patients taking anti-TNF drugs, and for this reason the British Society for Rheumatology RA guidelines on the safety of anti-TNF therapies recommend regular full blood count (FBC) monitoring. In our department—as in many—patients are required to have an FBC, LFT and urea and electrolytes (U&E) every 3–6 months in order to continue treatment. In this retrospective study we examined the frequency of abnormal results in a cohort of AS patients taking anti-TNF drugs as monotherapy.

Methods: The departmental biologics database was used to identify all patients with AS who had started an s.c. anti-TNF drug. Every blood result since starting anti-TNF therapy was examined for a significant abnormality, defined as a neutrophil count <1.0 x 10^9/L, alanine aminotransferase (ALT) >100 U/L or estimated GFR (eGFR) <45 ml min/1.73 m^2. Data were collected and analysed using Microsoft Excel and Stata.

Results: Of 281 patients starting anti-TNF therapy for AS, 238 (84.7%) received this as monotherapy. Four patients were excluded because their blood tests were performed at a neighbouring hospital and a further nine had received only i.v. anti-TNF therapy. The median age of the remaining 225 patients was 49 years [interquartile range (IQR) 39–59] and 183 (81.3%) were male. Patients were treated for a median of 42 months (IQR 20–87). Twenty-five (11.1%) switched to a second anti-TNF drug and 18 (8.0%) stopped treatment, 3 (1.3%) after a second anti-TNF drug. The total drug exposure and the number of significantly abnormal tests is given in Table 1. In total, 3026 FBCs, 2934 U&Es and 2945 LFTs were performed. No patient had severe neutropenia, and a single patient had stable renal impairment.

Disclosure: JL received funding from meeting attendance from MSD. L.H received funding for meeting attendance from MSD. All other authors declared no conflicts of interest.

134 EVALUATION OF THE ADVICE AND GUIDANCE SERVICE OFFERED BY THE RHEUMATOLOGY DEPARTMENT AT THE ROYAL DERBY HOSPITAL

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Background: The Advice and Guidance Service for Rheumatology at the Royal Derby Hospital (RDH) available via Choose and Book enables general practitioners (GPs) to obtain specialist advice without necessarily a secondary care referral. An evaluation of this service was made to assess the effectiveness of this system in managing patients.

Methods: A retrospective analysis of GP referrals to the Advice and Guidance Service from 1 September 2014 to 31 August 2015 was performed. A qualitative and quantitative analysis of GP letters and the response from rheumatologists or osteoporosis nurse specialist was performed. The number of queries received, nature of queries, number of referrals advised or not advised and number of cases referred were recorded.

Results: A total of 95 GP queries were received and analysed. Forty-four requests were regarding aid in diagnosis, while the other 51 were regarding clinical management. Sixty-five were regarding rheumatology and 30 were regarding osteoporosis. Of the osteoporosis referrals, most (28/30 (93%)) were related to management and a referral was advised for 11 of 28 patients, most of which related to parental therapy. In 43 (45%) cases the Advice and Guidance Service saved a new patient referral. In a further 9 (5%) patients a follow-up visit was advised for 11 of 28 patients, most of which related to parental therapy. In 43 (45%) cases the Advice and Guidance Service saved a new patient referral. In a further 9 (5%) patients a follow-up visit was advised. A referral was advised in 41 patients, of which 11 may require a referral depending on further information or patient progress. Where a referral was suggested, for 10 patients a referral at RDH never occurred. It is unknown whether these patients had been referred elsewhere or the decision was ultimately made by the GP not to refer. The length of time spent dealing with the queries was estimated at 5–25 minutes, with a median of 10 minutes. Low-complexity issues tended to take a shorter time to address. However, there was no significant difference between times taken to address issues for patients who were going to be referred compared with those who did not require a referral. Advice given to those where a referral may be required involved assessing investigations and previous correspondence or advice was given to the GP regarding how to manage the interim. These may have been some reasons why there was no difference in the time to address issues.
Conclusion: This evaluation of the advice and guidance referral system provided by the pharmacy department at RDH appears to provide an additional resource for GPs to reduce unsuitable referrals to secondary care, hence reducing GP referrals to secondary care and providing financial relief to the Clinical Commissioning Group. This work should be remunerated, as queries can take significant time to resolve.

Disclosure statement: The authors have declared no conflicts of interest.

135 AUDIT OF STEROID TAPERING IN TEMPORAL ARTERY BIOPSY-NEGATIVE PATIENTS: GUIDELINES MAY HELP REDUCE TOTAL STEROID DOSE

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Background: GCA is a sight-threatening large vessel vasculitis. Diagnosis is confirmed by temporal artery biopsy (TAB) and patients are commenced on high-dose steroids prior to diagnosis confirmation. The British Society for Rheumatology (BSR) published guidelines for the steroid-tapering regimen for patients with a GCA diagnosis, confirmed by TAB or clinical judgement. However, no guidelines exist for a tapering regimen in TAB-negative patients with low clinical suspicion for GCA. The aim of this study was to compare whether it is safe to recommend a faster tapering regimen in patients with negative TABs to minimize cumulative steroid exposure.

Methods: A retrospective audit was performed on the steroid-tapering regimen of all patients with suspected GCA who had a TAB at the Great Western Hospital. The TAB surgical lists were used to identify patients who had a TAB between 2009 and 2015 with a negative result and were followed up to establish a tapering regimen. Two groups were created within TAB-negative patients: those who were completely tapered within 6 months (considered fast tapering) and those who followed the BSR regimen. The relapse rate, reasons why the fast regimen was not initiated, biopsy size (mm) and delay from starting steroids were compared between the two groups.

Results: Forty-three TAB-negative patients were identified: 25 in the fast tapering and 18 in the standard regimen. Relapse rates were equivalent between groups: fast, 3/25 (12%) vs standard, 4/18 (22%). Twenty-two of 25 (88%) patients were successfully weaned in ≤ 6 months on the fast regimen. Reasons for using the standard steroid-tapering regimen in 18 TAB-negative patients were high clinical suspicion of GCA (8), lack of confidence in the biopsy result (7) and patient choice (3). It was also noted that in two cases inflammatory markers had not been taken prior to starting steroids. Biopsies were significantly longer in the fast group compared with the standard regimen: median 13 (interquartile range IQR) 10–18 vs 6 (IQR 5–10), P < 0.05. In contrast, days on steroids prior to TAB were similar in both groups: fast, 23 (IQR 17.5–29.5) vs standard, 24 (IQR 19.25–34.25), P = NS. The 36 day tapering regimen used in some cases led to a cumulative steroid dose of just 1170 mg prednisolone. This compares with the standard steroid-tapering regimen over 15 months that gives a total prednisolone dose of 4100 mg.

Conclusion: In patients with a low clinical suspicion of GCA, a fast steroid-tapering regimen is safe and effective in TAB-negative patients. This requires inflammatory markers to be taken before starting steroids and a timely, adequate TAB to be performed. The TAB size was significantly greater in our fast-tapering group. Guidelines for steroid tapering in TAB-negative patients may help in reducing cumulative steroid dose.

Disclosure statement: The authors have declared no conflicts of interest.

136 USE OF THE RHEUMATOID ARTHRITIS MEDICATION ASSESSMENT TOOL WITHIN PHARMACEUTICAL CARE PLANS

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Background: The RA Medication Assessment Tool (RhMAT) is a validated medication assessment tool designed specifically to analyse pharmacotherapy adherence to evidence-based guidelines in the management of RA. The outcome of the RhMAT is the ability to assess the degree of pharmacotherapy adherence to guidelines and the identification of gaps in adherence. The objective of the study was to implement the RhMAT within an ongoing pharmaceutical care service in order to help pharmacists systematically assess pharmacotherapy management against evidence-based recommendations and resolve pharmacological care issues.

Methods: Patients were eligible for inclusion in the study if they were >18 years of age, suffering from RA and regularly attending the rheumatology outpatient clinic at Mater Dei Hospital. The University of Malta Research Ethics Committee approved the study and patients’ consent was sought. During the pharmaceutical care session, the pharmacist assessed each patient’s pharmacotherapy regimen. The RhMAT adherence rate was calculated. Adherence rate is defined as low if the score achieved is ≤ 50%; intermediate if the score ranges between 51 and 74% and high if the score is ≥ 75%. The identified non-adherence issues of the RhMAT were subsequently discussed with the respective clinicians and the patients’ themselves. The RhMAT was run twice, during phase 1 (time = 0 months, baseline) and at the patient’s next visit (time = 12 ± 3 months).

Results: A total of 78 patients with a mean age of 64 years (s.d. 11.9) participated in the study. More than half of the patients (55% (n = 43)) had been prescribed traditional DMARDs (DMARDs), whereas 45% (n = 35) were on biologic DMARDs alone or in combination with DMARDs. The mean score of the total RhMAT adherence rate achieved at phase 1 (time = 0) was documented as 81.7%, indicating a high adherence rate. This was improved significantly for all patients by 8.5% (P < 0.05, Wilcoxon signed rank test) at phase 2 following the pharmacist’s discussion with the clinician on identified gaps and pharmacological care issues.

Conclusion: The RhMAT, which takes ~15 minutes to complete, can be used by pharmacists working in a busy clinical setting to capture the degree of adherence to guidelines and identify gaps leading to non-adherence. The pharmacist can therefore use the RhMAT as a quality control tool to identify and resolve pharmacological care issues, further improving the quality of care of RA patients.

Disclosure statement: The authors have declared no conflicts of interest.

137 BIOLOGICS ALERT CARD AUDIT: ARE PATIENTS CARRYING THEIR CARD?

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Background: All patients with rheumatological conditions who are treated with biologic therapies should carry an alert card informing health professionals of the treatment and the risks inherent with these therapies. The aim of the audit was to improve the quality of the biologic medication support and self-management education provided by the department through objective measurement and evaluation of current practice against recommended best practice.

Methods: Data were collected from a consecutive cohort of 100 patients who were receiving biologic therapy attending a routine specialist nurse lead clinic assessing disease management and control. There were no exclusions and all review visits were included. The data collection form required confirmation that a biologic alert card had been provided at initiation of therapy, if the patient carried the card to their visit and, for those with a card at the appointment, the details were monitored for correct therapy and contact numbers. The type of card was recorded, whether charity or commercial.

Results: A total of 100 patients were sampled. The majority [71% (n = 71)] remembered being supplied an alert card to carry on initiation of therapy and, of these, 76% (n = 54) had brought their card to the outpatient appointment. Therefore, 29% (n = 29) had not been provided with a card on commencement of therapy or could not recall this. Of those patients with an alert card at the clinic visit, 85% (n = 46) had the correct medication information and 80% (n = 43) had the correct contact details. Analysis of the type of card patients were carrying showed the majority [76% (n = 41)] were from the Arthritis Research Campaign, with 22% (n = 12) including cards provided by the drug company.

Conclusion: The results demonstrate that compliance with the standard of 100% of patients on biologic therapies both being provided with and carrying a biologics alert card is currently not being achieved within the service. Regularly reviewing patients’ alert cards to ensure they are up to date and educating patients on the importance of carrying the card to provide members of the health professions with information in case of emergency is an important task for both nurse specialists, supporting patients in achieving the best possible outcomes from their medication. An action plan has been developed to educate and remind members of the health care
team to provide a card on initiation or change of therapy and to include a check on the biologics alert card at each clinic visit. Visual reminders have been produced and displayed in relevant departmental areas. A re-audit is planned for 6 months.

Disclosure statement: The authors have declared no conflicts of interest.

138 RHEUMATOID ARTHRITIS: NOW AND THEN

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Background: There have been many changes in the approach to the management of RA in recent decades. The disease is now detected earlier and there is a wider range of DMARD and biologic drug treatments available.

Methods: We compared two cohorts of patients with RA to examine characteristics including demographics, extra-articular manifestations, drug treatments used and joint injections and replacements. We reviewed the charts of patients with RA who had been inpatients through the 1970s–1990s or diagnosed prior to 1990 (group 1) and compared third and fourth decade patients who were coded as seropositive RA (group 2). We examined 50 charts for each group.

Results: Demographics were similar, with 78% and 82% female in group 1 and group 2, respectively, and peak age at diagnosis being between 46 and 60 years. There was a greater proportion of patients diagnosed with late-onset RA in group 2. Group 1 included patients with multiple admissions. The most common reason for admission was flare of disease. Group 2 did not include any inpatient admissions.

Most significantly there was a reduction in radiographic erosions from 70% to 18%, although notably 36% of patients in group 2 had erosions evident on US. There was a substantial reduction in extra-articular manifestations, with cardiac involvement of 50% and 2%, arthropathy of 50% and 18%, cutaneous nodules 36% and 2%, lung disease 24% and 2%, osteoporosis 24% and 12%, vasculitis 10% and 0% and eye disease 8% and 0% in group 1 and group 2, respectively.

The use of DMARDs included dactinomycin in 62% and 0%, SSZ in 50% and 50%, gold in 44% and 2%, long-term steroids in 40% and 18%, MTX in 14% and 92%, HCQ in 14% and 50% and LEF in 0% and 36% in group 1 and group 2, respectively. Group 2 also included several patients on biologic agents. A much higher side effect profile was noted with the broader range and higher doses of DMARDs. In looking at joint injections being carried out, in group 1 these were predominantly knee and shoulder injections, while in group 2 there was a higher proportion of smaller joints being injected. Joint replacements are also much reduced, with hip and knee remaining the most commonly implanted joints.

Conclusion: The study has shown that as the treatment approach for RA has evolved, there have been improvements in several areas. There is a reduction in both the duration and frequency of inpatient admissions. Radiographic erosions are markedly reduced and erosions are now often detected on US before they are apparent on X-rays. There has been a reduction in the use of long-term steroids, with a subsequent reduction in rates of osteoporosis. There is a greater proportion of smaller joints being injected and a smaller number of joint replacements being carried out.

Disclosure statement: The authors have declared no conflicts of interest.

139 A SINGLE-CENTRE EXPERIENCE OF THE ISSUES DISCUSSED DURING PRE-PREGNANCY COUNSELLING OF PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASE

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Background: Inflammatory rheumatic diseases (IRDs), such as RA and SLE, have a predilection for women of childbearing age. Management of IRDs during pregnancy is complicated by a complex relationship with disease activity and often multiple medications that may be incompatible with pregnancy. Therefore, a multidisciplinary approach beginning with pre-pregnancy counselling is required, including consideration of disease manifestations and activity, obstetric history, drug history and autoantibody profile. Ideally, health care professionals should combine to offer expertise in the recognition and treatment of complications of pregnancy and relapses of inflammatory arthritis. A close collaboration between interdisciplin ary teams of rheumatologists and obstetricians allows appropriate risk assessment and provision of an individualized plan for antenatal and postnatal management of such high-risk pregnancies. In the UK, few specialist rheumatology-obstetrics clinics have been established, but one such service exists at University College London Hospital (UCHL). We have previously reported pregnancy outcomes from this clinic and now describe our pre-pregnancy counselling experience.

Methods: We performed a retrospective analysis to report the outcomes of all IRD patients attending UCHL’s joint rheumatology–obstetrics specialist counselling outpatient service during a 3 year period (January 2013–October 2015).

Results: Of a total of 222 patients referred to the specialist rheumatology–obstetric service, 77 patients (73 women, 4 men) were seen specifically for pre-pregnancy counselling in 79 consultations in the study period. The mean age was 35 years (s.d. 6.17, range 21–64); Diagnoses included SLE and lupus-like disease (n = 21); RA (n = 14), AS (n = 5), seronegative inflammatory arthritis (n = 6), PIA (n = 8); SS (n = 2), juvenile arthritis (n = 5), undifferentiated autoimmune rheumatic disease (n = 3), primary vasculitis (n = 1) and other chronic IRDs (n = 12). Disease activity (determined by the Physician Global Assessment) was judged to be moderate in 7 and mild/inactive in 72, with no cases of severe disease activity. Medication changes were advised for MTX (n = 17), LEO (n = 1) and rituximab (n = 1), to be stopped pre-pregnancy; infliximab to be stopped at the beginning of pregnancy (n = 2); etanercept (n = 8) and adalimumab (n = 8) to be stopped at the end of the second trimester; NSAIDs (n = 14) to be stopped at 32 weeks and coagulation switched to heparin upon a positive pregnancy test (n = 1). Continuation of medication during pregnancy was advised for AZA (n = 9), HCQ (n = 33), corticosteroids (n = 14), SSZ (n = 9), low-dose aspirin (n = 14), thyroxine (n = 2) and calcium/vitamin D (n = 8). Specific advice was given in relation to adverse autoantibody profiles and future pregnancy for patients with anti-RO (n = 12) and anti-La (n = 2).

Conclusion: Experience from this specialist rheumatology-obstetric pregnancy outpatient service shows that patients with IRDs require discussion of multiple counselling issues in pregnancy counselling consultations, particularly management of disease activity during pregnancy and alteration of medication in anticipation of a future pregnancy. Expectations regarding pregnancy outcome were also discussed.

Disclosure statement: The authors have declared no conflicts of interest.

140 ASSESSMENT AND DIAGNOSIS OF ANKYLOSING SPONDYLITIS: TREATMENT OPTIONS FOR PATIENTS BOTH ON AND NOT ON ANTI-TUMOUR NECROSIS FACTOR AT CHESTERFIELD ROYAL HOSPITAL

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Background: AS is a progressive inflammatory arthritis, mainly affecting the spine and sacroiliac joints, causing pain, stiffness and ankylosis. Currently for diagnosis of AS, X-ray evidence of sacroiliitis is required. The modified New York Criteria outlines the radiological and clinical criteria for a definite diagnosis of AS, while National Institute for Health and Care Excellence (NICE) guidance outlines recommendations for eligibility for treatment with anti-TNF. We decided to look at patients in the Ankylosing Spondylitis Clinic to establish whether they met the criteria for diagnosis and treatment with anti-TNF and hence whether NICE guidance was being followed. The audit objectives were to audit our own practice against national guidelines, to demonstrate compliance with national guidelines and to look at patients who are not currently on anti-TNF treatment.

Methods: Fifty-five patients with a diagnosis of AS, 20 receiving anti-TNF and 35 not receiving anti-TNF, were audited retrospectively using a pro forma at Chesterfield Royal Hospital. This included assessing the modified New York criteria for diagnosis and NICE guidelines for treatment with anti-TNF.

Results: Eighty-five per cent of patients on anti-TNF and 50% of patients not on anti-TNF were diagnosed within the first 3 years of symptoms. Of the patients on biologics, 80% met the New York criteria for diagnosis, 65% met the NICE criteria for biologics; 84% had a reduction in the pain visual analogue scale and 84% had a reduction in BASDAI after treatment. For the patients not on anti-TNF, 71% met the New York criteria for diagnosis and 22% met the criteria for anti-TNF.

Conclusion: Most people on anti-TNF meet the criteria for a diagnosis of AS, but 35% do not appear to meet the NICE guidelines for this treatment. Conversely, 22% of patients not on anti-TNF met the NICE guidelines for treatment. A more uniform approach to assessment is needed to ensure that eligibility for treatment is recognized and guidelines are followed. Communication between different members of the multidisciplinary team (MDT) is important to ensure that patients
The authors have declared no conflicts of interest.

Septic arthritis has a mortality rate of up to 11% and can be very difficult to diagnose and manage. We introduced a hot swollen joint bundle based on the British Society for Rheumatology (BSR) guidelines and conducted a full audit of this pathway.

Methods: All adults admitted in 2011 with a discharge diagnosis of septic arthritis were retrospectively analysed according to the BSR audit tool, which included appropriate initial investigations and treatment. A multidisciplinary hot swollen joint bundle was then introduced, aimed at reinforcing the BSR guidelines, including early joint aspiration, blood cultures, appropriate antibiotics and further investigations. The audit was then repeated in 2014 to assess the efficacy of the bundle.

Results: In 2011, there were 27 cases of septic arthritis and the majority of BSR standards were not met. More than half of patients did not have a joint aspirate prior to antibiotics or blood cultures taken during their admission (Table 1). In 2014, there were 33 cases of septic arthritis. Following bundle implementation, all areas of management had improved. We found statistically significant improvements in the number of patients having joint aspirates prior to antibiotics, the number of blood cultures taken, the number of joints being X-rayed and the number of antibiotic prescriptions according to guidelines. In 2011, the mortality rate of patients with septic arthritis was 7% and the average length of hospital stay was 22 days. In 2014, after bundle introduction, no patients died during their admission and the average length of hospital stay was 20 days.

Conclusion: The introduction of a hot swollen joint bundle is a cheap and effective method of improving the clinical care of patients with septic arthritis. We recommend that other hospitals adopt a similar bundle to ensure patient management is in accordance with BSR guidelines.

Disclosure statement: The authors have declared no conflicts of interest.
144 EVALUATION OF THE USE OF COMBINED IMMUNOSUPPRESSION TREATMENT REGIMENS IN THE SHEFFIELD ADULT UVEITIS/SCLERITIS SERVICE

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Background: Children and adults with uveitis are managed using similar treatments (MTX, MMF and biologic agents). Sheffield has established a uveitis transition clinic with staff from both children’s and adult services, providing the opportunity to examine treatment pathways and outcomes in both paediatric and adult services. We conducted a service evaluation to describe response to treatment in our adult service for individuals receiving combination therapy for uveitis and scleritis. The aims of the evaluation were to document the treatment pathway for adults with uveitis or scleritis receiving immunosuppression therapy with two or more agents and to describe response to treatment in terms of disease activity and visual acuity.

Methods: Patients receiving combination immunosuppression therapy (MTX, MMF and biologic agents) were identified from a medical notes review of patients attending uveitis clinics between July 2014 and February 2015. Data collected included anterior chamber activity for each eye (according to Standardization of Uveitis Nomenclature criteria), flare, visual acuity (recorded as Snellen and converted to logMAR for comparison with paediatric data) and concomitant systemic corticosteroid use.

Results: Twenty-one patients received combination immunosuppression therapy during the study time points. Diagnoses were as follows: birdshot chorioretinopathy (n = 5), idiopathic uveitis (n = 5), AS (n = 2). Behcets disease (n = 2), granulomatosis with polyangiitis (n = 2), sarcoidosis (n = 2), Vogt–Koyanagi–Harada disease (n = 1) and RA (n = 1). One patient had both RA and birdshot chorioretinitis and was included in both. Sixteen patients had uveitis, four had scleritis and one had sclera uveitis. The initial immunosuppression agent chosen varied as follows: MTX (n = 7), MMF (n = 11), biologic agent (n = 3). Biologic agents used included infliximab (n = 3), adalimumab (n = 11) and rituximab (n = 1). In some cases patients were changed from one biologic to another. A downward trend in mean average anterior chamber cell activity (from 0.38 to 0.05) was documented. When confounding factors (e.g. eye surgery) were removed, there was an improvement in visual acuity (logMAR 0.33 to 0.12) in individuals receiving anti-TNF therapy as part of combination immunosuppression therapy. A significant decrease in mean average oral corticosteroid dose (from 26 to 3.5 mg/day; P < 0.05) in individuals receiving immunosuppression therapy was documented. Time from decision to start biologic therapy to the first dose was as follows: <1 month, 10%; 1–2 months, 60%; >2 months, 30%; (range 2 weeks–5 months). No significant infectious episodes (requiring hospital admission) were noted during the period individuals were receiving combination immunosuppression therapy.

Conclusion: An improvement in visual acuity was documented in individuals receiving biologic treatment as part of immunosuppressive therapy. A downward trend in disease activity following combined immunosuppressive treatment was documented. A significant decrease in concomitant oral corticosteroid use was noted following initiation of combined immunosuppression therapy. Combination immunosuppression therapy appeared well tolerated in our cohort.

Disclosure statement: The authors have declared no conflicts of interest.

145 SUSPECTED TEMPORAL ARTERITIS: AN AUDIT OF A PATIENT PATHWAY

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Background: Temporal arteritis (TA), a rheumatological emergency, may present a diagnostic challenge for clinicians. Temporal artery biopsy (TAB) may secure the diagnosis, but the considerable false-negative rate means that the diagnosis of TA relies strongly on clinical experience and judgement. In the absence of generally accepted diagnostic criteria for TA, classification criteria such as those of the ACR (1990), which were originally developed and intended for research purposes only, are often used to assist clinicians in diagnosing the condition. We conducted an audit of the Dudley Group Foundation Trust suspected TA pathway and looked at the sensitivity and specificity of ACR criteria as a diagnostic tool.

Methods: We prospectively collected data from patients referred to the rheumatology department with suspected TA from both the primary care and acute medicine departments between February and June 2015. Data included demographics, time from referral to first rheumatology assessment, symptoms and signs, inflammatory markers, TAB results, time from steroid commencement to TAB date and whether the patient met the ACR GCA criteria. The clinical diagnosis at 4 weeks following first assessment was used to calculate sensitivity and specificity for ACR criteria when used as a diagnostic tool and for TAB.

Results: Data were available for 30 patients; 21 (70%) were female and the median age was 74 years (range 40–99). The median ESR was 51 mm/h and the median CRP was 29 mg/l. Twenty-two patients (73%) were treated as TA at 4 weeks. The median time from referral to first rheumatology assessment was 4 days (range 1–15). At least three of five ACR criteria were positive in 21 (70%) patients: 27 (90%) for age ≥50 years, 27 (80%) for new headache, 21 (70%) for clinical temporal artery abnormality, 13 (43%) for ESR ≥50 mm/h and 4 (13%) for positive TAB. Nine (30%) had visual symptoms. The sensitivity and specificity of the ACR criteria were 86% and 75%, respectively. TAB was performed in 17 (57%) patients. The median time from steroid commencement to TAB was 8 days (range 3–17). TAB was negative in 13 of the 17 patients, 12 of which were treated as TA regardless of their negative TAB result. Only 1 of the 13 was not treated as TA; however, this patient was not suspected as GCA when initially assessed by a rheumatologist and the biopsy was requested by the referrer team beforehand. The sensitivity and specificity of TAB were 25% and 100%, respectively.

Conclusion: This audit demonstrated rapid access to first rheumatology assessment and TAB in our pathway. Temporal artery histology had a lower than historically reported sensitivity and did not influence the initial management in the majority of our patients. The use and impact of TAB on clinical management may merit re-evaluation by clinicians requesting TAB.

Disclosure statement: The authors have declared no conflicts of interest.

146 ASSESSING THE USE OF INTRAVENOUS ZOLEDRONIC ACID IN A RHEUMATOLOGY POPULATION

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Background: Osteoporosis is a metabolic bone disease characterized by low bone mass, leading to an increased risk of fracture. Zoledronic acid is a bisphosphonate used to treat and prevent osteoporosis and bone metastases. A recent Cochrane review highlighted the effectiveness of zoledronic acid and concluded that intravenous zoledronic acid at 5 mg once in 6 months is the best choice. Although zoledronic acid is recommended for all osteoporotic patients, it is not generally used in practice.

Methods: The purpose of our study was to assess the reasons why zoledronic acid is not generally used in practice. A retrospective audit of patients prescribed zoledronic acid at Cannock Chase Hospital between January 2013 and December 2015 was conducted.

Results: The total number of patients prescribed zoledronic acid was 506. Of these, 303 (60%) were on zoledronic acid therapy for osteoporosis and 203 (40%) for treatment of bone metastases. The reasons why zoledronic acid was not used in practice were as follows: 147 patients (29%) were on oral bisphosphonates, 14 patients (3%) were not prescribed zoledronic acid by the prescribing consultant, 12 patients (2%) were not prescribed zoledronic acid by the consultant because of an adverse event and 113 patients (23%) were not prescribed zoledronic acid by the consultant because of cost constraints.

Conclusion: The reasons why zoledronic acid was not generally used in practice were predominantly related to cost constraints. A cost-benefit analysis of zoledronic acid is required to determine whether zoledronic acid is a cost-effective therapy for osteoporosis.

Disclosure statement: The authors have declared no conflicts of interest.
This retrospective cohort study included all patients who had been treated with i.v. zoledronic acid between 2010 and 2015 in the University Hospital Coventry and Warwickshire (UHCW) NHS Trust (Coventry). Ethics approval was obtained from the University Hospital Coventry and Warwickshire (UHCW) NHS Trust Research and Development Department. We developed a pro forma to collect information from these patients’ electronic notes relating to comorbidities, previous treatment, response to oral bisphosphonates, fracture rates, drug tolerance, side effects and post-treatment management. The main outcome measures were reason for changing from oral bisphosphonates, completion of baseline blood tests, BMD data and fracture rates.

Results: A total of 116 patients fulfilled inclusion criteria, of which 97 were female and 18 were male. Thirty-four per cent had co-morbid RA and 53% were on steroids; 87.1% had tried oral bisphosphonates previously. For 37.6% of these patients, the reason for transfer to zoledronic acid was not adequately documented. DEXA scans were performed in 90.5% of the cohort prior to their first infusion. All baseline blood work (bone profile, urinalysis and electrolytes), vitamin D levels were completed before the infusion. Correction of low vitamin D was required before 29 infusions but was only corrected before 22. Of the 41 patients who had completed treatment, 63% had post-treatment DEXA scans and 27% were awaiting scans. No patients experienced new-onset atrial fibrillation at any point during or after treatment. All patients tolerated the drug; side effects were experienced with few infusions. BMD in patients who completed treatment showed no statistically significant increase. However, a statistically significant (P < 0.015) decrease in the number of pathological fractures patients experienced was seen.

Conclusion: There are several gaps in the documented data due to incomplete documentation in clinical letters and non-completion of tests. Creating a checklist for clinicians to use should help improve documentation and thereby help standardize patient management. Zoledronic acid was well tolerated, caused few side effects and significantly reduced fracture rates, showing it to be safe and efficacious in this real-life setting.

Disclosure statement: The authors have declared no conflicts of interest.

HEALTH SERVICES RESEARCH, ECONOMICS AND OUTCOMES RESEARCH

148 PSYCHOLOGICAL INTERVENTIONS FOR RHEUMATOID ARTHRITIS: AN OVERVIEW OF SYSTEMATIC REVIEWS

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Background: RA is a long-term, progressive autoimmune disease. Many patients with RA continue to experience symptoms despite pharmacological intervention. RA medications also have a variety of side effects, especially when taken over long periods. These factors make psychological interventions an important but often overlooked option for patients with RA. In recent years the number of trials of psychological interventions has increased. There have been several systematic reviews of this literature but no overview of systematic reviews to summarize the evidence. The aim of this overview is to summarize evidence from multiple systematic reviews of randomized controlled trials (RCTs) of psychological interventions for patients with RA to determine their effectiveness in improving outcomes.

Methods: A systematic search of published scientific literature was conducted using bibliographic databases (Cochrane Library, Embase, Medline, CINAHL, PsycINFO) from January 2000 to June 2015. The inclusion criteria were systematic reviews of RCTs of psychological interventions; including participants with a diagnosis of RA (participants with a mixed diagnosis were included if outcomes were reported separately for adults with RA); age ≥18 years; findings reported for at least one of the following outcomes: pain, fatigue, functional disability, psychological status and disease activity and published in the English language. The quality of the selected reviews was assessed using the validated Assessment of Multiple Systematic Reviews (AMSTAR) checklist.

Wednesday 27 April 2016
Results: Eight systematic reviews published between 2002 and 2013, including a total of 65 RCTs published between 1981 and 2012, were selected for inclusion in the overview of systematic reviews. According to the AMSTAR checklist, five reviews were of moderate quality, two were of high quality and one was of low quality. A narrative approach was used to synthesize the findings from the reviews. Psychological interventions have small positive short-term effects on the following outcomes: pain, functional disability, depression, fatigue, coping, self-efficacy and patient global assessment. Limited evidence was found for any long-term effects on outcomes.

Conclusion: Psychological interventions have small positive effects on outcomes in adults with RA. These improvements in symptoms are in addition to pharmacologic treatment, and there is certainly a place for psychological interventions to be used adjunctively to enhance treatment response. Future research with high-quality RCTs is needed to refine these examinations, examine whether they are more beneficial for certain types of patients and develop strategies to increase and maintain improvements over time.

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149 IMPACT OF NEW ARTHRITIS ON ABILITY TO WORK: OBSERVATIONS FROM THE NATIONAL CLINICAL AUDIT FOR RHEUMATOID AND EARLY INFLAMMATORY ARTHRITIS

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Background: Inflammatory arthritis often presents in patients of working age and may impact negatively on work; it has previously been estimated that 30–50% of individuals diagnosed with RA leave their employment within 5 years. Despite this, a national survey by the National Rheumatoid Arthritis Society found that the majority of respondents could not recall being offered employment advice in their rheumatology consultations in the last 12 months. Here we present observations on work status for patients participating in the National Clinical Audit for rheumatoid and early inflammatory arthritis.

Methods: Data were collected in the National Clinical Audit for rheumatoid and early inflammatory arthritis between 1 February 2014 and 31 January 2015. Participants were individuals > 16 years of age with early inflammatory arthritis presenting to secondary care rheumatology units in England and Wales for the first time. Data were collected for 3 months from the initial assessment in a rheumatology clinic. The audit includes questions relating to patients’ ability to work, specifically regarding employment status, time required off work because of arthritis and whether patients recalled being asked about work.

Results: At recruitment, 2,444 (39%) patients were working full time in paid employment, 846 (14%) patients were working part time in paid employment, 2,286 (36%) were not working in paid employment and responses were missing for the remainder of patients. Data on work status were reported here on patients of working age (> 66 years). A total of 748 audit participants > 66 years of age returned a patient follow-up form at 3 months that detailed the impact of their condition on their ability to work. Nationally, 54 (7%) patients were not working because of their arthritis, 37 (5%) reported that they frequently required time off from work, 116 (15.5%) reported occasionally needing time off from work and 273 (36.5%) reported that they rarely needed time off from work. A total of 198 (26.5%) patients were not working, but this was not because of arthritis, or were working in a voluntary capacity only. Of note, 19% of patients reported that they had never been asked about their work by clinicians, 42% recalled being asked about employment during their consultation and no response was recorded for 39%.

Conclusion: Our findings suggest that most patients in work at the time of diagnosis with inflammatory arthritis are still working at 3 months, although a significant proportion report frequently needing time off because of their condition. This suggests that early disease may be a crucial time for assessing work instability in this patient group and offering work-related interventions before work instability translates into long-term work incapacity. Of note, the level of missing data in this first year of the audit is high; further confirmation of findings with more complete data is warranted.

Disclosure statement: The authors have declared no conflicts of interest.

150 PATIENT-REPORTED 28-JOINT DISEASE ACTIVITY SCORE IN RHEUMATOID ARTHRITIS: ITS RELIABILITY IN A LONGITUDINAL STUDY

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Background: There have been increasing studies focusing on patient-derived joint counts in RA. Patient self-reported 28-joint DAS (DAS28) with training has not been observed longitudinally in the UK. The aims of this study were to evaluate the reliability of patient self-assessment of DAS28 compared with physician DAS28 and to determine whether the agreement between patient-reported and physician-reported DAS28 improves over time with training.

Methods: This was a longitudinal study with a total of three study visits 6 weeks apart carried out at two hospital sites in the UK. All 42 patients had training on joint count self-assessment. A single physician performed joint assessments on patients independently blinded to the patients’ data. Correlations between patient and physician measurements were analysed using Spearman’s correlation coefficient, whereas agreement between patient and physician was analysed with Bland-Altman plots.

Results: There was very strong correlation between patient- and physician DAS28 with CRP, DAS28 with ESR, total joint count (TJC) and swollen joint count (SJC) (> 0.86). The limits of agreement of the DAS28 were consistent (range = –0.65 to 0.69) but exceeded the set difference of 0.6, although with a very small mean difference. The mean differences in both the TJC and SJC were small. The difference in the number of tender joints was constant, ranging from zero to four. The mean differences in SJC were similar throughout the study; with the difference in the number of swollen joints ranging from an underestimated four joints to an overestimated six joints. The difference in the number of swollen joints became smaller during the third study visit. This proved the positive effect of patient training.

Conclusion: Overall, it is reasonable to conclude that there was good agreement of tender and swollen joint assessments between patient and physician. Patient training has positive effects in increasing the reliability of patient self-assessment of joint counts. Our study showed the patient-reported DAS28 was not exactly the same as the physician-reported DAS28, although DAS28, TJC and SJC from both patient and physician were all very strongly correlated. Patient-reported joint counts were shown to have a strong predictive value and therefore could be incorporated in clinical practice. Patient DAS28 and physician DAS28 could act synergistically to reach a consensus evaluation of RA in order to achieve treatment optimisation.

Disclosure statement: The authors have declared no conflicts of interest.

151 IS THERE A LINK BETWEEN BODY HABITUS AND RHEUMATOID DIAGNOSIS?

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Background: Obesity is one of the biggest problems facing rheumatology and the wider health service and points to the need to...
We conducted a small-scale study on BMI of randomly selected AS, RA and PsA outpatients to attempt to characterize any relationship between diagnosis and BMI. A total of 254 sets of records were selected at random from an existing outpatient database. Information on each patient’s gender, date of birth, weight at diagnosis, weight at most recent consultation, height and date of diagnosis were collected. Weight and height were used to calculate a BMI at diagnosis and at present for each patient.

Results: There is a clear trend in increasing mean BMI for both sexes (Table 1) with AS < RA < PsA, although only AS males vs PsA males reached significance (P < 0.05). Correcting for age at diagnosis made no difference. The majority of patients were classified as overweight or obese both at diagnosis and currently. Only one male AS and female RA patients were classified as underweight. Against national population trends, females had a higher mean BMI than males. However, more males overall were classified as overweight or obese: AS, males 54%, females 33%; RA, males 66%, females 61%; PsA, males 86%, females 69%). With the exception of AS females, BMI increased with time in all groups.

Conclusion: The numbers are too small to draw a clear statistical conclusion, but the data support our impression of a gradation in BMI between patient diagnostic groups, with AS being smallest and PsA being largest.

Disclosure statement: The authors have declared no conflicts of interest.

152  PATIENT PERCEPTION OF TREATMENT EFFICACY, DISABILITY AND HEALTH SATISFACTION
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Background: Patient satisfaction encompasses experiences of care and treatment outcomes such as efficacy, health state and disability. Addressing these factors should improve satisfaction and patient outcomes.

Methods: A total of 115 questionnaires were randomly distributed to patients with inflammatory arthritis attending rheumatology clinics at University College Hospital, London between November 2014 and January 2015. The response rate was 90%. Questions were semi-structured, using Likert/Visual analogue scales, and focused on diagnosis, symptomatology, treatment history, health status and clinic attendance experience.

Results: RA represented 69% of inflammatory arthritis patients, 64% were female, the mean age was 50.44 years (s.d. 17.98), 5.94% of patients had a disease duration < 1 year and 57% of patients had a duration > 10 years. The current treatment regimen showed 23% to be on DMARDs alone, 33% on biologics alone and 44% on combination therapy. The mean number of drugs before the current drug regimen was 1.52 (s.d. 0.73), mean GVAS 45.87 (s.d. 29.81%). Only 17% of this perceived effective treatment regime had an HAQ score < 0.5 and 44% had a GVAS < 30. A total of 68.6% of respondents identified themselves as having a disability [mean HAQ 1.52 (s.d. 0.73), mean GVAS 45.87 (s.d. 29.81%)]. Eighty per cent of those with a perceived disability had an HAQ score > 1. Significant differences were found between patient groups, as shown in Table 1.

Conclusion: Health satisfaction is significantly linked to perceived treatment efficacy but not perceived disability levels. A high perception of disability and low perception of treatment efficacy are strongly associated with factors less commonly discussed in consultations, such as fatigue and involvement in decision-making. Interestingly, those who had low perceived efficacy levels were significantly less likely to view themselves as having a disability despite there not being a difference in HAQ scores between the two groups. This may reflect differing levels of acceptability regarding loss of function and the stigma that this brings. It is important to address the factors that influence patients’ satisfaction levels, especially when making management decisions.

Disclosure statement: The authors have declared no conflicts of interest.

153  EFFECT OF A BRIEF EDUCATIONAL INTERVENTION ON MOTIVATION FOR SMOKING CESSATION
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Background: Smoking has been associated with increased risk of developing RA, more severe disease and poor response to DMARDs. Giving up smoking is difficult and requires awareness of the ill effects of smoking, motivation, self-confidence and support. We looked at the effect on patient motivation for giving up smoking through a process of creating awareness of the ill effects of smoking.

Methods: We surveyed rheumatology outpatients with an anonymous questionnaire of demographics, smoking status, education status, employment status and awareness of the ill effects of smoking. Motivation to stop smoking was assessed on a 10 cm visual analogue scale (VAS) before and after receiving information on the adverse effects of smoking on RA. The information provided included the increased risk of RA, the severity of disease and poor response to DMARDs.

Results: Eighty-two unselected patients completed the questionnaire; 61 (74%) were female and 42 (51%) had RA. Nineteen (23%) were current smokers, 30 (37%) were never smokers and 33 (40%) were ex-smokers. Sixty-five per cent of patients in all categories had attended secondary school. Never smokers had attended university more often compared with current smokers [20% (6/30) vs 5% (1/19), P = 0.07]. More current smokers were unemployed compared with never smokers [37% (7/19) vs 6% (2/30), P = 0.0039]. Fifty-two per cent (43/82) of patients felt that they were never asked about smoking status during consultations. Using a VAS asking how important smoking is in arthritis, 55% (45/82) of patients scored > 8/10 (0 = not bad, 10 = very bad). There was no significant difference in understanding the importance of smoking on arthritis between current smokers, those who never smoked and those who gave up smoking, (mean VAS 4.17 before vs 6.17 after, P = 0.01), while 26% (5/19) showed no improvement. No patient had decreased motivation. Fifty-three per cent (10/19) of patients felt a lack of support and help prevented them from stopping smoking. Thirty-seven per cent of patients wanted smoking cessation advice via leaflets, 10% preferred verbal advice and 16% wanted to see a general practitioner. Fifty-five per cent (18/33) of ex-smokers were happy to speak to current smokers to provide tips on stopping smoking.

<table>
<thead>
<tr>
<th>HAQ, mean (s.d.)</th>
<th>1.52 (0.73)</th>
<th>1.01 (0.82)</th>
<th>0.004</th>
<th>1.28 (0.82)</th>
<th>1.43 (0.69)</th>
<th>0.578</th>
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<tr>
<td>GVAS, mean (s.d.)</td>
<td>45.87 (29.81)</td>
<td>43.63 (48)</td>
<td>0.061</td>
<td>39.44 (29.55)</td>
<td>57.17 (27.51)</td>
<td>0.009</td>
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<tr>
<td>Disease duration &gt; 10 years</td>
<td>61.8</td>
<td>46.7</td>
<td>0.050</td>
<td>66.66</td>
<td>0.066</td>
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<tr>
<td>Arthritis health satisfaction</td>
<td>76.12</td>
<td>64.52</td>
<td>0.26</td>
<td>86.49</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Presence of nocturnal joint pain</td>
<td>47.8</td>
<td>28.1</td>
<td>0.283</td>
<td>33.3</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>60.9</td>
<td>37.5</td>
<td>0.079</td>
<td>45.3</td>
<td>0.164</td>
<td></td>
</tr>
<tr>
<td>Morning stiffness &gt; 30 min</td>
<td>39.1</td>
<td>53.1</td>
<td>0.510</td>
<td>36</td>
<td>0.0007</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>68.1</td>
<td>43.8</td>
<td>0.033</td>
<td>53.3</td>
<td>0.515</td>
<td></td>
</tr>
<tr>
<td>Low mood</td>
<td>18.8</td>
<td>12.5</td>
<td>0.019</td>
<td>10.7</td>
<td>0.116</td>
<td></td>
</tr>
<tr>
<td>Interest in self-management</td>
<td>65.7</td>
<td>70</td>
<td>0.075</td>
<td>61.6</td>
<td>0.143</td>
<td></td>
</tr>
<tr>
<td>Self-identify with having a disability</td>
<td>68.6</td>
<td>31.4</td>
<td>0.743</td>
<td>93.3</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Fear of developing low in the future</td>
<td>90.6</td>
<td>90.6</td>
<td>0.848</td>
<td>93.3</td>
<td>0.040</td>
<td></td>
</tr>
<tr>
<td>Involved in decision-making</td>
<td>94.2</td>
<td>93.7</td>
<td>0.820</td>
<td>80.6</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>Given emotional support</td>
<td>74.6</td>
<td>80.7</td>
<td>0.062</td>
<td>72</td>
<td>0.452</td>
<td></td>
</tr>
</tbody>
</table>

P-values in bold are statistically significant. GVAS: generalized visual analogue scale.
**Conclusion:** This small study suggests that a brief educational intervention may motivate patients to give up smoking. A lack of support and help is one of the common difficulties patients face when they try to give up smoking. Medical staff could be more proactive and outpatient appointments are a good opportunity to promote smoking cessation.

**Disclosure statement:** The authors have declared no conflicts of interest.

**154 BIOLOGIC USE IN NHS PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS**

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**Background:** Biologic therapies have revolutionized the treatment of a range of rheumatic conditions. Clinical trials suggest that there are differences in how patients with different diseases respond to and tolerate these therapies. We evaluated the demographics and response rates of patients with RA, PsA and AS receiving biologics in the Glasgow area.

**Methods:** The Greater Glasgow and Clyde (GGC) biologic register captures the details of rheumatology patients from across Glasgow starting biologic therapy, as part of their routine clinical care. Consententing patients complete baseline questionnaires at the time of starting their biologics. Available registry data for patients with RA, PsA and AS were analysed.

**Results:** Data were available for 1271 patients with RA (\(n = 854\)), PsA (\(n = 278\)) and AS (\(n = 139\)). The average age overall was 53.2 years and 69% were female. On average, patients with RA were 10 years older (56.5 years) than those with PsA (46.3 years) and AS (46.5 years) at the time of starting biologics. The average Carstairs index was 4.34, indicating significant deprivation. Overall, 20% of patients were current smokers, with the highest incidence in those with AS (26%) compared with RA (20%) and PsA (17%). Patients with RA had on average received more DMARDs (2.5) prior to starting biologics than those with PsA (2.7) or AS (1.5). The most commonly used biologics were adalimumab and etanercept, accounting for 80% of biologics. At the time of data extraction, more patients with AS (86%) and PsA (80%) remained on their biologic compared with RA (86%). We describe some of the factors associated with stopping biologics, although data for these items are less complete.

**Conclusion:** There are differences in the demographics of patients with RA, PsA and AS starting biologics in GGC. The average number of previous DMARDs exceeds guideline requirements, particularly for AS, suggesting a high proportion of patients with peripheral joint involvement. Patients with AS and PsA were more likely to remain on their biologic than those with RA, which may reflect in part the more limited options for the former conditions. Smoking, functional impairment and deprivation remain significant issues in this population group.

**Disclosure statement:** The authors have declared no conflicts of interest.

**155 PATIENTS’ PERCEPTION AND SATISFACTION WITH WAITING TIME AT MEDICAL OUTPATIENT APPOINTMENTS**

Rosalie Magro\(^1\) and Josianne Aquilina\(^1\)

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**Background:** Patient satisfaction is an important determinant of health care quality. Decreasing waiting time is imperative in achieving patient satisfaction. The aim of this study was to determine the mean waiting time at medical outpatient appointments and to assess waiting time satisfaction. A further aim was to identify factors that affect the patients’ perceived waiting time.

**Methods:** Data were collected through questionnaire responses from 190 patients attending medical outpatient appointments between 20 March and 9 April 2013. This included demographic data, waiting time and service satisfaction, expected and perceived waiting time, level of boredom and comfort while waiting. Moreover, the actual waiting time was noted by the observer. The relationships between expected and perceived actual and perceived waiting time were in turn analysed using scatter plots and correlation coefficients. Approval to carry out this study was obtained from the university’s research and ethics committee.

**Results:** The participants had a mean age of 53 years (range 19–86), and 59% were female. On a 10-point Likert scale, the mean waiting time satisfaction was 7.1, while the mean service satisfaction was 9.3. The mean expected waiting time was 65 minutes and the mean perceived waiting time was 55 minutes. The mean actual waiting time was 51 minutes. This study revealed that as perceived waiting time increased, patient satisfaction tended to decrease consistently and significantly (\(P < 0.001\)). On the other hand, regression analysis revealed that perceived waiting time has a positive and significant linear relationship with the actual waiting time (\(P = 0.001\)) and the boredom levels of patients (\(P < 0.001\)). Patients seated comfortably had a significantly lower perceived waiting time that those who were not (\(P < 0.001\)). Perceived waiting time was not influenced by whether the patient was accompanied (\(P = 0.313\)) or being seen for the first time (\(P = 0.712\)). The patients reported that the provision of free tea or coffee, magazines or television could help reduce boredom and divert their attention, thus reducing perceived waiting time and in turn enhancing satisfaction. Eleven per cent (21 patients) suggested that the operation of free wireless Internet in the waiting area would also reduce the level of boredom during their wait.

**Conclusion:** Overall service satisfaction was extremely positive, while waiting time satisfaction was moderate. Although reducing the actual waiting time may be difficult, altering patients’ perceived waiting time may be beneficial to increase their satisfaction. This could be done by increasing their comfort and decreasing their boredom while waiting.

**Disclosure statement:** The authors have declared no conflicts of interest.

**156 THE BEST PRACTICE TARIFF FOR EARLY INFLAMMATORY ARTHRITIS—THE FIRST YEAR OF EXPERIENCE IN A LARGE URBAN DISTRICT GENERAL HOSPITAL**

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\(^1\)Rheumatology, Croydon University Hospital, London, UK

**Background:** The Best Practice Tariff (BPT) for early inflammatory arthritis (EA) was released as a national incentive for high-quality, cost-effective care. This was supported by the British Society for Rheumatology, Arthritis Research UK and the Department of Health. Inspired by this, the rheumatology department at Croydon University Hospital reconfigured their inflammatory arthritis service in order to comply with best practice recommendations. A new EA referral form was introduced, new appointments were ring-fenced for suspected EA patients and two new consultants—an associate specialist and a part-time specialist nurse—were appointed to increase capacity. The aim was to see patients within 3 weeks of referral and treat confirmed EA patients within 6 weeks. This study assesses the service before and after the introduction of these changes.

**Methods:** Initially, patients were identified over a 6 month period in 2010. A total of 46 patients were identified to have a new diagnosis of RA during those 6 months or in the last 2 years (cohort 1). Next, we identified all patients referred for suspected EA in a 1 year period from August 2014 to August 2015 (cohort 2); a total of 322 patients were identified. Data were collected from paper and electronic patient records retrospectively.

**Results:** For cohort 1, the mean age of patients was 52 years, with 71.7% females. The average time from receipt of the referral letter to the first appointment was a mean of 54.6 days (7.8 weeks). Forty-four of 46 patients were started on a DMARD on average a mean of 11 weeks after their first rheumatology appointment (mode = 5 weeks). The average time from referral to initiation of a DMARD was 19 weeks (mode = 11 weeks). Forty-eight per cent received a diagnosis at their first appointment and 20% had DMARD therapy started the same day. For cohort 2, the mean age of patients was 53 years, with 307 (95%) females. The average time from receipt of the referral letter to the first appointment was 20.3 days (2.8 weeks). A total of 162 patients did not have EIA. Of 160 EIA patients, 157 were started on a DMARD. The mean time to starting a DMARD was 32 days (4.6 weeks; range 0–340 days; mode = 20 days). The average time from referral to initiation of a DMARD was 50 days (7.1 weeks; range 0–365 days; mode = 20 days). Eighty-eight of 157 (56%) patients received a DMARD at their first appointment.

**Conclusion:** The introduction of an EIA pathway based on the BPT criteria improved waiting times not only for time to first appointment, but also time to initiation of first DMARD. This has revolutionized
patient care in the borough of Croydon and we hope will translate into improved outcomes for our patients with inflammatory arthritis.

Disclosure statement: The authors have declared no conflicts of interest.

157 WHAT DO PATIENTS WANT FROM A RHEUMATOLOGY SERVICE?
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Background: Services within the NHS are constantly seeking to improve patient care and efficiency. Patients can provide sharp insights into what is valued and necessary and thus can help shape future service delivery.

Methods: A questionnaire was developed following consultation with our patient advisory group and further input from three research patient partners. Fifteen questions were included plus further demographic information. Questionnaires were handed out to all patients attending our rheumatology outpatient department over a 2 week period. A total of 356 questionnaires were completed and returned. Only two patients declined to participate. The data were collated and analysed by two clinicians.

Results: The mean age of patients was 54 years (range 18–91) and 72% were female. The majority of patients (83%) had an inflammatory condition. There was a mix of patients with early and chronic disease. Patients valued being seen quickly over being seen close to home (72 vs 14%) or being seen by their usual clinician (37 vs 14%). Very few patients wanted to be seen by a rheumatologist in a primary care setting (<5%), a similar finding to a previous study. Patients placed high value on allied health professional services being close to or within the rheumatology department (83% scoring >8 on a Likert scale). Almost half of our patients preferred to receive appointment information by letter, with the remainder opting for telephone, text message or email contact in equal measures. Ninety-two per cent liked to receive a copy of their clinic letter accompanied by investigation results. Almost 80% of patients preferred to be seen during standard working hours. Patients in full-time employment were more likely to opt for an ‘out-of-hours’ appointment.

Conclusion: Patient surveys can provide useful insights into exactly what is important to our patients and can often shed new light onto previously held assumptions regarding service delivery. It is clear that our patients value a cohesive team unit with all care being delivered within one department. Information and communication were other aspects that patients stated were of great importance. Patients valued being seen quickly over being seen by their regular clinician. Interestingly, there was no strong push for weekend clinics, contrary to recent pressure for 7 day working throughout the NHS. The results of our survey have led to a number of positive changes within our service and our patient advisory group will continue to play an integral role in shaping our service delivery.

Disclosure statement: The authors have declared no conflicts of interest.

158 INFLIXIMAB BIOSIMILARS—SWITCHING REMICADE TO REMSIMA IN ROUTINE CARE: PATIENT ACCEPTABILITY AND EARLY OUTCOME DATA
Ritu Malaiya¹, Zoe McKee¹ and Patrick Kiely¹
¹Rheumatology, St George’s University Hospitals NHS Foundation Trust, London, UK

Background: Infliximab biosimilars (Remsima and Inflectra) have been approved by the European Medicines Agency, offering financial savings to departments and the NHS. Pan-European agreements provide both a 44% cost savings, of which 50% is retained as revenue through a 50:50 gain share agreement. We report our experience in implementing the change and the early outcome data at a single UK centre (Table 1).

Methods: The principles, science, safety and effectiveness of Remsima were reviewed at the departmental level. Remsima patient information leaflets were produced in conjunction with the Trust patient information group. A cost/benefit analysis was undertaken with informal board/ABI agreement to use revenue generated for rheumatology patients requiring biologic therapy outside of National Institute for Health and Care Excellence guidelines, prior to an individual funding request decision. Clinician and patient choice in switching was paramount. A neutral approach was maintained to avoid a positive or negative placebo effect. Opportunities for questions, open dialogue and time for reflection were given. Pre- and post-switch data were collected prospectively to monitor risk. This included demographics, underlying diagnosis, DAS, HAQ, changes in medication (including steroid rescue) and side effects. A pharmacy champion as part of the key stakeholders helped implement this change. An agreed date for swichover (May 2015), prescribing by brand name and a pharmacy policy was published.

Results: All 31 patients on infliximab consented to Remsima (one requested more time to decide). One patient was not switched (consultant decision due to uncertain recent septic arthritis). Overall, 30 patients commenced Remsima. The cost from May to August was £15,792.

Conclusion: Our experience of switching from Remicade to Remsima has been on the whole been positive. Feedback showed that reviewing evidence and providing reassurance was key to gaining patient trust, with the option of switching back to Remicade offered; this option was needed in only one case where there was no objective evidence of flare. Overall patients were keen for others to benefit from more cost-effective drugs. Our prospective data collection will be key to risk management and evaluating effectiveness over time. Our anticipated annual cost for rheumatology alone is £350,000. We believe effective planning and education (of patients and staff) prior to switching was instrumental to our early success.

Disclosure statement: P.K. has received funding for organising regional rheumatology meetings and meeting attendance and has

158 Table 1. Early outcome data with biosimilar Remsima

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean disease activity</th>
<th>Equivalent response, n = 16; subjectively worse, n = 1; discontinued after first infusion (due to unrelated medical problem), n = 1</th>
<th>Equivalent response, n = 6; subjectively worse, n = 1</th>
<th>Equivalent response, n = 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>First infusion</td>
<td>Patients, n</td>
<td>Mean disease activity</td>
<td>DAS28 = 3.65</td>
<td>BASDAI = 4.9</td>
</tr>
<tr>
<td>Second infusion</td>
<td>Patients, n</td>
<td>Mean change in disease activity</td>
<td>DAS28 = 0.04</td>
<td>BASDAI = –2.1</td>
</tr>
<tr>
<td>Third infusion</td>
<td>Patients, n</td>
<td>Mean change in disease activity</td>
<td>DAS28 = 0.48</td>
<td>Not calculated because there was only one patient</td>
</tr>
<tr>
<td>Fourth Infusion</td>
<td>Patients, n</td>
<td>Mean change in disease activity</td>
<td>Not calculated because there was only one patient</td>
<td>Equivalent response, n = 1</td>
</tr>
</tbody>
</table>

PsARC: psoriatic arthritis response criteria; TJC: tender joint count; SJC: swollen joint count.
received honoraria for participating on speakers or advisory boards for AbbVie, Amgen, BMS, Celgene, Hospira, Eli Lilly, MSD, Napp, Pfizer Roche, Samsung and UCB. All other authors have declared no conflicts of interest.

159 SCREENING FOR LATENT TUBERCULOSIS PRE-BILOGICS: PRACTICE, ACTIONS, OUTCOMES AND MISDEMEANOURS—A CROSS-SPECIALITY OBSERVATIONAL STUDY

Megan MacDiamid1, Ashley Spencer1 and Paresh Jobanputra1
1Rheumatology, University Hospitals Birmingham, Birmingham, UK

Background: Patients being considered for biologics are screened or risk assessed for tuberculosis (TB) in all medical specialities, although practice and subspecialty guidance varies. A key element of pretreatment screening, now adopted across all specialities in our hospital, is screening for latent TB using the IFN-γ release assay (IGRA). We describe test data from medical subspecialties and focus on outcomes and the management of patients testing positive.

Methods: Patients tested by IGRA, either QuantiFERON or T-SPOT, between January 2013 and September 2015 were identified from immunology laboratory databases. Those testing positive or equivocal and where biologic treatment was being considered were identified and clinical data extracted from electronic records.

Results: Between 3 January 2013 and 10 September 2015, 1088 samples from 875 patients were sent to immunology for IGRA testing. Tests were done on more than one occasion in 113 patients (tested twice), 37 patients (tested three times), 4 patients (tested four times) and 2 patients (tested five times). Of patients tested on three or more occasions, 36/40 (90%) were dermatology patients. Positive IGRA was found in 30 (3.4%) patients and an equivocal test in 29 (3.3%). Details of patient characteristics and actions taken after testing are shown in Table 1. Of the positive patients, a majority (90%) had or are awaiting chemoprophylaxis; one was found subsequently to have active TB and the patient subsequently declined biologic therapy; and one underwent extensive medical testing, including body scans, to exclude active TB. Chemoprophylaxis, when used, consisted of rifampin and was generally well tolerated (Table 1).

Conclusion: A majority of patients tested by IGRA for proposed biologic therapy for an autoimmune disease were found to be positive or equivocal and did not commence biologic therapy. Repeated IGRA tests were done, most commonly in dermatology. A majority of patients testing positive did so despite being on immunosuppressive treatment and in most cases biologic therapy was postponed until chemoprophylaxis was completed.

Disclosure statement: The authors have declared no conflicts of interest.

Table 1. Demographic data and clinical outcomes in patients testing positive or equivocal

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Self-identified ethnicity</th>
<th>RA or unspecified inflammatory arthritis</th>
<th>seronegative SpA</th>
<th>Psoriasis</th>
<th>SpA, including psoriasis</th>
<th>Immunosuppression at testing</th>
<th>TB chemoprophylaxis</th>
<th>Months of follow-up</th>
<th>Relative rate of missingness</th>
<th>Missing composite outcome data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>57.4 (47-77)</td>
<td>10/20</td>
<td>46.7</td>
<td>13.3</td>
<td>16.7</td>
<td>13.3</td>
<td>73.3</td>
<td>17/23 (73.9)</td>
<td>3/39 (10.3)</td>
<td>3/6 (50.0)</td>
<td>3/34 (9%)</td>
</tr>
<tr>
<td>Female</td>
<td>48.3 (20-81)</td>
<td>17/12</td>
<td>34.5</td>
<td>6.9</td>
<td>13.8</td>
<td>20.7</td>
<td>24.1</td>
<td>22/23 (96.7)</td>
<td>29/29 (100)</td>
<td>1/6 (16.7)</td>
<td>1/34 (3%)</td>
</tr>
</tbody>
</table>

*Includes arthropy associated with inflammatory bowel disease and AS.

160 A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS IN RHEUMATOID ARTHRITIS: THE REPORTING AND HANDLING OF MISSING DATA IN COMPOSITE OUTCOMES

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Background: The most reported outcome measures in RA trials are composite outcomes, the 28-joint DAS (DAS28) and the ACR response criteria. Trials with measurements made on the same patient repeated over time nearly always have an outcome where patients have missing values at the end of follow-up. The aims of this review were to assess the range of missing data rates in primary composite outcomes and to document the current practice for handling and reporting missing data in published RA trials compared with the Consolidated Standards of Reporting Trials (CONSORT) recommendations.

Methods: A systematic search for randomized controlled trials was conducted for RA trials published between 2008 and 2013 in four rheumatology and four high-impact general medical journals. The proportion of missing primary outcome data at the primary time point was defined as the number of patients who completed the trial divided by number of patients in intention-to-treat (ITT) analysis.

Results: Fifty-one trials with a composite primary outcome were identified, of which 38 (75%) used the binary ACR responder index and 13 (25%) used the DAS28. Forty-four (86%) of the trials reported ITT analyses, while 7 (14%) of the trials analysed the primary outcome data according to a modified ITT population and 37 (73%) trials reported both a sample size calculation and a participant flow diagram. The median missing primary composite outcome rate was 17% (interquartile range (IQR) 10–25%) with a wide range from 2.1 to 52.7%. Typically 17% of the primary composite outcome data in ITT analyses were imputed data, and this was considerably higher for some trials. The rate of missing primary outcome data was >30% in 9 (18%) trials, >20–30% in 11 (22%) trials, 10–20% in 18 (35%) trials and <10% in 13 (25%) trials. Thirty-eight trials (76%) used non-responder imputation (NRI) and 20 (40%) used last observation carried forward (LOCF) to impute missing data at the primary time point. The differential rate of dropout between active treatment and placebo was on average 61% times higher in the placebo arm compared with the treatment arm in the 34 placebo-controlled trials (relative rate 1.61 (95% CI 1.29, 2.02) (Table 1). Thirty-seven (73%) trials did not report the use of sensitivity analysis in the primary analysis.

Conclusion: This review highlights some improvement in reporting of the participant flow diagram in rheumatology trials since revision of the CONSORT guidelines, although there is a need to continue improving the reporting of missing composite outcome data and their components. In particular, the use of multiple imputation methods and sensitivity analysis needs to be more widely used in RA trials.

Disclosure statement: The authors have declared no conflicts of interest.

Table 1. Rates of missing data in placebo relative to treatment arms in placebo-controlled trials (n = 34)

<table>
<thead>
<tr>
<th>Months of follow-up</th>
<th>Relative rate of missingness</th>
<th>Missing composite outcome data</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months (n = 12)</td>
<td>1.36 (0.80, 2.39)</td>
<td>False positive composite data</td>
</tr>
<tr>
<td>6 months (n = 16)</td>
<td>1.72 (1.26, 2.93)</td>
<td>False positive composite data</td>
</tr>
<tr>
<td>12 months (n = 5)</td>
<td>1.78 (1.19, 3.64)</td>
<td>False positive composite data</td>
</tr>
</tbody>
</table>

Total (n = 34) 1.61 (1.29, 2.02) False positive composite data

161 DEVELOPMENT OF A NATIONAL WEB-BASED AUDIT TOOL

Elizabeth A. Murphy1, Jodi Birning2, Duncan Porter2, Laura McGregor1, Adrian Tan1, Nicole Amft1, Jane Harkess1, Katie McAlarey1, Neil McKay1 and Garry Milne1
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Background: Since 2009, the Scottish Society for Rheumatology (SSR) Clinical Standards Group has undertaken a project to develop a web-based audit.

Methods: An electronic web-based tool has been developed in collaboration with the Edinburgh Clinical Trials Unit. Each audit has a
The results of the six audits are as follows: podiatry: There were 50% of patients who received their preferred treatment. RA baseline: Comparing baseline data with the previous CARA audit, there was a reduction in the time to the first appointment in a similarly severe group of patients. Median symptom duration: 24 weeks (CARA = 35, 44); patients seen within 12 weeks of symptom onset: 25%; median delay to see a general practitioner: 8 weeks; median delay from referral to OPA: 39 days (CARA 10 weeks); mean DAS: 5.27 (CARA 5.3, 5.2); mean HAG: 1.192 (CARA 1.38, 1.38). RA follow-up: Median DAS at 6 months, 2.94; median DAS at 12 months, 2.90. Vaccination: A total of 495 patients were recruited from six centres in the first cycle, 178 in the second. First cycle: 76% of those <65 years of age and 86% of those >65 years of age had received a pneumococcal vaccine; 21% had been screened for hepatitis B and C. Second cycle: Similar levels of influenza vaccination were reported. Use of pneumococcal vaccine ever increased to 67.4%. Employment issues in RA: A total of 431 patients enrolled (mean age 49 years, 78% female, 66% early RA, 27% employed). Six per cent of referrals reported work issues, however, occupational therapy screening revealed 63% of patients had work problems, with 54% reporting medium-high levels of work instability. Most patients had a history of up to 2 weeks absence. GCA audit: Access to timely temporal artery biopsy was suboptimal.

Conclusion: The web-based methodology is feasible and acceptable to most units. We can gather similar volumes of data from several centres across Scotland at a fraction of the cost of previous audits. The tool is sustainable. The audit is truly multidisciplinary and has the potential to contribute to team learning and revalidation requirements, as well as improving patient outcomes.

Disclosure statement: The authors have declared no conflicts of interest.

162 RECEIVING PREFERRED TREATMENT NOT ASSOCIATED WITH POSITIVE OUTCOME IN A RANDOMIZED TRIAL

Marcus Beasley1, Elizabeth Jones1, John McBeth2, Gareth T. Jones1, Philip Hannahford3, Karina Lovell3, Deborah Symmons3, Philip Keeley3, Steve Woby3, Gordon Prescott1 and Gary J. Macfarlane1

1Musculoskeletal Research Collaboration, University of Aberdeen, Aberdeen, 2Arthritis Research UK Centre for Epidemiology, University of Manchester, Manchester, 3College of Life Sciences and Medicine, University of Aberdeen, Aberdeen, 4School of Nursing, Midwifery and Dentistry, University of Manchester, Manchester, 5School of Human and Health Sciences, University of Huddersfield, Huddersfield, 6Research and Development, Pennine Acute Hospitals NHS Trust, Manchester and 7Medical Statistics Team, University of Aberdeen, Aberdeen, UK

Background: In a randomized trial of treatments for chronic widespread pain (CWP), participants were asked their treatment preference just prior to randomisation (baseline). This analysis examined whether treatment preference was associated with baseline factors and whether receiving a preferred treatment affected outcomes.

Methods: The MUSICIAN trial was a 2 × 2 randomized trial of cognitive behavioural therapy (CBT) or exercise for people with CWP. Participants were randomly allocated to one of three active treatments [CBT (n = 112), exercise (n = 109), both exercise and CBT (n = 112)] or usual care (n = 109). Before allocation participants were asked, if they had a choice, which active treatment they would choose. A positive outcome was self-reported improvement in health of much or very much better 6, 9 and 30 months after entering the study. Associations between preference and baseline characteristics were examined, including age, gender, chronic pain grade (CPG), passive and active coping, fatigue, psychological distress, sleep problems and kinesiophobia. Differences in gender and CPG between preferences were tested by chi-square tests. For continuous variables, comparison was by analysis of variance and, where a difference was observed, Tukey’s honest significant difference was used to identify which preferences differed and then the standardized mean difference (d) with 95% CIs were calculated. Among those allocated to active treatments, logistic regression was used to calculate odds ratios, adjusted for factors associated with preference, with 95% CIs of positive outcome in those receiving their preferred treatment and not receiving preferred treatment as the referent outcome.

Results: Of 442 participants, 144 (33%) expressed preference for exercise, 20 (5%) for CBT, 199 (45%) for combined exercise and CBT and 79 (18%) expressed no preference. Compared with females, males were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%). Those preferring CBT, compared with those preferring exercise, were more likely to prefer exercise only (44 vs 28%) and less likely to prefer combined treatment (55 vs 50%).

Conclusion: Exercise and exercise combined with CBT were the most preferred treatments. Participants with specific preferences differed from each other with respect to factors which might influence outcome. However, receiving preferred treatment did not appear to influence treatment response.

Disclosure statement: M.B. has received funding for the MUSICIAN Study from Arthritis Research UK. G.J.M. has received funding for the MUSICIAN Study from Arthritis Research UK. All other authors have declared no conflicts of interest.

162 Table 1. Positive outcomes according to treatment preference

<table>
<thead>
<tr>
<th>Time after study entry</th>
<th>Did not receive preferred treatment</th>
<th>Received preferred treatment</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>Did not receive preferred treatment</th>
<th>Received preferred treatment</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
<th>Did not receive preferred treatment</th>
<th>Received preferred treatment</th>
<th>OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
<td></td>
<td>%</td>
<td>%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBT only</td>
<td>30</td>
<td>33</td>
<td>1.19 (0.20, 0.92)</td>
<td>1.63 (0.22, 12.0)</td>
<td>30</td>
<td>67</td>
<td>4.64 (0.80, 27.0)</td>
<td>0.94 (1.08, 88.5)</td>
<td>37</td>
<td>17</td>
<td>0.34 (0.04, 3.06)</td>
<td>0.43 (0.04, 4.68)</td>
</tr>
<tr>
<td>Exercise only</td>
<td>36</td>
<td>33</td>
<td>0.90 (0.37, 2.18)</td>
<td>0.56 (0.30, 1.70)</td>
<td>23</td>
<td>26</td>
<td>1.20 (0.47, 3.26)</td>
<td>1.03 (0.33, 3.32)</td>
<td>25</td>
<td>37</td>
<td>1.81 (0.73, 4.52)</td>
<td>1.32 (0.44, 3.97)</td>
</tr>
<tr>
<td>Combined CBT</td>
<td>42</td>
<td>33</td>
<td>0.69 (0.30, 1.61)</td>
<td>0.70 (0.27, 1.81)</td>
<td>35</td>
<td>37</td>
<td>1.08 (0.48, 2.45)</td>
<td>0.86 (0.34, 2.18)</td>
<td>27</td>
<td>35</td>
<td>1.51 (0.62, 3.68)</td>
<td>1.16 (0.30, 3.46)</td>
</tr>
<tr>
<td>All active treatments</td>
<td>34</td>
<td>33</td>
<td>0.95 (0.56, 1.62)</td>
<td>0.96 (0.55, 1.68)</td>
<td>29</td>
<td>34</td>
<td>1.28 (0.76, 2.16)</td>
<td>1.07 (0.61, 1.89)</td>
<td>30</td>
<td>35</td>
<td>1.23 (0.71, 2.11)</td>
<td>1.13 (0.52, 2.09)</td>
</tr>
</tbody>
</table>

CBT: cognitive behavioural therapy.


Background: Early diagnosis and treatment of inflammatory arthritis is well established as a predictor of better long-term outcome for patients. The National Institute for Health and Care Excellence Quality Standard 1 (QS1) recommends that patients with persistent symptoms be referred to secondary care within 3 days of presentation to primary care.

Methods: The national audit for rheumatoid and early inflammatory arthritis (EIA) assesses care provided to individuals >16 years of age presenting for the first time to specialist rheumatology units in England and Wales with EIA. Data were collected from secondary care units for all such patients and included the date the patient first presented to primary care with persistent symptoms and the date of referral for specialist assessment. Data collected over the first year (1 February 2014–31 January 2015) of this ongoing audit are reported.

Results: In total, 135 secondary care units participated in data collection (84% of possible units in England and Wales). Data were available from 6354 patients, of whom 1072 (17%) were referred within 3 days of presentation. There was substantial variation in the ability to meet QS1 across geographical regions, with as few as 11% achieving QS1 in the Midlands and East of England, compared with 40% in Wales (see Table 1). The median interval between presentation to primary care and receipt of referral in secondary care was 34 days nationally. All NHS regions were receiving referrals from primary care on the day that the patient first presented to primary care. All NHS regions reported delays of >350 days from the date a patient reported >n1. Advice given by the NHS Choices and WebMD symptom checkers, according to clinical diagnosis

The authors have declared no conflicts of interest.

Disclosure statement: The authors have declared no conflicts of interest.

Background: The early introduction of DMARDs leads to improved outcomes in RA. Despite this, patients often wait for prolonged periods before seeking advice from health care professionals. Patients with early symptoms may seek information online when deciding whether they need to seek medical attention. Health information is increasingly obtained via the Internet: NHS Choices receives on average of >10 million visits each week. There are a number of online symptom checkers that direct patients to an appropriate source of health care and self-diagnosis tools that provide a specific diagnosis or a series of differential diagnoses. The objective of our study was to evaluate how patients with inflammatory arthritis use the Internet to look for health information and assess the advice given by the NHS symptom checker and WebMD symptom checker in relation to the patient’s actual diagnosis.

Methods: Thirty-four patients [23 females; ages 27–81 years; median (IQR) 65 (34–102) years] newly presenting to a secondary care rheumatology unit for the first time were recruited to this study. A questionnaire was used to evaluate how patients used the Internet regarding their symptoms but only two patients had used a WebMD review.

Results: Forty-seven per cent of patients had previously consulted the Internet regarding their symptoms, but only two patients had used a symptom checker. Neither age nor gender significantly influenced Internet usage. The advice given by the NHS symptom checker and the five most common differential diagnoses given by WebMD are summarized in Table 1. Forty-four per cent of patients were inappropriately advised to call an ambulance or attend an accident and emergency department by NHS Choices. The most common first differential diagnosis given by WebMD was OA (35%), with only 19% patients with inflammatory arthritis given a first diagnosis of PsA or RA.

Conclusion: Our data highlight that advice given online is often inappropriate and that suggested diagnoses are frequently inaccurate. NHS Choices inappropriately directs people to emergency care, whereas the suggestion of OA by WebMD might delay help-seeking from health care professionals.

Disclosure statement: The authors have declared no conflicts of interest.

Background: Physician–patient communication in the assessment and management of rheumatic diseases can have significant impact on patients’ health-related quality of life. The aim of this review was to synthesize and systematically appraise the literature reporting on this standard relies upon information supplied within a referral letter or upon patient recall of their first consultation with their GP and will be subject to some degree of bias. Despite limitations, there is sufficient evidence to indicate that there is a significant delay between first presentation to a GP and referral to rheumatology for most patients. These data indicate that rheumatology services, GPs, commissioners and patient organisations need to work together to raise public awareness of the importance of seeking early medical assessment and care if they have potential symptoms of inflammatory arthritis, promote timely referral by primary care, and highlight organisational barriers that impede access to specialist care and address them.

Disclosure statement: The authors have declared no conflicts of interest.

RHEUMATOLOGY: A SYSTEMATIC REVIEW

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Physician–patient communication in rheumatology: a systematic review

Background: Physician–patient communication in the assessment and management of rheumatic diseases can have significant impact on patients’ health-related quality of life. The aim of this review was to synthesize and systematically appraise the literature reporting on the use of communication skills to improve patient outcomes.

Methods: A systematic search of electronic databases and the Cochrane central register of controlled trials was conducted. Studies meeting the inclusion criteria were included. The quality of studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.

Results: Twenty-five studies met the inclusion criteria. The quality of evidence was rated as low for most of the studies. There was no evidence to support the use of specific communication skills to improve patient outcomes. However, several studies demonstrated that patient-centered communication improved patient satisfaction and satisfaction with care.

Conclusion: The evidence from this review suggests that patient-centered communication improves patient satisfaction and satisfaction with care. Further research is needed to explore the impact of communication skills on patient outcomes.

Disclosure statement: The authors have declared no conflicts of interest.
physician–patient communication in rheumatology with the goal of identifying potential gaps and challenges in this area.

**Methods:** We performed a systematic search of published scientific literature using five standard bibliographic databases (Medline, PsycInfo, Embase, CINAHL, Web of Science). Inclusion criteria included participants ≥18 years with a diagnosis of a rheumatological condition; quantitative, qualitative or mixed methods research studies; surveys, observational and interventional studies; papers published in the English language and studies reporting findings on either variable.

**Results:** A systematic search of online databases from earliest record to January 2015 identified 455 relevant articles. Keywords and text words focused on terms related to communication factors and clinician–patient interaction. Removal of duplicates and title and abstract filtering yielded a total of 20 studies. After full-text assessment for eligibility, 11 studies were included in the review: 7 qualitative and 4 quantitative papers. Following quality assessment, data were extracted. Overall, it appeared that higher levels of trust in the physician and more active patient participation in the medical consultation were linked to lower disease activity, better global health, less organ damage accrual, greater treatment satisfaction with fewer side effects from the medication and more positive beliefs about control over the disease as well as about current and future health. Specifically, more active patient participation in visits was associated with less permanent organ damage and less organ damage accrual over time; poor communication between patients and doctors was associated with medication non-adherence; mutual respect, trust and expert knowledge were factors for establishing good communication with rheumatology staff as well as taking on responsibility and being acknowledged as an expert on their own bodies; informativeness, sensitivity to concerns and patient–centredness were independently predictive of trust in physicians, which in turn was associated with the quality of the doctor–patient relationship, disease activity and poorer health.

**Conclusion:** Despite the limited number of papers included in this review, the evidence highlighted the importance of the role of communication and positive interaction between clinician and patient as well as its potential impact on patient outcomes. Future research could focus on the design and implementation of interventions incorporating communication skills and patient education training to increase physician–patient communication and improve patient outcomes.

**Disclosure statement:** The authors have declared no conflicts of interest.

166 METHOTREXATE LONGEVITY IS LIMITED BY NAUSEA: PROPHYLACTIC ANTI-EMETICS AND EARLY SUBCUTANEOUS PREPARATION MAY IMPROVE PATIENT COMPLIANCE AND SAVE MONEY Vishal P. Patel1, Elizabeth Price2, David Collins2 and Lyn Williamson2

1Faculty of Health Sciences, University of Bristol, Bristol and
2Rheumatology, Great Western Hospital, Swindon, Swindon, UK

**Background:** MTX is the anchor DMARD in current rheumatology practice because of its safety, efficacy and longevity profiles. It is common practice to commence patients on oral MTX and switch to the s.c. preparation for intolerance or inefficacy. During this time, patients suffer because of poor disease control and side effects. Furthermore, failure of MTX therapy leads to escalation to more costly combinations and biologic DMARDs.

**Methods:** We aimed to look at s.c. MTX use across 10 years (2004–2015), reasons for stopping and concomitant DMARD use. Patients with complete data sets prescribed s.c. MTX via our DAWN monitoring system were included. We retrospectively analysed data from the years 2004 to 2008 (139 patients) and 2014 (51 patients).

**Results:** The modal weekly starting dose of s.c. MTX was 15 mg [mean 16.2 mg (range 7.5–30)]. This increased to 25 mg [mean 18.5 (range 5–30)] after 1 year. A total of 45.0% (31/69) stopped because of nausea, 8.7% (6/69) stopped due to feeling unwell, 7.2% (5/69) in injection anxieties/difficulties, 5.7% (4/69) due to vomiting and preference for the oral preparation or another DMARD, 3.6% (2/69) due to economic circumstances, 3.6% (2/69) due to feeling unwell, 7.2% (5/69) had other reasons (alopecia, deranged liver function tests, shingles, interstitial lung disease, diarrhoea or lack of effect). From the 2004 cohort, 25/51 (49%) stopped in less than 1 year. Reasons for stopping included nausea [30% (25/83)], disease [40% (10/25)], because they wanted to have children [8% (2/25)] and other reasons [infective patients, unwell, patient preference, undocumented reasons; 26% (7/25)]. From the 2004–9 cohort, 6.5% (9/139) stopped before 1 year, 7.2% (10/139) stopped after 1 year, 25.9% (36/139) stopped after 3 years, 62.6% (87/139) continued for 5 years and 13.7% (19/139) had taken s.c. MTX for >10 years. In the 2004–09 cohort the modal number of additional DMARDs used before switching from oral to s.c. MTX was 2 (range 0–27) [27% (20/19); mean 2 (range 0–4)]. After switching, the modal number of additional DMARDs decreased to 1 (33% (46/139); mean 3 (range 0–6)) with a P-value < 0.05.

**Conclusion:** In our patients, switching from oral to s.c. MTX was associated with increased modal dose from 15 to 25 mg weekly and fewer concomitant DMARDs. Two-thirds of patients continued for >5 years and this shows its longevity. Nausea is the reason for failing s.c. MTX in almost half the patients. We suggest using prophylactic anti-emetic at initiation to prevent nausea and the development of avoidance patterns. This may pre-empt treatment failure and the associated costs of escalation to combination and biologic DMARDs.

**Disclosure statement:** The authors have declared no conflicts of interest.

167 QUANTIFYING THE USE OF NHS HEALTH CARE RESOURCES FOR PATIENTS WITH RHEUMATOID ARTHRITIS, COMPARING HIGH AND LOW/REMISSION DISEASE STATES Bruce Kirkham1, Alexandra Vincent1 and Alison Elliott2

1Rheumatology, Guy’s and St Thomas’ NHS Foundation Trust, London and 2Market Access Directorate, Roche Products, Welwyn Garden City, UK

**Background:** Efficient use of resources is a priority for the NHS. Patients with RA have many different needs and rely on a multi-disciplinary team for all aspects of their care. One of the main costs of treating patients with RA is the high cost of drugs. Guy’s and St Thomas’ NHS Foundation Trust (GSTT) and Roche Products entered into a collaborative project to identify the actual health care resources used by patients with RA were using in the Trust. The objective of this project was to identify the real medical costs of treating patients with RA who were in a high vs low disease state or remission.

**Methods:** Anonymized data from the GSTT RA Centre database of 1700 patients with RA was used to form two groups with high 28 joint DAS (DAS28 > 5.1) scores and low DAS scores or remission. The groups had 60 patients, matched in terms of age, sex and duration of disease. Patients with co-morbidities such as significant chronic medical conditions, cancer and fibromyalgia were excluded from either group to ensure comparable groups. We calculated mean HAQ Disability Index (HAQ-DI) and EuroQol five-dimensions questionnaire (EQ-5D) values for each group. This initial report contains data of pharmaceutical expenditures in the GSTT from August 2013 to September 2015.

**Results:** The mean for HAQ-DI and EQ-5D was 1.78 (range 0.15–2.92) and 0.286 (range 0.619 to 0.239), respectively, for patients with high disease activity and 0.70 (range 0–2.31) and 0.714 (range 0.258–1), respectively, for patients with low disease activity. The total GSTT pharmaceutical costs were £390 904 (with biologic drug costs of £377 507) for patients with high disease activity and £324 805 (with biologic drug costs of £321 401) for patients in low disease activity. Seventeen patients in the high DAS group took concomitant prednisolone compared with five in the low DAS group.

**Conclusion:** This study uses real-world evidence to identify the Trust level costs of treating patients with RA who have different disease activity. Poor function and quality of life for those people with high disease activity despite a greater use of concomitant steroids and biologic DMARDs.

**Disclosure statement:** B.K. has received consulting fees from Eli Lilly and Novartis; has received honoraria from AbbVie, BMS, Amgen, Celgene, Novartis and Eli Lilly; has participated in speakers bureaus for AbbVie, Janssen and MSD and has received research funding from AbbVie, Novartis and Roche. A.E. is an employee of Roche Products. The other author has declared no conflicts of interest.

168 DISEASE-MODIFYING ANTI-RHEUMATIC DRUG PRESCRIBING BY CLINICAL COMMISSIONING GROUP: A SURROGATE MARKER FOR SERVICE ACTIVITY David A. Collins1 and Rheumatology, Great Western Hospitals NHS Foundation Trust, Swindon, UK

**Background:** Raising the profile of early aggressive management of inflammatory arthritis and working towards uniformity of care across the country have been the thrust of recent initiatives by the British Society for Rheumatology and National Institute for Health and Care Excellence.
Methods: Openprescribing.net is a publically available resource to simplify analysis of NHS prescribing data published monthly by the Health and Social Care Information Centre. Analysis of all prescribed drugs is available by practice and by clinical commissioning group (CCG). Using this tool, we reviewed prescribing patterns for MTX, SSZ, LEF and HCQ with regard to the average number of prescriptions issued nationally per month between January and June 2011 compared with January–June 2015 and also prescriptions per 1000 population (Rx/1000) from January to June 2015 by the 211 CCGs in NHS England.

Results: Analysis of the numbers of prescriptions issued reveals an increase in utilization for all four drugs: MTX, +17.5% (140 442/month increasing to 165 025/month); SSZ, +10.2% (81 467/month to 72 755/month); LEF, +25.0% (11 028/month to 13 791/month); HCQ, +67% (48 356/month to 81 127/month). The number of prescriptions by CCG reveals a typical ski slope graph. As the data are based on primary care prescribing and in some CCGs the responsibility for DMARD prescribing lies wholly within secondary care, the lowest prescribing 10% of CCGs were excluded from the analysis. For all drugs there is considerable variation between the lowest and highest prescribing regions (Table 1), and although there is less difference between the mode and highest, there remains an up to 2.8-fold difference.

Conclusion: Although other disciplines use these medications, local analysis suggests that rheumatoid conditions are the main driver of prescriptions. There has been little change in the prescribing patterns for other disciplines, so we feel these data provide a reliable longitudinal surrogate marker of rheumatology activity. The lowest vs highest mode to highest difference in CCG prescribing suggests the bottom 10% cut-off is probably not enough and there is a greater reliance on secondary care prescribing than anticipated. The increase in the total number of prescriptions suggests that the message of early aggressive therapy is getting through. The marked increase in HCQ suggests that the message of combination therapy is likewise taking hold. However, the increase in LEF prescribing seems to coincide more with the price reduction as it came off patent. With different local policies, the lowest: highest ratio between CCGs is probably not reliable, but this variation between mean to highest suggests that there are still regional differences that need to be reviewed.

Disclosure statement: The authors have declared no conflicts of interest.

168 Table 1. A comparison of timelines pre- and post-pathway

<table>
<thead>
<tr>
<th>Time point from GP referral date to</th>
<th>Pre-pathway, median, days</th>
<th>Post-pathway, median, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commencing steroid therapy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Specialist consultation</td>
<td>8</td>
<td>4.5</td>
</tr>
<tr>
<td>Temporal artery ultrasound</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Temporal artery biopsy</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>Temporal artery histology report</td>
<td>19</td>
<td>12.5</td>
</tr>
</tbody>
</table>

169 STREAMLINING THE PATIENT PATHWAY: THE GIANT CHALLENGE IN TEMPORAL ARTERITIS

Nicholas R, Fuggle1, Chai Ling2, Matthew Martinucci1 and Nidhi Sofat1
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Background: GCA is a large vessel vasculitis associated with significant morbidity in the form of visual loss and stroke. It is important that GCA patients have a swift passage from diagnosis to the commencement of steroid therapy and to timely temporal artery biopsy (TAB) that will maximize diagnostic potential.

Methods: We gathered a cohort of patients with suspected GCA and retrospectively analyzed the management pathway. Following this initial data collection we convened a multidisciplinary committee (including rheumatologists, acute medics, vascular surgeons and ophthalmologists). The aim was to streamline the process from clinical review to commencing steroid therapy and performing TAB and temporal artery US. We then re-audited to evaluate the effectiveness of the intervention.

Results: Data were collected on 75 patients in total, 19 pre-pathway and 56 post-pathway. In keeping with the demography of the disease, 56 (75%) were female and the majority of those in whom race was identified were white British. Although there was no statistically significant difference between the pre- and post-pathway timeline (likely due to insufficient power), there was a strong trend towards a reduction in time to commencement of steroids, first specialist consultation, temporal artery US, TAB and histological reporting, as shown in Table 1. However, when post-pathway patients who were referred from general practice with a primary clinical suspicion of GCA were analysed, there was a significant reduction in the time to TAB (P = 0.002) and reporting (P = 0.003). There was also a marked increase in the number of patients seen first by patients seen first by rheumatologists (47% to 66%) and a concurrent reduction in those seen by general medicine on the acute medical unit (21% to 9%) following the commencement of the pathway.

Conclusion: The introduction of a coordinated, multidisciplinary patient pathway for GCA resulted in a reduction in the time taken for patients to receive specialist rheumatology clinical review, important investigations and more timely treatment and the avoidance of serious complications. It can also channel patients with GCA to specialist rheumatology review and relieve pressure on the acute medical unit.

We make recommendations for the replication of this model in other departments.

Disclosure statement: The authors have declared no conflicts of interest.
170 Table 1. New and follow-up patients attending rheumatology clinics in July 2015

<table>
<thead>
<tr>
<th>Follow-up patients</th>
<th>n (%)</th>
<th>Age, years (mean)</th>
<th>Discharged, n (%)</th>
<th>Next follow-up, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>AS/AxSpA</td>
<td>48 (5.3)</td>
<td>49.3 (16.6)</td>
<td>1 (2.08)</td>
<td>7.1</td>
</tr>
<tr>
<td>Crystal (gout/pseudogout)</td>
<td>21 (2.3)</td>
<td>61.0 (16.2)</td>
<td>3 (14.3)</td>
<td>5.1</td>
</tr>
<tr>
<td>FM/chronic pain</td>
<td>13 (1.4)</td>
<td>47.4 (12.5)</td>
<td>9 (69.2)</td>
<td>7.5</td>
</tr>
<tr>
<td>Other inflammatory arthritis</td>
<td>60 (6.7)</td>
<td>53.4 (16.3)</td>
<td>2 (3.3)</td>
<td>5.6</td>
</tr>
<tr>
<td>JA</td>
<td>4 (0.4)</td>
<td>26.8 (10.3)</td>
<td>0 (0)</td>
<td>4.0</td>
</tr>
<tr>
<td>Osteoporosis/MIBID</td>
<td>9 (1.0)</td>
<td>58.2 (19.9)</td>
<td>2 (22.2)</td>
<td>9.0</td>
</tr>
<tr>
<td>PsA</td>
<td>89 (9.9)</td>
<td>63.5 (12.6)</td>
<td>1 (11)</td>
<td>6.6</td>
</tr>
<tr>
<td>RA</td>
<td>447 (42.9)</td>
<td>67.2 (13.3)</td>
<td>3 (7)</td>
<td>6.7</td>
</tr>
<tr>
<td>Soft tissue/OA/other</td>
<td>96 (10.7)</td>
<td>58.0 (38.0)</td>
<td>40 (42.1)</td>
<td>6.2</td>
</tr>
<tr>
<td>Vasculitis/PmR/CTD, total</td>
<td>113 (12.6)</td>
<td>59.2 (15.6)</td>
<td>5 (45)</td>
<td>6.3</td>
</tr>
</tbody>
</table>

New patients

| RA                | 32 (9.9) | 57.4 (17.2) | 1 (3.2) | 29.9 |
| AS/AxSpA          | 11 (3.4) | 45.5 (13.8) | 0 (0)   | 3.0  |
| Crystal (gout/pseudogout) | 18 (5.6) | 55.3 (13.6) | 3 (16.7) | 12  |
| FM/chronic pain   | 38 (11.8) | 45.5 (11.6) | 28 (73.7) | 5.7 |
| Other inflammatory arthritis | 42 (32.9) | 49.1 (15.6) | 1 (2.4) | 3.0 |
| Osteoporosis/MIBID | 26 (11.8) | 67.7 (13.4) | 6 (23.1) | 5.2 |
| PsA               | 11 (3.4) | 58.1 (16.0) | 0 (0)   | 4.1  |
| Soft tissue/OA/other | 105 (32.9) | 52.5 (16.1) | 69 (65.1) | 3.8 |
| Vasculitis/PmR/CTD | 38 (11.8) | 57.5 (17.5) | 14 (33.3) | 6.0 |

Follow-up, total

| RA                | 900 (56.7) | 59.0 (15.0) | 66 (7.4) | 6.5 |
| AS/AxSpA          | 13 (12)   | 59.0 (15.0) | 1 (3.2) | 29.9 |
| Crystal (gout/pseudogout) | 18 (16)    | 59.0 (15.0) | 1 (3.2) | 29.9 |
| FM/chronic pain   | 38 (11.8) | 45.5 (11.6) | 28 (73.7) | 5.7 |
| Other inflammatory arthritis | 42 (32.9) | 49.1 (15.6) | 1 (2.4) | 3.0 |
| Osteoporosis/MIBID | 26 (11.8) | 67.7 (13.4) | 6 (23.1) | 5.2 |
| PsA               | 11 (3.4) | 58.1 (16.0) | 0 (0)   | 4.1  |
| Soft tissue/OA/other | 105 (32.9) | 52.5 (16.1) | 69 (65.1) | 3.8 |
| Vasculitis/PmR/CTD | 38 (11.8) | 57.5 (17.5) | 14 (33.3) | 6.0 |

**New patients**

As AxSpA, axial spondyloarthropathy; MIBD, metabolic bone disease.

* Patients also seen in treat-to-target clinic. Excludes patients discharged from clinic.

**171 CLINICAL AND PATIENT-REPORTED OUTCOMES FROM THE NATIONAL CLINICAL AUDIT FOR RHEUMATOID AND EARLY INFLAMMATORY ARTHRITIS**

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**Background:** The 28-joint DAS28 (DAS28) uses clinician and patient-derived measures to assess the activity of RA. High disease activity (HDA), intermediate disease activity (IDA) and low disease activity (LDA) are defined as DAS28 >5.1, 3.2–5.1 and <3.2, respectively; a DAS28 reduction of >1.2 represents a clinically meaningful response. The RA Impact Disease (RAID) score is a validated patient-reported outcome tool for RA; a decrease in score of 3 is considered clinically significant. Both these outcome measures have been collected within the National Clinical Audit for Rheumatoid and Early Inflammatory Arthritis (EIA).

**Methods:** The National Clinical Audit for Rheumatoid and EIA assesses care provided to individuals >16 years of age presenting for the first time to specialist rheumatologist units in England and Wales with EIA. DAS28 and RAID scores have been recorded, where available, for all EIA patients at baseline and for RA patients after 3 months of specialist care; data are presented for the first year of this audit.

**Results:** A total of 6354 baseline forms were submitted from 135 (94%) Trusts between 1 February 2014 and 31 January 2015 and 3107 clinician and 1217 patient follow-up forms by 30 April 2015. For those with available DAS28 at baseline, the mean score was 5.0 (SD, 1.4) with 50%, 45% and 10% of patients having HDA, IDA and LDA, respectively. Baseline DAS28 were unavailable in 277 (9%) RA patients.

**Disclosure statement:** The authors have declared no conflicts of interest.

172 ACUTE RHEUMATOID MIGRAINUS ARE INCREASING: A SERVICE EVALUATION OF MORE THAN 1000 CONSECUTIVE ACUTE INPATIENT REFERRALS FROM A TERTIARY CENTRE

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**Background:** Historical data suggest the inpatient workload forms a small proportion of a rheumatologist’s practice. There are limited contemporary data describing acute inpatient rheumatology provision. At Queen Elizabeth Hospital Birmingham, an electronic prescribing and management system has been used for many years, and since 2010 a full outpatient electronic record. Electronic systems allow cross-speciality referral for inpatients and a comprehensive record of referrals to the rheumatology service is available. The objective of this service evaluation is to describe the nature, pattern and source of these inpatient referrals.

**Methods:** All inpatient rheumatology referrals over a 41 month period from 1 January 2011 to 31 May 2014 were identified from electronic records. The setting was Queen Elizabeth Hospital Birmingham, a 1200-bed NHS teaching hospital. Referrals were exported to a database, including date, time, referring clinician, referring ward and typed referral text. Data were analysed in two steps. First, we explored demographic data, referrer location and referral trends. Second, we reviewed the case mix of the referrals. To do this we excluded repeat referrals for a single admission and referrals lacking sufficient data for a provisional diagnosis. Our project was registered with the Trust audit department. We coded each referral against a modified International Classification of Diseases, 10th Revision 2010 musculoskeletal system and connective tissue disease list, as a known or suspected diagnosis.

**Results:** There were 1386 new referrals sent to rheumatology (mean 33.8/month, 405.6/annum). Referrals increased significantly month to month (Pearson’s r = 0.54, P < 0.001, large effect size). Referrals per annum were 332 in 2011, 361 in 2012 and 503 in 2013. There were 2.8 referrals/month per 100 inpatient hospital beds. The most common referral location was the acute medical unit (369 (26.6%)), with significant referrals from surgical specialties (299 (21.57%)). After excluding repeat referrals for a single admission and those lacking referral information [222 (16.0%)], 1162 were left, and these were ultimately coded against 28 diagnoses. Overall there were 667 (57.4%) referrals for a pre-existing problem. The six most common suspected diagnoses were as follows (new referrals in parentheses): gout, 229 (80); RA, 152 (20); OA, 102 (19); SLE, 97 (19); vasculitis, 88 (88); GCA, 52 (35).

**Conclusion:** Our data indicate that the burden of inpatient referrals for rheumatology advice is increasing in substantially. We suspect our data, though based on a single large tertiary referral centre, are generalizable to other similar hospitals. Our data have implications for ensuring good rheumatology skills for trainees in medical specialties.

In particular, we perceive a need for better knowledge of gout. In addition, our data have implications for consultant and specialist registrar job plans, as many rheumatology services do not have
The authors have declared no conflicts of interest.

MUSCLE DISORDERS

173 MYOSITIS AUTOANTIBODIES: UTILITY OF AN EXTENDED PANEL TEST
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Background: Idiopathic inflammatory myopathies (IIMs) constitute a group of heterogeneous systemic diseases including polymyositis, dermatomyositis, sporadic inclusion body myositis, necrotising autoimmune myositis and overlap myositis. Autoantibodies, directed towards nuclear and cytoplasmic antigens, are present in 50 to 80% of patients with IIMs. Some are specific for autoimmune myositis [myositis-specific antibodies (MSAs)], while others are shared with several autoinimmune rheumatic diseases and are mostly found in myositis overlap syndromes [myositis-associated antibodies (MAAs)]. Antibodies are important to guide the diagnosis/classification and prognosis of IIMs. Our objective was to assess the utility of an extended panel of myositis antibodies in patients with suspected IIM.

Methods: We performed an observational retrospective study in all the patients who were tested for the extended panel of myositis antibodies (Euroline Myositis Profile 3, Euroimmun, Lübeck, Germany) in University College London Hospitals between February 2014 and June 2015. The panel comprises 10 antibodies: five antisynthetase antibodies (Jo-1, PL-7, PL-12, EJ and OJ), anti-SRP, anti-Mi-2, anti-Ku, anti-PM-Scl-100 and anti-PM-Scl-75. The list of patients was obtained through the immunology laboratory and then the individual clinical files were reviewed to obtain demographic data, creatinine kinase (CK), muscle weakness and/or myalgia associated with elevated serum CK was the main reason for the request (57%). Twenty-one patients (16%) had at least one autoantibody identified, however, only 18 of these patients had a definite diagnosis of IIM (Table 1). In 37 of 55 patients (67%) with a diagnosed IIM, no MSA or MAA were identified, although five of them had ANA.

Results: A total of 138 tests were performed, comprising 134 patients (53 males, 81 females) with a mean age of 53 years (s.d. 15). Most requests came from rheumatology (48%) and neurology (45%). Muscle weakness and/or myalgia associated with elevated serum CK was the main reason for the request (57%). Twenty-one patients (16%) had at least one autoantibody identified, however, only 18 of these patients had a definite diagnosis of IIM (Table 1). In 37 of 55 patients (67%) with a diagnosed IIM, no MSA or MAA were identified, although five of them had ANA.

Conclusion: Given that our previous panel of IIM antibodies was restricted to detection of anti-Jo-1 and anti-PM-Scl, our data showed nine IIM patients (50%) had myositis antibodies that would not have been discovered without the use of the extended panel. However, this extended panel seems to offer a limited advance, although a negative result, especially in the absence of an ANA test, should alert the clinician to the possibility of another condition, such as muscular dystrophy or cancer-associated myositis.

Disclosure statement: The authors have declared no conflicts of interest.

174 A DIAGNOSTIC AND TREATMENT CHALLENGE: THE PREVALENCE AND CLINICAL ASSOCIATIONS OF ANTI-HMG-COA REDUCTASE AUTOANTIBODIES IN A LARGE UK JUVENILE-ONSET MYOSITIS COHORT
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Background: Autoantibodies directed against 3-hydroxy-3-methylglutaryl-CoA reductase (HMGR) have been described in patients with necrotising autoimmune myositis (NAM) associated with statin use, although <60% of patients have a history of statin exposure. Data on those with juvenile-onset disease are very limited; anti-HMGR has been identified in juvenile NAM patients who, similar to adults, can present with both rapidly progressive and more insidious muscle weakness. We aimed to establish the prevalence and clinical associations of anti-HMGR in a large UK juvenile-onset myositis cohort.

Methods: Serum samples and matched clinical data were obtained from 386 patients with JDM recruited to the UK Juvenile Dermatomyositis Cohort and Biomarker Study. After initial screening for the presence of autoantibodies by immunoprecipitation, the presence of anti-HMGR was assessed by ELISA using recombinant antigen.

Results: Anti-HMGR autoantibodies were detected in four patients (1%). They were mutually exclusive and not found in conjunction with

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any other myositis-specific or -associated autoantibody. While results were insufficient for statistical analysis, based on the Childhood Myositis Assessment Score and Physician Global Assessment score, these children were both weaker and had greater disease activity than others (Table 1). Two children presented with severe disease that was difficult to control despite aggressive immunotherapy, including i.v. CYC, IVIG and biologics. Due to poor treatment response, both were subsequently investigated for possible muscular dystrophy. Two children presented with more insidious disease onset in the absence of any skin rash, again leading to diagnostic difficulty and the consideration of muscular dystrophy. All children had elevated serum creatinine kinase for prolonged periods and all ultimately received biologic therapies.

Conclusion: Anti-HMGCR autoantibodies are rare in UK children with juvenile-onset myositis but are associated with severe disease that is poorly responsive to treatment. All children identified had absent or minimal skin involvement, and anti-HMGCR testing may help to confirm the diagnosis of myositis and prevent further potentially unnecessary investigations. Patients with anti-HMGCR require long-term aggressive treatment and have a very slow recovery. Autoantibody testing would also be clinically useful to inform prognosis, so that patients and their parents can be forewarned they should not expect a quick recovery.

Disclosure statement: The authors have declared no conflicts of interest.

175 MYOSITIS-SPECIFIC AUTOANTIBODIES RARELY COEXIST WITH EACH OTHER: AN ANALYSIS OF THE UKMYONET AND EUMYOonet COHORTS

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Background: Myositis autoantibodies have traditionally been divided into myositis-specific (MAAs) and myositis-associated autoantibodies (MAAs). The MSAs are nearly exclusively found in PM or DM, whereas the MAAs are found in patients with myositis-CTD overlap conditions. While an individual patient may have multiple MAAs, it has generally been regarded that the MSAs are mutually exclusive. To test this assumption, we screened a large cohort of adult PM and DM patients for MAAs/MAAs and analysed the data for the presence of coexisting autoantibodies.

Methods: A total of 1637 adult myositis PM or DM patients recruited to the UKMyoNet or EuMyoNet cohorts were investigated for MAAs/MAAs by radiolabelled immunoprecipitation using K562 cell extracts. Patients immunoprecipitating a band at approximately 140kDa where further investigated by NXP2 or MDA5 ELISAs to confirm the presence of these autoantibodies.

Results: Autoantibodies (MAAs: PMScI, snRNP, Ku, uRNP, P060, La, RNA Pol II/III, ARA, Topo isomerases; MAAs: Jo-1, PL12, P17, EJ, KS, Zo, OJ, SRP, Mz-2, TIF1, SAE, NXP2 and MDA5) were found in 1009 (61.6%) patients recruited to the study. Of the autoantibody-positive patients, 856 (84.7%) had a single MSA or MAA, 131 (13.0%) had two MSAs/MAAs and 23 (2.3%) had three or more MSAs/MAAs. When two or more MSAs/MAAs occurred simultaneously, 80 incidences were of coexisting MAAs, 120 occurrences were between an MSA and MAA and only 3 instances were due to coexisting MSAs (see Table 1).

Conclusion: While many hospitals have limited availability for testing of the full myositis autoantibody repertoire, most routine labs are able to screen for the more common MSAs/MAAs. While the majority of patients will only have one MSA/MAA, the results from our study demonstrate that when an MAA alone is found by standard testing, it is still worth continuing with additional specialist screening for a further MSA. Furthermore, the coexistence of MSAs is extremely rare, emphasising their importance in identifying pathogenic pathways and potential biomarkers for precision medicine.

Disclosure statement: The authors have declared no conflicts of interest.

200 WHEN INTERSTITIAL LUNG DISEASE REPRESENTS THE MAJOR CLINICAL FEATURE IN ANTSYNTHETASE SYNDROME CASES WHICH ARE CLEARLY AMYOPATHIC, IS IT JUSTIFIABLE TO STILL REGARD DETECTED ANTISYNTHETASES AS MYOSITIS-SPECIFIC ANTIBODIES?

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Background: Antisynthetase syndrome (ASS) is usually characterized by the presence of myositis, a skin rash in DM cases, interstitial lung disease (ILD), RP, mechanic’s hands and non-erosive arthritis. ASS associates with the presence of antisynthetase antibodies, which target one of eight known amino-acyltransfer RNA synthetases.

Methods: We report three CTD cases presenting with ILD in association with an antisynthetase, but without detectable evidence of myositis.

Results: Patient 1 is a 42-year-old female who presented with a 9 month history of dry cough and RP. Examination revealed ‘mechanic’s hands’ changes and bilateral end-inspiratory crackles, but without evidence of muscle weakness. Creatinine kinase (CK) levels were normal, as was muscle histology, but myositis serology by Euroimmun Line-Blot 4 testing demonstrated anti-PL-12 positivity. High-resolution CT (HRCT) confirmed the presence of ILD, and early immunosuppression was induced by i.v. CYC and prednisolone to target the respiratory disease. Patient 2 was a 60-year-old male who presented with increasing dyspnoea. He denied any generalized CTD symptoms. Examination revealed bilateral end-inspiratory crackles but no other CTD signs or clinically detectable muscle weakness. His CK at presentation and throughout was normal. HRCT showed a non-specific interstitial pneumonia (NSIP) pattern, but lung biopsy demonstrated an organising pneumonia. The ILD responded well to steroid treatment. Myositis serology by Line-Blot 4 ultimately confirmed anti-PL-12 positivity. Patient 3 was a 47-year-old male who presented with progressive dyspnoea. HRCT suggested an organising pneumonia, which was confirmed histologically. No general CTD features or underlying muscle weakness were ever detected. His CK was normal when tested, although by then he had received steroid treatment for some weeks. His ILD responded well to therapy. Routine serology confirmed anti-Jo-1 positivity.

Conclusion: These ILD cases were confirmed as antisynthetase antibodies positive, but presenting without any evidence of an associated myositis. Moreover, as all cases are now receiving long-term immunosuppression, myositis may never become a component of their ASS. Amyopathic DM is a recognized term describing patients with hallmark cutaneous DM sine myositis. None of the presented cases had DM, so their phenotype could potentially be termed amyopathic polymyositis, although amyopathic antisynthetase syndrome appears more accurate. Given the cleary amyopathic nature of these cases, and that the antisynthetases detected were indeed apparently acting as ILD biomarkers, employing myositis-specific antibodies (MSAs) as an umbrella term comprising antisynthetases appears somewhat inappropriate. Further research to determine the relative prevalence of amyopathic vs myopathic ASS is now required to determine the validity of rigidly categorising antisynthetases as MSAs.

Disclosure statement: The authors have declared no conflicts of interest.
ORTHOPAEDICS AND REHABILITATION

177 THE FEASIBILITY OF USING SONEOELASTOGRAPHY TO IDENTIFY THE EFFECT OF JOINT HYPERMOBILITY SYNDROME ON ELASTICITY OF GASTROCNEMIUS MUSCLE

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Background: Joint hypermobility syndrome (JHS) is a heritable connective tissue disorder in which multiple synovial joints demonstrate a painful and extraordinary range of motion. Genetically there are abnormal changes in the connective tissue matrix in people with JHS, and that may alter the viscoelasticity of their muscular tissue. Soneoelastography (SEG) is a new technique in musculoskeletal practice for assessing tissue elasticity. This study aimed to determine the feasibility of using SEG to distinguish between those with and without a diagnosis of JHS. Gastrocnemius muscle (GM) elasticity was examined, as it is essential for balance and walking.

Methods: Twenty participants were examined in a cross-sectional feasibility study: 10 participants diagnosed with JHS and 10 age- and gender-matched healthy controls. The dominant GM was scanned three times, once at the same level or at the level of the ankle (red), intermediate (green) and hard (blue) tissues. ImageJ software was used to analyse the images by identifying the mean percentage of pixels each colour.

Results: For the JHS group, nine females and one male were examined, with a mean age of 38.9 years (s.d. 15.53). Similarly, for the non-JHS group, nine females and one male were examined, with a mean age of 38.9 years (s.d. 13.77). The groups were comparable in terms of age, gender and BMI (P = 1.00, 1.00, and 0.77, respectively). The JHS group had a significantly higher percentage of blue (hard tissue) pixels when compared with the control group (P = 0.035). No significant differences were found in the mean percentage of green (intermediate) and red (soft) pixels (P = 0.55 and P = 0.051, respectively).

Conclusion: SEG required a reasonable amount of training for clinicians with sufficient background in musculoskeletal anatomy, ~4 h of observation and practical training. The examination was completed in ~5 min, so it may be reasonable for use in clinical practice, and it was well tolerated by patients. The SEG image was analysed in <5 minutes.

Disclosure statement: The authors have declared no conflicts of interest.

178 DOES PHYSICAL ACTIVITY CHANGE FOLLOWING HIP AND KNEE REPLACEMENT? AN ANALYSIS OF DATA FROM THE OSTEARTHRITIS INITIATIVE

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Background: Total hip (THR) and knee replacement (TKR) procedures aim to reduce debilitation associated with end-stage OA to increase quality of life and physical performance. While it is assumed that this would automatically translate into increased engagement in physical activity, this has been recently questioned. The purpose of this analysis was to determine whether the type and level of physical activity increases during the initial 24 post-operative months compared with pre-operative levels, and how this change compares with people without arthroplasty or OA.

Methods: This study was an analysis of a North American prospective cohort dataset [Osteoarthritis Initiative (OA1)] of community-dwelling individuals. Data from all people who underwent THR or TKR with a minimum of baseline and 24 month follow-up data were identified. These were compared with data from people who had not undergone a THR or TKR and who did not have a diagnosis of hip or knee OA during the OA1 follow-up period. Data collected included demographic characteristics, medical morbidities, musculoskeletal health and physical activity/active living measures of function reported pre-THR/TKR and then at the 12 and 24 month follow-up collection intervals. Data were analysed using inferential statistical tests to compare within-individual and between-group differences in physical activity correlated during each follow-up interval.

Results: In total, 116 participants were analysed in the THR group and 105 in the TKR group. They were compared with 3441 control participants. While physical activity largely increased from pre-operative levels during the first 12 months post-operatively, this change reverted at the 24 month assessment to pre-operative levels in people who underwent THR. In contrast, there appeared to be limited change in physical activity at 12 or 24 months post-operatively compared with pre-operative levels in people who underwent TKR. Compared with the non-arthroplasty cohorts, physical activity was consistently greater in the non-arthroplasty group at 12 and 24 months post-operatively.

Conclusion: There is limited change in the level or type of physical activity undertaken between people before or after THR or TKR in the first 24 post-operative months. Physical activity levels are lower in people following THR and TKR compared with people with similar characteristics who have not had arthroplasty or have OA. There appears to be a difference in the physical activity pursuits undertaken by people following THR compared with TKR. The findings indicate that those who undergo THR are less likely to engage in different types of physical activity or to the same level compared with THR, who are more active during the initial 24 post-operative months.

Disclosure statement: The authors have declared no conflicts of interest.

179 DURATION OF PHYSICAL ACTIVITY FOLLOWING TOTAL HIP OR KNEE REPLACEMENT: AN ANALYSIS OF THE EPIC-NORFOLK COHORT

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Background: It has been suggested that following total hip (THR) and knee replacement (TKR) people increase their levels of physical activity as a result of reduced pain and increased range of motion. Engagement in physical activity is important for promoting physical and mental health and reducing the burden of non-communicable diseases on primary and secondary care services. Therefore, joint replacement is hypothesized to have wider health benefits in addition to improvement of joint pain and disability. However, the degree to which physical activity increases following THR and TKR is unknown.

This study answered this question with a UK population cohort: the European Prospective Investigation of Cancer (EPIC)-Norfolk. We determined whether there was a change in the duration of physical activity following THR or TKR, if the duration of physical activity changes following THR or TKR, which specific forms of physical activity are altered and by how much; and which characteristics or variables predicted an absolute change in duration of physical activity following THR or TKR.

Methods: In total, 653 people from the EPIC-Norfolk community cohort were identified who had undergone primary THR or TKR between EPIC Health Check 2 (1998-2001) and 3 (2006-2011). Paired t-test and multivariable regression analyses were conducted to determine whether there was a change in pre- vs post-arthroplasty duration of physical activity [assessed through duration of waking hours, stair climbing, activities of extended daily living (in and around the home), time spent undertaking physically active recreational pursuits]. Paired t-test analyses were undertaken to assess the change in physical activity over time, while a multivariable regression analysis modelled the absolute change in physical activity measures against potential explanatory factors such as age, gender and co-morbidities.

Results: There was a statistically significant reduction from pre- to post-arthroplasty duration of daily stair climbing at home [THR: mean difference 6.19 (95% CI 2.86, 9.50), P < 0.01; TKR: mean difference 9.42 (95% CI 3.00, 15.43), P = 0.01] and time spent participating in recreational activities [THR: mean difference 1.10 (95% CI 0.26, 1.95),
180 A HOME-BASED BIOMECHANICAL TREATMENT REDUCES PAIN AND IMPROVES FUNCTION AND GAIT PATTERN IN PATIENTS WITH CHRONIC NON-SPECIFIC LOW BACK PAIN
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Background: Chronic nonspecific low back pain (CNSLBP) accounts for the consumption of major portions of health care funds and financial compensation for temporary or permanent inability to work. Patients with CNSLBP after their gait pattern and suffer from diminished physical function and increased pain. Rehabilitation programs aim to reduce the disability of CNSLBP patients. The purpose of the current study was to assess the changes in pain, function and gait pattern in patients suffering from CNSLBP following 6 months of home-based biomechanical treatment.

Methods: Sixty patients with CNSLBP underwent a spatio-temporal gait evaluation using an electronic walkway mat and completed the Oswestry Disability Index (ODI) and the 36-item Short Form Health Survey (SF-36) at three time points: pre-treatment and after 3 and 6 months of home-based biomechanical treatment (AposTherapy). The treatment consists of a foot-worn biomechanical device that is individually calibrated to each patient based on his gait pattern and symptoms. Patients were instructed to walk with the device during their daily routine for a specified amount of time over 6 months. Twenty-four healthy, age-matched individuals served as a reference group.

Results: Significant differences were found in all gait parameters between CNSLBP patients and healthy people at baseline (P < 0.01 for all). There were no significant differences between groups in the gait parameters following therapy. Significant improvements were found in all gait parameters following 3 months of therapy, including an increase in gait velocity (10.6%), step length (5.6%), cadence (5%) and single limb support phase (2.1%) and a decrease in stance phase (1.5%). These improvements were maintained following 6 months of therapy (P < 0.01 for all). A significant reduction of 3.7 points was found in the ODI score (a decrease of 13.5%; P < 0.03) and also in the SF-36 physical score (an increase of 15.9%; P < 0.02) and SF-36 mental score (an increase of 10.5%; P < 0.05) following 6 months of therapy. There were significant differences between CNSLBP patients and healthy people in the ODI score and in the SF-36 physical and mental scores both pre-treatment and following 6 months of therapy (P < 0.007).

Conclusion: The examined home-based biomechanical treatment led to significant improvements in spatio-temporal gait pattern, reduction in pain, improved function and increased quality of life. Furthermore, after 6 months of therapy CNSLBP patients had a gait pattern similar to healthy age-matched people. The level of pain, function and quality of life, however, did not reach those of healthy people.

Disclosure statement: The authors have declared no conflicts of interest.

181 PAIN SENSITIVITY IN HEALTHY VOLUNTEERS AND PEOPLE WITH KNEE OSTEOARTHRITIS
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Background: OA is the most common form of arthritis worldwide and a major cause of pain and disability, and yet underlying mechanisms of OA pain are not entirely understood. There is compelling evidence that altered central pain processing plays an important role in maintaining pain and increasing pain severity in some people with OA. Quantitative sensory testing (QST) is psychophysical testing of somatosensory function and can be used to investigate somatosensory abnormalities. The aims of this study were to evaluate the clinical feasibility and practicality of QST measurements in healthy participants and people with knee OA and to determine if there are any differences in QST measurements between people with knee OA and controls. We also aim to investigate the relationship between pressure and punctate thresholds in people with knee OA.

Methods: Twenty-six knee OA participants and 25 age- and sex-matched healthy volunteers were recruited. All participants completed a self-report questionnaire set [Intermittent and Constant Osteoarthritis Pain (ICOAP), PainDETECT and Hospital Anxiety and Depression Scale (HADS)]. Two mechanical QST modalities (pressure and punctate) were performed. For the pressure modality, the pressure pain threshold (PPT) was assessed with an electronic pressure algometer. For the punctate modality, three outcome measures were assessed using pinprick stimulators (mechanical pain threshold, mechanical pain sensitivity and wind-up ratio). Principal Components Analysis (PCA) was performed on QST data from the sternum to investigate whether a single common factor could be determined from the measures.

Results: Knee OA participants displayed lower pressure pain thresholds at the index knee (P = 0.003) and at the tibia (P = 0.015). However, there were no significant differences in other QST measurements between knee OA and controls (Table 1). A single-factor PCA of data from the sternum gave scores that were significantly correlated with each of the three punctate QST modalities (r > 0.50 and P < 0.001) for all, but not the pressure QST modality (r = 0.10, P = 0.552). Single-factor PCA scores were also not significantly different between OA and controls (P = 0.600).

Conclusion: This suggests PPT may be more useful in determining augmented pain mechanisms in people with knee OA. Punctate QST measurements appear to share a common factor that is distinct from PPT measures.

Disclosure statement: The authors have declared no conflicts of interest.

181 TABLE 1. QST measurements in knee OA and controls

<table>
<thead>
<tr>
<th>QST</th>
<th>Site</th>
<th>Knee OA</th>
<th>Controls</th>
<th>P-value</th>
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<tr>
<td><strong>Pressure pain threshold</strong></td>
<td></td>
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</tr>
<tr>
<td>Sternum</td>
<td>289 (226–365)</td>
<td>358 (213–492)</td>
<td>0.290</td>
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<tr>
<td>Tibia</td>
<td>414 (239–526)</td>
<td>681 (517–848)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td><strong>Mechanical pain threshold</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sternum</td>
<td>13.0 (8.4–24.9)</td>
<td>20.4 (9.4–43.3)</td>
<td>0.326</td>
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<tr>
<td>Tibia</td>
<td>61.8 (23.4–108.4)</td>
<td>74.1 (26.7–119.6)</td>
<td>0.659</td>
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<td><strong>Mechanical pain sensitivity</strong></td>
<td></td>
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<tr>
<td>Sternum</td>
<td>4.5 (2.8–5.6)</td>
<td>5.2 (3.0–7.2)</td>
<td>0.206</td>
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<tr>
<td>Tibia</td>
<td>4.7 (5.6–12.0)</td>
<td>4.3 (2.6–6.8)</td>
<td>0.433</td>
<td></td>
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<td><strong>Wind-up ratio</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Sternum</td>
<td>1.6 (1.0–2.0)</td>
<td>1.93 (1.30–2.22)</td>
<td>0.792</td>
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</tbody>
</table>

Data are presented as median (interquartile range). QST: quantitative sensory testing.
182 THE EFFECTS OF SELF-REPORTED KNEE JOINT INSTABILITY ON MUSCLE CO-ACTIVATION IN OSTEOARTHRITIS OF THE KNEE

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Background: Individuals with OA of the knee (KOA) frequently report knee joint instability and episodes of buckling and giving way. It has been suggested that muscle co-activation may be a mechanism utilized to promote stability at the risk of faster disease progression whereby a certain level of muscle co-activation is required to stabilize the joint. High levels of muscle co-activation are thought to increase joint contact pressures, and combined with high joint loads associated with KOA, these may be detrimental to KOA progression. The purpose of this study was to determine the effect of self-reported knee joint instability on muscle co-activation in individuals with KOA.

Methods: Muscle co-activation was assessed in 77 KOA participants (mean age 62.5 years (s.d. 8.1); 29.4 kg/m² (s.d. 6.0)) using electromyography (EMG) and ground reaction forces during walking and four-step stair negotiation. EMG was recorded from seven sites (medial/lateral gastrocnemius, biceps femoris, semitendinosus, vastus lateralis/medialis and rectus femoris). All trials were normalized to maximal voluntary isometric contraction. Muscle co-activation was calculated from normalized EMG using the following equation: muscle co-activation = (antagonist + agonist) x (antagonist + agonist). The same posture was assessed for level walking and stair negotiation. Stair negotiation was split into transition (floor to stairs) and continuous (step to step) for ascent and descent. Instability was assessed using an adapted version of Felson’s self-reported instability questionnaire. The study was approved by the local NHS and institutional ethics committees and was conducted in accordance with the Declaration of Helsinki; all participants provided written informed consent. T-tests were performed to assess the differences in muscle co-activation between individuals with and without instability.

Results: Knee joint instability was reported in 37 (48%) individuals with KOA. The self-reported instability group had significantly higher muscle co-activation for the quadriceps–gastrocnemius (P = 0.029), gastrocnemius–hamstrings (P = 0.021) and vastus lateralis–medialis (P = 0.005) during level walking. There was no difference for hamstrings–quadriceps, semitendinosus–biceps femoris and medial–lateral gastrocnemius. During stair ascent and descent, muscle co-activation was higher in the self-reported instability group for quadriceps–gastrocnemius (P = 0.024) continuous descent. There was no difference in muscle co-activation between individuals with and without self-reported instability for any other muscle combination.

Conclusion: Individuals with KOA who self-reported knee joint instability demonstrated higher muscle co-activation during level walking compared to the stability group. The results suggest that muscle co-activation may be a mechanism to promote dynamic joint stability. High muscle co-activation demonstrated in the instability group has previously been associated with high joint contact pressures. Combined with high joint loads associated with KOA, this suggests knee joint instability may be detrimental to the incidence and progression of KOA. During stair negotiation, muscle co-activation was higher in the instability group, however, this was not significant.

Disclosure statement: The authors have declared no conflicts of interest.

183 THE MOST FREQUENT SITE AFFECTED IN PATIENTS WITH STICKLER SYNDROME IS THE KNEE AND THIS IS SIGNIFICANTLY ASSOCIATED WITH PAIN SEVERITY AND INTERFERENCE

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Background: Stickler syndrome is an autosomal dominant disorder with characteristic ophthalmological and orofacial features, deafness, and arthropathy that was first described in 1986. There is a substantial risk of retinal detachment. The majority of families with Stickler syndrome have mutations in the COL2A1 gene and show the characteristic type 1 vitreous phenotype. The remainder with the type 2 vitreous phenotype have mutations in COL1A1, COL1A2 and COL5A1. This musculoskeletal complications of the condition are joint hypermobility and OA, which can develop in the third or fourth decade. Mild spondyloepiphyseal dysplasia is often apparent radiologically.

Occasional findings include slender extremities and long fingers. Stature and intellect are usually normal.

Methods: A total of 101 patients attending the Rheumatology Department at Addenbrooke’s Hospital were supplied with a Brief Pain Inventory. All patients had been genotyped. Baseline demographic and medication usage were also collected.

Results: Sixty-nine patients had type 1 Stickler syndrome and 32 had type 2. Sixty-four patients were female and 37 were male. The average age was 38.0 years (range 6–75, s.d. 17.6). Ninety-one patients completed the questionnaire. The average pain score was 4.1/10, with the average best and worst scores being 2.5 and 5.5. Forty-seven patients did not take medication for their pain, which on average they rated 3.4/10. Forty-four patients took medication for their pain, which on average they rated 4.8/10 and this medication provided on average 48% pain relief. The most common medications used were either a sole NSAID or a combination of an NSAID and paracetamol (31/44). There were no differences in demographics, medication use or pain between type 1 and type 2 Stickler patients. The knee was the most common site affected (Table 1). Patients with Stickler syndrome who had their knee affected suffered more pain on average (4.4 vs 3.3/10; P < 0.05) and this pain interfered more with their general activities, walking and normal work (P < 0.05), but not their mood, relations with other people, sleep or enjoyment of life.

Conclusion: Patients with Stickler syndrome appear to have more pain from their knee joint than their other joints and this pain affects their ability to walk and work. There does not appear to be a significant difference between the pain reports in patients with type 1 vs type 2 Stickler syndrome.

Disclosure statement: The authors have declared no conflicts of interest.

184 KNEE OSTEOARTHRITIS FUNCTIONAL CLASSIFICATION SCHEME: VALIDATION OF TIME-DEPENDENT TREATMENT EFFECT—1 YEAR FOLLOW-UP OF 518 PATIENTS

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Background: The purpose of the current study was to validate time-dependent changes of a recently published novel functional classification for patients with knee OA (KOA) following a home-based biomechanical treatment (HBBT).

Methods: A retrospective analysis of 518 patients with KOA was conducted. Patients were graded using a novel KOA functional grade (KOFG) classification based on spatio-temporal gait analysis. Patients were reclassified after 3 months and 1 year of HBBT. The time-dependent changes in the classification were compared to gold standard self-assessment questionnaires, WOMAC and 36-item Short Form Health Survey results.

Results: Changes in KOFG were demonstrated over time. Most changes were observed after 3 months of treatment, with consolidation of the effect at 12 months. For example, of 427 patients that were KOFG 2–4 at baseline, 44.9% and 9.1% had lower (better) KOFG at 3 and 12 months of treatment, respectively. The changes in KOFG were validated with WOMAC and SF-36 questionnaires that showed similar trends. The SF-36 pain subscale showed improvements of 33.0% and 38.0% following 3 and 12 months of treatment, respectively (P < 0.0001).

Conclusion: The KOFG classification scheme offers an objective measurement tool for the assessment of function in the KOA
osteoarthritis: treatment

186 Multiple small hand joint injections are an effective treatment in hand osteoarthritis

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Background: OA is a chronic condition that causes significant pain and disability. Current National Institute for Health and Care Excellence (NICE) guidance recommends the use of conventional analgesic medications, including topical NSAIDs and opioids. Often these have significant side effects, so there is a need for a safer and long-term treatment for chronic pain and disability, particularly in hand OA. Intra-articular steroid injections are a safe and effective form of treatment, particularly for large joints. We provide a joint injection service, where multiple small hand joints are injected during the same visit. Sedation is also provided if the patient wishes it. We review this service, in addition to NICE-approved treatment.

Methods: Patients attended the service if they had painful hand joints due to OA, confirmed by hand X-Rays. All patients had tried NICE-approved treatment previously. Written consent was always obtained. A trained anaesthetist, for patients who wished it, provided sedation. Only painful joints were injected. Dexamethasone 10mg and 1% lignocaine 0.2ml were injected into each painful joint using a 30G needle.

Patients completed questionnaires after the procedure. This included a visual analogue score (VAS) for the effectiveness of analgesics previously received compared with the multiple small hand joint injections.

Results: Eleven patients attended the service over a 3 month period. A total of 104 small hand joints were injected. The main joints injected were thePIP and DIP joints. All patients had multiple small hand joint injections before with a good response. The mean time for repeat injection was every 6 months (range 4–12). Eight patients had sedation (usually needle-phobic or patient wishes). Two patients had the injections with cryogenic spray as anaesthetic cover (fewer than eight joints injected). In comparison to previous treatment received, the mean VAS for regular oral paracetamol was 2.3/10, topical NSAIDs 3.8/10 and regular oral NSAIDs 4.8/10. Overall, the mean effectiveness of the multiple joint injections was 8.6/10. No patient had a side effect from the injections or sedation. All of them would recommend the service as an effective means of analgesia.

Conclusion: Multiple small hand joint steroid injections are an effective treatment in addition to NICE-approved treatment. Although patients return for further injections, it provides a window of improvement in their quality of life. We plan to conduct further studies to see whether these patients have any Doppler activity on US. Our service is safe, reliable and provides a solution for patients suffering from chronic pain due to hand OA.

Disclosure statement: The authors have declared no conflicts of interest.

Osteoporosis and metabolic bone disease

187 towards consensus guidelines for the prevention of medication-related osteonecrosis of the jaw: survey results among general dental practitioners and rheumatologists in the south west of england

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Background: Bisphosphonates and newer bone-active drugs used in fracture prevention are linked with osteonecrosis of the jaw. Medication-related osteonecrosis of the jaw (MRONJ) refers to persistent (>8 weeks), non-healing exposed dental bone in patients with exposure to an implicated medication, with neither metastases nor therapeutic irradiation. Patients, general (dental and medical) practitioners and colleagues expressed mixed views about MRONJ informally. We therefore planned surveys of our local dentists and of rheumatologists in the South West to explore their experience with MRONJ.

Methods: A postal questionnaire asked general dental practitioners if they had encountered a patient with MRONJ, whether they recommended specific checks or dental work prior to patients commencing bone prophylaxis and about the practitioner’s source(s) of information about MRONJ. Second, selected rheumatology units across the South West were emailed inquiring about experience with MRONJ (encounters and management), the existence of local guidelines and the advice given to patients starting bone prophylaxis.

Results: Sixty of 182 (33%) dental practitioners responded. Eleven of the 60 (18%) reported they had encountered MRONJ over the previous 12 months. Fifteen of 60 (25%) recommended dental checks/treatment prior to starting any bone prophylaxis. Dentists identified 15 different sources of information/guidance they used in addressing MRONJ. Comments suggested local guidelines linking dental and medical care would be useful. Seven rheumatology centres responded. Five of the seven centres had encountered patients with MRONJ. 9 patients were identified in all, most with additional risk factors. Six of seven centres discuss MRONJ with all patients about to start bone prophylaxis, but only one with those about to start parental treatment. Of the seven centres, two recommend dental screening for all new patients, two for those starting parental treatment with poor dentition, one for poor dentition and one where there were multiple risk factors. Advice to patients already receiving
bone prophylaxis was similarly inconsistent, and no centre had established formalized guidance with their dental colleagues.

Conclusion: The incidence of MRONJ reported by dentists in a geographical area serving just two of the rheumatology units surveyed suggests they encounter the condition more frequently than rheumatologists. There is apparent discrepancy among both sets of professionals about how they approach bone prophylaxis with respect to the potential side effect of MRONJ. The surveys revealed a lack of consensus locally among dentists and regionally in what rheumatologists advise new and existing patients. The findings led to a workshop meeting attended by rheumatologists and our dental, oncological and general practitioner colleagues. The number of patients with MRONJ attending the dental hospital is now being monitored. Pathways for early dental review of high-risk patients (such as those with malignancy or osteogenesis imperfecta) have been successful and will be audited. Consensus guidance is planned.

Disclosure statement: The authors have declared no conflicts of interest.

188 ATYPICAL FEMORAL FRACTURES ASSOCIATED WITH BISPHOSPHONATE USE IN NORTH STAFFORDSHIRE: A 5 YEAR RETROSPECTIVE ANALYSIS

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Background: There is a growing awareness of atypical femoral fractures (AFFs) and mounting evidence for the association between these fractures and bisphosphonate (BP) use. In October 2013 the American Society for Bone and Mineral Research (ASBMR) published a review of the evidence, suggesting an incidence of AFF of 11 per 100 000 patient-years of bisphosphonate treatment using a revised case definition. The objective of this study was to identify the incidence of AFF using the ASBMR revised case definition within North Staffordshire. We also aimed to audit post-fracture osteoporosis management, in line with guidance that BPs should be stopped after AFF.

Methods: A retrospective analysis was performed through interrogating a comprehensive orthopaedic database of all admissions between July 2009 and June 2014. A list of all femoral fractures was generated and subsequently this was refined by exclusion of all fractures outside of the ASBMR defined anatomical region, high-energy fractures, pathological fractures and peri-prosthetic fractures. The radiographs of the remaining cohort (112) were assessed using the ASBMR revised case definition within North Staffordshire. We also aimed to audit post-fracture osteoporosis management, in line with guidance that BPs should be stopped after AFF.

Results: We found 11 cases of AFF, as defined by ASBMR, in the 5 year period studied. Among them, seven patients were receiving bisphosphonate therapy, one patient was on denosumab and three were not on any bone anti-resorptive treatment. In five patients, in whom the diagnosis was not recognized, bisphosphonates were continued after the fracture. The general practitioners of these patients have subsequently been informed. Two patients on bisphosphonates had concomitant vitamin D deficiency. No patients were on steroids. The incidence of AFF in our region is approximately 7/35 167 patient-years of bisphosphonates treatment.

Conclusion: The estimated incidence of AFF in North Staffordshire is markedly less than the latest published estimates suggest. This single-centre study has demonstrated that bisphosphonate therapy is not always stopped after these events, which may be related to a lack of recognition/diagnosis of AFF. The rarity of these fractures and the resulting low number expected to be seen by any single clinician in their career may explain this finding. Local pathways need to be developed to facilitate communication between orthopaedics and rheumatologists to enhance the recognition and medical management of these patients. The determinants or risk factors for AFF are still not well evaluated; we also therefore propose that AFF should be incorporated in a national register to permit further investigation of possible associations and risk factors, possibly as part of the National Hip Fracture Database.

Disclosure statement: The authors have declared no conflicts of interest.

189 ARE WE OPTIMISING THERAPIES IN PSORIATIC ARTHRITIS? A SURVEY OF UK PRACTICE

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1Rheumatology, Guy’s and St Thomas’ NHS Foundation Trust, London, 2Rheumatology, University of Leeds and Bradford Hospitals NHS Trust, Bradford, 3Pharmacology, University of Bath, 4Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, 5Rheumatology, Kellgren Centre for Rheumatology, Manchester Royal Infirmary, Manchester and 6Rheumatology, Imperial College, London, UK

Background: A treat-to-target strategy significantly improves outcomes for RA. Recently a PsA disease activity state equivalent to remission in RA, called minimal disease activity (MDA), has been defined and a strategy study using MDA as a target for treating early PsA (TICOPA Study) has been reported. We performed an audit of routine practice among attendees at educational meetings on the assessment and treatment of PsA.

Methods: Prior to the meeting, attendees were asked to complete a questionnaire on how they assessed PsA, treatment strategies and practice arrangements. Responses were anonymous, but an indication of their region of practice and professional role was requested.

Results: Fifty-six health care professionals participated: 36% consultant rheumatologists and 37% rheumatology nurse specialists from the following regions: Midlands (7), Scotland (7), South East (10), North East (2), Northern Ireland (6), South West (6), North West (6), not specified (13). A total of 89% of respondents review patients in general rheumatology clinics; new patient consultations lasted 21–30 min and follow-up lasted 11–20 min. National Institute for Health and Care Excellence and British Society for Rheumatology guidelines were referred to by 80% and 64%, respectively; all Scottish respondents also used SIGN guidelines. Sixty-three per cent of 45 respondents used 66/68 joint counts and 31% used 28-joint counts/DAS28. To assess skin, 36% used patient global score, 32% physician global score, 22% Psoriasis Area and Severity Index, 11% Dermatology Life Quality Index and 9% body surface area. Forty per cent did not use any listed score. Fifty-five per cent of 45 responding participants were not aware of MDA, but when asked about the use of treatment targets, of 39 respondents, 8% used MDA at 6 months, 3% at 1 year and 38% at an indeterminate time. Remission with an unspecified tool was assessed by 64% and DAS28 remission by 59%, at 3 or 6 months or an unspecified time. Forty-one per cent used the Psoriatic Arthritis Response Criteria at 6 months, 10% at 3 months and 26% at an indeterminate time. Fourteen per cent of 45 respondents reported they treated to target and have resource to do so, while 32% said they were underresourced. New patients with PsA were reviewed monthly by 48% of 41 respondents and 45% every 3 months. Sixty-seven per cent do not define personalized goals with patients. Challenges in PsA care included limited resources, arranging dedicated PsA clinics, patient heterogeneity and assessment, difficulty achieving remission and managing some patients, including co-morbidities such as psychological and obesity issues.

Conclusion: These findings show that UK rheumatologists are interested in learning more about PsA; generally assess arthritis well, although not all use 66/68 joint counts, are unclear about skin assessment and many are not aware of the MDA concept. Many respondents included remission assessment and saw early PsA patients regularly after diagnosis. Treat-to-target in PsA will be possible in many centres in the future.

Disclosure statement: E.K. has received consulting fees from Eli Lilly and Novartis; has received honoraria from AbbVie; has participated in speakers bureaus for BMS, Janssen and MSD and has received research funding from AbbVie, Novartis and Roche. P.H. has received consulting fees from BMS, Celgene, Novartis and Eli Lilly; honoraria from AbbVie, BMS, Amgen, Celgene, Novartis and Eli Lilly; has participated in speakers bureaus for BMS, Janssen and UCB and has received research funding from AbbVie and Pfizer. N.M. has received consulting fees from AbbVie.
Background: Myeloid-related protein (MRP) 8/14 complexes are calcium-binding proteins that act as endogenous ligands to TLR4. Thus we studied the levels of MRP8/14 in adult AS patients.

Methods: The median serum MRP8/14 levels in patients (29.90 μg/ml (range 0.50–109.37)) were significantly higher than in healthy controls (6.07 μg/ml (range 0.079–20.51), P < 0.0001). Patients with pure axial disease (n = 50) had lower median levels than those with peripheral arthritis (n = 27) (19.65 μg/ml (range 0.51–109.37) vs 38.76 (11.92–100.0), P = 0.02). Levels of MRP8/14 correlated with BASDAI (r = 0.379, P = 0.039) and Ankylosing Spondylitis Disease Activity Score (ASDAS) with ESR (r = 0.44, P = 0.015) and ASDAS with CRP (r = 0.485, P = 0.007) in early disease (disease duration ≤5 years; n = 30) but not in patients with longer disease (disease duration >5 years, n = 47). ASDAS: r = 0.064, P = 0.66; ASDAS-ESR: r = 0.015, P = 0.91; ASDAS-CRP: r = 0.009, P = 0.95.

Results: By activating TLR4, MRP8/14 may be contributing to inflammation in AS and its levels may be used as a biomarker for activity in early disease.

Conclusion: The authors have declared no conflicts of interest.

Disclosure statement: The authors have declared no conflicts of interest.

191 TOCILIZUMAB IN SPONDYLOARTHITIS: EVIDENCE FOR A ROLE IN PERIPHERAL SYNOVITIS–ASSOCIATED REFRACTORY DISEASE

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Background: The spondyloarthropathies are complex polygenic inflammatory disorders with mixed, sometimes evolving clinical phenotypes. Pro-inflammatory cytokines, such as TNF-α and IL-17/IL-23, are keys in the pathogenesis of axial SpA and PsA. Whereas there is ample evidence to suggest a crucial role for TNF inhibition in the treatment of these conditions, not all patients respond or maintain a response. IL-6 inhibition effectively suppresses synovitis in RA and in systemic juvenile arthritis but failed to show efficacy in clinical trials in SpA, namely AS.

Methods: Here we report four cases of refractory AS with different phenotypic expressions successfully treated with tocilizumab (TCZ), all of whom had previously been exposed to TNF inhibitor (TNFi).

Results: All the cases fulfilled the modified New York criteria for AS at 5 years; all had at least 3 months after starting one of the following biologic therapies: adalimumab, etanercept, infliximab or golimumab.

Conclusion: IL-6 inhibition was efficacious in refractory SpA where there was severe associated synovitis as part of the phenotype. This suggests a role for TCZ in a subset of patients with a clinical phenotype of aggressive, destructive, primarily synovial joint involvement resembling that of RA. The role of IL-6 in the pathogenesis of axial and peripheral SpA merits further consideration.

Disclosure statement: The authors have declared no conflicts of interest.

192 BIOLOGIC THERAPIES IMPROVE AXIAL SPONDYLOARTHRITIS PATIENTS’ WORK PRODUCTIVITY AND REDUCE ACTIVITY IMPAIRMENT

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1Rheumatology, Professor Maddison Rheumatology Centre, Llandudno, UK

Background: Biologic therapies reduce disease activity and improve functional outcomes measured using validated BATH indices in AS and non-radiographical axial SpA (nraxSpA), together referred to as axSpA. Since a significant proportion of axSpA patients are of working age, the impact of the disease on work productivity can be significant. The aim of this audit was to investigate the benefit of biologic therapy on work productivity using the Work Productivity and Activity Impairment Score (WPAI), previously validated in conditions such as RA and adapted to axSpA.

Methods: AxSpA patients completed the WPAI questionnaire before and at least 3 months after starting one of the following biologic therapies: adalimumab, etanercept, infliximab or golimumab. Percentage impairment while working, percentage overall work impairment and percentage activity impairment were calculated.

### TABLE 1. Clinical manifestations and response to treatment after TCZ

<table>
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<tr>
<th>Diagnosis</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
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<tbody>
<tr>
<td>Disease duration, years</td>
<td>30</td>
<td>49</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>RF, CCP and ANA</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Skin psoriasis</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>IBD</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Peripher joint involvement</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Previous biologics (reason for discontinuation)</td>
<td>Infliximab (shortness of breath) and Gol intolerance</td>
<td>Adalimumab (shortness of breath and Gol intolerance)</td>
<td>Infliximab</td>
<td>Adalimumab</td>
</tr>
<tr>
<td>CRP, mg/l</td>
<td>103</td>
<td>26</td>
<td>149</td>
<td>171</td>
</tr>
<tr>
<td>Tender joints</td>
<td>&lt;5</td>
<td>20/66</td>
<td>33/66</td>
<td>10/66</td>
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<tr>
<td>Swollen joints</td>
<td>6/66</td>
<td>20/66</td>
<td>20/66</td>
<td>10/66</td>
</tr>
</tbody>
</table>

G1: gastrointestinal; N: no; Y: Yes; +: positive; -: negative.
using Reilly Associates WPAI scoring equations set out in the Specific Health Problem version. The effects of biologic drug therapies on work impairment were analysed by comparing the average percentage scores before and after drug therapy.

Results: WPAI scores for a total of 23 axSpA patients before and after biologic therapy were determined, of which 22 (96%) patients were in the working age group. Of these, 13 (58%) were on adalimumab, 6 (26%) on etanercept, 2 (8%) on infliximab and 2 (8%) on golimumab. There were 14 (61%) males and 9 (39%) females with a mean age of 45 years (range 24–71). A total of 18 (78%) had a diagnosis of AS and 5 (22%) of PsA. The mean disease duration was 8.4 years (range 3–23). The number of patients working increased from 29%, from 15 before biologic therapy to 18 after biologic therapy (Table 1). The number of working hours increased from 26 h per person per week to 33 h after biologic therapy, on average an increase of 6 h per person per week. Activity impairment decreased from 52% to 28%. Impairment at work decreased from 44% to 23%. Overall work impairment decreased from 49% to 24% following biologic therapy and was statistically significant.

Conclusion: The number of axSpA patients performing hours of paid work and the number of hours per patient increased following biologic therapy. Patients were significantly more productive while at work, as shown by reductions in overall work impairment. This correlates with reduced average BASDAI scores over the same time period. Despite the small sample size, the data provide confirming evidence that biologic therapy improves work productivity by reducing work and activity impairment in patients with axSpA. This can have a significantly positive social and economic impact in patients with persistently working age populations, offsetting some of the cost of biologic therapies.

Disclosuer statement: The authors have declared no conflicts of interest.

Table 1. Work hours and percentage impairment before and after biologic therapy.

<table>
<thead>
<tr>
<th>Pre-biologic</th>
<th>Post-biologic</th>
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<tbody>
<tr>
<td>BASDAI (range)</td>
<td>5.4 (2.8–8.7)</td>
<td>2.3 (0.1–5.1)</td>
</tr>
<tr>
<td>Patients working (%)</td>
<td>15 (60)</td>
<td>18 (76)</td>
</tr>
<tr>
<td>Total hours worked per person per week</td>
<td>26</td>
<td>33</td>
</tr>
<tr>
<td>% activity impairment due to axSpA</td>
<td>52</td>
<td>28</td>
</tr>
<tr>
<td>% impairment while working due to axSpA</td>
<td>44</td>
<td>23</td>
</tr>
<tr>
<td>% overall work impairment due to axSpA</td>
<td>49</td>
<td>24</td>
</tr>
</tbody>
</table>

193 IMMUNOPATHOGENIC ROLE OF CHLAMYDIA TRACHOMATIS HEAT SHOCK PROTEIN 60 (CT-HSP60) VERSUS CYTOKINE RESPONSES IN UNDIFFERENTIATED SPONDYLOARTHROPATHY PATIENTS

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Background: Undifferentiated SpA (uSpA) patients are generally asymptomatic, however, they have been reported to be chronically infected with Chlamydia trachomatis. Although India has a high burden of genital chlamydial infection, uSpA due to C. trachomatis is grossly underestimated. C. trachomatis heat shock protein 60 (CT-Hsp60) is abundantly produced during chronic persistent infection. CT-Hsp60 is able to stimulate the production of pro-inflammatory cytokines in endothelial cells, smooth muscle cells and macrophages and can also promote the activation of specific immune cells. However, its role in uSpA patients is yet unexplored. Since C. trachomatis infection may be aetiological for uSpA, we aimed to delineate the immunopathogenic role of CT-Hsp60 vis-à-vis inflammatory cytokines (IFN-γ and IL-17) and IL-6 in uSpA patients.

Methods: With the permission of the hospital ethics committee and informed written consent, patients with uSpA and RA were enrolled in accordance with European Spondyloarthropathy Study Group and ACR criteria, respectively. Clinical and epidemiological details were collected in specific questionnaires. Circulatory CT-Hsp60 was estimated by a commercially available ELISA kit, both semi-quantitatively and quantitatively. Cytokines (IFN-γ, IL-6, IL-17A) were estimated in serum by commercially available ELISA kits and cytokine differences were statistically analysed between group I (CT-Hsp60-positive uSpA patients; n = 9), group II (CT-Hsp60-negative uSpA patients; n = 20) and group III (controls; CT-Hsp60-negative patients; n = 14). RA: n = 20 patients. Statistical analysis was performed with GraphPad Prism software version 5.0 (GraphPad Software, La Jolla, CA, USA).

Results: The majority of patients with CT-Hsp60 were males, had an oligoarticular joint profile and were younger. Significant upregulation (P = 0.04) was observed in IFN-γ in CT-Hsp60-positive patients (group I) as compared with group III (controls). There was no significant difference in IL-6 and IL-17A cytokine levels between group I and group II. However, IL-6 was found to be significantly higher (P < 0.05) in group I patients compared with controls. Individually, the level of cytokines (IFN-γ, IL-6 and IL-17A in the CT-Hsp60-positive patients (group I) were compared with each other: IFN-γ (P = 0.04) and IL-17A (P = 0.0001) were significantly increased compared with IL-6, while IL-17A was significantly higher than IFN-γ (P = 0.01).

Conclusion: Increased levels of IFN-γ and IL-17A in group I indicates that CT-Hsp60 plays a protective role in cell-mediated immunity in uSpA patients. However, downregulation of cytokine IL-6 indicates that activation of IL-17A takes place possibly by other regulatory cytokines.

Disclosure statement: P.K. has received a Senior Research Fellowship (no. 80/635/ECR-1/2009) from ICMR, New Delhi, India. All other authors have declared no conflicts of interest.

194 APREMILAST, AN ORAL PHOSPHODIESTERASE 4 INHIBITOR, IS ASSOCIATED WITH LONG-TERM (104 WEEK) IMPROVEMENT IN FATIGUE IN PATIENTS WITH PSORIATIC ARTHRITIS: POOLED RESULTS FROM THREE PHASE III RANDOMIZED CONTROLLED TRIALS

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Background: Substantial fatigue, particularly with chronic diseases such as PsA, affects quality of life (QoL). The 2014 OMERACT PsA Working Group identified fatigue measurement as an important outcome to include in PsA core assessments. PALACE 1, 2 and 3 (NCT01172938, NCT01212757 and NCT01212770) compared apremilast (APR) efficacy and safety with placebo in patients with active PsA despite prior conventional DMARDs and/or biologics, including fatigue level assessment. We report the treatment impact of APR on fatigue over 104 weeks in a pooled PALACE 1–3 analysis.

Methods: Patients were randomized (1:1:1) to placebo, APR 30 mg twice a day (APR30) or APR 20 mg twice a day (APR20). At week 24, the remaining placebo patients were re-randomized to APR30 or APR20. Double-blind APR treatment continued to week 52; patients could then continue to receive APR or placebo for >4 additional years. Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy fatigue scale (FACT-F) version 4, a 13-item questionnaire initially developed to assess anaemia-associated fatigue. Questions are scored on a scale of 0–4. Total FACT-F scores range from 0 to 52; higher scores denote lower levels of fatigue. As a point of reference, mean fatigue scores of 4.0–4.63 in the general population, 35.8 in PsA patients and 23.9 in anemic cancer patients have been reported. The FACT-F minimum clinically important difference (MCID) in PsA has not been determined; the FACT-F MCID in patients with RA (3–4) was used in this analysis.

Results: Baseline mean FACT-F scores in APR patients at weeks 52 and 104 ranged from 29.2 to 31.2, markedly below population norms and indicative of fatigue-related, impaired QoL. Long-term improvement in fatigue was seen in APR patients at 52 weeks, with improvements in FACT-F scores (Table 1). At week 104, APR30 patients had sustained improvements in fatigue (mean FACT-F = 35.0), marking a shift towards population FACT-F norms. The APR30 mean change was 5.6, exceeding the MCID for this measure in the general population, 35.8 in RA patients; 50.9% of APR30 patients achieved the FACT-F MCID at 52 weeks. The APR30 mean percentage change in FACT-F was 44.5%. Week 104 findings were similar for APR20. Over 104 weeks, most adverse events were mild to moderate; in general, no increases in the incidence/severity of adverse events with longer-term exposure.

Conclusion: Over 104 weeks, APR continued to improve fatigue in PsA patients. APR demonstrated an acceptable safety profile and was generally well-tolerated up to 104 weeks.

Disclosure statement: A.K. has received research funding from Abbott, Amgen, AstraZeneca, Bristol-Myers Squibb, Celgene,poster viewing II
194 Table 1. FACIT-F at weeks 52 and 104 (data as observed)

<table>
<thead>
<tr>
<th></th>
<th>Week 52</th>
<th>Week 104</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>APCDI</td>
<td>APCDI</td>
</tr>
<tr>
<td></td>
<td>(n = 55)</td>
<td>(n = 54)</td>
</tr>
<tr>
<td>Mean baseline score</td>
<td>29.2</td>
<td>30.4</td>
</tr>
<tr>
<td>Mean score at time point</td>
<td>34.0</td>
<td>35.1</td>
</tr>
<tr>
<td>Mean change from baseline score</td>
<td>4.8</td>
<td>5.3</td>
</tr>
<tr>
<td>Mean change from baseline score, %</td>
<td>35.4</td>
<td>21.5</td>
</tr>
<tr>
<td>Proportion of patients achieving MCID, %</td>
<td>50.8</td>
<td>49.0</td>
</tr>
</tbody>
</table>
| n represents the number of patients who completed weeks 52 and 104 weeks of treatment, respectively, regardless of when treatment started (baseline, week 16 or week 24), with a baseline value and a post-baseline value at the time point.

195 SECUKINUMAB SIGNIFICANTLY IMPROVES THE SIGNS AND SYMPTOMS OF ACTIVE PSORIASIS ARTHRITIS IN PATIENTS PREVIOUSLY EXPOSED TO ANTI-TUMOUR NECROSIS FACTOR THERAPY AND ANTI-TUMOUR NECROSIS FACTOR-NAIVE PATIENTS: 52 WEEK RESULTS FROM THE PHASE III FUTURE 2 TRIAL

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Background: Additional treatment options for patients with PsA who inadequately respond to or are intolerant of anti-TNF therapy remains an unmet need. In the randomized, double-blind, placebo-controlled phase III FUTURE 2 study (NCT01752634), secukinumab, a human anti-IL-17A monoclonal antibody, demonstrated significant efficacy in patients with PsA. Here we report the efficacy and safety of secukinumab up to 52 weeks by anti-TNF history in patients enrolled in FUTURE 2.

Methods: Patients were randomized to receive s.c. secukinumab 300 mg, 150 mg or placebo at baseline, weekly until week 4 and then every 4 weeks (q4w) from week 8. At week 16, placebo-treated patients were re-randomized to receive s.c. secukinumab 300 mg or 150 mg q4w from week 16 (non-responders) or week 24 (responders). Randomisation was stratified by anti-TNF history; anti-TNF-naive or inadequate response/intolerance to three or fewer anti-TNF agents (anti-TNF-IR). The primary endpoint was the proportion of patients achieving a 20% improvement in ACR criteria (ACR20) at week 24. Secondary endpoints included the proportion of patients achieving Psoriasis Area and Severity Index (PASI) 75/90 scores, ACR50 response and changes from baseline in 28-joint DAS with CRP, 28-joint Short Form Health Survey Physical Component Summary, HAQ Disability Index; resolution of dactylitis or enthesitis. ACR70 was an exploratory endpoint. Analyses used non-responder imputation (binary variables) and mixed-model repeated measures (continuous variables). Analysis of primary and secondary endpoints stratified by anti-TNF history was pre-specified.

196 PUBLIC AWARENESS AND EDUCATION OF INFLAMMATORY BACK PAIN IMPROVES THE QUALITY OF REFERRALS AND DETECTION OF AXIAL SPONDYLOARTHRITIS

Antoni Chan and Susan Hicks

Rheumatology, Royal Berkshire NHS Foundation Trust, Reading, UK

Background: The advance in therapies in SPA has not been matched with the time taken for diagnosis of AS. There is an average delay of 8.5 years from symptom onset to diagnosis. To reduce the time to diagnosis of SPA, we organized awareness events for both the public and also health care professionals in the community in Berkshire.

Methods: A baseline pre-event audit was undertaken from January to June 2014. All referrals to the AS Clinic in Reading were analysed. Patient demographics, time from symptom onset to referral, presence of an adequate response (IBP) and final diagnosis were collected. Awareness events were held in July 2014. Roadshows were held for health professionals in primary care to raise awareness of IBP and SPA. A public event, Don’t Turn Your Back On It, was held in the Reading town centre with access to the IBP symptom checker. A post-event audit was undertaken from August 2014 to January 2015 with the same data set collected.

Results: Pre-event, there were 87 new referrals for back pain to the AS clinic. The median age was 33 years and the female:male ratio was 1:2. The time from symptom onset to referral was 12 months–10 years.
Forty-seven patients (54% of referrals) had mechanical back pain and 40 patients (46% of referrals) had IBD. In patients with IBD, 25 of them did not have any MRI changes of axial SpA (axSpA). Eleven patients had an alternative diagnostic and four patients (5% of total referrals) had a diagnosis of axSpA. Of these four patients, three (75%) had IBD >12 months and one (25%) had IBD <12 months. Post-event, the median age of patients was 29 years. The female:male ratio was 1:2. The time from symptom onset to referral was 3 months–7 years. Seventy-one new referrals for back, buttock pain, hip pain, and 28 patients (40% of referrals) had mechanical back pain and 43 patients (60% of referral had IBD). Referrals were received from both general practitioners and physiotherapists. Of the 43 who had IBD, 27 did not have MRI changes of axSpA. Five patients had alternative diagnoses and 11 patients (15% of total referrals) had a new diagnosis of axSpA. Of these 11 patients, 5 (45%) had IBD >12 months and 6 (55%) had IBD <12 months.

Conclusion: The awareness programmes do not necessarily increase the quantity of referrals or do improve the quality of referrals. There was an increased number of patients with IBD and a reduction in mechanical back pain referrals. This led to an increase in the diagnosis of SpA post-event. Awareness events also reduce the time to diagnosis of SpA patients. Public awareness programmes increase the detection of IBD and presentation of SpA.

Disclosure statement: The authors have declared no conflicts of interest.

197 INCREASED CD4 T CELL GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR PRODUCTION IN SPONDYLOARTHRITIS

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1Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford and 2Orthopaedic Surgery, Oxford Universities NHS Foundation Trust, Oxford, UK

Background: Immunological, genetic and therapeutic studies have implicated the IL-17A/IL-23 inflammatory axis in SpA. GM-CSF is emerging as a cytokine that marks a pathogenic subset within those with inflammatory arthritis and inhibition of this cytokine pathway is currently in clinical trials for RA. We sought to investigate the role of GM-CSF in SpA pathogenesis.

Methods: Blood, SF and synovial tissue from patients with SpA were studied ex vivo in vitro using SpA joint tissue explant assays. GM-CSF production from different cell types was characterized using multicolour flow cytometry (FACS) and time-of-flight cytometry (CyTOF).

Results: CyTOF analysis revealed ex vivo GM-CSF production from multiple lymphoid and non-lymphoid cell lineages, with CD4 cells clearly the main producers upon whole peripheral blood mononuclear cell (PBMC) stimulation. CyTOF findings were validated with flow cytometry. The percentage of CD4 cells producing GM-CSF was significantly increased in AS PBMCs ex vivo compared with healthy controls (mean 7.73 vs 4.96%, n = 38, P = 0.005). Further characterisation of GM-CSF-producing T cells showed an overlap with both classical Th1 and Th17 phenotypes. The mean percentage of GM-CSF-positive CD4 cells from ex vivo synovial fluid mononuclear cells (SFMCs) was 32.2%, and significantly higher compared with matched PBMCs (n = 5, P = 0.005). CD4 cells from SpA synovial tissue mononuclear cell explant cultures also showed high levels of GM-CSF production by CD4 cells (n = 6).

Conclusion: Increased numbers of CD4 T cells produce GM-CSF in the blood and joint in SpA. GM-CSF may be a key pathogenic cytokine in SpA and can potentially be targeted therapeutically. Anti-GM-CSF monoclonal antibodies are already in phase 3 clinical trials for other inflammatory diseases and have shown an acceptable safety profile.

Disclosure statement: The authors have declared no conflicts of interest.

198 NEW ASSESSMENT OF SPONDYLOARTHRITIS INTERNATIONAL SOCIETY OUTCOME MEASURES ARE MORE SENSITIVE IN DETECTING RESPONSE IN BIOLOGIC-TREATED AXIAL SPONDYLOARTHRITIS PATIENTS

Antoni Chan1, Kathryn Rigler2 and Linda Herdman1

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Background: Outcome measures have been used to measure disease activity and severity in axial SpA (axSpA). The Assessment of SpondyloArthritis International Society (ASAS) outcome measures were developed in 2009. They included the AS Disease Activity Score (ASDAS), ASAS 20 improvement, ASAS 40 improvement and ASAS partial remission. We measured the sensitivity of the ASAS scores against the standard outcome measures BASDAI 50 and spinal visual analogue scale (VAS) in anti-TNF-α-treated axSpA patients.

Methods: The ASAS outcome measures were compared with National Institute for Health and Care Excellence (NICE) standards for response (BASDAI 50, 2 cm reduction in BASDAI and spinal VAS) and non-response to anti-TNF-α in AS. The standard of the audit was NICE TA 143 (May 2008) and TA 233 (August 2011). All patients meeting ASAS criteria for axSpA between April 2014 and March 2015 and on anti-TNF-α treatment were studied. There were 115 patients, with males comprising 77% [median age 44 years (range 21–62)], ASAS outcomes (ASDAS, ASAS20, ASAS40 and ASAS partial remission) were measured.

Results: A total of 65.6% of patients responded to anti-TNF-α based on NICE criteria at week 12. Using ASDAS in the responder group, 80% had major improvement (change >92% and 20% had minor improvement (change >2% and <50%) of ASDAS moderate disease activity, so ASDAS performs well against BASDAI 50 and NICE criteria for axSpA. Five patients had alternative diagnoses and 11 patients (15% of total referrals) had a new diagnosis of axSpA. Of these 11 patients, 5 (45%) had IBD >12 months and 6 (55%) had IBD <12 months.

Conclusion: The awareness programmes do not necessarily increase the quantity of referrals or do improve the quality of referrals. There was an increased number of patients with IBD and a reduction in mechanical back pain referrals. This led to an increase in the diagnosis of SpA post-event. Awareness events also reduce the time to diagnosis of SpA patients. Public awareness programmes increase the detection of IBD and presentation of SpA.

Disclosure statement: The authors have declared no conflicts of interest.

199 ASSESSMENT OF DISABILITY LEVELS IN A COHORT OF 1449 PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS: AN ADAPTED ASAS RESPONSE CRITERIA TO MEASURE THE EFFECT OF APREMILAST TREATMENT: POOLED DATA FROM THREE PHASE III RANDOMIZED CONTROLLED TRIALS

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Background: PsA reduces physical function. PALACE 1–3 compared apremilast (APR) efficacy and safety with placebo in patients with active PsA despite prior conventional DMARDs and/or biologics. The impact of treatment with APR 30 mg twice a day (APR30) on disability over 104 weeks was assessed using the HAQ Disability Index (HAQ-DI) in a pooled analysis of the PALACE 1–3 database.

Methods: Patients were randomized (1:1:1) to placebo, APR30 or APR 20 mg twice a day (APR20). At week 24, the remaining placebo patients were re-randomized to APR30 or APR20. HAQ-DI scores were collected at baseline and weeks 16, 24, 40, 52, 65, 78, 91 and 104. Data were analysed by intention to treat and last observation carried forward (LOCF) for week 16 and descriptive data observed to week 104. The proportion reaching the minimum clinically important difference (MCID) was calculated. Disability levels were calculated using HAQ-DI cut-off levels <1.0 (clinically important difference), <0.5 (minimal disease activity criteria) and <0.25. Category shifts showing changes in functionality were observed using 0.25 increments.

Results: Patients exhibited significant physical disability baseline mean HAQ-DI = 1.2. Major disability was noted in 13% with baseline HAQ-DI >1.875. By week 16, physical function improved with APR30 vs placebo, with a mean HAQ-DI change of −0.23 vs −0.08
and hip was calculated and compared using OPG-Ab status and achieved spatial BMD (g/cm²) is greater than hip BMD, there is likely syndesmophyte formation. Simple descriptive statistics were performed using Fisher’s exact test and Student’s t-test.

Results: We studied 134 patients, of whom 75% were male. The mean age was 47 years (±15) and the median disease duration from diagnosis was 6.5 years. Sixteen patients (11.9%) tested positive for OPG-Ab. In those with longer disease duration, 100% of OPG-Ab positive patients had higher spinal BMD compared with 65% of negative patients (P = 0.026). This was not significant in those with shorter disease duration. The difference between spinal and hip BMD increased with disease duration, and in those with >6.5 years duration, OPG-Ab positivity was associated with greater differences.

Conclusion: This cross-sectional study demonstrates that in patients with longer disease duration, those positive for OPG-Ab seemed to have higher spinal than hip BMD. This may be a result of increased loss of BMD at the hip with increasing disease duration. Another explanation could be that OPG-Ab are associated with dysregulation of bone remodelling and redistribution of bone from the vertebral bodies to form syndesmophytes. These findings warrant further studies into the role of OPG-Ab in axSpA.

Disclosure statement: P.L.R. has a patent application relating to the detection of osteoprotegerin antibodies in the diagnosis of osteoporosis. S.H.R. has a patent application relating to the detection of osteoprotegerin antibodies in the diagnosis of osteoporosis. All other authors have declared no conflicts of interest.

201 RETROSPECTIVE STUDY OF THE MANAGEMENT OF PSORIATIC ARTHRITIS WITH TUMOUR NECROSIS FACTOR INHIBITORS IN THE UK: CAPTURE STUDY PRELIMINARY ANALYSIS

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Background: Several TNF inhibitors (TNFi) are available to treat PsA in the UK, with Psoriatic Arthritis Response Criteria (PsARC) recommended for assessment of response. Patients may remain on the first TNFi for prolonged periods, and while this indicates sustained clinical effectiveness, it may also reflect a lack of alternative therapeutic options. The objective of this study was to characterize PsA management with TNFi during normal clinical care in the UK NHS.

Methods: CAPTURE was a retrospective observational study in 11 centres that included 141 consenting NHS patients with a documented diagnosis of PsA (according to Classification of Psoriatic Arthritis (CASPAR) criteria) who were initiated on their first TNFi ≥3 years previously and ≥18 years of age. Data were collected from medical records, including patient and clinical characteristics at initiation of the first TNFi (baseline), TNF prescribed and PsAR variables. The median duration of the study period (initiation of the first TNFi to the date of data collection) was 4.5 years (range 3.4–5.5). Where data were not available for all patients, the denominator is shown.

Results: Seventy-one (50.4%) patients were female. The median age at PsA symptom onset was 38.1 years (range 11.9–67.3; n = 130) at PsA diagnosis 40.0 years (15.0–67.4; n = 138) and at initiation of first TNFi 50.0 years (23.2–76.8). At baseline, 29.8% (42/141) of patients had PsA-related nail involvement, 19.1% (71/141) had enthesitis and 18.4% (26/141) had dactylitis. During the study period, 68.1% (96/141) of patients received one TNFi only, 19.9% (28/141) received two and 12.1% (17/141) received three or more. Adalimumab [57.4% (81/141)] and etanercept [40.4% (57/141)] were the most frequently prescribed first-use TNFis. Forty-one of 141 patients had data available to calculate PsARC response 12 weeks post-initiation of the first TNFi; 73.2% (30/41) had a PsARC-defined response, of which 29% did not discontinue the first TNFi. Eleven of 41 (26.8%) patients did not have a PsARC-defined response, but of these only 6 switched to a second TNFi. Three years post-initiation of the first TNFi, 64.5% (91/141) of patients remained on the first TNFi, 24.1% (34/141) were receiving an alternative TNFi and 11.3% (16/141) had permanently discontinued TNFi therapy. The most common reasons for discontinuation of the first TNFi at any time were...
In this study of a representative patient group treated with TNFis and where data were available approximately three-quarters of patients achieved a PsARC response after 12 weeks, comparable with published trial data. While missing data are a limitation of any retrospective study, the extent of PsARC data not documented in the patients’ medical notes was unexpected. Missing data may reflect that the PsARC response is not always appropriately documented and/or routinely assessed. This is despite clear guidance from the National Institute for Health and Care Excellence, and may indicate the need to establish specialized PsA clinics in order to optimize patient management.

**Disclosure statement:** N.B. has been a speaker for Pfizer and AbbVie; has received research funding from Novartis and AbbVie and has received a travel grant from Pfizer. G.C. has received honoraria from Janssen Cilag, Pfizer and Amgen. B.K. has received consulting fees from AbbVie, Eli Lilly and Novartis; has received honoraria from Celgene, Janssen Cilag, Eli Lilly and UCB; has participated in speakers bureaus for BMS and MSD and has received research funding from AbbVie, Novartis and Roche. H.M.O. has received honoraria from AbbVie, Celgene, Janssen Cilag, MSD, Novartis, Pfizer and UCB and has received research funding from Pfizer and Janssen Cilag. I.M. has received consulting fees from Janssen, Pfizer, Novartis, Amgen, MSD and Celgene and research funding from Janssen Cilag and Pfizer. J.F. has received honoraria from AbbVie and has only received non-pharma grants (NASS and NIHR). Y.F. has received honoraria from Pfizer, BMS, Novartis and AbbVie; has participated in speakers bureaus for BMS and Pfizer and has received research funding from Roche, BMS, Novartis, AbbVie, Amgen and Pfizer. A.B.-B. is an employee of pH Associates, contracted by Novartis to manage the CAPTURE study. S.M. is an employee and shareholder of Novartis (sponsor of the CAPTURE study). N.M. has received consulting fees from Celgene and GSK; honoraria from AbbVie, Celgene and Novartis and research funding from Novartis, Pfizer and Celgene. The other author has declared no conflicts of interest.

### 202 PERFORMANCE OF THE SPADE TOOL TO IDENTIFY SPONDYLOARTHRITIS IN PATIENTS REFERRED TO A SPECIALIST

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**Background:** Many referral strategies have been devised to optimize the early diagnosis of SpA and these result in the diagnosis of SpA in 30–40% of patients. Strategies to reduce the delay in diagnosis of SpA and optimize the appropriateness of referrals to secondary care should be explored. The Spondyloarthritis Diagnosis Evaluation (SPADE) tool (http://www.spadetool.co.uk) has been designed to assist health care professionals in determine the probability of axial SpA (axSpA) in patients <45 years of age with chronic back pain and no definite changes on radiographs. The probability of axSpA derived from the SPADE tool is displayed on a chart with clear instructions for the user on what action should be taken next. The aim of this study was to assess the performance of the SPADE tool in the secondary care setting.

**Methods:** The Royal National Hospital for Rheumatic Diseases runs a weekly early back pain (EBP) clinic. Data on all patients (axSpA and mechanical back pain) was collected. The SPADE tool, which consists of questions pertaining to clinical features, CRP, HLA-B27 and MRI findings, was applied on all EBP patients with a diagnosis to obtain the probability of SpA in this group of patients in one of the four categories: category 1, improbable; category 2, additional tests needed (HLA-B27 or MRI, consider referral to a specialist); category 3, probable SpA; and category 4, definitive SpA. This was compared with the diagnosis made by the physician. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were estimated using observed ratios of patient numbers from this sample. The 95% CIs on the NPV were generated by assuming a binomial model for x, where x is the number of patients with SpA who are not referred at a given SPADE threshold.

**Results:** We looked at a total of 87 patients (49 males). Forty-four (50.5%) had SpA subsequently diagnosed: 0/21 in category 1, 1/21 in category 2, 7/9 in category 3 and 31/36 in category 4. Estimates of PPV, NPV, sensitivity and specificity obtained by using each of the SPADE categories as a threshold for referral are given in Table 1.

**Conclusion:** The SPADE tool is a valuable resource to assist clinicians in determining the probability of SpA in patients with chronic back pain. The high NPV, especially with the referral threshold set at 2 or 3, implies that the test is most useful in ruling out SpA. Note that the prevalence in this sample is likely to be higher than in the target population (primary care), meaning that these estimates of NPV are likely to be underestimates. The tool needs to be validated in a primary care setting.

**Disclosure statement:** The authors have declared no conflicts of interest.

### Table 1. Sensitivity, specificity and predictive values of the SPADE thresholds

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Sensitivity, %</th>
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<th>PPV, %</th>
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<td>100</td>
<td>49</td>
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<td>70</td>
<td>88</td>
<td>86</td>
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BACTERIAL TOXINS IN THE URINE OF PATIENTS WITH RHEUMATOID ARTHRITIS: A CAUSE OF THE CONDITION OR AN OPPORTUNISTIC RESULT OF IT?
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Background: RA is an autoimmune disease of unknown aetiology with a pathogenesis that is due to a mixture of genetic, immunological and environmental factors. A T-cell immune response to the presence of pyrogenic toxin superantigens (PTSAsgs) in the joints of RA patients has previously been described. A link has been proposed between pathogenic microorganisms and the development of chronic autoimmune conditions. Potential pathogenic mechanisms include the hygiene hypothesis and molecular mimicry. Due to the widespread prevalence of RA, it has been hypothesized that the pathogenesis could involve a common bacterium. Previously, Porphyromonas gingivalis, a periodontal pathogen, had been suggested due to its ability to citrullinate proteins. In RA, one potential bacterial candidate that has been suggested is Staphylococcus aureus. Current published data average the general presence of S. aureus at 30% (nasal/nasopharyngeal swabs). However, our unpublished data suggest immune complexes containing S. aureus antigens are detectable in urine. Approximately 18% of the general population present S. aureus toxins in their urine. The aim of this study was to investigate the presence of staphylococcal enterotoxins B and C (SEB/SEC), toxic shock syndrome toxin 1 (TSST-1) and alpha haemolysin (AH) in the urine of patients with RA to support the hypothesis that they may play a role in RA.

Methods: After ethical approval, patients with RA with no active infection(s) were recruited from a North West rheumatology department. Midstream urine samples were collected and processed aseptically. These samples were analysed by western blot using commercially available primary (sheep) antibodies to SEB, SEC, TSST-1 and AH and a rabbit anti-sheep horseradish peroxidase conjugated secondary antibody.

Results: The patient population included 110 females and 38 males ages 25–90 years (median 65–74). Western blot analysis of 140 RA patient urine samples demonstrated the presence of AH/SEC/SEC in 74 (52.9%) samples. TSST-1 was not identified in any of the samples.

Conclusion: Our work demonstrates the presence of bacterial toxins in urine from RA patients, with 52.9% demonstrating the presence of at least one staphylococcal enterotoxin. This study is the first to demonstrate the presence of common staphylococcal enterotoxins in RA patient urine, raising the question of what role they may have in the disease pathogenesis, given that these patients have no active infections. We also show that S. aureus toxins are present in the urine of nearly three times more of the RA population than the general population. This raises questions of whether the bacteria and their toxins are involved in an individual’s likelihood of getting RA; are those people with RA more likely to have S. aureus infections due to their immunological state? The presence of S. aureus in RA patient tissues warrants further investigation to determine if it is causative of or a result of the RA diagnosis.

Disclosure statement: The authors have declared no conflicts of interest.
cohort of 34 SLE patients were subjected to flow cytometry to correlate serum biomarkers with B cell subsets.

Results: By adjusting for the baseline level (at the first visit), delta ELISpot of \( \geq 10 \) activated memory B cells (\( P = 0.01 \)) and improved sensitivity (86.4%) and specificity (83.9%) for identifying SLE responders vs non-responders compared with conventional SLE biomarkers including anti-dsDNA antibody titre and C3. To account for serial measurements over time, we used a mixed effects model analysis that identified deltaVCAM-1 as the best marker of SLE clinical response (6.6 \( \times 10^{-3} \)). sVCAM-1 levels were significantly correlated with CD95+/CD27+ activated memory B cells (\( P = 0.01 \)), CD95+ plasmablasts (\( P = 0.006 \)) and circulating plasma cell numbers (\( P = 0.009 \)) in SLE patients.

Conclusion: Subtracting a baseline level of sVCAM-1 for each individual substantially improved its utility as a biomarker. deltaVCAM-1 was superior to conventional SLE biomarkers for monitoring changes in disease activity. This suggests that serial monitoring of serum sVCAM-1 trends should be considered in SLE patients to document responses to treatment. We hypothesize that the correlation between activated B cell subsets and circulating plasma cell numbers with sVCAM-1 serum levels in SLE may relate to the important role of VCAM-1 in B lymphocyte survival and maturation in bone marrow and secondary lymphoid tissues.

Disclosure statement: The authors have declared no conflicts of interest.

206 THIS POSTER IS NOW AN ORAL PRESENTATION

207 THE ABILITY OF RECOMBINANT DOMAIN I OF BETA-2 GLYCOPROTEIN I TO INHIBIT THE LUPUS ANTICOAGULANT EFFECT OF IgG FROM PATIENTS WITH ANTI-PHOSPHOLIPID SYNDROME IS ENHANCED BY PEGYLATION

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Background: APS is an autoimmune rheumatic disorder caused by aPLs and is characterized by vascular thrombosis (VT) and pregnancy morbidity. aPLs are detected by three tests, the anti-cardiolipin and anti-\( b_{2} \)-glycoprotein I (\( b_{2} \)GPI) ELISAs and the lupus anticoagulant (LA) test. The LA test measures prolongation of clotting time caused by aPL present in the plasma of patients. LA positivity is strongly associated with thrombosis and is the strongest predictor of pregnancy morbidity in patients with APS. In testing the potential efficacy of new therapeutic agents for APS it would useful to assay their ability to inhibit LA effects of polyclonal IgG-aPL in samples from patients. Here we describe a novel method for carrying out such tests and its application to test PEGylated human recombinant domain I (\( \text{DI} \)) of \( b_{2} \)GPI. Recombinant DI has been shown to block the binding and prothrombotic properties of purified IgG antibodies from APS patients. PEGylation (the chemical addition of polyethylene glycol) can increase the half-life and reduce the immunogenicity of small molecules, enhancing their development as therapeutic agents.

Methods: We used a Symex-CX coagulometer with a dRVLT Plus kit. The principle of the assay is that the sample to be tested is allowed to clot either in the presence or absence of a reagent containing excess phospholipid (LR) (a two-step test). aPLs that cause an LA effect prolong clotting time in the lupus anticoagulant sensitive test (LS) but not in the lupus anticoagulant resistant test (LR). Thus the ratio of LS to LR clotting time is a measure of the LA effect. We purified IgG from the serum of patients with APS (n = 4, all fulfilling Sydney criteria and known to be LA positive) and added it to normal human plasma at a concentration of 500 \( \mu \text{g} / \text{ml} \). These samples were then tested in the coagulometer assay either with or without pre-incubation with DI alone or DI PEGylated with three different sizes of PEG (20, 30 or 40kDa).

Results: For all four patients, purified IgG in the absence of inhibitor gave an LS:LR ratio > 1.15, showing an LA effect. For all patients, the addition of PEGylated DI reduced the LA effect on the LS:LR ratio and the effect of PEGylated DI was greater than the effect of non-PEGylated DI in three of four cases. This finding is particularly interesting since PEGylation generally reduces the biological effects of small molecules. A minimal effect was seen with PEG alone. Conclusion: Using this assay, we demonstrated it is possible to test a putative therapeutic agent’s ability to inhibit the LA effect. PEGylation of DI did not reduce its ability to inhibit the LA effect of APS-IgG, but actually increased inhibition. This finding may be beneficial in the development of PEG DI as a therapeutic.

Disclosure statement: T.C.R.M. is an inventor on the patent for PEGylated Domain I. C.P. is an inventor on the patent for PEGylated Domain I. I.G. is an inventor on the patent for PEGylated Domain I. Y.I. is an inventor on the patent for PEGylated Domain I.

208 ANTI-TUMOUR NECROSIS FACTOR THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS DOES NOT ATTENUATE CUTANEOUS TUMOUR NECROSIS FACTOR ACTIVITY FOLLOWING A TUBERCULIN SKIN TEST

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Background: Anti-TNF therapy has revolutionized the treatment of RA. However, the mechanisms underlying its effectiveness are poorly understood. We used the tuberculin skin test (TST) as an in vivo challenge model to investigate whether TNF activity is attenuated by anti-TNF therapy in a prototypic cell-mediated immune response.

Methods: Fifty stable RA patients (treated with adalimumab, etanercept or MTX) and healthy volunteers with immunological memory to tuberculosis (TB) antigens were identified using an IFN-\( \gamma \) ELISPOT of peripheral blood. TST or saline (controls) was injected into the forearm of study participants and 3mm punch skin biopsies were taken from the injection site after 72 hours. Samples were collected for RNA analysis and histology. Genome-wide transcriptional profiling was performed to compare gene expression changes in response to the TST challenge between treatment groups. As a surrogate marker for TNF activity, the expression of TNF-regulated genes was quantified using a modular approach.

Results: Clinical TST responses were significantly diminished in RA patients compared with healthy controls. Anti-TNF therapy did not have a further significant effect on skin induration compared with those treated with MTX. However, clinical TST skin induration did not correlate with peripheral blood response to TB antigens, as IFN-\( \gamma \) responses to TB antigens in peripheral blood were not attenuated by rheumatoid disease or treatment. Genome-wide transcriptional profiling showed that TNF was induced following the TST, and this was not attenuated by anti-TNF therapy compared with RA patients treated with MTX or healthy controls. Furthermore, downstream activity of this induced TNF was preserved in patients on anti-TNF therapy.

Conclusion: Attenuated cellular TST responses have been previously shown in RA patients with active disease. Our results expand these findings to patients with stable disease, where the clinical TST responses were also diminished. Intriguingly, based on the transcriptional response to a TST challenge, we did not observe any reduction in TNF activity in patients on anti-TNF therapy. We conclude that anti-TNF therapy is unable to block a surge in TNF activity following an acute challenge. Therefore we infer that anti-TNF therapy is more likely to have biological effects on basal levels of TNF activity in steady state rather than blocking TNF activity at the site of acute inflammation.

Disclosure statement: R.B.-M. has received research funding from Arthritis Research UK (Clinical Fellow). All other authors have declared no conflicts of interest.

209 VACCINATIONS AND BIOLOGIC THERAPY: PATIENT PERSPECTIVE AND AUDIT FINDINGS FROM THE SOUTHAMPTON BIOLOGICS SERVICE

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Background: The British Society for Rheumatology guidelines recommend that patients on anti-TNF therapy should receive influenza and pneumococcal immunisations unless contraindicated. Live-attributed vaccines are not recommended in patients receiving anti-TNF
therapy. This audit aims to assess the current vaccination status of rheumatology patients on biologic therapy under the care of the Southampton biologics service.

Methods: It is local practice that patients are advised on the required vaccinations and the avoidance of live-attenuated vaccines at biologic screening. Questionnaires were distributed to consecutive patients receiving biologic therapy who attended the Southampton biologics review clinic between September and October 2015. The question- naire asked whether patients recalled being informed of the vaccinations they should and should not receive while receiving a biologic, about their current vaccination status and their reasons for not having had appropriate vaccinations.

Results: A total of 101 forms were analysed (42 males, 59 females); 31 patients (30.7%) were >65 years of age and 70 (68.3%) were <65 years. Although 86 patients (85.1%) reported that they recalled being advised to have the yearly influenza vaccine, only 66 (63.3%) received the vaccine. Of the 32 (31.7%) who did not receive the influenza vaccine, 6 reported not realising the vaccination was needed, 12 decided not to be vaccinated, 4 reported previous adverse reactions or side effects and 8 were planning to have their vaccination at a later date. Sixty patients (59.4%) did not recall being advised to have the pneumococcal vaccine. Only 21 (20.8%) reported that they had been administered the vaccination in the last 5 years. Five patients (5%) were vaccinated >5 years ago, 3 of whom were >65 years old. Only 48 (45.5%) who reported not having had the vaccine, 40 did not realize they needed the vaccine. Fifty patients (49.5%) were not aware of the recommendation to avoid live-attenuated vaccines. One patient had been administered a live-attenuated varicella vaccine. This was a female patient, >65 years old, who was not aware that live-attenuated vaccines were not recommended while on biologic therapy.

Conclusion: Although the majority of patients (85.1%) receiving biologic therapy recalled being advised to have the influenza vaccination, a sizeable proportion of these patients (27.9%) did not have this, with 58.3% of these actively declining. A much higher percentage of patients (59.4%) did not recall being advised to have the pneumococcal vaccination and, as a result, only 25.7% of patients received this. Only half of the patients could not recall being advised to avoid live-attenuated vaccines. This highlights a need to not only equip patients with information about vaccinations when first assessed in the biologics clinic, but also to provide ongoing patient education to ensure better understanding of the vaccinations they should and should not receive while on biologic therapy.

Disclosure: C.R. Holroyd: Honoraria; C.R.H. has received Honoraria; Hadija Trojer: NHS; Kate David: C.R.Holroyd: Honoraria; C.R.H. has received Honoraria. All other authors have declared no conflicts of interest.

210 RETROSPECTIVE ANALYSIS OF ADULT REFERRALS TO THE PERIODIC FEVER SERVICE AT THE NATIONAL AMYLOIDOSIS CENTRE: INCREASING RECOGNITION OF ADULT-ONSET GENETIC AUTOINFLAMMATORY DISEASE

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Background: Autoinflammatory diseases are most commonly diagnosed in childhood, but there is increasing awareness that patients with these disorders may present in adulthood. We sought to analyse the outcomes of adult referrals to the Periodic Fever Service at the National Amyloidosis Centre (NAC) over 1 year and to further characterize the atypical inflammatory disorders among adults in whom the aetiology remained undetermined.

Methods: All patients >16 years of age who were referred to the Periodic Fever Service during 2014 were identified from the NAC database. Data were collected on baseline demographics, age at referral, referrer’s specialty, diagnosis and management and outcomes.

Results: A total of 141 adult patients were referred to the Periodic Fever Service in 2014. The most common referring specialty was rheumatology (49%), followed by general practice, dermatology and immunology. The mean age at initial appointment was 41 years (range 18–80). Forty-one per cent of patients were diagnosed as having a recognized autoinflammatory syndrome, of whom 50 (35%) of referrals had a monogenic disorder [mean age at diagnosis 42 years (range 16–79)]; FMF, n = 21 [mean age 42 years (range 19–78)]; cryopyrin-associated periodic syndrome, n = 14 [mean age 42 years (range 19–78)]; TNF receptor-associated periodic syndrome, n = 13 [mean age 42 years (range 19–78)]; recurrent idiopathic pericarditis, n = 3 [mean age 50 years (range 24–77)]; Schnitzler syndrome, n = 2 [mean age 53 years (range 47–58)]; mevalonate kinase deficiency, n = 1 (age 36 years); deficiency of the IL-36 receptor antagonist (DIRTA), n = 1 (age 59 years); and adult periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA), n = 1 (age 20 years). Two patients had adult-onset Still’s disease [mean age 38 years (range 30–45). A gene mutation was not identified in 57 (40%) individuals [mean age 42 years (range 18–60)], who did not fulfill the criteria for non-heritable autoinflammatory syndromes but in whom there was evidence of substantial inflammation; these patients were categorized as having a chronic inflammatory disorder of undefined type. Seventeen per cent of patients referred were not considered to have an autoinflammatory disease. Pathogenic mutations were identified in 33% of the patients referred from rheumatology centres compared with 39% of patients referred from the other main referring specialties. General practice contributed a large number of monogenic referrals reflecting knowledge of family history.

Conclusion: Greater knowledge and clinical experience has led to systemic autoinflammatory syndromes being diagnosed more often in adulthood. In this series, most patients were in their fifth decade when referred. The most common diagnoses were monogenic diseases; diagnosis of these in middle age was attributed to delayed recognition of characteristic symptoms in some patients, but there was a true late onset of symptoms in others, very notably among those identified to have somatic mosaicism. The representation of referring specialists to the service and appear to be increasingly alert to the possibility of adult-onset autoinflammatory disease in their clinics.

Disclosure statement: The authors have declared no conflicts of interest.

211 RHEUMATOLOGY PATIENTS’ EDUCATIONAL RESOURCES: THE PATIENTS’ PERSPECTIVE

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Background: Approximately 400 000 people in the UK are living with RA and ~6000 new cases are diagnosed every year, causing significant disability and morbidity. Patient education has shown to have a significant effect on disability, joint counts, patient global assessment, psychological status and depression at first follow-up of patients with RA. The aims of the survey were to investigate patients’ opinions of rheumatology education resources for newly diagnosed inflammatory arthritis and to identify the preferred information resource format.

Methods: Forty-one patients diagnosed with an inflammatory arthritis completed questionnaires handed out in outpatient rheumatology clinics across three hospital sites in Manchester (University Hospital of South Manchester, Stepping Hill Hospital and Tameside Hospital). The surveys investigated patients’ views on the information they were given at the time of their diagnosis, their satisfaction with this information and in what format they would prefer to receive information.

Results: Twenty-nine females and 12 males completed the questionnaire: 95% of patients were 30–75 years of age. Eighty-eight per cent of patients were given verbal information and 83% received information via a booklet at the time of diagnosis. Twenty per cent received information on a website, 2% were offered group educational sessions and 2% were provided with a DVD. Forty-six per cent of patients would like to participate in group educational sessions. Eighty per cent of patients have access to a computer. The most popular topics for further information were drugs, self-management, diet, physiotherapy and pain control.

Conclusion: Patients wish to have more information when diagnosed with an inflammatory arthritis. The preferred format is via a website, with a focus on drugs, self-management, diet, physiotherapy and pain control. The results of this survey have informed the production of a website with links to educational resources that we hope will enable
patients to have a greater understanding of their disease and therefore improved outcomes.

Disclosure statement: The author has declared no conflict of interests.

212 SHOULD THERE BE INFORMATION AND SUPPORT AVAILABLE FOR CHILDREN WHOSE PARENTS OR GRANDPARENTS HAVE A CHRONIC RHEUMATIC CONDITION?

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Background: Within the UK, national rheumatology charities such as Arthritis Research UK are well known for their educational leaflets for patients. Families also need information and resources to enable them to understand and support the person with the rheumatic condition. While there are information leaflets for adult caregivers, there are no age-appropriate information or educational materials available specifically for the children within these families. It is not known what information would be useful to children, nor the content, format, timing and delivery of such information for children. Indeed, it has not been established whether parents/grandparents would welcome such resources for their children to use.

Methods: Using a cross-sectional study design, a questionnaire was developed as part of a two-phase study. The second phase of the study involved in-depth semi-structured interviews and visual data collection (cultural icons) to develop the questionnaire. The questionnaire contained closed, multiple-choice and open-ended free text questions. Data were collected from adult patients (>18 years of age) within the local secondary care rheumatology service and the National Rheumatoid Arthritis Society (NRAS), National Ankylosing Spondylitis Society (NASS), Scleroderma Society (SS) and Lupus UK.

Results: A total of 1079 participants completed the questionnaire, covering 65% of all UK postcode areas (excluding islands). Most participants (93%) had either a child or grandchild <18 years of age. More than 90% of responses said that providing information to children (or grandchildren) whose parents/grandparents have a chronic rheumatic condition was a good idea. Additionally, information should be available whenever the parent or child asked for it. Those who did not want children to have information felt that it would protect them from worry. The most popular modes of delivery were leaflets, websites or delivery by a person. Participants with children both younger and older than 18 years felt that the rheumatology nurse would be the best person to help them talk to their children about their rheumatic condition. The most popular content was felt to be information that outlined the physical impact of the condition and its treatments, disease symptoms and ways in which the child could help and information about preventative steps the child could take to avoid similar conditions. There should be encouragement to seek early screening or diagnosis and information on the likelihood of heritability.

Conclusion: There should be information for the children of people with chronic rheumatic conditions that is provided in a number of formats, for different age-appropriate ways and available from diagnosis onwards. Patients would welcome support from health care professionals in talking to their children about their rheumatic condition.

Disclosure statement: E.D.P.H. has received research funding from Arthritis Research UK. All other authors have declared no conflicts of interest.

213 MUSCULOSKELETAL TRAINING IN RHEUMATOLOGY: WHAT DO TRAINEES THINK?

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Background: One in four adults are affected by musculoskeletal (MSK) problems, accounting for up to 30% of general practitioner consultations. With a move towards providing rheumatology services in the community, there is a need to ensure rheumatology trainees become competent in diagnosing and managing MSK conditions. Rheumatology trainees have expressed the view that training in MSK is compromised, partly due to the reduction in referrals of MSK conditions to secondary care and partly due to the focus on more complex inflammatory conditions.

Methods: An online survey was carried out on behalf of the RHEUMATOLOGY SPECIALIST ADVISORY COMMITTEE TO ASSESS rheumatology trainees’ confidence and ability in dealing with MSK conditions during and upon recent completion of training. The survey was disseminated to rheumatology trainees via their Local Education and Training Board (LETB) trainee representatives.

Results: From an estimated total of 223 trainees, we received 77 responses, with 20 deemed incomplete due to missing answers. Trainees in all career grades from ST3 to 2 years post Certificate of Completion of Training (CCT) and across 15 geographical deaneries/LETBs participated in the survey. The majority of responders (92%) thought MSK medicine is an important part of rheumatology training, with 64% managing patients with MSK and soft tissue pathology on a daily basis and 30% on a weekly basis. However, 32% of trainees felt they were not yet confident in diagnosing and differentiating between different types of soft tissue pathologies. Exposure to and experience with MSK medicine in their current posts and throughout training ranged from poor to excellent. Although 16% of trainees felt they were lacking confidence in dealing with certain areas of MSK medicine, when competencies were mapped out to the rheumatology curriculum (Joint Royal Colleges of Physicians Training Board 2010), most trainees felt they were achieving appropriate competency for their level of training. Trainees were more confident in dealing with upper limb MSK pathologies than lower limb pathologies, with trainees feeling least confident in diagnosing and managing foot and ankle pathologies specifically. Interestingly, only 67% rated their training in injection techniques as at least adequate. Free text comments highlighted that some trainees were self-taught in some injection procedures.

Conclusion: Albeit limited, this survey exploring the views of 77 trainees shows that training in MSK could be improved at all levels. Trainees were keen to have further MSK training, specifically in sports medicine. Qualitative feedback on ways to improve skills repeatedly mentioned shadowing physiotherapists and exposure to direct teaching and supervision focusing on examination techniques. A need for better structured injection technique training was also identified. With changes in the nature and geography of rheumatology services, we feel these aspects of training should not be overlooked, ensuring trainees are equipped to independently manage MSK conditions by completion of training.

Disclosure statement: The authors have declared no conflicts interest.

214 FEASIBILITY OF RANDOMIZED CONTROLLED TRIAL INVESTIGATION OF EDUCATION AND VITAMIN D ADHERENCE IN ETHNIC POPULATIONS

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Background: Many people in the UK are recommended to supplement their vitamin D intake and yet most do not. This suggests an educational need. Darker-skinned ethnic minorities are preferentially affected. The Osteomalacia Mind-Map was developed with culturally sensitive images, translated into Urdu and made interactive on a DVD. This has been well received by the Urdu-speaking community. We were interested to explore the feasibility of a randomized study to measure an effect of education in improving vitamin D adherence as measured by blood levels of vitamin D and parathormone.

Methods: This was a pilot study, Group randomisation was used to avoid interperson contamination. Two South Asian women’s groups were recruited and randomized to get either the interactive DVD or the ARUK leaflet in a presentation about osteomalacia. Knowledge before and after was tested with a knowledge questionnaire and blood samples were taken for vitamin D and parathormone levels.

Results: The groups were found to be mismatched for many things—knowledge, educational attainment, language and other sources of information—and there were organisational difficulties with different tutors and translators. The DVD group had high knowledge at baseline, but this did not improve, although the low scores improved. The knowledge score went from 18 range (3–20) to 23 range (16–29). The DVD group had lower parathormone levels at 5.39 pg/ml (range 3.62–7.74), which did not change at follow-up (5.63 (3.53–8.12)), which did not change at follow-up. Vitamin D actually fell from 49 to 33.2 nmol/l. The leaflet group had an increase in vitamin D from 43 to 57 nmol/l, but parathormone remained higher going from 9.78 to
10.21 pg/mL. Correlation between knowledge and parathormone level was r = -0.407 and the change in knowledge with a change in parathormone was r = -0.324. These were not statistically significant on these small numbers but are stronger than the correlations with vitamin D at r = +0.13 and +0.192, respectively.

Conclusion: Performing a randomized study on this sort of population-level educational intervention seems impractical. A correlation between knowledge and parathormone levels is worth testing and one may act as a surrogate for the other. Parathormone is a more stable outcome measure than vitamin D.

Disclosure statement: The authors have declared no conflicts of interest.

215 VALIDATION OF A NEW FATIGUE SELF-HELP LEAFLET REVEALS BENEFIT FOR PATIENTS AND STAFF
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Background: Fatigue is a heavy burden for rheumatology patients. It can present as a syndrome on its own, a side effect of medication or a symptom of disease. It is also a common consequence of a busy lifestyle. At the request of our patients, we created a self-help leaflet containing information on likely causes of fatigue, management advice and lifestyle tips. Colleagues validating the leaflet commented that fatigue affects them too. We decided to try to answer the questions: Who gets fatigued? How widespread is this problem?

Methods: Outpatients and hospital staff from a variety of departments completed a leaflet validation questionnaire. Patients were given a paper questionnaire and staff completed an online survey. Participants were also invited to complete a 13-item Functional Assessment of Chronic Illness Therapy fatigue scale (FACIT-F) self-assessment tool, providing a score from 0 to 52. (A score <30 indicates severe fatigue and higher scores indicate less fatigue.) Data were collected on demographics, medical conditions, job role, fatigue leaflet feedback, influence of fatigue on life and FACIT score.

Results: A total of 98 people participated: 53 patients and 65 hospital staff completed the questionnaire [24 males, 70 females; mean age 51 years (range 24–87)]. In the patient group, the mean fatigue scores were males 26.8 (range 0–51) and females 24.6 (range 0–45). The mean fatigue scores by outpatient clinic were diabetes 47.0 (one patient), rheumatology 30.8 (six patients; range 16–42), neurology 27.0 (two patients; range 14–40) and oncology and haematology 18.6 (five patients, range 0–31). In the staff group, the mean fatigue scores were males 35.9 (range 6–52) and females 36.7 (range 13–53). The mean fatigue scores by job role (least to most fatigued) were nurses 38.5, trainee doctors 37.5, qualified doctors 36.9, administrative staff 34.3. The most fatigued individual was a male registrar who scored 6. The least fatigued individual was a male consultant who scored 52. Staff with medical conditions scored 8% lower (33) on average than those who deemed themselves as healthy (36). Overall, 44% of patients and 28% of staff scored <30, deeming them severely fatigued. For leaflet validation, 89% of patients (29) and 86% of staff (57) thought the leaflet was either quite or very helpful. No one from either group found it unhelpful.

Conclusion: Fatigue is a widespread problem not exclusive to rheumatology patients. It affects individuals of all genders, ages, job roles and health statuses, although the highest levels are among those with medical conditions, in particular the female patient group. Diagnosis and job role appear to influence levels of fatigue, however, a larger sample group is needed to fully examine this. Both patients and staff felt that this self-help leaflet would benefit those suffering with fatigue. Although this resource was designed for rheumatology patients, it is clearly of wide relevance to all medical and demographic groups and is freely available at http://www.gwh.nhs.uk/media/195287/fatigue-mindmap-trifold150731.pdf.

Disclosure statement: The authors have declared no conflicts of interest.

216 QUANTITY AND QUALITY OF FEEDBACK ON CLERKING ORBITED BY 4TH-YEAR MANCHESTER MEDICAL STUDENTS IN RHEUMATOLOGY AND ORTHOPAEDICS
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Background: Feedback is the cornerstone of effective clinical teaching, allowing students to improve by reinforcing good practice and improving poor practice. The ability to take a clinical history is a key skill required to practice effectively as a doctor. The 4 week Rheumatology and Orthopaedics placement for University of Manchester medical students requires them to take a minimum of 12 case histories, at least 4 of which must be presented to clinicians to obtain feedback.

Methods: A questionnaire survey of 4th-year medical students studying rheumatology and orthopaedics at the University Hospital of South Manchester was performed to review clinical history taking and feedback during this module. It consisted of 13 questions designed around the four levels of training evaluation described by Kirkpatrick’s evaluation framework. It was given to two cohorts of students on the day that they completed their Rheumatology and Orthopaedics block.

Results: Twenty-six of 42 (62%) students responded to the questionnaire, of which 16 students (38%) either agreed or strongly agreed that it was easy to find patients from whom to take clinical histories during the placement. However, 30.7% of students reported not achieving the minimum of 12 case histories required. A total of 42.3% of students agreed that it was easy to identify staff from which feedback could be sought, and 53.8% received feedback for at least four clinical histories. Almost all of the students (96%) agreed that feedback was useful. The content of the feedback varied greatly, with very few students receiving feedback covering positive and negative comments as well as ways to improve (orthopaedics 19.2%, rheumatology 31.7%). Feedback varied in length of time, with 65.4% taking <5 min, 19.2% lasting 5–10 min and 11.5% lasting 11–15 min.

Conclusion: Our survey demonstrates that there are some issues within the current system for facilitating student history taking and obtaining feedback. The vast majority of feedback received is perceived as useful. Approximately half of students are not achieving the amount of feedback that they should receive, hence students are potentially missing out on an important opportunity to improve their clinical performance. Considering the results of this survey, the authors plan to develop an intervention to try to increase the quality and quantity of feedback given, similar to the feedback postcard project being piloted in Edinburgh, which seems on track to improve both the quality and quantity of feedback during clinical placements.

Disclosure statement: The authors have declared no conflicts of interest.

217 AXISAL SPONDYLOARTHRITIS KNOW-HOW: A QUALITATIVE INVESTIGATION OF PATIENT EXPERIENCES OF A BRIEF EXERCISE AND SELF-MANAGEMENT GROUP PROGRAMME
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1Rheumatology, Guy’s and St Thomas’ NHS Foundation Trust, London and 2School of Health Science, University of Brighton, Eastbourne, UK

Background: Axial SpA (axSpA), a long-term seronegative inflammatory arthritis, causes back pain, reduced spinal mobility, fatigue, disability and work incapacity. Exercise and self-management education are key recommendations of international management guidelines for axSpA. The Axial Spondyloarthritis Know-How (ASK) programme aims to increase knowledge, exercise participation and self-management and comprises a 2 h group education, gym-based exercise and hydrotherapy session for up to six people, facilitated by a specialized physiotherapist and a self-management education handbook. This qualitative focus group study explored the acceptability and experience of the ASK programme in adults with axSpA.

Methods: A purposive sample of adults with established AxSpA (Assessment of Spondyloarthritis International Society classification criteria 2009) who attended the ASK group between April and June 2014 were enrolled in the study. Focus groups were facilitated by a rheumatology specialist physiotherapist not involved with the delivery of the ASK programme and followed a topic guide developed a prior. The focus groups were audio recorded and transcribed verbatim. Manual coding was utilized to build categories (through natural inquiry as a permutation of constructivist grounded theory), resulting in the identification of a thematic framework linking the theoretical concepts. The themes were checked for resonance with participants. Ethical approval was obtained from the National Research Ethics Service Committee West Midlands (13/WM/0360).

Results: Two focus groups including nine participants (five males; mean age 43 years; range 21–74; mean disease duration 12 years; range 1–44) were conducted. Overall, patients reported the ASK group was a positive and acceptable experience. Four overarching themes were identified: Exercise behaviours. Participants described increased knowledge and confidence to exercise following the
programme. Three participants commenced exercising with local National Ankylosing Spondylitis Society groups and four adapted the content of a home exercise programme after attendance. Disease positioning. Participants reported comparing their mobility and posture with others in the ASK group and positioned themselves along a disease severity spectrum in relation to other group members. Temporal effects of self-management education. The time between diagnosis and attending the ASK group influenced participation in the ASK programme and the extent of learning acquired. Newly diagnosed interviewees reported that the ASK group provided information and promoted their self-management, whereas those with longer disease duration, who considered themselves to be knowledgeable, enjoyed acting as experts and supporting the learning of the newly diagnosed attendee (referred to as beginners) but reported gaining less knowledge. Group effect. Participants reported that they learned from their peers, particularly self-management strategies for dealing with flares.

Conclusion: The ASK programme is an acceptable and positive experience for adults with axSpA. It promotes understanding and self-management and may be easily implemented into clinical practice. However, it may be more appropriate for those with early disease.

Disclosure statement: The authors have declared no conflicts of interest.

GENETICS

218 THE ASSOCIATION OF A COMMON FUNCTIONAL POLYMORPHISM IN THE TUMOUR NECROSIS FACTOR RECEPTOR 1 GENE (TNFRSF1A) AND DISEASE SEVERITY IN ANKYLOSING SPONDYLITIS

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Background: AS is a highly heritable spondyloarthropathy to which many genes contribute. Its severity is also genetically influenced, but this is not well characterized. A common functional TNFRSF1A polymorphism (rs1800693) results in exon 6 skipping, encoding a soluble truncated form of the p55 (type 1) TNF receptor with potentially anti-inflammatory effects. The G allele predisposes strongly to multiple sclerosis (MS) but is weakly protective against AS. These opposite genetic associations mirror the contrasting effects of anti-TNF medications in these two conditions; anti-TNF therapy is highly effective for AS but may precipitate or worsen MS. We investigated whether rs1800693 was associated with disease severity or response to anti-TNF therapies in AS.

Methods: A total of 2917 UK Caucasian patients with AS were genotyped for rs1800693. A structured questionnaire was used to obtain demographic information, medication use, a visual analogue scale (VAS), 0–10 of how effective they felt their treatment had been and the Bath AS measures of disease activity (BASDAI, BAS-G) and functional impairment (BASFI). Participants were also genotyped for the HLA-B27 tagging SNP rs4349869. Unadjusted and adjusted linear and logistic regression were used to analyse genotypes and outcome measures.

Results: After allowing for failed genotyping (67/2917 cases), there were 2850 cases for analysis. Genotype groups at rs1800693 did not significantly differ by age, gender, disease duration, HLA-B27, age of onset, proportion on biologics or proportion with iritis, psoriasis, joint swelling or IBD. Although the differences were small, rs1800693 GG homozygotes actually had significantly worse BASDAI scores (mean 4.2 [95% CI 4.0, 4.4]) than AA homozygotes [mean 3.8 [95% CI 3.7, 4.0)] in unadjusted (difference = 0.4, P = 0.006) and adjusted analyses (difference = 0.2–0.5, P = 0.002-0.04) depending on the adjustment model used. The rs1800693 genotype had no significant effect on BASFI [unadjusted GG mean BASFI 4.4 [95% CI 4.0, 4.7]] vs AA 4.1 (95% CI 3.9, 4.3), P = 0.1] or BAS-G [GG mean BAS-G 4.3 [95% CI 4.0, 4.6 vs AA 4.2 [95% CI 4.0, 4.3], P = 0.4]. It also did not influence the requirement for (intended biologic treatment G [n = 84340] (24.7%) vs AA 2089104 (20.6%), odds ratio 1.2, P = 0.2) or the efficacy of anti-TNF treatment.

Conclusion: The TNFRSF1A polymorphism rs1800693 shows a weak relationship between AS and BASDAI, but in the opposite direction to that predicted. There is no association with other markers of disease severity and responses to anti-TNF treatment are not predicted by the TNFRSF1A genotype.

Disclosure statement: The authors have declared no conflicts of interest.

219 VALIDATION OF A DISTINCT PSORIATIC ARTHRITIS RISK VARIANT AT IL23R

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Background: PsA is an inflammatory arthritis that is associated with psoriasis and is estimated to present in ~14% of psoriasis patients in the UK. PsA is a complex disease that is influenced by both genetic and environmental factors. Genetic studies have aided the discovery of PsA risk loci, the majority of which also confer a risk for psoriasis. We have recently reported evidence of specific loci that confer a risk for PsA and not psoriasis, including a variant at IL23R that was also found to be independent of a psoriasis variant reported at the same locus.

Methods: In this study we attempted to identify additional PsA-specific risk variants by genotyping 32 single nucleotide polymorphisms (SNPs), which included those found to have nominal significance in our recent Immunochip study (P < 0.05). These were analysed in 914 PsA cases and 9845 controls from the UK, Crete, Spain and Germany, which were independent from those genotyped as part of the Immunochip study. Genotyping was performed using the Life Technologies QuantStudio genotyping platform and association testing was carried out using PLINK. Genotype data were also available from the psoriasis WTCCC2 study (excluding known PsA, n = 1784). Multinomial logistic regression was carried out in Stata to compare effect estimates in PsA and psoriasis using PsA Immunochip data (n = 1962). A direct comparison of PsA and psoriasis genotypes was also performed.

Results: We found a significant association for the SNP rs12044149 mapping to IL23R (P = 4.03 × 10−4). A weak association was found with the psoriasis risk variant rs9988642, which has been reported at the same
locus (P = 0.04). The association with rs12044149 was significant when conditioning upon rs9988642 (Pcond = 4.86 × 10^{-10}). Likewise, rs9988642 remained significantly associated with psoriasis when conditioning upon rs12044149 (P = 1.0 × 10^{-2} vs Pcond 1.63 × 10^{-4}), indicating that they represent independent effects. Effect estimates for rs12044149 were significantly different between PsA and psoriasis (P = 2.0 × 10^{-7}). When genotypes for rs12044149 were directly compared between PsA and psoriasis, the risk allele was significantly increased in PsA (P = 1.91 × 10^{-2}; odds ratio = 1.2).

Conclusion: For the first time we have been able to successfully validate a PsA-specific (associated with PsA but not psoriasis) risk variant at the IL33 locus in an independent cohort, confirming rs12044149 to be independent of rs9988642 (P = 0.01). This now gives a total of four PsA-specific associations that have been identified. Such variants could potentially provide markers to identify psoriasis patients who are prone to developing PsA. IL-23 is a target for the psoriasis drug ustekinumab, which has also shown efficacy in PsA during clinical trials. Therefore it would be interesting to explore the role of disease-specific risk variants in treatment response.

Disclosure statement: The authors have declared no conflicts of interest.

### 220 SUSCEPTIBILITY TO ANYKLOSING SPONDYLITIS IS INFLUENCED INDEPENDENTLY BY TWO CLOSELY ADJACENT RUNX3 SINGLE NUCLEOTIDE POLYMORPHISMS THAT SHOW STRONG FUNCTIONAL EFFECT IN DIFFERENT CELL TYPES

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**Background:** More than 60 genes are associated with AS, many of which (RUNX3, EOMES, TBX21, ZM21, IL23R, IL6R, ERAP-1, IL7 and IL7R) are involved in diverse immunological processes. To understand the functional basis for these genetic associations is one of the greatest scientific challenges in complex polygenic diseases. For example, the association between AS and the single nucleotide polymorphism (SNP) rs4648889 located in a 2 kb regulatory locus upstream of the promoter of RUNX3 can be explained by allele-specific effects on transcription factor (TF) recruitment (including IRF4) that alter gene expression, specifically in CD8+ T cells. Of the 22 SNPs in the RUNX3 locus that were initially found to be associated with AS, we focus here on an independently associated SNP adjacent to rs4648889 that affects gene regulation in CD14+ monocytes.

**Methods:** We used the Encyclopedia of DNA Elements (ENCODE) data to dissect the epigenetic and transcriptional landscape of the RUNX3 locus; we performed in silico analysis and in vitro functional studies to characterize the effects of this particular genetic variant, providing critical functional evidence for its role in AS.

**Results:** Conditional analysis on 4230 AS cases and 9700 matched controls established the primacy of the rs4648889 association (1.3 × 10^{-10}) with AS in this region. However, there was also an independent second signal (1.7 × 10^{-10}) with rs4265380, adjacent to rs4648889, highlighting the importance of this locus and a likely functional role for rs4265380. ENCODE data on CD14+ monocytes revealed a robust peak for DNA accessibility (DNase1 hypersensitivity) and TFs ChIP-seq overlapping rs2465380. There was also a strong overlying peak for histone modification, H3K4Me1, normally associated with the active regulatory region. The effect of the rs2465380 dimorphism on TF binding was evaluated by electrophoretic mobility shift assays (EMSA) using nuclear extract from U937 and THP-1 (monocyte-derived cell lines) focusing on specific TFs involved in monocyte regulation and inflammation (C-Fos, Jun-D, p53). Analysis of the expression of inflammasome-related genes revealed some striking differences (i.e. CARD6 and IL-6, upregulated 5- and 177-fold, respectively) influenced by the rs2465380 genotype.

**Conclusion:** We identified functional differences in the transcriptional regulation of RUNX3 associated with AS-associated SNPs at this locus. Two individual adjacent SNPs exert their independent effects in two separate cell types (CD8+ T cells and monocytes). These observations are critically important not only in identifying cell types that play a pathogenic role in AS, but also in defining potential therapeutic drug targets.

**Disclosure statement:** The authors have declared no conflicts of interest.
**Background:** It is well established that early recognition and treatment of synovitis is integral to the prevention of permanent joint damage and co-morbidity in RA. PET is being increasingly recognized as a sensitive means of detecting and quantifying early synovitis. PET ligands to translocator protein (TSPO), a mitochondrial cholesterol transporter known to be upregulated on activated macrophages, are increasingly being demonstrated to have utility in detecting and quantifying synovitis. The TSPO PET tracer [11C]PBR28 has a higher affinity for TSPO and less signal/noise ratio, thus it may be a more sensitive and specific tracer for imaging synovitis. Binding of second-generation tracers is affected by a single nucleotide polymorphism (SNP), rs6971, with homozygotes binding tracers with low affinity. Our group has so far demonstrated rs6971 homozygote prevalence at 12% in the RA population, comparable to healthy populations. Here we present findings from a proof-of-principle pilot study using [11C]PBR28 to image synovitis in patients with RA.

**Methods:** Patients with RA affecting the knees or ankles were included, as well as healthy controls. Homozygotes for rs6971 were excluded. Patients underwent a US scan and clinical examination of the group of joints to be imaged with PET-CT. Semi-quantitative scores for synovitis on clinical examination and US were applied. [11C]PBR28 was injected as an i.v. bolus at the start of a 90 min dynamic PET acquisition. PET data were reconstructed using filtered back-projection correcting for attenuation and scatter (based on a low-dose CT acquisition). Regions of interest (ROIs) were drawn on synovial tissue in the knee or ankle joints. Standard uptake values (SUVs) for all ROIs were calculated.

**Results:** To date, six PET-CT images have been acquired: four from patients with known RA and 2 from those without inflammatory arthritis. SUVs of [11C]PBR28 positively correlate with synovitis scoring on clinical and US assessment, with no significant uptake in healthy joints. Interestingly, elevated SUVs were observed in the knee joint of an RA patient with no clinical or US evidence of synovitis. Further patients are required to confirm these initial findings. The impact of binding affinity due to the rs6971 SNP on [11C]PBR28 PET-CT of inflamed joints remains to be fully assessed.

**Conclusion:** We demonstrate a significant increase in the uptake of [11C]PBR28 in inflamed joints, with significant positive correlation of SUVs with clinical and US assessments of synovitis. The potential of [11C]PBR28 to detect subclinical synovitis is demonstrated by the fact that elevated SUVs were seen in the knee joint of an RA patient without clinical or US evidence of synovitis. Further patients are required to confirm these initial findings. The impact of binding affinity due to the rs6971 SNP on [11C]PBR28 PET-CT of inflamed joints remains to be fully assessed.

**Disclosure statement:** The authors have declared no conflicts of interest.

### Table 1. Clinical correlates of DECT results

<table>
<thead>
<tr>
<th>Patient</th>
<th>Synovial aspirate</th>
<th>Urate level, mmol/l</th>
<th>X-ray results</th>
<th>US</th>
<th>DECT indication</th>
<th>DECT region</th>
<th>DECT result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ND</td>
<td>580</td>
<td>Erosions in hands, normal</td>
<td>Normal</td>
<td>Inflammatory symptoms, chronic kidney disease and elevated urate</td>
<td>Hands and feet</td>
<td>Urate deposition, MTP joint/P joint in feet, no erosions in feet, no urate deposition in hands</td>
</tr>
<tr>
<td>2</td>
<td>ND</td>
<td>406</td>
<td>Normal</td>
<td>ND</td>
<td>Inflammatory arthritis or chronic gout</td>
<td>Left ankle, right hand</td>
<td>No urate deposition, degenerative changes seen</td>
</tr>
<tr>
<td>3</td>
<td>ND</td>
<td>351</td>
<td>Fracture of the scaphoid</td>
<td>Normal</td>
<td>Inflammatory arthritis or chronic gout</td>
<td>Hands</td>
<td>No urate deposition, degenerative changes seen</td>
</tr>
<tr>
<td>4</td>
<td>ND</td>
<td>633</td>
<td>Normal</td>
<td>ND</td>
<td>High urate with longstanding foot pain over MTP joints</td>
<td>Feet</td>
<td>Extensive uric acid deposition on first MTP joints bilaterally and within tarsometatarsal, mid-tarsal and tibiotalar joint with associated gouty tophi</td>
</tr>
<tr>
<td>5</td>
<td>ND</td>
<td>590</td>
<td>Normal</td>
<td>ND</td>
<td>Possible gout</td>
<td>Hands</td>
<td>Extensive uric acid deposition along distal radio-ulnar joints of both hands, index finger and little finger PIP joints of right hand, PIP joints of index and middle finger of left hand</td>
</tr>
</tbody>
</table>
| 6       | ND               | 910                 | OA | ND | Possible gout | Elbows, hands, feet | Urate deposition in small hand joints, left first MTP joint and on triceps insertions on the olecranon (
| 7       | ND               | 425                 | Double contour | Normal | Attacks in right first MTP joint, high urate and family history, but very unusual in a young female | Right foot | Small marginal focus of urate deposition at the medial aspect of the first metatarsal head, no erosions |
| 8       | MSU crystals (historic) | 240 | Periarticular osteopenia and erosions | Normal | Histologic positive asperite but CCP, ANA and ANC positive | Left hand | No urate deposition, erosive changes seen |
| 9       | ND               | 479                 | Normal | Normal | Possible gout | Left foot | No urate deposition, degenerative changes seen |
| 10      | ND               | 402                 | Normal | Normal | Discharging lesion right ring finger DIP joint | Hands | No urate deposition |
| 11      | ND               | 315                 | OA | Normal | Possible chronic gout | Right foot | No urate deposition |

ND: not done; DECT: dual-energy CT.
Data from six HBs in Wales were obtained, totalling 190 scan requests in a 4 week period. Three HBs had radiology-only MSUS service, 2 had rheumatology and radiology service and 1 had a rheumatology-only service. A total of 145 (76%) MSUS requests were made to define or confirm synovitis, of which 35 (24%) were for same day in two rheumatology departments. The mean waiting time for synovitis scans across Wales was 8.1 weeks (range 0.1-14 weeks). The shortest waiting time was 2.7 weeks (range 0.1-12) and the longest was 32 weeks (range 6-43). Forty-five (24%) requests were for non-synovitis scans, with a mean waiting time of 11.9 weeks (range 1-50); the shortest waiting time was 5 weeks (range 1-8) and the longest was 35 weeks (range 26-50). Where MSUS was provided by rheumatology (with or without radiology), the mean waiting time for synovitis scans was lower, at 6.6 weeks (range 0.1-21 weeks; n = 91) compared with that of 14 weeks (range 3.5-43 weeks; n = 33) where MSUS was only provided by radiology. Of the 32 respondents completing the online survey, 15 (47%) felt that longer waiting times for MSUS caused delay in early arthritis treatment, 9 (28%) felt it caused inequality of patient care, 7 (22%) felt it caused patient dissatisfaction and 9 (28%) felt it caused unnecessary follow-up appointments.

Conclusion: Access to MSUS for rheumatology patients is variable within Wales between HBs. There is a significant delay in synovitis scanning if only performed by radiology without facilities for same-day scanning, leading to potential delays in patient management. If MSUS is to play a role in managing inflammatory arthritis, rheumatology departments within Wales need equitable access to US.

Disclosure statement: The authors have declared no conflicts of interest.

225 AUDIT OF POSITRON EMISSION TOMOGRAPHY–COMPUTED Tomography USE IN RHEUMATOLOGY: TOWARDS A REGIONAL REFERAL PATHWAY

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Background: PET-CT has emerged as a useful tool in the modern rheumatologist’s armoury when facing certain diagnostic challenges. The Royal College of Physicians’ (RCP) guidance on the indications for PET-CT includes large vessel vasculitis (LVV), sarcoidosis and pyrexia of unknown origin (PUO) in specific circumstances. Within the North West England rheumatology community, potential barriers to the use of PET-CT were identified, including uncertainties about the availability of PET-CT for non-ocular indications, referral route and waiting times. Discussion with the regional PET-CT centre highlighted variability in the clinical information provided on referrals, which may impact on the urgency or interpretation of imaging. Thus development of a regional referral pathway for PET-CT was proposed. As the first step, we aimed to undertake a retrospective audit of referrals from rheumatologists to a regional PET-CT centre in addition to reviewing referrals for suspected LVV from other specialties.

Methods: The audit standard was the 2013 RCP guidelines on the indications for PET-CT. Cases were identified from December 2013 to August 2015. Referral letters and reports were reviewed. Recorded variables included referring centre and specialty; clinical details, including referral reason, inflammatory markers, steroids/immunosuppressant therapy and previous imaging; time from referral to scan and key findings.

Results: A total of 39 cases were reviewed. Nineteen patients were female (48.7%) and the median age was 40 years (interquartile range (IQR) 63-57). The median time from referral to scan was 14 days (range 1-57). Thirty of (77%) referrals were made by rheumatologists from 12 Trusts. Indications and key findings are described in Table 1. In all cases referrals met the audit standard. Intermediate vascular uptake was reported on nine scans but was inconclusive for vasculitis. In some cases vascular uptake was reported using a semi-quantitative scale and in others in descriptive form. Information on inflammatory markers was provided in 16/39 (41%) cases. Steroid/immunosuppression use was reported in 32/39 (82%) cases. In cases where intermediate vascular uptake was seen, two patients were on steroids and in four cases no information was provided. Previous imaging information was provided in 16/39 (41%) cases. Prior to referral, 11 patients had a CT scan, 5 had an MRI, 1 had a labelled white cell scan and another had an isotope bone scan.

Conclusion: While all referrals were for appropriate indications, important information regarding inflammatory markers and medication was lacking in some cases, which may have an impact on scan interpretation. There were variations in reporting methods and intermediate cases may benefit from multidisciplinary team discussion. Going forward, a regional user survey is being undertaken. Collaboration with other regional PET-CT centres has been initiated with the aim of optimising acquisition and reporting methods. A referral pathway including a pro forma with minimal clinical information is being designed. As a result, we aim to optimize the use of PET-CT within the region.

Disclosure statement: The authors have declared no conflicts of interest.

225 Table 1. Indications for PET-CT and key findings

<table>
<thead>
<tr>
<th>Indication</th>
<th>Number of cases</th>
<th>Key findings, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVV</td>
<td>28</td>
<td>Steroids = 8; No steroids = 9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other immunosuppression = 2; Not documented = 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Steroids = 5; No steroids/immunosuppression = 2; Other immunosuppression = 2; Not documented = 0</td>
</tr>
<tr>
<td>PUD</td>
<td>2</td>
<td>Granulomatous disease = 1; Not documented = 2</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>1</td>
<td>Not documented = 1</td>
</tr>
</tbody>
</table>

LVV: large vessel vasculitis; PUD: pyrexia of unknown origin.
Methods: Thirty consecutive MSK US scans over four clinics were reported by two consultant rheumatologists. One rheumatologist (T.J.A) scanned and both reported using the images obtained. The scans were undertaken using a GE Logiq E US machine. Reports were evaluated for concordance by R.R. The scans included hands, wrists, feet, ankles or a combination of joints. The concordance was graded from 1 (complete concordance) to 4 (complete discordance). Grade 2 was a minor discrepancy unlikely to affect patient care. The aim of the study was to assess concordance and its degree between the reports of the two sonographers.

Results: Nineteen of 30 scans were for hands and wrists. The majority were diagnostic scans assessing disease activity in established patients. The main indications for the scans were polyarthralgia, early inflammatory arthritis or a synovitis screen. Table 1 shows the concordance of the scans. Twenty-four of 30 grade 1 concordant and 6/30 were grade 2. No scans were grade 4 discordant. Of the six scans that had discrepancies, the main discrepancy (S6) seen was discordant grading grade 1 syndesmophytes.

Conclusion: Eighty per cent of scans were grade 1 concordant and 20% of scans were grade 2. The discrepancies were minor and did not affect patient care. The rate of concordance between sonographers varies widely in the literature and this study shows that our service lies in the higher end of this range. It is important to establish quality assurance for any new MSK US service.

Disclosure statement: The authors have declared no conflicts of interest.

226 Table 1. Levels of concordance for each US scan

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</table>

Grade 1, complete agreement; grade 2, minor discrepancy; grade 3, potentially significant discrepancy; grade 4, discrepancy likely to have adverse consequences for the patient.

227 DEVELOPMENT OF A NOVEL IMAGING METHOD FOR TibIAL BONE MINERAL DENSITY MEASUREMENT In PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Density fractionation and chemical analysis studies have demonstrated that subchondral bone is less highly mineralized in patients with knee OA than age-matched controls. It can be hypothesized, therefore, that BMD decreases around osteoarthritic joints. It has been reported however, that osteoarthritic subchondral bone may also increase in volume, by up to 20%. DXA measures BMD per area of bone, meaning potential changes in bone depth are unaccounted for. This may be particularly problematic for longitudinal evaluation of subchondral BMD in patients with knee OA. As such, this study aimed to develop a method for measuring tibial depth at sites of DXA BMD measurement in patients with knee OA and to explore whether adjusting for bone depth has implications for BMD interpretation.

Methods: Participants with Kellgren–Lawrence grade ≥2 OA who were enrolled in a longitudinal parent epidemiological study of knee OA (the VIDEO study) were included in this analysis. Participant DXA and MRI data were retrospectively consecutively retrieved from the parent study until a sample size of 31 was achieved. Areal BMD (aBMD) was measured using DXA at the medial and lateral proximal tibia. MATLAB software was written to co-register DXA and MRI data in order to calculate tibial depth. A volumetric BMD (vBMD) score was calculated for both the medial and lateral tibial compartments. Paired samples t-tests were used to determine the difference between medial and lateral compartment scores. Pearson’s correlation coefficient was used to test correlation between aBMD and vBMD scores.

Results: In both the medial and lateral compartments the mean aBMD was significantly higher than the vBMD [medial aBMD: 0.830 (s.d. 0.235), vBMD: 0.189 (s.d. 0.046); lateral aBMD: 0.774 (s.d. 0.220), vBMD: 0.185 (s.d. 0.050); P < 0.001]. In both medial and lateral compartments, aBMD and vBMD had a significant positive correlation, r = 0.793 and 0.910, respectively (P < 0.001). With a mean difference of 0.057 (t = 4.432), the medial compartment aBMD was significantly higher than the lateral compartment aBMD (P < 0.001). However, there was a non-significant difference of −0.003 (t = −0.901) between the medial and lateral compartment vBMD (P = 0.375). The difference between medial and lateral tibial depth was 0.390 (t = 7.595, P < 0.001).

Conclusion: This study provides preliminary evidence that differences in aBMD between the medial and lateral compartment of the subchondral tibia could be primarily due to tibial depth differences in patients with knee OA. Adjusting for tibial depth demonstrates a potential under-/overestimation in aBMD, and thus possibly fracture risk, in this patient group. vBMD is an alternate measure of tibial bone density for use in patients with altered bone morphology related to knee OA.

Disclosure statement: C.B. has received research funding from NIHR.

228 KEY DIFFERENCES BETWEEN OSTEOARTHRITIS AND SEROPOSITIVE RHEUMATOID ARTHRITIS ON HAND ULTRASOUND

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Background: The US features characterising active and chronic inflammation in RA are synovial hypertrophy (SH) and positive power Doppler (PD) signal. Erosive OA (EOA) shows increased synovial thickening, rarely associated with PD signal, never found in patients with non-inflammatory joint pain. Our findings suggest an overlap between US features of OA and RA.

Methods: A retrospective, observational study was conducted using 654 patients with inflammatory hand joint pain referred to the University College London Hospital US outpatient clinic, comparing 73 OA and 224 seropositive RA patients by age, sex, CRP, CRP, US and clinical joint examination (CJE). On US, SH, PD signal, number of osteophytes (OPs) and erosions were noted. On CJE, tender joint count (TJC), swollen joint count (SJC) and global assessment score (generalized visual analogue scale (GVAS)), were obtained. We compared the 22-joint score of the hand (including wrist, MCP and PIP joints) with smaller, predefined joint scores, including 20, 18, 16, 14 and 10 and two sets of 4-joint for RA and scoring systems comprising 20, 12, 10 and 4 joints for OA.

Results: In the 22-joint system, OA patients [mean age 60.6 years (s.d. 9.93)] were older than RA patients [mean age 53.8 years (s.d. 15.4)] (P < 0.0028). Inflammatory markers were similar (CRP, P = 0.690; ESR, P = 0.100) between groups. US showed more OPs in OA patients [median 7 (interquartile range (IQR) 8)] than RA patients [median 1 (IQR 3)] (P < 0.001). PD signal was more frequent in RA [median 0 (IQR 2)] than OA [median 0 (IQR 0)] (P < 0.001). RA patients had more erosions [median 2 (IQR 8)] than OA patients [median 0 (IQR 4)] (P = 0.002). CJE showed higher TJC scores in RA compared with OA [P = 0.001], likewise with SJC scores (P < 0.001) and GVAS scores (P < 0.001). When comparing OA joint scores, the 20-joint score was the most comprehensive in assessing changes compared with the scores from 12, 10 or 4 joints. In RA, the 22-joint score was most informative; however, similar information was captured by two different sets of 4-joint scores (wrist + MGS and MCP-C3 bilaterally) (P < 0.05).

Conclusion: Our findings reflect known differences between hands in RA and OA. OA is a degenerative condition, affecting older patients and associated with more OPs on US. RA patients showed more inflammation on US (SH, PD and erosions) and higher CJE. Interestingly, some OA joints were also characterized by inflammatory changes. Hand US can help differentiate OA from RA. The effectiveness of using smaller joint scores in RA may benefit time-constrained clinical settings. Further work is needed to determine objective cut-offs for inflammatory changes, which can help reliably differentiate RA associated with joint degenerative changes from inflammatory OA.

Disclosure statement: The authors have declared no conflicts of interest.

229 PREDICTION OF PERSISTENT INFLAMMATORY ARTHRITIS WITH ULTRASOUND: A DATA-DRIVEN METHOD

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Thursday 28 April 2016 POSTER VIEWING III
College, University of Oxford, Oxford and 4Wolfson Computer Laboratory, University Hospital Birmingham NHS Foundation Trust, Birmingham, UK.

Background: Prediction of disease persistence in early inflammatory arthritis is important to enable timely initiation of appropriate therapy. Musculoskeletal US is a sensitive and specific modality for the detection of subclinical synovitis. Currently available predictive algorithms for persistent arthritis do not include US variables. We used a data-driven method to identify the minimal core set of US, clinical and serological variables predicting persistent inflammatory arthritis in a cohort of patients with early arthritis.

Methods: A total of 107 patients (60 females, median age 51 years) with clinically apparent synovitis at least one joint and symptom duration ≤3 months underwent clinical, laboratory and US assessments. The final diagnosis was determined during 18 months of prospective follow-up. US assessment determined the presence of grey scale (GS) and power Doppler (PD) synovitis at 36 joints (bilateral MCPs 1–5, PIPs 1–5, wrists, shoulders, elbows, ankles and MTPs 2–5) using a Siemens Acuson Antares scanner. First, univariate analysis was performed to identify all clinical, serological and US variables significantly associated with persistent disease at 18 months. Second, principal component analysis (PCA) was performed on clinical and serological variables (age, gender, symptom duration, ESR, CRP, RF, ACPA, duration of early morning stiffness, tender joint count and swollen joint count), US GS variables and US PD variables to identify variables that reflected similar themes. Finally, one variable from each component was extracted and made available in a forward-stepwise multivariate logistic regression analysis to test for independent predictive effect.

Results: Sixty-three patients developed persistent inflammatory arthritis and 44 patients had resolving disease. On PCA, three components were identified within the clinical and serological variables, four components were identified within the GS US variables and four components were identified within the PD US variables. Table 1 shows the variables with the highest magnitude of factor loading from each component, together with the univariate odds ratio (OR). The final multivariate logistic regression model included RF positivity (OR 5.83, P = 0.003), MCP2 PD positivity (OR 4.33, P = 0.002) and MTP2 PD positivity (OR 10.72, P = 0.030). In seronegative patients, the final multivariate logistic regression included early morning stiffness >60 min (OR 3.62, P = 0.011) and PIP2 PD (OR 8.41, P = 0.003). In seropositive patients, the final multivariate logistic regression included RF positivity (OR 8.41, P = 0.001), MCP2 PD positivity (OR 6.19, P < 0.001) and PIP3 PD positivity (OR 4.17, P = 0.002). In seronegative patients, the final multivariate logistic regression included early morning stiffness >60 min (OR 3.62, P = 0.011) and PIP2 PD (OR 8.41, P = 0.003).

Conclusion: This is the first study using a data-driven method to show that US provides independent data beyond clinical and serological variables in the prediction of persistent arthritis, even in RF and ACPA-negative patients. Bilateral MCP2 and MTP2 is the minimal joint subset that provides independent predictive data in this cohort.

Disclosure statement: The authors have declared no conflicts of interest.

229 Tau: 1. Factor loading and ORs

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230 THE IMPACT OF A NEW RHEUMATOLOGY-BASED MUSCULOSKELETAL ULTRASOUND SCAN SERVICE ON INFLAMMATORY ARTHRITIS MANAGEMENT IN A LARGE DISTRICT GENERAL HOSPITAL

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Background: Musculoskeletal (MSK) US scanning is increasingly used to aid clinical decision-making in the management of early and established inflammatory arthritis. In patients suspected of having early inflammatory arthritis (EIA), we analysed the autommune profile (RF and ACPA). For the whole cohort we studied the rate of synovitis detected and interventions as a result of the scan, namely, start, escalate or stop DMARDs, joint aspiration or injection or referrals to allied health professionals (AHPs) (e.g. physiotherapy). Some patients had more than one intervention.

Methods: A total of 167 MSK US scans (hands, feet, ankles and wrists) were carried out in a 6 month period between January and June 2015. Scans were carried out using a GE Logic E machine. Synovitis was defined using OMERACT grey scale and power Doppler grading protocols, including tenosynovitis and erosions. Data were collected from paper and electronic patient records.

Results: Of 167 scans, 79 were performed for patients with suspected EIA and 75 for non-EIA patients; 13 patients were not defined. In the suspected EIA group, 29 patients (36.7%) had synovitis. In the suspected EIA synovitis subgroup, 20 patients were double seronegative (negative RF and ACPA) and 7 patients were seropositive (RF or ACPA positive or both). In the suspected EIA non-synovitis subgroup, 40 patients were double seronegative and 5 patients were seropositive. These data were not available for seven patients. Sixty of 79 patients (76.9%) in the suspected EIA group developed double seronegative and, of these, 20 (30%) had synovitis. In the suspected EIA group, for 25 patients a DMARD was started, for 1 patient the DMARD was stopped, for 3 patients the DMARD was increased and 35 were referred to AHPs. Thirty-two patients were not started on a DMARD and seven patients continued with the same DMARD; three patients are awaiting decisions. Sixty-one of 79 patients had at least one therapeutic intervention. For the non-EIA group, 23 patients (30.7%) had synovitis. In the non-EIA group, 12 patients a DMARD was initiated, for 5 the DMARD was stopped, for 3 the DMARD was increased and 17 were referred to AHPs. Three patients had joint aspiration or injection. Twenty-three patients were not started on a DMARD and 18 patients continued with the same DMARD; 5 patients are awaiting decisions. Twenty-six of 75 patients received at least one therapeutic intervention. In both groups, suspected EIA and non-EIA, the most common therapeutic intervention was referral to AHPs followed by starting a DMARD.

Conclusion: This study shows that the introduction of a rheumatology-based MSK US service had a significant impact on patient management, with approximately three-quarters of suspected EIA and one-third of non-EIA patients requiring a therapeutic intervention following the scan.

Disclosure statement: The authors have declared no conflicts of interest.

PAEDIATRIC AND ADOLESCENT RHEUMATOLOGY

231 ASSESSING THE IMPACT OF CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING ON CLINICIANS’ DECISION-MAKING IN JUVENILE IDIOPATHIC ARTHRITIS OF THE HIP

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1Medical School, University of Sheffield, 2Radiology and 3Rheumatology, Sheffield Children’s Hospital and Adolescent Rheumatology, Sheffield Teaching Hospitals, Sheffield, UK

Background: Contrast-enhanced MRI (CE-MRI) is considered the gold standard imaging modality for suspected hip arthritis in children. A recent study at our institution identified discrepancies in radiological interpretation of CE-MRI hip scans and we report this separately. Acknowledging potential variability of reporting, we conducted the present study to explore the impact of CE-MRI on clinical decision-making.

Methods: We conducted a retrospective case-note review of patients who underwent hip CE-MRI at our Institution between January 2011 and September 2014 to confirm or exclude the presence of hip inflammation. The impact of CE-MRI findings on clinical management was assessed using clinic data and contemporaneous radiological reports. Clinical data included inflammatory markers, reported symptoms and medication changes before and within 3 months following CE-MRI. Clinician suspicion of inflammation or lack of it was determined if explicitly recorded by the clinician at the visit when the CE-MRI was requested. Decision-making was based on changes made to the patient’s treatment following CE-MRI.
Results: Eighty-four patients with a median age of 13 years (range 1–18) under the care of three pediatric rheumatologists and one adolescent/adult rheumatologist were included. Twenty-two scans (26%) demonstrated inflammation. A significant difference (P = 0.001) in decision was observed between those receiving an inflammatory vs non-inflammatory CE-MRI report (Table 1). Nineteen (86%) of the 22 patients in whom CE-MRI reported evidence of synovitis received increased treatment (steroid/GMAR and/or biologic drug). Clinician suspicion of inflammation or non-inflammation was compared against CE-MRI report (gold standard). Clinician specificity for inflammation was 45.6% and sensitivity 70.6%; positive and negative predictive values were 31.6% and 81.5%, respectively. The number of patients with an inflammatory diagnosis increased from 28 to 42 (33% to 50%) following CE-MRI scanning.

Conclusion: A CE-MRI report influenced the rheumatologists’ decision-making. Most notably an inflammatory scan result was associated with an increase treatment. When CE-MRI was negative, clinical suspicion of inflammation had a greater impact on the decision to treat than the scan result (active inflammation of other joints may also have influenced decision-making). Clinicians were able to reliably identify non-inflamed hips. Clinician specificity for hip inflammation was low, resulting in a high number of unnecessary MRI scans.

Disclosure statement: F.M.Y. has received research support from the University of Sheffield Medical Athena Swan Bursary to support a Biomedical PhD that included this research. All other authors have declared no conflicts of interest.

232 EVALUATING THE RHEUMATOLOGY TRANSITIONAL CARE SERVICE FOR YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS IN NEWCASTLE UPON TYNE

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Background: Transitional care is the purposeful, planned movement of adolescents and young adults with chronic conditions from a child-centred to an adult-oriented health care system. Currently in Newcastle, a transitional care service is in place for young adults with JIA. The young adults get the opportunity to meet a consultant from the adult service while still in the paediatric service as part of the transition process. They are then seen by the same consultant in a specialized young adult clinic. In 2010, the Department of Health (DoH) issued You’re Welcome guidelines, which are a set of quality criteria for young people-friendly health services. There are 10 key themes in these guidelines, and for a service to achieve You’re Welcome accreditation, they must audit their service against these guidelines. One overarching theme of the You’re Welcome document is that young people should be actively involved in monitoring and evaluating their service. The aim of this audit was to evaluate the young adult transition service for young adults with JIA from the perspective of young adults using the service in Newcastle upon Tyne.

Methods: Two questionnaires were developed and handed out to 27 consecutive patients attending the young adult clinic. The first questionnaire was the DoH You’re Welcome questionnaire and the second questionnaire was developed with questions specific to our service.

Results: Of the 27 patients who completed the questionnaires, there were 12 males [median age 19 years (range 16–23)] and 15 females [median age 19 years (range 16–22)]. The results of both questionnaires were largely favourable but highlighted areas for development. Transition was discussed and planned prior to attending the young adult service in 96% of cases. Eighty-nine per cent of patients who had met the consultant from the adult service while still in the paediatric service had found this a helpful and reassuring experience. Eighty-two per cent of patients who had not had the opportunity to meet the consultant from the adult service while still in the paediatric service reported that they would have found this a useful experience. All patients reported that they would be happy to use the service again. You’re Welcome themes that scored low included understanding of confidentiality, how to make comments or complaints and information on display regarding religion, sexuality and mental health.

Conclusion: Transition plays an important role when patients with chronic conditions move from paediatric to adult services. The audit was reassuring and demonstrated that young adults with JIA valued a transitional care service. However, the audit also highlighted areas that needed improving. The transitional care and young adult service in Newcastle is currently implementing these changes with a view to re-auditing and applying for You’re Welcome accreditation in the near future.

Disclosure statement: The authors have declared no conflicts of interest.

233 MYELOID-RELATED PROTEINS 8 AND 14 (MRP 8/14): POTENTIAL BIOMARKERS OF ARTHRITIS IN CHILDREN WITH TRISOMY 21?

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Background: To date, no specific markers exist in clinical practice to predict disease activity and outcome in JIA. MRP8 and MRP14 are calcium-binding proteins secreted by infiltrating phagocytes in synovial inflammation. Studies have shown that their serum concentrations correlate sensitively and specifically with synovial inflammation in JIA. To date there have been no studies looking specifically at serum or SF levels of MRP8/14 in Down’s arthropathy (DA). We attempted to answer the question, are MRP8/14 serum/SF levels accurate markers of inflammation in DA, and do levels differ in DA compared with JIA?

Methods: New cases of JIA and DA attending our centre had blood drawn to measure CRP, ESR and MRP8/14 levels. The corresponding active joint count (AJC) was documented. Paired SF samples were taken for analysis from children requiring steroids. Serum and SF concentrations of MRP8/14 were determined by sandwich ELISA.

Results: Serum MRP8/14, ESR and CRP were measured in DA (n = 34) and JIA (n = 50) patients. In a subgroup, MRP8/14 levels were also quantified in paired SF, DA (n = 3) and JIA (n = 21). At diagnosis, ESR and CRP levels were elevated in a lower percentage of DA cases compared with our JIA cohort, even though, on average, a higher AJC was observed in the DA cohort. Serum MRP8/14 levels were significantly higher in JIA compared with DA, levels of which correlated with ESR (r = 0.312, P < 0.05). No correlation between serum MRP8/14 and systemic clinical markers (CRP and ESR) was observed for DA. We therefore examined if MRP8/14 levels were higher at the site of inflammation, i.e. in SF from the joints of children with active DA. Preliminary data have shown MRP8/14 levels are higher in SF compared with serum in DA. Our CRP, ESR and serum/SF MRP8/14 observations in DA may suggest that there is dissociation between systemic and local inflammation in this cohort.

Conclusion: DA is a more challenging condition than JIA in light of confounding illness and the often-associated developmental delay and non-verbal state. In DA, a simple biomarker of disease would be invaluable. Our preliminary results suggest that children with DA (and who may have SF levels of MRP8/14 that correlate to disease activity) in JIA, SF concentrations of MRP8/14 are significantly higher than their paired serum samples, however, our results show significant positive correlation between the two. This suggests that serum MRP8/14 levels are potentially accurate markers of SF levels, and in turn are accurate markers of disease activity in JIA. This was not the case in our DA cohort and may suggest a functional role for MRP8/14 at the site of inflammation in DA.

Disclosure statement: The authors have declared no conflicts of interest.

234 HOW COMMON IS REMISSION IN JUVENILE IDIOPATHIC ARTHRITIS? A SYSTEMATIC REVIEW

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Background: Children with active JIA are at risk of pain, disability and joint damage. The treatment target for patients is remission, where there is no evidence of disease activity. Many definitions of remission have been developed for JIA populations. In addition, the frequency of remission in contemporary patient cohorts has not been described. The aim of this systematic review was to investigate how remission is defined across JIA clinical cohorts and the frequency of remission in these cohorts.

Methods: For this systematic review, studies were selected if they were observational in design and estimated remission from inception of JIA cohorts of ≥ 50 patients. Articles were excluded if they focused on remission following specific medical interventions, did not define remission clearly or were dated prior to the publication of ACR
classification criteria for juvenile arthritis. Studies were selected from Medline, Embase and PubMed and from bibliographies of those already selected. Outcomes were classified as inactive disease (ID), where no disease activity was evident at a single time point, and remission, where ID was maintained for a specific length of time and/or off medication.

Results: Sixty studies were reviewed. Overall, patients’ ages ranged from 1 month to 68 years at recruitment and disease duration ranged from a minimum of 6 months to 30 years. Fifty distinct definitions of remission were identified. Single criteria, such as no active joints or zero on the physician’s global, were frequently utilized. Validated composite scores such as the ACR 2011 criteria and Wallace’s preliminary criteria were used but were frequently altered to suit the data collected. Within the first 5 years of disease, the frequency of ever having achieved ID increased from 30% by 1 year to 85% by 5 years. The frequency of ever having achieved remission was lower (0% to 58%, respectively), but no clear trend over time was evident. Across studies looking at the prevalence of remission, higher frequencies were generally achieved after longer disease duration. Higher estimates were not achieved from studies that recruited in the biologics era post-2000. Across ILAR subtypes, patients with persistent oligoarthritis disease tended to fare particularly well, while patients with RF-positive polyarthritis had the poorest prognosis.

Conclusion: ID was achieved at once by the majority of children in the first 5 years of disease. The frequency of current remission increased with longer disease duration, but the majority of patients remain in active disease in the long term. A large variation existed between estimates of both ID and remission, but it is unclear whether variation is due to population characteristics, study design or the vast variation in definitions applied. Multiple definitions need to be applied in a single patient population to disentangle the reasons for this variation.

Disclosure statement: The authors have declared no conflicts of interest.

235 A SURVEY OF RHEUMATOLOGY PATIENTS’ TRANSITION FROM PAEDIATRIC TO ADULT SERVICES IN THE UNITED KINGDOM AND HOW THIS EXPERIENCE AFFECTED PATIENTS’ OUTCOMES AND ADHERENCE TO MEDICATION

Hannah L. Power,1 Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK

Background: Health care transition is the period of time when a patient moves from a paediatric clinic to an adult clinic at the appropriate age and the process of ensuring the patient and parent/carer are prepared for this. Many paediatric rheumatology conditions are chronic and therefore require paediatric patients to transition their care to an adult setting. A review of the data established that there were limited data from the patient perspective, so this research was carried out to address this knowledge deficit and assess what improvements can be made to the transition process.

Methods: The research undertaken collected both quantitative and qualitative data using an online 27-question survey at the end of 2014 that was completed by rheumatology patients who had undergone transition or were undergoing transition into the adult services. The survey collected data on demographics, the experience for the patient when transitioning from paediatric to adult services, how the patient felt about the experience and the effect the transition had on the patient.

Results: There were 48 respondents to the survey who had experienced transition. The socio-economic status demonstrated that 35% of participants were in education, 38% of participants were employed and 3% were full-time homemakers. Those that were either unemployed or on long-term sick leave equated to 24% of participants. This is considerably higher than the unemployment rate for 16-24-year-olds not in full-time education, which was 14.4% between October and December 2014, and demonstrates that adolescent rheumatology patients are less likely to be employed or in education compared with their healthy peers, and the reason for this goes beyond any physical disability. Only 17% of participants reported attending an adolescent clinic and only 3% remember receiving a transition plan, which were two points from the qualitative data collected that patients thought could help their transition. Comparing those patients that attended an adolescent clinic and those that did not have the opportunity, these patients were statistically more adherent with their medication during transition ($P = 0.04$), however, it did not affect their adherence to medication currently ($P = 0.78$) when from back over the previous 6 months.

Conclusion: This research demonstrates that attendance at an adolescent clinic improves adherence at the time of transition but not current adherence to the adolescent clinic. In addition to adolescent clinics, transition plans, preparation on what to expect and seeing both (paediatric and adult) doctors in the same clinic provided a positive transition experience. Adequate and appropriate transition procedures are of importance to ensure the patient is equipped with the necessary skills and empowered to take responsibility for their health care and medications.

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236 THE USE OF A COMBINATION OF IL-1 AND IL-6 INHIBITION IN THE MANAGEMENT OF SEVERE, AGGRESSIVE, EROSIIVE, SYSTEMIC-ONSET JUVENILE IDIOPATHIC ARTHRITIS

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Background: Systemic-onset JIA (SoJIA) is a form of JIA that typically presents with prominent systemic features (i.e. quotidien fever, rash, lymphadenopathy) and accounts for ~10-15% of children with JIA. Pro-inflammatory cytokine pathways are thought to be involved in its pathogenesis, including IL-1 and IL-6. Laboratory tests demonstrate a prominent inflammatory response. Patients with SoJIA are at risk of developing macrophage activation syndrome (MAS).

Methods: We present the case of a 17-year-old young man who was initially diagnosed with SoJIA at age 7 years after presenting with a 3 week history of fever, arthralgias and a rash.

Results: The patient was diagnosed with SoJIA at age 7 years and treated initially with i.v. methylprednisolone. He was seronegative for ANA, RF and anti-CCP antibodies. In December 2006 he was started on oral MTX in combination with oral prednisolone. In September 2006 he was still symptomatic despite s.c. MTX and oral prednisolone, so he was started on etanercept. Between September 2006 and July 2012, despite the combination of s.c. MTX and etanercept, his disease continued to be active and he required oral prednisolone, repeated intra-articular steroid injections and pulses of i.v. methylprednisolone. In July 2012, the etanercept was switched to i.v. monthly infliximab, but his disease continued to be active. In April 2014 he presented with a severe flare of arthritis and the infliximab was switched to i.v. monthly tocilizumab. Despite this, he developed further arthritis affecting his left hip and right ankle and an MRI scan confirmed severe erosive disease. In November 2014 the tocilizumab was switched to adalimumab. He continued on s.c. MTX throughout. In March 2015, he re-presented with fevers, rash, myalgias and arthritis. His CRP was elevated at 325 mg/l. He was admitted for i.v. methylprednisolone and the adalimumab was switched to anakinra 100 mg s.c. once a day. On review, he actually felt well on the combination of s.c. anakinra and MTX. However, his inflammatory markers were still very high (CRP 185 mg/l), he had developed an anaemia of chronic disease (haemoglobin 8.1 g/dl) and he had active disease in his right knee. After further discussion with colleagues and a special funding request, tocilizumab 1 mg/kg i.v. monthly was added to his anakinra 100 mg s.c. once a day and MTX 10 mg s.c. weekly in June 2015.

Conclusion: We present a patient with SoJIA resistant to multiple biologic therapies currently being treated with the novel combination of IL-1 and IL-6 inhibition (in the form of anakinra and tocilizumab). So far his treatment response has been good and there have been no complications. Our aims of treatment are to help the patient feel better, prevent flares of his arthritis and further erosive disease and also treat his inflammatory response (and potential complications such as MAS and amyloidosis).

Disclosure statement: The authors have declared no conflicts of interest.

237 EVALUATION OF THE USE OF COMBINED IMMUNOSUPPRESSION TREATMENT REGIMENS IN THE SHEFFIELD PAEDIATRIC UVEITIS SERVICE

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Children and adults with uveitis are managed using similar treatments (MTX, MMF and biologic agents). Sheffield has established a uveitis transition clinic with staff from both the children’s and adult services, providing the opportunity to examine treatment pathways and outcomes in both paediatric and adult services. We conducted a service evaluation to describe response to treatment in our paediatric service with individuals receiving combination therapy. Here we report data from the paediatric service. The aims of the study were to document the treatment pathway for children and young people with uveitis ultimately receiving triple immunosuppression therapy and to describe response to treatment in terms of disease activity and visual acuity.

Methods: A keyword search of a comprehensive ophthalmic electronic clinic letter storage system was conducted. The keywords ‘methotrexate’ and ‘mycophenolate’ were used to identify patients who were diagnosed with uveitis at ≤16 years of age and who received combination therapy between April 2012 and April 2014.

Results: Of 64 patients with uveitis, 11 patients (18 affected eyes) met the inclusion criteria: 6 males, 5 females; 6 idiopathic uveitis, 5 JIA-associated uveitis. The mean age at diagnosis was 7 years 7 months (range 3–14 years). Seven patients had bilateral disease and four had unilateral disease. MTX and MMF were used to achieve disease control in 8/18 eyes. Eight patients (10 eyes) required the addition of anti-TNF to control their uveitis. Seven patients received infliximab and one patient was entered into the Sycamore trial to receive either adalimumab or placebo. Forty-one per cent of eyes showed a reduction in anterior chamber cells with MTX alone, compared with 76% with MTX plus MMF and 100% with MTX, MMF and anti-TNF. All patients receiving anti-TNF achieved remission (anterior chamber cells <1+ in 100% (10/10) eyes). Table 1 shows the improvement in mean visual acuity with the addition of each therapeutic agent.

Conclusion: Children in our cohort followed the same treatment pathway: MTX followed by the addition of MMF followed by the addition of anti-TNF if required. Improvement (in control of inflammation and visual acuity) was noted with the addition of each therapeutic agent.

Disclosure statement: The authors have declared no conflicts of interest.

Table 1. Mean visual acuity according to treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean visual acuity (logMAR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At presentation</td>
<td>0.365</td>
</tr>
<tr>
<td>MTX</td>
<td>0.212</td>
</tr>
<tr>
<td>MTX + MMF</td>
<td>0.143</td>
</tr>
<tr>
<td>Methotrexate + MMF + anti-TNF</td>
<td>0.125</td>
</tr>
</tbody>
</table>

238 TO DISCHARGE OR NOT TO DISCHARGE? OUTPATIENT DID NOT ATTEND RATES IN A YOUNG ADULT RHEUMATOLOGY CLINIC COMPARED WITH OLDER ADULT PATIENTS

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Background: We wanted to determine the did not attend (DNATT) rate of young adult patients (16–24 years of age) in a young adult rheumatology clinic compared with older adult patients and determine the outcome of the DNATT appointments if there were any differences in management between young adult and adult patients.

Methods: Seventy patients who were offered appointments in the Young Adult Rheumatology Clinic of the Dudley Group of Hospitals and 70 older adults offered a standard rheumatology outpatient follow-up appointment in the same Trust were identified. A retrospective review of clinic letters on the hospital intranet (3 April 2012–30 December 2014) was undertaken. Data were collected on patient demographics, attendance or DNATT, diagnosis and outcome of the appointment using an Excel spreadsheet.

Results: In the young adult clinic, 14/70 (20%) of the distinct appointments were DNATT. This compared with 5/70 (7%) for the older adult follow-up clinic. Eight of 11 (72%) young adults in the study were given a further appointment following the DNATT event, compared with 7/10 (70%) older adults.

Conclusion: This audit was carried out in the face of the increasing financial pressure on the NHS and the ever-present need for efficiency gains. In the adult rheumatology population, the drive is to discharge patients from secondary care at the first DNATT appointment. The DNATT rate for young adult patients at post-transition to adult care is clinically perceived to be higher than for older adults, but there is a lack of published data in rheumatology. Work in diabetes suggests that up to 30% of patients are lost to secondary care follow-up at transition to adult services, with a DNATT rate of ~15%. In this audit the DNATT rate for young adult patients was higher than for older adults (20 vs 7%), with a small group of young adults being multiple non-attenders. All young adults with chronic inflammatory conditions and those on immunosuppression were offered further appointments even if they failed to attend on multiple occasions, unlike the older adult population, who were more likely to be discharged to primary care. The Trust utilizes a text reminder service for appointments across its outpatient services, but other avenues that have been successful in improving outpatient attendance in young adult diabetic care should be investigated, including varying the time of clinics, providing appointment times outside of college/work hours, access to health care staff outside of clinic appointments and rapid access to appointments when required. These interventions are costly to develop and will require review to assess their effectiveness, but if successful they are likely to lead to improved long-term outcomes for individuals with JIA.

Disclosure statement: The authors have declared no conflicts of interest.

PAIN

239 USING MAGNETIC RESONANCE SPECTROSCOPY TO DEVELOP A BRAIN BIOMARKER OF PAIN IN PEOPLE WITH HAND OSTEOARTHRITIS

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Background: OA is the most common arthritis worldwide, with pain being a major symptom in this condition. During established disease, chronic pain due to OA may be aggravated by the process of central sensitisation, whereby pain processing pathways of the CNS become sensitized to peripheral nerve stimulation caused by degenerative and inflammatory disease processes. Newer brain imaging techniques involving MRI have recently enhanced research into the mechanisms of OA pain. We aimed to establish if there are distinct brain regions activated during hand OA pain that could be used as biomarkers of OA pain.

Methods: We conducted a brain neuroimaging study using a Philips 3T MRI scanner with 46 participants. We investigated whether biochemical changes in the brain detectable by 1H magnetic resonance spectroscopy (MRS) were related to clinical measures of perceived pain and related symptoms, including functional activity, depression and anxiety. Brain imaging using 1H MRS was performed in brain regions including the anterior cingulate cortex and the insula cortex, which are areas involved in pain processing and implicated in central sensitisation identified from our previous work. Quantified metabolites included the inflammatory marker myo-inositol and the neurotransmitters Glx (a sum of the neurotransmitters glutamate and glutamine). Clinical scores were measured using a visual analogue scale (VAS) for pain, the Australian and Canadian Hand OA Index (AUSCAN) and the Hospital Anxiety and Depression Scale (HADS).

Results: We investigated 32 hand OA participants and 14 controls with an age range of 43–74 years. All hand OA participants fulfilled ACR criteria for hand OA. MRS analysis demonstrated there were no metabolite differences between controls and OA participants in the anterior cingulate gyrus, nor age-related changes. In contrast, in the insula cortex the myo-inositol/Glx ratio correlated with age (R² = 0.29, P = 0.0018) and correlated with the VAS pain score (R² = 0.52, P = 0.018) after co-varying for age. In addition, principal component analysis demonstrated the myo-inositol/Glx ratio was the best single predictor of the VAS pain score.
index across all clinical scores relating to pain and depression indicated the VAS pain score and AUSCAN stiffness correlated to the myo-inositol/Glx ratio (P = 0.041) with age as a covariate. Conclusion: In conclusion, we have found using MRS that a high myo-inositol/Glx ratio is seen in the insula cortex of OA patients. The MRS activation we detected is associated with high pain, and the age dependence of myo-inositol/Glx ratio suggests age-dependent and/or duration-dependent effects of OA on the brain. Our data show that specific brain biomarkers could be useful in characterising OA pain. Disclosure statement: The authors have declared no conflicts of interest.

240 IDENTIFYING CONSTRUCTS OF HEALTH BELIEF AND THEIR ROLE IN DISABLING DISTAL UPPER LIMB PAIN

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Background: Pain in the distal upper limb affects approximately 1 in 12 UK adults annually and is often disabling. Evidence has demonstrated the importance of health beliefs in predicting pain. Epidemiological studies have investigated the role of health beliefs in disabling upper limb pain by analysing responses to single statements about pain cognitions or groupings of statements based on similarity. It is unclear if these approaches have captured distinct constructs and therefore calls into question the meaningfulness of reported associations. This study aimed to identify underlying health belief constructs in individuals referred to physiotherapy with distal upper limb pain and investigate whether these constructs predict moderate or severe disabling distal upper limb pain.

Methods: This cross-sectional study used baseline data from the Arm Pain Trial (ISRCTN79080562). Eligible participants were adults referred to physiotherapy with distal upper limb pain. Information on demographic factors (sex, age, employment), pain (severity, duration, widespread symptoms), disability (modified Disabilities of the Arm, Shoulder and Hand Questionnaire) and health beliefs (11 statements, 5-point Likert agreement scale) were captured through questionnaires prior to trial randomisation. Exploratory factor analysis (EFA) used responses to health belief statements to identify underlying constructs. Due to ordinal data, output from a polychoric correlation matrix was used for EFA using principal axis factoring. Oblim promax rotation determined the association of statements with constructs, maximized to produce the clearest structure (factor loadings >0.3 regarded as significant). The number of underlying constructs was determined after consideration of findings from parallel analysis, balanced against clinical plausibility. Factor loadings were used to calculate scores for each participant for each construct. The predictive and moderating effect of each construct on disabling pain was assessed using linear regression. A multivariant model adjusted for demographic and pain-related factors. Results: A total of 476 trial participants contributed data [age range 18-85 years, mean 48.8 (s.d. 13.7), 54% female, 69% employed]. EFA identified five health belief constructs: hereditary factors, movement and pain, locus of control, life course/lifestyle factors and prognosis. In multivariable analysis only greater pessimism about prognosis predicted disabling distal upper limb pain [β = 1.20 (95% CI 2.07, 0.32)]. This was also the only health belief construct that moderated the pain–disability relationship [β = 0.16 (95% CI 0.031, 0.29)]. Conclusion: Results suggest that at the time of referral to physiotherapy, individuals with mild to moderate distal upper limb pain but higher than expected disability may benefit from reassessment regarding prognostic outlook. These findings support a stratified model of care based on recovery expectations. Future investigations should confirm and validate the health belief measure’s ability to predict longitudinal impact on chronic disabling distal upper limb pain. Disclosure statement: R.M. has received a Medical Research Student Scholarship, Undergraduate Vacation Scholarship. All other authors have declared no conflicts of interest.

241 IDENTIFICATION OF NERVE ROOT INVOLVEMENT IN PRIMARY CARE CONSULTANTS WITH LOW-BACK-RELATED LEG PAIN: DIAGNOSTIC CLASSIFICATION USING ALTERNATIVE APPROACHES

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Background: There is no recognized gold standard for diagnosing nerve root involvement (NRI) in patients with low-back-related leg pain (LBPLP) and the consensus on which clinical items might best identify NRI. Diagnostic models have mainly been developed in secondary care with conflicting reference standards and predictor selection. In the absence of a gold standard, clinical opinion and/or imaging findings are often used. Clinical opinion has issues of incorporation bias and imaging can incorrectly classify patients. This study explores the challenges of reference standard selection in NRI diagnostic modelling and aims to ascertain which combination of clinical assessment items best identify NRI in primary care LBPLP consulters. Classification using clinical diagnosis is compared with a statistical approach that circumvents the need for a reference standard.

Methods: Two definitions of NRI formed the reference standards for diagnostic modelling: high confidence (>80%) NRI clinical diagnosis; and high confidence (>80%) NRI clinical diagnosis with confirmatory MRI findings. Cross-sectional data on 394 LBPLP consulters were used to develop the model. Potential NRI indicators were seven clinical assessment items. Multivariable logistic regression models were constructed and compared for both reference standards. Model performances were summarized using the Hosmer-Lemeshow statistic and area under the curve (AUC). Bootstrap assessed model stability. The same variables were analysed using latent class analysis (LCA).

Results: The NRI clinical diagnosis model 1 retained five items. The clinical diagnosis plus MRI model 2 retained six items. Four items remained in both models: below knee pain, leg pain worse, positive neural tension and neurological deficit. The NRI clinical diagnosis model was well calibrated (P = 0.17) and discrimination was an AUC of 0.95 (95% CI 0.93, 0.98). The clinical diagnosis plus MRI model showed good discrimination [AUC 0.82 (95% CI 0.78, 0.86)] but poor calibration (P = 0.004). Overfitting was minimal in both. LCA identified three LBLP groups. Group 1 (n = 147) had high pain intensity (6.9/10) and very high probability (>0.85) of three clinical indicators being positive [leg pain worse (P = 0.86), below knee pain (P = 0.92), positive neural tension (P = 0.92)]. Group 2 (n = 165) had moderate pain (4.8/10) and high probability (>0.7) of below knee pain (P = 0.78) and neurological deficit (P = 0.73). Group 3 (n = 83) had low pain (3.3/10) and low probability (<0.33) of any positive clinical indicators. There was very high agreement between the clinically diagnosed NRI group and latent class groups 1 and 2.

Conclusion: Following diagnostic modelling, four clinical assessment items were common in both reference standard definitions. Three of these items were highly probable in one LCA subgroup and two of the four items were probable in the second subgroup. This work suggests a combination of items that identify two diagnostic subgroups of LBPLP consulters with NRI that could be used clinically and in research to improve homogeneous patient identification.

Disclosure statement: The authors have declared no conflicts of interest.

242 PATIENT SUBGROUPS AND PAIN PROGNOSIS IN EARLY RHEUMATOID ARTHRITIS

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Background: Pain is the major concern for many people with RA. RA inflammatory disease activity is measured using the 28-joint DAS (DAS28), which includes pain-related components, visual analogue scale (VAS) for global health and tender joint count (TJC). We hypothesize that pain characteristics and active inflammation can be used to subgroup people with RA and that pain might follow different trajectories in early RA.

Methods: Data from the Early RA Network inception cohort at baseline (n = 856) and bodily pain scores until year 3 were analysed (n = 856). Latent class analysis (LCA) used variables directly reflecting pain, central pain mechanisms or inflammation (normal 36-item Short Form Health Survey including bodily pain, vitality and mental health, ESR, swollen joint count (TJC) and VAS). Growth mixture modelling (GMM) identified pain trajectories for cases with complete pain data from baseline to 3 years (validated using imputation). Differences between
Five classes were identified at baseline, two of which (27% and 11%) were interpreted as displaying mild or severe disease, with concordant pain and inflammation. Two classes (38% and 12%) displayed discordantly high pain compared with inflammation and one class (11%) displayed discordantly high levels of inflammation compared with pain. Bodily pain improved from a mean of 34 (SD 11) at baseline to 39 (SD 11) at year 3. Pain displayed three discrete trajectories. The mean pain scores for two trajectories showed consistently high (58% of cases; mean of 31 at year 3) or consistently low pain (23% of cases; mean of 47 at year 3), whereas a third category displayed normalisation of initially severe pain (19% of cases; mean of 51 at year 3). Lower BMI at baseline was associated with the pain normalisation trajectory (mean BMI for pain normalisation group 26.4 (SD 4.5) compared with 28.7 (SD 5.8) for consistently high pain; P = 0.019).

The five latent classes at baseline segregated heterogeneously into the three trajectories for pain progression (P < 0.001). The mild latent class at baseline intersected with the consistently good pain trajectory. Other latent classes were almost exclusively distributed between the other two trajectories, but with non-significant differences in pairwise comparisons.

Conclusion: Subgroups of people with RA can be identified that display discordantly high pain despite apparently low levels of inflammation. Mean outcomes in the cohort suggest only modest improvements in pain. However, these conceal a subgroup that displayed normalisation of pain over time. These data support the concept of pain responders and non-responders in routine care. The subgroup that displayed pain improvement had normal rather than high BMI, but could not be distinguished from non-improvers using baseline total DAS28 or baseline latent class.

Disclosure statement: D.F.M. has received research funding from Pfizer. D.A.W. has received research funding from Pfizer. All other authors have declared no conflicts of interest.

244 DETERMINANTS OF LOW BACK PAIN AMONG WORKERS FROM 18 COUNTRIES: THE CUPID STUDY

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Background: Low back pain (LBP) is the most common regional pain syndrome and contributes importantly to the burden of sickness absence and work disability throughout the developed world. Prevention often hinges on ergonomic approaches, but systematic reviews suggest very small effects of this approach. We investigated those factors that might underlie the lack of efficacy of an ergonomic approach.

Methods: This is a cohort study of musculoskeletal pain and disability among 47 occupational groups from 18 countries.

Results: Among 12 197 subjects at baseline, 4429 (36.3%) workers reported LBP. The majority (3820) reported pain associated with musculoskeletal pain at other sites and only 4.9% reported localized LBP. Localized LBP was associated with less sciatica (30.0 vs 48.1% of cases), less disability (67.3 vs 64.1% of cases), less medical consultation and less sick leave. Localized LBP was also less likely to persist at follow-up after a mean duration of 14 months (54.1 vs 65.6%). LBP with pain at other sites was more common among women, older workers, people with higher somatisation scores, those with poorer mental health and those feeling pressured for time at work. There was marked variation in the prevalence of LBP (localized and non-localized) between people doing the same jobs in different countries.

Conclusion: We are to make strides reducing work disability from LBP, we need to take a broader approach to prevention. Our results suggest that new approaches should take into account the propensity towards any musculoskeletal pain rather than factors specific to the spine.

Disclosure statement: The authors have declared no conflicts of interest.

SCLERODERMA AND RELATED DISORDERS

245 MODELLING OF LONGITUDINAL CHANGES IN LUNG FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS AND THEIR ASSOCIATION WITH THE DEVELOPMENT OF PULMONARY HYPERTENSION

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Background: The diffusing capacity of the lungs for carbon monoxide (DLCO) and forced vital capacity (FVC) are powerful predictors of the development of pulmonary hypertension (PH) in patients with SSC, but...
the majority of published models for the prediction of PH use cross-
sectional data. We examine the changes in FVC and DLOC over time in a large cohort of SSC patients and explore their association with the development of PH.

Methods: Subjects with SSC with follow-up data for ≥10 years and pulmonary function tests (PFTs) performed on at least two occasions were included. Linear mixed models were used to explore associations between repeated measurements of FVC and DLOC and the development of PH.

Results: We included 371 SSC subjects; 13% were male and 36% had dcSSC. Of the entire cohort, 15% had developed PH. PFTs were performed on average every 15 months, between 2 and 20 times (median 6 times). Patients who developed PH had an 8.5% lower baseline FVC compared with those who did not develop PH (P = 0.008). Over time, FVC decreased by 0.4% per year in PH while in non-PH subjects it increased by 0.6% on average (P = 0.001). The rate of change in FVC was influenced by a number of other clinical characteristics (Table 1). Even after adjustment, baseline FVC was on average 7.1% lower in PH subjects compared with non-PH subjects (P = 0.014). While in non-PH patients FVC increased by ~1% per year, in those who developed PH, the increase was ~0.1% (P = 0.003). PH subjects had on average 12.6% lower baseline DLOC compared with non-PH (P = 0.001). In PH patients, DLOC decreased by 2.6% per year while in non-PH patients the yearly decrease was 0.8% (P = 0.001). When adjusting for other covariates, PH was still associated with a substantially lower baseline DLOC (11.2% difference, P = 0.001) and this decreased by 1.9% per year compared with 0.5% (P = 0.001) in non-PH patients, when keeping all other covariates constant (Table 1).

Conclusion: Our findings confirm the particular value of serial measurements of lung function in the identification of patients at risk of PH. Subjects who develop PH have lower baseline FVC and DLOC levels with increased rates of DLOC reduction over time.

Disclosure statement: The authors have declared no conflicts of interest.

246 IDENTIFICATION OF NOVEL MEDIATORS OF FIBROSIS IN SCLERODERMA

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Background: Fibrosis is a major pathological feature of many chronic diseases such as SSCs, an autoimmune rheumatic disease characterized by activation of fibroblasts, accumulation of extracellular matrix (ECM) and persistent inflammation that can lead to impaired organ function. Fibrotic disorders share common features, although it is unclear which of these occur as a result of shared mechanisms and pathways and which are mediated by unique organ-specific mechanisms. The aims of this project were to identify common and unique genes whose expression is altered in three fibrotic organs (lung, skin and kidney), to validate their expression in SSc cells and tissues and to explore their function in normal and SSC fibroblasts.

Methods: An extensive literature search from 1988 to 2015 (PubMed) was carried out to identify common and unique genes involved in fibrosis of diverse aetiologies. In addition, a thorough in alca data-

mining exercise was conducted using all published microarray data (GEO database). A short list of genes was compiled based on several criteria, including common/specific targets for lung, skin and kidney fibrosis, druggability and availability of validated siRNA for knock-down of expression. The expression levels of the short-listed genes was performed in human primary fibroblasts (n = 3) by quantitative PCR (mRNA), western blotting (protein) and immunohistochemistry (IHC). Fibroblasts were derived from normal, SSC lung and skin tissue and normal kidney. TGF-β was used to induce fibrogenic genes in fibroblasts from healthy controls as a model of generic fibrosis since TGF-β is regarded a major profibrotic cytokine.

Results: A list of the 100 most altered (up- or downregulated) genes was compiled, from which 12 genes were short-listed. Pathway analysis of all 100 altered genes highlighted the hyaluronic acid (HA) pathway, a major component of ECM, from which 2 genes were in the 12-gene short list, hyaluronan synthase 2 (HAS2) and cell migration-inducing protein (CEMP). HAS2, responsible for hyaluronan polymerization, was the most significantly upregulated gene. Significantly elevated mRNA and protein levels of HAS2 were observed in skin and lung SSC fibroblasts and in TGF-β-treated fibroblasts from all 3 organs. The IHC data showed that HAS2 was higher in skin and lung tissues from SSC patients compared with controls. CEMIP, an HA binding protein, was significantly downregulated in fibroblasts from SSC lung and skin and in TGF-β-treated fibroblasts from all 3 organs.

Conclusion: Taken together, these data reveal that HAS2 is significantly upregulated and CEMIP is significantly downregulated in lung and skin fibroblasts from SSC patients compared with controls and in fibrotic conditions in all three organs. These data suggest an important role of the HA pathway for HAS2 and CEMIP in SSC. These findings suggest that potential mediators of fibrosis could be novel targets for antifibrotic therapies.

Disclosure statement: The author has declared no conflict of interest.

247 A PILOT STUDY USING HIGH-FREQUENCY ULTRASOUND TO MEASURE DIGITAL ULCERS AS AN OUTCOME MEASURE IN SYSTEMIC SCLEROSIS CLINICAL TRIALS

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Background: Although digital ulcers (DUs) are often used as the primary endpoint in SSC-related clinical trials, the reliability of rheumatologists grading DUs is poor to moderate at best, therefore more objective measures are required. Against this background our aim was to assess the feasibility, tolerability and measurement capability of high-frequency US (HFUS) in SSC-related DUs.

Methods: Eleven patients with 15 DUs (4 fingertip, 7 extensor, 2 palmar) and cell migration- and cell migration-related genes and a visual analogue scale (VAS) of 0–100 (100 = most severe pain imaginable by the patient) associated with HFUS was documented. The acquired HFUS images of DUs were reviewed by three raters who decided by consensus agreement whether the image was classifiable (i.e. that a measurement could be made). The raters identified the edges/margins/borders of the DU at the surface of the skin by identifying changes in the surface layers or an appreciable change in the surface profile. Two lines were then drawn perpendicular to the surface of the skin at each edge and a third line was drawn parallel to the surface of the skin at the deepest level of skin structure disruption (depth).

Results: HFUS was considered by the majority (n = 10) of patients to be feasible (either completely or very feasible) and in most patients (n = 7) to take just the right amount of time. The pain VAS associated with HFUS was low (median 0 (interquartile range 0–2)). The majority of DUs (n = 13) had at least one image that was considered classifiable, allowing measurements to be made. The majority (n = 13) of DUs had at least one width and depth measurement. The mean DU depth was 0.99 mm (s.d. 0.45) and width was 0.57 mm (s.e. 0.2). Conclusion: HFUS imaging of DUs was considered feasible and was well-tolerated in most patients. The majority of DUs had at least
Background: Selenium possesses antioxidant, anti-inflammatory and antifibrotic properties. Previous studies have demonstrated lower circulating selenium levels in patients with SSc compared with healthy controls. The pathogenesis of SSc is unclear, but fibrosis of the skin and internal organs, vascular injury and immune dysfunction all play a role. The aim of this study was to determine whether circulating selenium levels change over time in patients with SSc and whether longitudinal measurements of selenium correlate with modified Rodnan skin score (mRSS). Associations between selenium levels and different disease characteristics were also investigated.

Methods: A total of 200 longitudinal serum samples from 42 patients with SSc (collected over 8 years, 4-5 samples/patient) were selected. Selenium was measured using inductively coupled plasma (ICP) mass spectrometry. Linear mixed models were used to investigate selenium trends over time and associations with clinical and demographic characteristics. The association between each of disease duration (≤5 or >5 years from onset) and disease subtype (diffuse or limited cutaneous) and selenium trends were examined. The association between selenium levels and mRSS, presence of pulmonary hypertension and pulmonary fibrosis were also assessed.

Results: No systematic patterns of selenium levels over time for each patient were identified. No difference was found in the selenium level trends between patients with limited and diffuse disease (P = 0.354) or between patients with early and late-stage disease (P = 0.138). Table 1 shows the estimated effect of each disease characteristic as the change in selenium associated with a 1 unit increase in the factor (for continuous variables) or the difference in selenium associated with the factor shown in brackets compared with a reference category (for categorical variables). Increased skin score was found to be associated with slightly reduced contemporaneous selenium levels (P = 0.015). There was some evidence for lower levels of selenium in patients with pulmonary hypertension (P = 0.015) but not in patients with pulmonary fibrosis (P = 0.270).

Conclusion: There was a modest signal of lower circulating selenium levels with worse skin score and with pulmonary hypertension. These results suggest that the role of selenium in SSc deserves further investigation in larger prospective studies.

Disclosure statement: The authors have declared no conflicts of interest.

249 Table 1. Estimated effects of covariates on selenium level

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Estimated effect (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodnan skin score</td>
<td>-0.006 (-0.006, -0.003)</td>
<td>0.015</td>
</tr>
<tr>
<td>Limited or diffuse disease (limited)</td>
<td>0.048 (-0.067, 0.166)</td>
<td>0.451</td>
</tr>
<tr>
<td>Early or late onset (early)</td>
<td>0.006 (-0.009, 0.001)</td>
<td>0.191</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>-0.154 (-0.209, -0.047)</td>
<td>0.217</td>
</tr>
<tr>
<td>Pulmonary fibrosis</td>
<td>-0.076 (-0.104, 0.041)</td>
<td>0.270</td>
</tr>
<tr>
<td>ACA</td>
<td>-0.008 (-0.036, 0.011)</td>
<td>0.191</td>
</tr>
<tr>
<td>Anti-ScI 70 antibody</td>
<td>-0.001 (-0.017, 0.006)</td>
<td>0.299</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.002 (-0.002, 0.007)</td>
<td>0.279</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>0.003 (-0.004, 0.006)</td>
<td>0.110</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>-0.019 (-0.032, -0.006)</td>
<td>0.012</td>
</tr>
<tr>
<td>Smoking status (current)</td>
<td>-0.014 (-0.011, 0.005)</td>
<td>0.360</td>
</tr>
</tbody>
</table>

250 MODELLING THE INTERACTION BETWEEN DISEASE MICROENVIRONMENT AND MESCENYMPHAL CELLS IN SYSTEMIC SCLEROSIS: ROLE OF IL-31

Zeinab Taki, Sara Zafar, Bahia Ahmed-Abdi, Henrique Rosario, Xu Shiwen, David Abraham, Christopher Denton and Richard Stratton

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Background: SSc has a complex aetiology with many potential driving forces, one of which is the microenvironment in lesional skin. This comprises activated mesenchymal cells, aberrantly expressed growth factors and cytokines and excessively stiffened and abundant extracellular matrix. We hypothesise that mesenchymal stem cells (MSCs) are persistently activated within this microenvironment, leading to chronic aberrant tissue repair and fibrosis. The expression of stem cell blastifer fluid (BF) and IL-31, the maximally induced cytokine in SSc BF, were studied in models of interaction between the disease microenvironment and MSCs. MSCs were studied in situ using amniotic nuclear division as a marker of their activation.

Methods: Staining of tissue spreads for metakaryotic nuclear divisions was used as a method to identify MSCs in SSc tissue. SSc BF sampled from control skin (each dial 1:125 in 0.2% DMEM) and IL-31 were studied as possible agonists in the following model systems using adipose-derived MSCs: scratch wound

248 DIGITAL ULCERS IN SYSTEMIC SCLEROSIS ARE ASSOCIATED WITH ABNORMALITIES OF PERI-LESIONAL SKIN AS ASSESSED BY CAPILLAROSCOPY

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Background: Digital ulcers (DUs) are a common, visible manifestation of the progressive microangiopathy in SSc, impact negatively on hand function and occupation and are a biomarker of internal organ involvement. Nailfold capillaroscopic abnormalities have been reported to be strongly predictive of future DUs. Against this background, our aim was to investigate the capillary architecture surrounding DUs in SSc.

Methods: Capillaroscopy was performed (Optilia MediScope, >200 magnification) at four equidistant quadrants surrounding the DU and at the contralateral position on the opposite hand (unless at the nailbed, or if the patient indicated that they did not wish to proceed). Sterile water and/or US gel was used for the optical interface. Two graders agreed by consensus on the capillary structure (either normal size and morphology, slightly or grossly enlarged capillaries, neoangiogenesis or vessel an unclear classifiable category). Patient-reported opinion on the feasibility of the technique was collected (not feasible, indifferent, very or completely feasible).

Results: Ten patients with SSc-spectrum disorders with 15 [8 extensor (one nailbed), 6 fingertip, 1 lateral] DUs were recruited. Capillaroscopy was performed around all the DUs and at the contralateral position in most patients (n = 7); 11 DUs. Most DUs (n = 11) and almost all contralateral images (n = 10) had one or more classifiable quadrant. Image acquisition of DU perielsional skin was possible in four quadrants in six DUs and three quadrants in nine DUs. Most DUs (n = 12) and almost all contralateral images (n = 11) had one or more classifiable quadrant. Almost all (n = 11) the classifiable DUs (7 extensor, 4 fingertip) had enlarged capillaries (7 slightly and 4 grossly) in at least one quadrant, 2 (DUs) with neoangiogenesis. Although the majority (n = 10) of contralateral counterparts were graded as ‘normal’, one revealed slightly enlarged capillaries. Both fingertip (n = 4) and extensor (n = 7) DUs demonstrated abnormalities of perielsional skin (including slightly or grossly enlarged capillaries). Capillaroscopy was well tolerated and considered by the majority (85%) as (very or completely) feasible, with two patients considering it not feasible.

Conclusion: Capillaroscopy of DU perielsional skin revealed SSc-associated microangiopathic changes, consistent with a vascular drive to DUs. Both fingertip and extensor DUs revealed similar capillary abnormalities, suggesting that microangiopathy contributes to both. Perielsional DU capillaroscopy was well tolerated and considered feasible by the majority of patients. Further research (including non-contact capillaroscopic systems to optimize image acquisition) is warranted to investigate perielsional DU capillary abnormalities and provide novel insights into the pathophysiology of both DU development and healing in SSc.

Disclosure statement: The authors have declared no conflicts of interest.

249 THE ROLE OF SELENIUM DEFICIENCY IN THE PATHOGENESIS OF SYSTEMIC SCLEROSIS

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1Musculoskeletal Research, 2Biostatistics, Institute of Population Health, University of Manchester, 3Research and Development, 4Rheumatology, Salford Royal NHS Foundation Trust, Salford, UK

Background: There was some evidence for lower levels of selenium in SSc. Staining of tissue spreads for metakaryotic nuclear divisions was used as a method to identify MSCs in SSc tissue. SSc BF sampled from control skin (each dial 1:125 in 0.2% DMEM) and IL-31 were studied as possible agonists in the following model systems using adipose-derived MSCs: scratch wound
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251 MULTIPLEX SERUM PROTEIN ANALYSIS IDENTIFIES MARKERS OF RESPONSE TO HYPERIMMUNE CAPRINE SERUM IN SYSTEMIC SCLEROSIS

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1Rheumatology, University College London, London, 2Statistics and Actuarial Science, University of Kent, Canterbury and 3Scientific Development, Daval International, London, UK

Background: Hyperimmunone caprine serum (HICS) administered by s. injection over 26 weeks has shown benefit for the modified Rodnan skin score (mRSS) in dcSSc in a recent phase 2 placebo-controlled trial. We report multiplex protein analysis of serum samples from the trial to explore mechanisms of action of this novel biologic agent and identify potential biomarkers in SSc.

Methods: In a parallel group, placebo-controlled trial patients were treated with HICS (n = 10) or placebo (n = 10) over 26 weeks, with a follow-up open-label treatment for 26 weeks. Serum samples at baseline and 6, 26 and 52 weeks were analysed using a multiplex assay for 40 cytokines and growth factors (Q-plex) and additional individual solid phase immunoassays for procollagen III N-terminal propeptide (P-precursor), serum IL-2R, cartilage oligomeric matrix protein (COMP), IL-31, and von Willebrand factor (vWF). To explore patterns of change over multiple analytics, heat maps were constructed using Cluster software. String analysis was performed using coexpression and Pearson coefficient and significance analysis of microarrays (SAM) for correction.

Results: Cluster analysis defined factors that were increased or decreased from baseline after 26 weeks of treatment with HICS. Results for key analytes are summarized in Table 1. Consistent with previous preclinical studies, there was evidence for marked upregulation of the hypothalamic–pituitary–adrenal axis from 6 weeks after HICS treatment, and this effect was maintained at 26 weeks. This was evidenced by increase in α-MSH and ACTH in cases treated with HICS. There were changes in markers of fibroblast biology, including changes in bFGF, PIINP and COMP. Novel findings include a consistent increase in PIINP associated with improved mRSS, suggesting that this may be a marker of extracellular matrix turnover rather than fibrogenesis. Other factors that were frequently reduced, though not reaching statistical significance, included TIMP2, fractalkine and TGF-β1 levels.

Conclusion: This study identifies the feasibility of conducting relatively short-term parallel group placebo-controlled trials in established dcSSc to target skin fibrosis. The benefit of including multiplex analysis of serum proteins in early phase trials to better understand treatment mechanisms and disease biology is confirmed. This study suggests possible mechanisms of action for HICS, including upregulation of α-MSH, which has been shown to be antifibrotic in preclinical studies, and indicates potential serum markers that may be included in future clinical trials in SSc.

Disclosure statement: J.V. is an employee of Daval International. D.M. is an employee of Daval International. C.P.D. has received consulting fees from GSK, Actelion, Sanofi and Inventiva and has received research funding from GSK and CSL Behring. All other authors have declared no conflicts of interest.

252 INVESTIGATING THE MISFOLDED PROTEIN RESPONSE IN SYSTEMIC SCLEROSIS

Matthew Delaney, Bahija Ahmed Abdi, Christopher Denton, David Abraham, Nikita Arumalla, Mark Gibson1 and Richard Stratton
1Rheumatology, Royal Free Hospital, London, UK

Background: Much progress has been made in understanding the role of inflammatory, immune and vasculopathic mechanisms in SSc, but the initiating aetiology remains to be fully determined. Using a broad proteomic methodology, it was demonstrated that proteins involved in the metabolism of misfolded proteins were increased in the disease. Congo red staining of urinary protein extracts is a recent method developed in pre-ecrampia to demonstrate the presence of significant burden of misfolded proteins. We have applied this method in SSc and used database screening and String analysis to characterize the proteomic changes seen in this severe disease.

Method: Skin biopsy material from 12 healthy controls, and 12 patients with recent-onset diffuse SSc was sampled by 4 mm punch biopsy. Samples were stored in liquid nitrogen and then subjected to 2D gel PAGE. Proteins of a 2-fold increase were studied further by mass spectroscopy. String 9.1 was used to associate proteins that are functionally related. Urine samples from SSc patients and healthy controls (both n = 5) were assayed for total protein by bicinchoninic acid assay and the protein levels normalized to 6.6 mg/l. Samples of urine (100 µl) were mixed with Congo red 2 µl and applied to a nitrocellulose filter (Hybond c) and allowed to adhere for 15 min prior to washing with ethanol in order to elute the non-bound fraction. Congophilic binding was quantified by imaging before and after washing.

Results: Of 17 proteins of altered abundance > 2-fold in SSc samples, 3 were functionally related to misfolded protein response [α1-antitrypsin: 849 in control vs 4484 in SSc (P < 0.0001); serum amyloid P-precursor: 1183 vs 3505 (P < 0.0003); cytochrome c: 627 vs 1911 (P < 0.0005)]. String analysis linked these proteins and revealed other functionally related groups including cytokeratins, and myofibroblast contractile proteins preliminary Congophilic urinary analysis showed that one of five SSc patients had positive Congophilic binding compared with no healthy controls. Results of Congo red staining of skin biopsy material plus immunochrometry of sections for serum amyloid P and α1-antitrypsin is awaited.

Conclusion: Using an unbiased approach, it was demonstrated that factors involved in misfolded protein response are of altered abundance in SSc skin biopsy material and show functional associations by String analysis. Preliminary analysis of urine for Congophilic showed positive results in a single patient (severe diffuse recent-onset SSc). Protein misfolding may occur in the endoplasmic reticulum of highly synthetic myofibroblasts seen in SSc fibrotic lesions.

Disclosure statement: The authors have declared no conflicts of interest.

251 Table 1. Change in serum protein level after 26 weeks HICS or placebo treatment

<table>
<thead>
<tr>
<th>Direction of change</th>
<th>Serum protein</th>
<th>Basal, mean (s.c.)</th>
<th>Week 26, mean (s.c.)</th>
<th>26 weeks vs basal, fold change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up</td>
<td>α-MSH, pg/ml</td>
<td>3.7 (3.6)</td>
<td>31.1 (35.8)</td>
<td>0.0035</td>
</tr>
<tr>
<td></td>
<td>bFGF, pg/ml</td>
<td>1.9 (2.4)</td>
<td>27.6 (42.3)</td>
<td>0.0009</td>
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<tr>
<td></td>
<td>SFSG, pg/ml</td>
<td>3.4 (6.5)</td>
<td>21.5 (21.9)</td>
<td>0.0185</td>
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<tr>
<td></td>
<td>PIINP, pg/ml</td>
<td>6.9 (5.8)</td>
<td>14.5 (10.1)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Down</td>
<td>COMP, ng/ml</td>
<td>1.0 (1.0)</td>
<td>1.0 (1.0)</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>FRACT, ng/ml</td>
<td>3.7 (4.4)</td>
<td>3.3 (6.1)</td>
<td>0.108</td>
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</table>

HICS change during study

<table>
<thead>
<tr>
<th>Direction of change</th>
<th>Serum protein</th>
<th>Basal, mean (s.c.)</th>
<th>26 weeks vs basal, fold change (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up</td>
<td>α-MSH, pg/ml</td>
<td>1.8 (0.9)</td>
<td>2.2 (1.9)</td>
</tr>
<tr>
<td></td>
<td>bFGF, pg/ml</td>
<td>1.1 (1.1)</td>
<td>1.0 (0.7)</td>
</tr>
<tr>
<td></td>
<td>SFSG, pg/ml</td>
<td>2.7 (6.3)</td>
<td>27.6 (42.3)</td>
</tr>
<tr>
<td></td>
<td>PIINP, pg/ml</td>
<td>21.3 (43.3)</td>
<td>23.6 (51.6)</td>
</tr>
<tr>
<td></td>
<td>COMP, ng/ml</td>
<td>1.3 (0.5)</td>
<td>1.4 (0.6)</td>
</tr>
<tr>
<td></td>
<td>FRACT, ng/ml</td>
<td>1.1 (0.7)</td>
<td>1.0 (0.6)</td>
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</table>

HICS vs placebo change

<table>
<thead>
<tr>
<th>Direction of change</th>
<th>Serum protein</th>
<th>Basal, mean (s.c.)</th>
<th>Fold change (HICS)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up</td>
<td>α-MSH, pg/ml</td>
<td>1.8 (0.9)</td>
<td>2.2 (1.9)</td>
<td>0.399</td>
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<td></td>
<td>bFGF, pg/ml</td>
<td>1.1 (1.1)</td>
<td>1.0 (0.7)</td>
<td>0.036</td>
</tr>
<tr>
<td></td>
<td>SFSG, pg/ml</td>
<td>2.7 (6.3)</td>
<td>27.6 (42.3)</td>
<td>0.005</td>
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<tr>
<td></td>
<td>PIINP, pg/ml</td>
<td>21.3 (43.3)</td>
<td>23.6 (51.6)</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>COMP, ng/ml</td>
<td>1.3 (0.5)</td>
<td>1.4 (0.6)</td>
<td>0.012</td>
</tr>
<tr>
<td></td>
<td>FRACT, ng/ml</td>
<td>1.1 (0.7)</td>
<td>1.0 (0.6)</td>
<td>0.318</td>
</tr>
</tbody>
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253 COMPLEMENTARY VALUE OF THE ELF TEST AND NT-proBNP IN REFLECTING FIBROSIS AND VASCULOPATHY IN SYSTEMIC SCLEROSIS

Giuseppina Abigiano1, Jelena Blagoevic1,2, Lesley Anne Bissell1, Raluca Bianca Dumitru1, Sookheong Eng1, Nicola Calder2, Michael Messenger3, Maya Buch1, Paul Emery1 and Francesco Del Gatto1
1Rheumatic and Musculoskeletal Medicine and NIHR Leeds Musculoskeletal Biomedical Research Unit, University of Leeds and Leeds Teaching Hospitals NHS Trust, Leeds, UK, 2Experimental and Clinical Medicine, Division of Rheumatology, Florence, Italy and 3NIHR Diagnostic Evidence Co-operative Leeds, St James University Hospital, Leeds Teaching Hospital NHS Trust, Leeds, UK

Background: The ELF test and its components (PIIINP, TIMP-1 and HA) have been shown to correlate with skin, lung and overall fibrosis and not with any vascular manifestation of SSC. In contrast, NT-proBNP has been suggested to be useful for stratification of SSC patients, especially to identify those at risk of pulmonary hypertension. The aims of this study were to validate the ELF score and its single analytes on an independent cohort of scleroderma patients and to evaluate whether NT-proBNP could provide additional value to the discrimination of an SSC-specific algorithm.

Methods: A total of 250 sera from SSC patients from a single UK centre were analysed employing a high-throughput in vitro diagnostic of a routine NHS pathology lab to measure ELF score, its analytes and NT-proBNP levels. All patients fulfilled 2013 ACR/EULAR classification criteria for SSC. Clinical, laboratory and instrumental data were collected at the time of sampling. Statistical analysis was performed using SPSS. P-values < 0.05 were considered statistically significant.

Results: Multivariate analysis of the ELF score (including the variables found statistically significant in univariate analysis) identified age, modified Rodnan skin score and diffusing capacity percentage of the lungs for carbon monoxide (DLCO%) as independently associated with ELF score (P < 0.0001 for all), confirming results previously published on an independent Italian cohort. As previously shown, the ELF score single analytes were not associated with heart and vascular manifestations of the disease. However, NT-proBNP significantly correlated with disease severity (P < 0.0001) and peripheral vasculopathy (P = 0.056). Its levels were higher in patients with current digital ulcers (P = 0.001), digital pitting scars (P = 0.01), telangectasia (P = 0.01), systemic arterial hypertension (P = 0.004), pulmonary artery hypertension (PAH) (P = 0.01), diastolic dysfunction (P = 0.002), reduced ejection fraction (P = 0.0002), arrhythmias (P < 0.0001) and dyspnoea (P = 0.003) compared with those without the manifestation. Multivariate analysis identified the presence of arrhythmias (P < 0.0001), age (P < 0.0001), PAH (P < 0.001) and DLCO% (P = 0.006) as independently associated with NT-proBNP. All the biomarkers significantly correlated with the total Medsger’s severity and ESSGActivity index (P < 0.0001).

Conclusion: Our findings validate the value of the ELF score in a second independent cohort of 250 SSC sera and suggest that NT-proBNP has a complementary value correlating with other aspects of the disease, such as PAH and heart severity. Longitudinal multicentre studies are warranted to determine the sensitivity to change and the predictive value of these biomarkers in SSC patients and to build a new combined scleroderma-specific algorithm including markers of fibrosis and vasculopathy.

Disclosure statement: The authors have declared no conflicts of interest.

254 THE USE OF PHOSPHODIESTERASE-5 INHIBITORS IN SECONDARY RAYNAUD’S PHENOMENON: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Patients with RP secondary to CTDo have to manage severe disease compared with those with primary RP, resulting in substantial functional impairment and ischaemic complications such as digital ulcerations. They often require pharmacological therapy. The escalation beyond first-line treatment with calcium channel blockers (CCBs). Phosphodiesterase-5 (PDE-5) inhibitors are commonly used as second-line agents in patients intolerant to or with inadequate response to CCBs. This systematic review aims to determine the efficacy of PDE-5 inhibitors in improving symptoms, severity and functional impact of secondary RP.

Methods: The Medline and Embase databases were searched using the OVID platform for potentially relevant studies. Additional sources of data included the Cochrane Controlled Trials Register, the ClinicalTrials.gov registry and the reference lists of identified studies. Randomized controlled trials comparing PDE-5 inhibitors to placebo or to an alternative agent in the management of secondary RP were evaluated. Trial subjects were adults with a diagnosis of secondary RP. Outcome measures assessed were frequency, duration and severity of attacks [measured by the Raynaud’s Condition Score (RCS)], patient and physician’s global assessment of the impact of RP, quality of life/functional impact (measured by the HAQ or Sclerodema HAQ (SHAQ)] and digital ulcers (development of new ulcerations and healing of existing ulcers). All data analyses were performed using the generic inverse variance method (RevMan 5.3). A fixed-effects model was used to estimate the effect size for continuous variables.

Results: Six studies were included in the final quantitative review. Overall, this review showed that PDE-5 inhibitors have demonstrable efficacy over placebo in reducing the frequency of RP attacks [weighted mean difference (WMD) −0.71/day (95% CI −0.93, −0.48)], the duration of RP attacks (WMD −17.58 min/day (95% CI −21.82, −9.70)) and the RCS (WMD −0.77 (95% CI −1.07, −0.47)). The improvement in objective measures was translated to improvement in patient-reported outcomes such as patient global assessment score, HAQ and SHAQ. PDE-5 inhibitors also appear to be effective in healing existing digital ulcers and preventing new digital ulcer formation, although these outcomes were only assessed in two studies as secondary outcome measures. A sensitivity trial that evaluated the efficacy of PDE-5 inhibitor against CCBs did not demonstrate any significant difference between the two groups.

Conclusion: PDE-5 inhibitors are efficacious in reducing the symptoms and severity of secondary RP as well as improving patient reported function, compared with placebo. More limited evidence also suggests efficacy in healing existing digital ulcers and preventing new digital ulcer formation.

Disclosure statement: The authors have declared no conflicts of interest.

255 MICROARRAY ANALYSIS MAPS GLOBAL EFFECTS OF EPIDEMIC BROMODOMAIN INHIBITOR JO1 IN ON GENE EXPRESSION IN TRANSFORMING GROWTH FACTOR-β- STIMULATED ADULT LUNG FIBROBLASTS

Carmel Stock1, Mike Hubank2, Charalambios Michaeloudes3, Fan Chung4, Athol Wells1, Ian Adcock5, Elisabetta Renzoni6 and Gisela Lindahl1
1Intestinal Lung Disease Unit, National Heart and Lung Institute, Royal Brompton Hospital and Imperial College London, 2Child Health, University College London and 3National Heart and Lung Institute, Imperial College London, London, UK

Background: Pulmonary fibrosis represents one of the most prevalent and serious disease complications in SSC, affecting >70% of patients, and currently has no effective treatment. Chronic paracrine and autocrine TGF-β1-signalling to fibroblasts is believed to be a central driver of fibrotic processes in SSC and can serve as an in vitro disease model of activated fibroblasts to identify suitable therapeutic strategies. Recently, epigenetic regulation and aberrant histone modification has been implicated in fibrosis. Bromodomain and extraterminal (BET) proteins, including BRD2, 3 and 4, are epigenetic readers recognising histone acetyl marks and thus regulate gene transcription. Here we examine the global effect on gene expression in human activated lung fibroblasts of the bromodomain inhibitor JO1, a new antifibrotic compound, which has demonstrated potential beneficial effects on fibroblast phenotype and limited gene expression in vitro, and in the murine bleomycin model of lung fibrosis.

Methods: Adult pulmonary fibroblasts were obtained by explant culture from histologically determined unaffected lung from patients undergoing cancer resection surgery and maintained under standard culture conditions. Fibroblasts were treated with 2ng/ml TGF-β and 500nM JO1 or its inactive enantiomer JO1* for 24 h in triplicate. RNA from cell lysates was subjected to analysis on Affymetrix Human Exon 1.0ST arrays. Hybridisation signals were normalized for each array by Affymetrix software and GeneSpring software was used to determine differentially expressed (DE) genes, with DE = 1.3-fold filtered out. A number of DE genes were verified by quantitative real-time PCR (qRT-PCR).

Results: Preliminary analysis revealed 731 genes (401 upregulated and 330 downregulated) responsive to TGF-β. In the presence of TGF-β, 509 genes were significantly regulated by JO1 compared with JO1*. Of the genes regulated by TGF-β, 218 were significantly affected by JO1* and 516 were not. Of these genes, 132 genes upregulated by TGF-β were downregulated by JO1*, i.e. expression levels were normalized to varying degrees ranging from 60 to 167% of TGF-β-induced expression levels. This group included IGF-1, IL-6, EGR2, EDN1 and NOX4 genes. A total of 79 genes downregulated by TGF-β
were upregulated by JQ1, including HGF and PLAT. Interestingly, 7 genes downregulated by TGF-β were further downregulated by JQ1. Among the 516 genes regulated by TGF-β but unaltered by JQ1 are also fibrosis-related genes such as CTGF and SERPIN1 (PAI-1) downregulated in SSC fibroblasts.

Conclusion: These data provide greater insight into the effects of JQ1 on fibroblast gene expression, which is essential in understanding its impact on phenotype, and may help in developing this and related drugs for use in diseases like SSC.

Disclosure statement: The authors have declared no conflicts of interest.

256 INVESTIGATING THE ROLE OF C-KIT-POSITIVE SUBPOPULATION IN SCLERODERMA LUNG FIBROBLASTS

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Background: Using a broad screening methodology, c-Kit was identified as an induced phosphoprotein in migrating lung fibroblasts. Minority stem cell populations expressing c-Kit have been demonstrated in lung tissue, capable of regenerating epithelial and endothelial cells after injury. We went on to study the c-Kit subpopulation of cells using stem cell factor (SCF) as the growth factor ligand and investigate SCF/c-Kit as a potential driving factor in the fibrogenic process of SSC and as a possible therapeutic target.

Methods: Aligned collagen matrices designed to model fibroblast migration, as well as scratch wound assay, were used to measure cell migration following treatment with SCF or anti-Kit antibodies. Kinexus phosphoprotein arrays were used to assay phosphoproteins in 40 × 2500 cell foci migrating vs matched non-migrating cultures. Proliferation was assessed using WST-1 and crystal violet assays. Protein levels and mRNA gene expression of SCF and c-Kit lung fibroblasts were measured by western blotting and quantitative PCR. Known inhibitors of signalling pathways were also analysed for their capacity to suppress gene expression. The levels of SCF and c-Kit in SSC and control plasma, blister fluid and fibroblast conditioned media were assessed by ELISA. A microbead kit was used to select CD117+ populations in peripheral blood and lung fibroblasts while CD117− cells were also analysed by flow cytometry.

Results: Phosphokinexus arrays identified c-Kit as among the top induced phosphoproteins in lung fibroblasts undergoing migration on aligned collagen matrices (770 phosphoproteins were assayed). The addition of neutralizing anti-c-Kit resulted in a significant decrease of induced phosphoproteins in migrating lung fibroblasts (770 phosphoproteins were assayed). The levels of SCF and c-Kit were further downregulated by JQ1 and 24 h (P < 0.01). The SCF-treated SSC fibroblasts migrated more rapidly after 32 h upon scratch wounding compared with the untreated cells (P < 0.007). Full-length SCF transcript mRNA was increased and more abundant in SSC lung fibroblasts (P < 0.008) and epidermal sheet, whereas the membrane bound spliced variant mRNA level did not differ between SSC and control samples (relative copy number 1.1 and 0.76, respectively; P = NS). C-Kit mRNA expression was confirmed present at low levels in both SSC and control lung fibroblasts (P = NS). Plasma and tissue fluid analysis by ELISA did not reveal systemic activation of SCF/c-Kit in SSC plasma levels. CD117+ cells were not detected using the microbeads, however, a small subpopulation of CD117+ cells was found in both SSC (2.3%) and healthy control (4.5%) lung fibroblasts through FACScan.

Conclusion: Lung fibroblasts maintained in tissue culture contain a c-Kit-positive minority cellular subpopulation. A potential autocrine function for SCF/c-Kit is proposed, acting in SSC fibroblasts to maintain proliferation and migratory potential, which could be targeted by therapeutic antibodies.

Disclosure statement: The authors have declared no conflicts of interest.

257 CARPAL TUNNEL BIOPSY AS A DIAGNOSTIC TOOL TO IDENTIFY EARLY CASES OF CARDIAC AMYLOIDOSIS: RESULTS OF A PILOT STUDY

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Background: Carpal tunnel syndrome (CTS) is the only known early clinical manifestation of systemic transthyretin amyloidosis (wild-type ATTR amyloidosis, formerly known as senile systemic amyloidosis). In our cohort, 98% of those with proven cardiac ATTR amyloidosis had evidence of median nerve entrapment on neurophysiological studies and 48% had a history of carpal tunnel decompression as much as 12 years prior to clinical presentation with advanced heart failure symptoms. ATTR amyloidosis is currently diagnosed in ~100 individuals in the UK annually, but cadaveric studies suggest the disease prevalence of cardiac ATTR amyloidosis may be as much as 20% in those >60 years of age. The diagnosis of ATTR amyloidosis (Tc-DPD) has lately been repurposed as a highly sensitive tool for the diagnosis of cardiac ATTR amyloidosis, which has largely abrogated the need for cardiac biopsy. Amyloid deposition can be readily identified in carpal tunnel biopsies taken at routine decompression surgery. Immunohistochemistry is able to type amyloid deposits, with ATTR amyloid deposits found in up to 25% of carpal tunnel biopsies from international cohorts with idiopathic CTS. Rheumatologists are ideally placed to request biopsy at routine decompression surgery. Developing this underused but diagnostic test is of particular importance in light of emerging therapies for ATTR amyloidosis.

Methods: Carpal tunnel biopsies were taken at decompression surgery from individuals with proven median nerve entrapment. Biopsies were stained with Congo red and viewed under cross-polarised light. Immunohistochemistry was used to type amyloid deposits.

Results: We analysed 21 carpal tunnel biopsies (76% female, mean age 65 years [range 35–87]). Three biopsies (14%) contained definitive ATTR amyloid deposits. One further case was equivocal. Of the four definitive cases, two were typed as ATTR amyloid using immunohistochemistry (9.8% of the total cohort, male:female 50%) and one demonstrated no specific staining. Proteomic analysis is under way. Neither case with proven ATTR amyloid had a history of heart failure symptoms at the time of carpal tunnel decompression. Of these, a 74-year-old man attended the neurosciences ambulatory centre for further diagnostic workup. He had no cardiac symptoms, normal ECG and echocardiogram and wild-type TTR gene sequence, however, Tc-DPD scintigraphy demonstrated low-grade uptake within the intraventricular septum and left ventricular wall on SPECT, indicative of early cardiac amyloidosis.

Conclusion: Carpal tunnel biopsy can readily identify ATTR amyloid deposition and may identify those at risk of developing systemic ATTR amyloidosis at an earlier and potentially treatable stage. This pilot study has informed the design of a prospective study to identify the UK prevalence of ATTR amyloid in those with CTS. Long-term follow-up of this cohort will inform us of the natural history of ATTR amyloidosis and permit early administration of potential disease-modifying therapeutic agents.

Disclosure statement: The authors have declared no conflicts of interest.

SYSTEMIC LUPUS ERYTHEMATOSUS AND ANTIPHOSPHOLIPID SYNDROME

258 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LOW BONE MINERAL DENSITY HAVE NO SIGNIFICANT INCREASED SUBCLINICAL ATHEROSCLEROSIS COMPARED WITH THOSE WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND NORMAL BONE DENSITY

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Background: Osteoporosis and osteopenia are inversely associated with atherosclerosis in the general population. This relationship appears to be independent of age and other shared traditional risk factors. Inflammation has been proposed to be important, with pro-inflammatory cytokines and the RANK pathway implicated as a link between these two conditions. Therefore we studied the association between atherosclerosis and low BMD in patients with SLE.

Methods: One hundred patients with SLE and no history of previous cardiovascular disease had carotid and femoral high-sensitivity US scans. Various US parameters were measured to estimate the burden of atherosclerosis: presence of plaque, number of plaque sites, total plaque area (TPA), intima-media thickness (IMT) and grey scale median (GSM), where lower values imply echolucent inflammatory
plaque. Bone density was measured by DXA. Statistical analysis was performed using PRISM.

Results: Of the 100 patients, 95% were female with a mean age of 45.2 years (range 20–66, s.d. 12.4). Thirty-six per cent had plaque and 64% had no plaque. Eighty-one per cent had available DXA scan results. Normal BMD was found in 32.14% (n = 27), osteopenia in 53.57% (n = 45) and osteoporosis in 10.31% (n = 9). Of the 81 patients for whom we had available scan and DXA results, the presence of plaque was more common in patients with low BMD compared with those with normal BMD (40.74% (n = 22/54) vs 37.03% (n = 10/27); Table 1), but we did not find a statistically significant association between plaque and low BMD (χ2-squared test, P = 0.7479). We noted that of the 32 patients with plaque, the mean number of plaque sites, mean GSM, mean TPA and mean overall IMT were higher in those with low BMD vs normal BMD (Table 1). None of these differences, however, were statistically significant (Mann–Whitney U-test; Table 1). The mean common carotid IMT was similar in patients with low BMD and those with normal BMD (Table 1).

Conclusion: We did not find a significant difference in atherosclerotic plaque burden or stability between patients with SLE and low BMD compared with those with SLE and normal BMD. Further research is required.

Disclosure statement: The authors have declared no conflicts of interest.

258 Table 1. SLE and BMD

<table>
<thead>
<tr>
<th>Presence of plaque, n (%)</th>
<th>SLE and normal BMD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>32/54 (40.74)</td>
<td>10/27 (37.03)</td>
<td>0.7479</td>
</tr>
</tbody>
</table>

Results: Of the 81 patients, 71% were female with a mean age of 45.2 years (range 20–66, s.d. 12.4). Overall, 36% had plaque and 64% had no plaque. Anti-factor Xa IgG was found in 44% and anti-Thr IgG in 31% of all patients. Anti-factor Xa IgG positivity was seen in 33/64 (52%) patients without plaque and 11/36 (31%) patients with plaque (P < 0.04). Among the 36 patients with plaque, the number of plaque sites per patient was lower in anti-factor Xa-positive than in anti-factor Xa-negative patients (P < 0.02). Although anti-Thr IgG positivity was also higher in patients without plaque [22/64 (34.3%)] compared with patients with plaque [9/36 (25%)], but this difference did not reach statistical significance (P = 0.3). There was no association between anti-Thr positivity and the number of plaque sites.

Conclusion: Patients with SLE who were positive for anti-factor Xa IgG had reduced atherosclerotic plaque burden (presence and total number of sites) compared with patients who were anti-factor Xa IgG negative. However, a similar relationship was not found between anti-Thr IgG and plaque. Further research is now required to determine whether anti-factor Xa IgG may be protective against the proatherogenic effects of factor Xa in patients with SLE.

Disclosure statement: The authors have declared no conflicts of interest.

260 HOW MUCH DIFFERENCE CAN WE MAKE BY STANDARDIZED ASSERTIVE MANAGEMENT OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A REAL-LIFE CLINIC STUDY

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Background: Patients with SLE have an increased risk of developing cardiovascular disease (CVD) compared with healthy people of the same age and gender. It is recognized that general CVD risk factors contribute to this increased risk. There are no consensus standards on how to manage these conventional risk factors in SLE patients. Challenges include establishing a simple, effective protocol that can be operated within a busy NHS clinic, setting standards for investigation and intervention and identifying patients who would benefit.

Methods: We designed a simple one-page protocol with input from doctors working in the lupus clinic and the CVD risk team. The aim was to capture information on age, sex, ethnicity, BMI, smoking status, blood pressure (BP) measurements and lipid levels for every SLE patient attending our lupus clinic. We report the results collected over 9 months. Criteria for intervention were as follows: serum low-density lipoprotein (LDL) >2.6 mmol/l in patients >40 years of age (liaise with the general practitioner to recommend treatment), offer all smokers referral to a smoking cessation service using the Smoking in Lupus leaflet and BP >140/90 mmHg (elevated as defined by the National Institute for Health and Care Excellence), confirmed by repeat reading, should lead to 24 h BP monitoring.

Results: Of a potential cohort of 448 SLE patients, data were collected on 309 patients (69%) with an average age of 47 years; 94% were female, 55% were Caucasian, 25% were Afro-Caribbean/African, 14% were Asian and 6% other. LDL was measured in 256 (82%) patients, of whom 64 were >40 years of age with LDL >2.6 mmol/l, but this only led to intervention being recommended in 13 patients. Smoking was less common among women in this cohort (10%) than in UK women generally (17%), but only one patient accepted referral to smoking cessation. Forty-three of 309 (14%) patients were eligible for 24 h BP monitoring and 32 were referred, of whom 6 were hypertensive. Three have had their BP drugs increased and the other three have been referred to a hypertension clinic. However, 48% of all patients were already on antihypertensives. Obesity (BMI >30 kg/m2) was seen in 62/309 (20%) patients, of whom 52% were on steroids, 47% on BP drugs and 11% on statins. Twenty-six per cent of obese patients were hypertensive, 5% diabetic and 26% had LDL >2.6 mmol/l.

Conclusion: All data were collected during normal clinical consultations and the protocol could readily be applied to >300 patients within 9 months. The results suggest that smoking and hypertension would not be rewarding targets for intervention. Our patients are very reluctant to change smoking behaviour and, in this cohort, BP is already managed appropriately in most patients. However, high LDL may represent an unmet need for intervention, and the one-fifth of patients who are obese may be a group with clustering of cardiovascular risk factors who could be targeted more stringently.

Disclosure statement: The authors have declared no conflicts of interest.

261 WHAT LEVELS OF VITAMIN D SHOULD WE AIM FOR IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS? A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Patients with SLE have an increased risk of developing cardiovascular disease (CVD) compared with healthy people of the same age and gender. It is recognized that general CVD risk factors contribute to this increased risk. There are no consensus standards on how to manage these conventional risk factors in SLE patients. Challenges include establishing a simple, effective protocol that can be operated within a busy NHS clinic, setting standards for investigation and intervention and identifying patients who would benefit.

Methods: We designed a simple one-page protocol with input from doctors working in the lupus clinic and the CVD risk team. The aim was to capture information on age, sex, ethnicity, BMI, smoking status, blood pressure (BP) measurements and lipid levels for every SLE patient attending our lupus clinic. We report the results collected over 9 months. Criteria for intervention were as follows: serum low-density lipoprotein (LDL) >2.6 mmol/l in patients >40 years of age (liaise with the general practitioner to recommend treatment), offer all smokers referral to a smoking cessation service using the Smoking in Lupus leaflet and BP >140/90 mmHg (elevated as defined by the National Institute for Health and Care Excellence), confirmed by repeat reading, should lead to 24 h BP monitoring.

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Disclosure statement: The authors have declared no conflicts of interest.
Background: There is increasing evidence for the role of vitamin D in the reduction of disease activity in SLE. The objective of this study was to compile the evidence for vitamin D supplementation in SLE patients with regards to helping develop guidelines.

Methods: The PubMed and Cochrane databases were searched (systemic lupus erythematosus[MeSH Terms] OR systemic lupus erythematosus[Title/Abstract]) OR lupus [MeSH] AND ([vitamin D[MeSH Terms]] OR vitamin D[Title/Abstract]) AND (last 10 years [PData] AND adult[MeSH] AND Humans[MeSH] AND English). A total of 190 papers that met the criteria were assessed for relevance and parameters measured, leaving 77 papers. Duplicates, case reports and papers not measuring vitamin D were removed. Final selection using the Critical Appraisal Skills Programme screening tool and again for relevance gave 52 papers. This process was repeated and papers checked by another medical student. Papers were then graded using the Centre for Evidence-Based Medicine scale. P-values, number of patients and strength of association between vitamin D level and disease activity were extracted, as were the vitamin D levels defined as ‘replete’. Papers were divided into positive (those finding a significant relationship between vitamin D and the parameter measured) and negative.

Results: A total of 32 papers were graded and results analysed. Twenty-six found that lower levels of vitamin D corresponded to higher disease activity as measured by SLEDAI (22, BILAG (1), biomarkers (9) and fatigue scores (2)). Two randomized controlled trials (RCTs) met the criteria; the trial confirmed SLEDAI > 11 was associated with < 0.26 nmol/l vitamin D (P = 0.038), while the negative trial measured vitamin D over 12 weeks as opposed to existing levels. It also assessed the IFN signature, which is yet to be validated as a marker for SLE activity. Of the SLEDAI measuring papers, 14 found a significant (P < 0.04) inverse correlation between SLEDAI and serum vitamin D (3852). Seventeen papers found vitamin D levels < 20 ng/ml correlated with higher SLEDAI (levels 1b–2b). There is a discrepancy over the level of vitamin D considered replete. One study found a reduced SLEDAI with vitamin D < 40 nmol/l, while others saw 20 ng/ml as replete with narrow confidence intervals. Six papers quoting no relationship were grade 2b or below (205 pooled patients). Two studies looked at carotid plaque thickness and atherosclerosis in 199 patients (2b > 3b). The lack of a gold standard disease marker causes difficulty in the interpretation. Of the two studies measuring fatigue, the positive study was a stronger retrospective cohort study and found a greater negative correlation (r = -0.364). This study included 19 more patients than the negative study (r = -0.12), which was not considered significant.

Conclusion: Patients with >20 ng/ml vitamin D have lower disease activity measured by various parameters. Those with <30 ng/ml have an even greater reduction in disease activity. This is valuable evidence for the role of vitamin D supplementation in the practical management of SLE. There is a need for more RCTs and the agreement of a biomarker for disease activity.

Disclosure statement: The authors have declared no conflicts of interest.

262 LONGITUDINAL ASSESSMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY: BRITISH ISLES LUPUS ASSESSMENT GROUP 2004, SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY INDEX 2000 OR BOTH?

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Background: Various different ways of analysing the BILAG-2004 index, SLEDAI (and its derivatives) and combinations of the two have been employed in longitudinal studies of SLE, especially clinical trials. However, there has not been a direct comparison of these two indices and their various combinations to determine the best way of using them. This study was to compare the performance of BILAG-2004 [including the BILAG-2004 systems tally (BST) and simplified BST (sBST)] and SLEDAI-2000 and to determine if there was any added value in combining BILAG-2004 and SLEDAI-2000.

Methods: This was a multicentre longitudinal study of SLE patients (data collected on BILAG-2004, SLEDAI-2000 and therapy at every visit). The external responsiveness of the indices was assessed by determining the relationship between change in disease activity and change in therapy between two consecutive visits. Comparison of the indices and derivatives was analysed by assessing the main effects of the indices using logistic regression. Receiver operating characteristics curves analysis was used to describe the performance of these indices individually and in various combinations and comparisons of the area under the curve (AUC) were performed (Table 1). Wald tests were used for model comparison where needed.

Results: There were 1414 observations from 347 patients. Both BILAG-2004 and SLEDAI-2000 maintained an independent relationship with change in therapy when compared. There was no evidence that the BILAG-2004 system scores and the continuous SLEDAI-2000 variables (change in score and score of previous visit) were less predictive of changes in therapy individually than each other (P = 0.69, Wald test). There was some improvement in performance when SLEDAI-2000 variables were combined with BILAG-2004 system scores (P < 0.001 for the addition of one index to the other, Wald test). Dichotomisation of the indices resulted in poorer performance, especially with SLEDAI-2000 (lower AUC). BST, sBST and BILAG-2004 numerical score variables (change in numerical score and previous visit numerical score) were more predictive of an increase in therapy compared to BILAG-2004 system scores (P < 0.001, P < 0.002 and P < 0.001, respectively; Wald test) and SLEDAI-2000 variables (P = 0.001, P = 0.013 and P = 0.001, respectively; Wald test) individually, but are comparable to or slightly better than the combination of the two (P = 0.63, P = 0.26 and P = 0.03, respectively; Wald test). There was little benefit in combining SLEDAI-2000 variables with BST, sBST or BILAG-2004 numerical score variables (P = 0.60, P = 0.16 and P = 0.22, respectively; Wald test). BST (AUC 0.66) and sBST (AUC 0.65) have superior overall performance to the Systemic Lupus Erythematosus Responder Index 4 (AUC 0.59) and BILAG-based Composite Lupus Assessment-90 (AUC 0.59) combinations.

Conclusion: The BILAG-2004 had comparable performance to SLEDAI-2000. There was some benefit in combining both. Dichotomisation of BILAG-2004 and SLEDAI-2000 leads to suboptimal performance. BST and sBST performed well on their own; they are recommended for their simplicity and clinical meaningfulness.

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262 Table 1. AUC values from ROC analysis of BILAG-2004, SLEDAI-2000 and a combination of the two indices

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Increase in therapy vs no increase in therapy</th>
<th>Decrease in therapy vs no decrease in therapy</th>
</tr>
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<tbody>
<tr>
<td>BILAG-2004 systems score</td>
<td>0.75 (0.71, 0.78)</td>
<td>0.65 (0.62, 0.67)</td>
</tr>
<tr>
<td>sBST</td>
<td>0.83 (0.81, 0.86)</td>
<td>0.66 (0.63, 0.68)</td>
</tr>
<tr>
<td>BILAG-2004 numerical score variables</td>
<td>0.85 (0.82, 0.88)</td>
<td>0.67 (0.66, 0.70)</td>
</tr>
<tr>
<td>SLEDAI-2000 variables</td>
<td>0.76 (0.73, 0.79)</td>
<td>0.63 (0.60, 0.66)</td>
</tr>
<tr>
<td>Combination of BILAG-2004 index score variables</td>
<td>0.81 (0.78, 0.84)</td>
<td>0.64 (0.61, 0.67)</td>
</tr>
<tr>
<td>SLEDAI-2000 variables</td>
<td>0.76 (0.73, 0.79)</td>
<td>0.63 (0.60, 0.66)</td>
</tr>
<tr>
<td>Combination of BST and SLEDAI-2000 variables</td>
<td>0.84 (0.81, 0.87)</td>
<td>0.67 (0.64, 0.70)</td>
</tr>
<tr>
<td>Combination of sBST and SLEDAI-2000 variables</td>
<td>0.83 (0.80, 0.86)</td>
<td>0.67 (0.64, 0.69)</td>
</tr>
<tr>
<td>Combination of BILAG-2004 numerical score variables and SLEDAI-2000 variables</td>
<td>0.85 (0.83, 0.88)</td>
<td>0.68 (0.65, 0.71)</td>
</tr>
</tbody>
</table>

BST: BILAG-2004 systems tally; sBST: simplified BST.
263 THE USE OF RITUXIMAB IN NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: LONG-TERM STEROID-SAVING CAPACITY AND CLINICAL EFFECTIVENESS

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Background: We assessed the long-term steroid-sparing capacity and clinical effectiveness of B cell depletion therapy (BCDT) in newly diagnosed SLE patients.

Methods: Sixteen female SLE patients were treated at or shortly after diagnosis with BCDT, aiming to avoid the routine use of oral steroids. Post-treatment, most patients were given HCQ (n = 14) and AZA (n = 10). The BILAG disease activity index was used for clinical assessments. Serum anti-dsDNA (normal ≤50 IU/mL), C3, ESR, circulating B lymphocytes (CD19+) and total immunoglobulins were tested every 2–6 months for an average of 5.5 years (s.e. 8.9) post-treatment. Disease activity and steroid requirements over the follow-up period (ranging from 1 to 6.5 years) were compared with three SLE patients treated conventionally (usually with steroids), each carefully matched for ethnicity, sex, age, clinical features and disease duration at diagnosis.

Results: All patients given rituximab achieved B cell depletion. Clinical flares were present in up to 50% of the BCDT group and in 70.8% of the control group, although this was not significant (P = 0.145). The mean number of flares during the follow-up period (defined as new BILAG A or B) was 3.75 (s.e. 4.04) in the BCDT group and 4.27 (s.e. 4.03) in the control group (P = 0.69). Post-BCDT, mean dsDNA antibody level fell from 1114 (s.e. 1699.3) to 194 (s.e. 346.7) for 18 months (P = 0.043), mean serum ESR fell by >70% at 6 months and was maintained during the follow-up and serum C3 level normalized during the follow-up in seven patients. The mean cumulative prednisolone dose at 60 months for the BCDT patients (n = 11) was 4995.67 mg (s.e. 6090 vs 12 553.92 (s.e. 12 672) for the controls (P = 0.01) (Table 1).

Conclusion: Early treatment of SLE patients with BCDT is safe and effective and enables a reduction in the overall steroid burden.

Disclosure statement: The authors have declared no conflicts of interest.

264 A META-ANALYSIS OF TACROLIMUS USE IN LUPUS NEPHRITIS

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Background: Current treatments for LN are associated with significant adverse effects, therapy failure and relapse rates, so there is an ongoing search for more effective, less toxic options. There is growing interest in the role of tacrolimus as a potential therapeutic agent in SLE. This meta-analysis therefore evaluates the evidence for tacrolimus use in the management of LN. The incidence of adverse effects when compared with currently used therapies is also evaluated.

Methods: A systematic review was carried out and 13 controlled studies were identified (9 suitable for inclusion) using Cochrane databases, SCOPUS, Web of Science and Ovid (Medline and Embase). Data on complete and partial remission rates, proteinuria reduction and adverse events were extracted and analysed using RevMan software.

Results: The meta-analysis showed that overall tacrolimus is more effective at inducing complete renal remission than i.v. CYC (P = 0.004), but there is no significant difference compared with MMF (P = 0.87). Multitarget tacrolimus + MMF therapy is more effective than i.v. CYC only when partial remission is included (P = 0.0026). It is unknown what the long-term outcomes are following tacrolimus use. Although none of the studies detected any calcineurin-induced nephrotoxicity, there are valid concerns raised from studies in solid organ transplantation that report almost universal nephrotoxicity with long-term use beyond 10 years. Overall, the meta-analysis suggests the frequency of some key adverse effects to be comparable with other agents used in the management of LN, with fewer gastrointestinal side effects, leukopenia, menstrual disorders, infections and episodes of liver dysfunction reported, but more new-onset hypertension and hyperglycaemia. Mortality also appeared to be lower in the tacrolimus groups, but this was not statistically significant (P = 0.15). There is some suggestion that tacrolimus may be more effective at reducing proteinuria. Other epidemiological studies have suggested those with lower levels of proteinuria after 6 months have lower mortality, less end-stage renal disease and better long-term outcome, therefore tacrolimus could potentially be a useful adjunctive agent in the management of patients with persistent proteinuria. There are no controlled studies in the special cases of pregnancy and juvenile patients, however, case reports suggest that tacrolimus may also be safe and effective in these groups.

Conclusion: In moderately severe LN there is some evidence supporting the efficacy of tacrolimus or multitarget tacrolimus + MMF over i.v. CYC, but no evidence supporting tacrolimus over MMF. Tacrolimus may be more effective at reducing proteinuria, having potential implications for long-term outcomes. Key limitations of this study are the lack of long-term outcome data and the lack of high-quality, large, blinded controlled trials in multi-ethnic groups.

Disclosure statement: The authors have declared no conflicts of interest.

265 CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN NAIROBI, KENYA

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Background: SLE, a chronic multisystem autoimmune disease with a wide spectrum of manifestations, shows considerable variation across the globe, although data from Africa are limited. Quantifying the burden of SLE across Africa can help raise awareness and knowledge about the disease. It will also clarify the role of genetic, environmental and other causative factors in the natural history of the disease and help us to understand its clinical and societal consequences in Africa.

Methods: To determine the clinical profile of SLE patients at a tertiary care centre in Nairobi, we reviewed the case records of patients attending the Nairobi Arthritis Clinic seen between January 2002 and January 2013. This was a cross-sectional study done on 100 patients fulfilling the 2012 SLICC criteria for SLE attending the Nairobi Arthritis Clinic. The patients were evaluated for sociodemographic, clinical and immunological manifestations and drugs used to manage SLE.

Results: One hundred patients diagnosed with SLE were recruited into the study. Ninety-seven per cent of the study participants were female with a mean age of 36.6 years and a mean age of diagnosis of 33 years. The mean duration of disease was 3 years (range 0–13). There was extensive disease, as many had multi-organ involvement. The majority of the study participants (83%) met between four and six manifestations for the diagnosis SLE. Non-erosive arthritis and cutaneous disease were the most common initial manifestations. The patients had varied cutaneous, haematological, pulmonary, cardiac, renal and neuropsychiatric manifestations. ANA assay and anti-dsDNA were positive in 82 and 52%, respectively. Patients on steroids, non-steroidal drugs and synthetic DMARDs were 84, 45 and 43%, respectively. None of the patients were on biologic DMARDs.

Conclusion: In Nairobi, SLE is a multisystem disorder affecting predominantly young females. Polyarthitis and cutaneous disease were the most common clinical feature. This is comparable to other studies done in black African populations. We found a higher prevalence of haematological and lower rate of renal disease as compared with other studies done in black Africans. The ANA assay and anti-dsDNA positivity were lower than in other studies on black Africans. The majority of the patients are on steroids.

Disclosure statement: The author has declared no conflicts of interest.

Table 1. Prednisolone total doses (mg)

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266 AN EVALUATION OF QUALITY OF LIFE IN AMBULATORY PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ATTENDING A RHEUMATOLOGY CLINIC IN KENYATTA NATIONAL HOSPITAL

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Background: SLE is a chronic autoimmune disease that affects all organs of the body. It is becoming increasingly clear that SLE is not as rare in Kenya as was previously thought. Due to its chronicity SLE has been known to affect patients’ quality of life. There are minimal data on SLE in East Africa, and especially in Kenya. The quality of life of SLE patients in Kenya has never been assessed.

Methods: Patients who satisfy the ACR criteria were consecutively recruited. All patients with SLE attending the clinic were included in the study. Consent was obtained from the patients, after which their demographic data were obtained. Patients were examined for the presence of malar rash, icssoid rash, arthritis/arthritis, photosensitivity, CNS symptoms, serositis and oral ulcers. The patients then completed the Lupus QoL questionnaire. The information acquired was then analysed using SPSS version 17.0 using Student’s t-test and regression analysis. The quality of life was calculated and then correlated with age, duration of illness and drug management.

Results: Sixty-two patients were analysed (60 females and 2 males). The mean age of the population was 37.3 years (range 14–71 years). All patients had some level of education, with 61.3% of the population having some form of secondary education. Most patients (54.8%) were married. The mean age of diagnosis was 34.5 years and the mean duration of disease was 1.5 years. A majority (88.7%) had arthritis/arthralgia, followed by oral ulcers (62.8%), malar rash (59.7%), photosensitivity (58.1%), serositis (32.3%), CNS symptoms (27.4%) and discoid rash (17.7%). Patients scored globally low in all domains of the Lupus QoL. The highest domain was planning [83.7 (28.3)], followed by emotional health [81.3 (28.6)], burden to others [58.9 (31.2)], fatigue [57.5 (30.0)], pain [56.6 (29.6)], physical health [54.0 (23.3)], body image [47.1 (24.2)] and intimate relations [41.1 (38.4)]. The most common drug in use in our population was prednisone (74.2%). This was followed by HCO (89.4%), NSAIDs (54.8%), AZA (37.1%), MTX (22.6%), MFM (8.1%), calcium channel blockers (11.3%) and colchicin (3.2%). Health-related quality of life (HRQoL) correlated positively with advance in age for the domains physical health, burden to others, emotional health and fatigue. There was no correlation between HRQoL and duration of illness or drugs used by the population.

Conclusion: The HRQoL of our SLE patients was found to be low in all domains and to correlate with advance in age in the domains of physical health, burden to others, emotional health and fatigue. However, there was no correlation with duration of illness or drugs used.

Disclosure statement: The authors have declared no conflicts of interest.

267 FLARE RATES AND TREATMENT OF LUPUS FLARES MEASURED BY THE BRITISH ISLES LUPUS ASSESSMENT GROUP 2004 INDEX

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Background: The BILAG index is based on the physician’s intention to treat. It is becoming increasingly clear that SLE is not as rare in Kenya as was previously thought. Due to its chronicity SLE has been known to affect patients’ quality of life. There are minimal data on SLE in East Africa, and especially in Kenya. The quality of life of SLE patients in Kenya has never been assessed.

Methods: Patients who satisfy the ACR criteria had been taken and stored at University College London over 12 months (January 2014–December 2014). A total of 323 patients regularly attending were assessed using BILAG-2004 at each visit.

Results: During the study period, 135 patients (41.8%) had flares (mild, moderate or severe). There were 229 flare episodes, as some patients had more than one flare. Among the 229 flare episodes, 15.7% were severe, 14% were moderate and 70.3% were mild.

Twenty-seven of the 323 patients (8.4%) had had severe flares during this period. 30 (9.3%) had moderate flares and 113 (35.0%) had mild flares. In the previous study with the classic BILAG, 10.4% of patients had A flares and 51.2% had B flares. We stratified the treatment of flares into cytotoxic drugs/high-dose steroids, low-dose steroids, antimalarials or symptomatic drugs and no change in treatment. For severe flares, 41.7% were treated with cytotoxic/high-dose steroids, 36.1% with low-dose steroids and 22.2% had no treatment change for various reasons. For moderate flares, the largest proportion (40.6%) was treated with low-dose steroids. For mild flares, most (57.8%) had no treatment change. The treatment strategies of severe, moderate and mild flares were significantly different ($\chi^2 = 49.16, P < 0.001$) (Table 1).

Conclusion: These results are consistent with the principle of the physician’s intention to treat. The severe flare rate in BILAG-2004 was comparable to the A flare rate using the classic BILAG.

Disclosure statement: The authors have declared no conflicts of interest.

268 DIFFERENT PATTERNS OF POSITIVEITY FOR IGG ANTI-CARDIOLIPIN, ANTI-¿2-GLYCOPROTEIN I AND ANTI-DOMAIN I ANTIBODIES WITHIN THE FIRST YEAR OF DISEASE IN 501 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: ASSOCIATIONS WITH DIFFERENT CLINICAL OUTCOMES

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Background: APS is an autoimmune rheumatic disorder in which aPLs cause clinical sequelae including vascular events (VEs) and pregnancy morbidity. The key antigen in APS is β2-glycoprotein I (β2GPI), which consists of five domains. The N-terminal domain (D1) carries the main immunodominant epitope. Current clinical ELISAs used in APS test for aCL and anti-β2GPI antibodies, but increasing evidence suggests that anti-DI levels may be more strongly associated with VEs and pregnancy morbidity. Patients with SLE are often screened using current tests for aPL, and up to 40% are positive, but the implications of a positive test for the future health of the patient are unclear. In this study we retrospectively explored the prevalence of IgG aCL, anti-β2GPI and anti-DI antibodies in stored serum samples that had been collected prospectively within 1 year of diagnosis in 501 patients with SLE and analysed associations between these serological profiles and clinical outcomes.

Methods: Samples from 501 patients with SLE fulfilling revised ACR criteria had been taken and stored at –20 °C within 1 year of diagnosis. All samples were tested for levels of IgG aCL, anti-β2GPI and anti-DI by ELISA. Results were expressed in absorbance units (AU) by comparison with standard positive controls loaded on every plate. A positive test was defined as an AU >99th percentile of 100 healthy controls and high positive was defined as double that level. Data on VEs (venous or arterial thrombosis or coronary disease) and pregnancy were obtained from medical records and patient interviews. Fisher’s exact test was used to analyse statistical associations between particular serological profiles and VEs or pregnancy morbidity.

Results: The mean age of the 501 patients was 30 years (s.d. 12.2, 91% were female and 91% were white. In the early disease samples, 68 were positive for aCL, 24 for anti-β2GPI and 146 for anti-DI. Thirty patients were double positive for two of these aPLs and 9 were triple positive. Using higher cut-off levels, 31, 6 and 36 patients were high positive for aCL, anti-β2GPI and anti-DI, respectively. The mean follow- up time post-sample was 12.1 years (maximum 36). Full data on VEs and pregnancy morbidity were available for 338 and 275 patients,
respectively. Table 1 shows associations between particular serologi-
cal profiles and the occurrence of VEs or pregnancy morbidity.

Conclusion: Thirty-eight per cent of patients were positive for one or
more aPLs in early disease, but only 15% showed high positivity.
Both double or triple positive was most strongly associated with VEs
(but not pregnancy morbidity): 40% of the double-/triple-positive
patients suffered VEs in the follow-up period. Positivity for anti-FGPI
was also associated with VEs. High positivity for anti-D showed the
strongest association with pregnancy morbidity.

Disclosure statement: D.A.I. has received research funding from
Bristol-Myers Squibb. All other authors have declared no conflicts of
interest.

Results: Dietary restriction resulted in significantly lower serum
25(OH)D after 6 weeks [mean 21.6 nmol/l (s.d. 65.0; P < 0.0001)] but normal serum calcium. Vitamin D-deficient mice had
significantly worse endothelium-dependent vasorelaxation (difference
in relaxation P = 0.041 and P = 0.018 at the two highest concentrations
of ACh). Neangiogenesis was also significantly reduced in the vitamin
D-deficient mice (P = 0.023), although there was no change in the total
number of EPCs [105 (s.d. 37) vs 123 (35); P = 0.398]. There was no
difference in the anti-dsDNA titre, proteinuria or glomerulonephritis
(either activity or chronicity, or C3/G3 deposition) between deficient or
replete mice. Deficient mice did however have increased ISG
expression (notably MCP1; P = 0.036). In support of this finding, the
ISG score (calculated as the mean fold increase of six ISGs compared
with healthy subjects) was significantly higher in vitamin D-deficient
(10.7 (s.d. 2.9) compared with replete [2.9 (s.d. 3.9)] SLE patients
(P = 0.047).

Conclusion: Vitamin D deficiency is a novel cause of abnormal
vascular repair and reduced endothelial function in SLE and may
exacerbate disease through effects on type I IFN responses.

Disclosure statement: The authors have declared no conflicts of
interest.

270 PATIENTS WITH EARLY INCOMPLETE LUPUS HAVE
ELEVATED TYPE 1 INTERFERON ACTIVITY

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2NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds, UK

Background: Autoantibodies can be present several years before
the onset of clinical diseases such as SLE. Therefore, identifying
biomarkers that may predict progression is needed and will allow
early intervention to prevent organ damage. Type 1 IFN plays a key
role in the pathogenesis of SLE, however, its role in pre-clinical
disease has not been fully elucidated. The aim of this study was to
calculate expression of IFN-stimulated genes (ISGs) in patients
with early incomplete lupus erythematosus (E-ILE) and undiffer-
entiated CTD (UCTD) with established SLE, RA and healthy
controls.

Methods: We conducted a cross-sectional study of patients with
established SLE, E-ILE and UCTD at a single centre. SLE was
defined by ACR/SLICC 2012 criteria (n = 163). E-ILE was defined
by the presence of ANA and one or two ACR/SLICC clinical criteria
with <12 months from onset. UCTD was defined as for E-ILE, but
>12 months from onset. Healthy (n = 20) and disease controls [RA
(n = 32)] were used for comparison. Thirty-three ISGs were
measured from whole blood using TaqMan quantitative PCR.
Relative expressions were log transformed and expressed as
s.o.s from the mean of healthy controls. The overall IFN signature
score was derived by adding these values. Kruskal-Wallis and
Bonferroni-corrected Mann-Whitney U tests were used for statis-
tical analysis.

Results: As expected, most SLE patients had elevated IFN scores
(median 21.6 [interquartile range (IQR) 4.1–31.0]). RA patients had
elevated IFN scores, but significantly lower than SLE (P < 0.05). In
E-ILE, the IFN score was lower than SLE, but significantly higher than in
healthy controls [mean 14.5 (IQR 1.1–24.4); P < 0.05]. In UCTD, the
IFN score was lower than in E-ILE and SLE, but not significantly different
from healthy controls [mean 3.1 (IQR 15.7 to 5.7)]. However, a subset of
UCTD patients had elevated IFN scores.

Conclusion: We found an intermediate level of IFN expression in
early incomplete SLE. The level was higher after SLE progression, but
lower in persistently undifferentiated disease. IFN expression at the
onset of symptoms may predict progression, or IFN response may
worsen after the first year. Longitudinal analysis will investigate these
explanations further. These results indicate that IFN dysregulation is
apparent early in the disease and support the notion of early intervention
studies.

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Pfizer, MSD, Roche and UCB. All other authors have declared no
conflicts of interest.
271 INTERRATER AND INTRARATER ANALYSIS OF ULTRASOUND AND HISTOLOGICAL FINDINGS IN PATIENTS WITH SUSPECTED GIANT CELL ARTERITIS

Raashid A. Luqmani1, Ellen Lee2, Sunjeet Singh3, Michael Gillett4, Wolfgang A. Schmidt5, Mike Bradburn6, Bhaskar Dasgupta7, Andreas P. Diamantopoulos8,9, Wulf Forrester-Barker10, William Hamilton11, Shaura Masters12, Brendan McDonald12, Eugene McNally13, Colin T. Pease14, Jennifer Piper15, John Salmon16, Allan Wai10, Konrad Wolfe17 and Andrew Hutchings18 for the TABUL Sonographers Group and TABUL Pathologists Group.


Background: US is emerging as an alternative test to performing a temporal artery biopsy in the diagnosis of GCA. Little is known of the variability in interpretation of these tests by sonographers and pathologists. We undertook an interobserver analysis to assess agreement between sonographers in interpreting US videos and between pathologists for biopsy images in patients with suspected GCA.

Methods: We developed a web exercise with 30 cases randomly sampled from patients with suspected GCA recruited to a large multicentre study comparing US with biopsy for the diagnosis of GCA. We used 5 practice cases, followed by the 30 unique cases and 6 interspersed repeats, showing US videos of both temporal arteries and high-quality scanned images of biopsies. Trained sonographers and pathologists from the study were asked to assess the compatibility of the videos and images with a diagnosis of GCA and indicate how confident they were of the diagnosis. Interobserver agreement between sonographers and between pathologists was evaluated using two-way random effects analysis of variance to estimate the intraclass correlation coefficient (ICC) for agreement. Intra-observer reproducibility was evaluated using x statistics for the six repeated cases.

Results: All 12 sonographers agreed unanimously on 10/30 cases; 4 as GCA and 6 as not GCA. In five cases at least three sonographers differed from the majority. All 14 pathologists agreed unanimously on 11 cases; 6 as GCA and 5 as not GCA. In five cases at least three differed from the majority and in one case the pathologists were evenly divided. Overall agreement (based on ICCa) was similar between the sonographers (0.61 (95% CI 0.48, 0.75)) and pathologists (0.62 (95% CI 0.49, 0.76)). After allowing for confidence in interpretation of videos and images, interobserver agreement between sonographers (ICC 0.58 (95% CI 0.44, 0.72)) was lower than between pathologists (ICC 0.72 (95% CI 0.60, 0.83)). Giant cells were reported in 8/30 cases; in 6/8 the pathologists unanimously judged the biopsy images to be consistent with GCA. For intra-observer reproducibility of the repeated cases the sonographers (raw agreement 86%, k = 0.69) performed less well than the pathologists (raw agreement 92%, k = 0.83).

Conclusion: The level of agreement between sonographers is similar to that between pathologists for assessing the compatibility of videos and images with a diagnosis of GCA. Pathologists performed better, after allowing for certainty in interpretation and for intra-observer reproducibility. However, the level of agreement was lower than expected. We suggest that training is required in interpreting both temporal artery-US and histological abnormalities (especially in the absence of giant cells).

Interpreting results to support or overturn a diagnosis of suspected GCA should be undertaken in the light of these findings.

Disclosure statement: R.A.L. has received research funding from Chemocentryx, GSK, Nordic and Medimmune and honoraria from Roche Products and UCB. A.H. has received research funding from the NIHR HTA programme and Medical Research Council. All other authors have declared no conflicts of interest.

272 ANTICOAGULATION AND LONG-TERM OUTCOMES IN PATIENTS WITH RENAL ARTERY STENOSIS AND ANTI-PHOSPHOLIPID SYNDROME

Alina Casian1, Shirish Sangle1, Natasha Jordan6, Sotiria Maroukathopoulou1 and David D’Cruz1
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Background: Our previous data showed that renal artery stenosis (RAS) is more prevalent in APS (26%) compared with the general hypertensive population (8%), and anticoagulation (international normalized ratio >3) was associated with an initial reduction of chronic kidney disease (CKD) and hypertension.

Methods: We identified 37 patients with RAS and APS fulfilling Sapporo criteria: anti-cardiolipin IgG/IgM titre >40 units or >99th percentile (or positive lupus anticoagulant) on two or more occasions ≥6 weeks apart AND vascular thrombosis (or pregnancy morbidity). RAS was diagnosed by magnetic resonance angiography (MRA).

Results: Fifteen patients had APS alone and 22 APS associated with autoimmune conditions and 15 lupus, 5 ANCA vasculitis, 4 myositis, 4 mixed connective tissue disease, 4 SLE, 2 CRPS, 1 Takayasu arteritis, 1 thoracic outlet syndrome and 1 diabetic nephropathy. Twenty-six had hypertension and 15 diabetes. Median age at RAS diagnosis was 48 years, 31 (83.8%) were female and the median follow-up was 10.4 years. Twenty-five (67.6%) had previous thrombosis. Seven (19.1%) had bilateral RAS and three with artery occlusion. Six (16.2%) had concurrent coeliac stenosis. Recanalization of RAS occurred after HCQ in 3, and 9 (24.3%) underwent angioplasty with/without stenting. MRA was repeated in 11 (29.7%) patients after 2 years. Twenty-three (62.2%) were anti-coagulated, with 9 (24.3%) on antiplatelet therapy. Thirteen (35.1%) received HCQ, 10 (45.5%) immunosuppressives and 18 (48.6%) antihypertensives. Nine (24.3%) died after a median of 10 years since RAS diagnosis. Twenty-one (56.8%) developed CKD; 6 end-stage renal failure and 15 with a median eGFR of 39 ml/min.

Conclusion: The majority of patients with RAS and APS were female, developed CKD and did not benefit from renal angioplasty. Anticoagulation was not associated with a long-term reduction of end-stage renal disease or death, suggesting a non-thrombotic pathogenetic process underlying RAS, such as intimal hyperplasia. Treatment of associated vascular risk factors and autoimmune disease is paramount. Anti-cardiolipin antibodies and renal MRA are useful screening tests for lupus patients with difficult blood pressure control.

Disclosure statement: The authors have declared no conflicts of interest.

273 THE ROLE OF HYDROXYCHLOROQUINE IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY–POSITIVE AND NEGATIVE VASCU Lis TIS

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Lupus Unit, Guy’s and St Thomas’ NHS Foundation Trust, London, UK.

Background: There is an unmet need for a less toxic, corticosteroid-sparing therapy in ANCA vasculitis (AAV), as up to 50% of patients relapse by 5 years and 20% have suboptimal disease control. HCQ has been effective and safe in autoimmune diseases such as SLE and RA. There is a mechanistic rationale for the effectiveness of HCQ in vasculitis, considering its effect on immune mediators involved in pathogenesis, including B cell activating factors, Toll-like receptors, autoreactive T cells and cytokines. Here we assess retrospectively the efficacy and safety of HCQ in patients with systemic vasculitis.

Methods: Patients were identified by searching our departmental vasculitis database, including 248 patients in total, and electronic clinical records. Twenty-six patients received HCQ along with corticosteroids and immunosuppressants (Table 1). We assessed the effect of HCQ on clinical symptoms and the median dose of corticosteroids required.
Results: Twenty-six patients with various vasculitides were treated with HCO (median dose 200 mg once a day); 6 patients with Henoch–Schönlein purpura (HSP), 6 urticarial vasculitis, 6 with ANCA-positive vasculitides (AAV) (4 PPR-ANCA, 2 MPO-ANCA), 1 eosinophilic granulomatosis with polyangiitis (EGPA), 2 Takayasu arteritis, 2 Behçet’s disease, 1 adult Still’s disease (AOSD), 1 relapsing polychondritis, 1 polycystitis nodosa (PAN). The female:male ratio was 21:5 and the median age was 53 years. The median duration of HCO treatment was 3 years. Sixteen patients experienced a reduction in anarthria and skin rashes improved in 8 patients and completely resolved in a further 4. Eight patients could reduce corticosteroid doses (from 9 to 6 mg) and three discontinued corticosteroids. Four patients developed fewer vasculitic relapses, six felt less fatigued, two no longer experienced abdominal pain and diarrhoea and two improved their mood and ability to think clearly. The six patients with AAV experienced improvement in anarthria, reduced their prednisolone dose by a third, had fewer relapses and felt less tired. One patient developed asymptomatic QT prolongation and stopped the HCO, with no other adverse events reported.

Conclusion: All 26 patients reported symptomatic benefits associated with HCO treatment, especially improvement in joint pain, fatigue and rash. Vasculitic relapses were less frequent, with a reduction in corticosteroid doses. HCO was generally well tolerated.

Disclosure statement: The authors have declared no conflicts of interest.

273 Table 1. Additional immunosuppressive therapy

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<td>MTX + prednisolone</td>
<td>5</td>
<td>2 HSP, 1 AAV, 1 AOSD, 1 polychondritis</td>
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PAN: polyarteritis nodosa; HSP: Henoch–Schönlein purpura; AAV: AAV.

274 FEATURES OF ORBITAL INFLAMMATORY DISEASE AND RESPONSE TO IMMUNOSUPPRESSIVE THERAPY

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Background: Here we characterize a single-centre retrospective case series of patients with intra-orbital inflammatory masses with autoimmune disease, including granulomatosis with polyangiitis (GPA); formerly Wegener’s granulomatosis), eosinophilic granulomatosis with polyangiitis (EGPA) and IgG4-related disease (IgG4-RD).

Methods: We identified 30 patients with intra-orbital inflammation on MRI imaging. Clinical and laboratory data were collected from electronic clinical records. Comprehensive diagnostic criteria were used for IgG4-RD and Chapel Hill criteria for GPA and EGPA. Statistical analysis was performed using GraphPad software. Continuous variables were compared between IgG4-RD and GPA groups using non-parametric Mann–Whitney test and categorical variables were compared by Fisher’s exact test.

Results: The study included 21 Caucasians, 6 Asians and 3 patients of African descent (Table 1). There were 19 female and 11 male patients. The median age of the patients was 44 years (range 29–76). Thirteen patients were diagnosed with GPA, 1 with eGPA, 12 patients with HCO (median dose 200 mg once a day); 6 patients with Henoch–Schönlein purpura (HSP), 6 urticarial vasculitis, 6 with ANCA-positive vasculitides (AAV) (4 PPR-ANCA, 2 MPO-ANCA), 1 eosinophilic granulomatosis with polyangiitis (EGPA), 2 Takayasu arteritis, 2 Behçet’s disease, 1 adult Still’s disease (AOSD), 1 relapsing polychondritis, 1 polycystitis nodosa (PAN). The female:male ratio was 21:5 and the median age was 53 years. The median duration of HCO treatment was 3 years. Sixteen patients experienced a reduction in anarthria and skin rashes improved in 8 patients and completely resolved in a further 4. Eight patients could reduce corticosteroid doses (from 9 to 6 mg) and three discontinued corticosteroids. Four patients developed fewer vasculitic relapses, six felt less fatigued, two no longer experienced abdominal pain and diarrhoea and two improved their mood and ability to think clearly. The six patients with AAV experienced improvement in anarthria, reduced their prednisolone dose by a third, had fewer relapses and felt less tired. One patient developed asymptomatic QT prolongation and stopped the HCO, with no other adverse events reported.

Conclusion: All 26 patients reported symptomatic benefits associated with HCO treatment, especially improvement in joint pain, fatigue and rash. Vasculitic relapses were less frequent, with a reduction in corticosteroid doses. HCO was generally well tolerated.

Disclosure statement: The authors have declared no conflicts of interest.

274 Table 1. Patient characteristics

<table>
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<tr>
<td>Age, median, years</td>
<td>46</td>
<td>38</td>
</tr>
<tr>
<td>Gender distribution</td>
<td>8 female, 6 male</td>
<td>8 female, 4 male</td>
</tr>
<tr>
<td>Ethnic distribution</td>
<td>10 Caucasian, 3 Asian, 1 African</td>
<td>7 Caucasian, 3 Asian</td>
</tr>
<tr>
<td>ANCA status</td>
<td>11 ANCA+, 2 ANCA−</td>
<td>3 ANCA−, 10 ANCA−</td>
</tr>
<tr>
<td>Bilateral orbital inflammation</td>
<td>4/14</td>
<td>2/12</td>
</tr>
<tr>
<td>Extra-ocular manifestations</td>
<td>14/14</td>
<td>3/12</td>
</tr>
<tr>
<td>Number of DMARDs, median</td>
<td>3 (range 1–9)</td>
<td>1 (range 0–3)</td>
</tr>
<tr>
<td>Rituximab treatment</td>
<td>10/14</td>
<td>3/12</td>
</tr>
<tr>
<td>Surgical debulking</td>
<td>1/14</td>
<td>6/12</td>
</tr>
</tbody>
</table>

275 MISSED OPPORTUNITIES LEADING TO A DELAYED DIAGNOSIS OF VASCULITIS: A RETROSPECTIVE STUDY

Chris Record, Frances Edwards and Shahi Hamdulay

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Background: Vasculitis has a broad range of clinical presentations determined by the type of vasculitis and the organ system involved. Delayed diagnosis increases the risk of disease progression, and in the worst cases, organ failure and death. This retrospective study aims to review the number of presentations prior to diagnosis, their nature and the time intervals involved.

Methods: The hospital records of non-renal vasculitis patients attending a secondary care vasculitis clinic over 1 month were retrospectively analysed for demographics, type of vasculitis and number of presentations prior to diagnosis.

Results: A total of 41 vasculitis patients were identified with a mean age 58.8 years (range 21.8–85.6) and 56% (23/41) were female. The first presentation was most commonly as a medical admission [18/41 (44%)], then to a general practitioner (GP) [10/41 (24%)], accident and emergency [7/41 (17%)] and other medical specialty clinics [6/41 (15%)]. The diagnoses were 16 large vessels (GCA, 14, Takayasu arteritis, 2), 1 polycystitis nodosa, 14 ANCA (MPO positive, 4; granulomatosis with polyangiitis, 8; eosinophilic granulomatosis with polyangiitis, 2) and 10 IgA vasculitis. The median number of presentations prior to diagnosis was 2 (range 0–14) and the median number of days between first presentation and diagnosis was 14 (range 0–721). In patients diagnosed with IgA vasculitis, the median number of days from presentation to diagnosis and the median number of prior presentations were both zero. The first clinical presentation in all cases was abdominal pain and/or rash (10/10), and this presentation was an inpatient hospital stay in 70% (7/ 10). The ANCA vasculitides had a median of 3 (range 0–14) prior presentations with a median number of days from presentation to diagnosis of 200 (range 0–721). The initial presenting symptoms were most commonly respiratory in nature (29%), Patients with GPA had a median of 5 (range 2–14) presentations prior to diagnosis and a median of 359 days from presentation to diagnosis. The symptomatology and medical setting of the first presentation was highly variable in this patient group. The large vessel vasculitides were typically diagnosed with only 1 (range 0–6) presentation prior and only 17 days (range 0–324) elapsing between these attendances. For the GCA patients, the initial presenting
complaint was exclusively headache or constitutional symptoms (14/14) and the location of this first presentation was their GP in 64% (9/14).  

**Conclusion:** The number of presentations and time taken to make a diagnosis of vasculitis is highly variable. Patients with IgA vasculitis are diagnosed most rapidly, followed by GCA. There is significant delay in the diagnosis of ANCA-positive vasculitis, particularly GPA, with patients waiting months or years before diagnosis. This may reflect the diverse symptomatology and the multiple resulting specialty doctors they see prior to being diagnosed. An increased awareness of vasculitis is required among health care professionals to guide early rheumatology referral and improve outcomes.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**276 THE SHORT-TERM DAMAGE BURDEN IN VASCULITIS AND VASCULITIS MIMICS AS MEASURED BY THE VASCULITIS DAMAGE INDEX**

Alberto Fiori 1,2, Jan Szajno³ 1,2, Katarzyna Wawrzyczka-Adamczyk 1,2, Joanna Robson 2, Anthea Craven 2, Peter A. Merkell 2, Richard A. Watts 1 and Raashid A. Luqmani 2

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**Background:** Damage in vasculitis, due to both the vasculitic process itself and the complications of treatment, accumulates over time and accounts for significant morbidity across a variety of organs. It is not known whether conditions mimicking vasculitis are associated with a similar spectrum and extent of damage. We aimed to compare short-term damage accrual in vasculitis with vasculitis mimics using the Vasculitis Damage Index (VDI).

**Methods:** Using data from the ACR/EULAR Diagnostic and Classification Criteria in Vasculitis Study (DCVAS), we analysed VDI scores and individual items (recorded at 6 months from diagnosis) in granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA), polyarteritis nodosa (PAN), Takayasu arteritis (TAK), GCA and their comparators. We used the submitting physician’s diagnosis as the gold standard (recorded certainty >75%) and predetermined criteria to identify comparators.

**Results:** A total of 1243 patients with vasculitis and 506 comparators were analysed. The median (interquartile range) VDI score was significantly higher in each vasculitis vs comparators: GPA 1 (0–3) vs 0 (0–2); EGPA 2 (1–4) vs 0 (0–2); MPA 2 (0–3) vs 1 (0–2); PAN 1 (0–2) vs 0 (0–1); TAK 2 (0–2) vs 0 (0–1) (P < 0.001 for all); GCA 0 (0–1) vs 0 (0–1) (P = 0.006). On multivariate analysis, average VDI scores were significantly higher in vasculitis than comparators, except for GCA. The frequency of VDI score ≥ 1 was significantly higher in all vasculitides vs comparators: GPA 71 vs 48%; EGPA 85 vs 49%; MPA 73 vs 50%; PAN 69 vs 28%; TAK 77 vs 44% (P < 0.001 for all); GCA 49 vs 35% (P = 0.009). We identified several systems/organ involved significantly (P < 0.025) more frequently in vasculitis than comparators: ENT, renal and neuropsychiatric systems in GPA; ENT, pulmonary and neuropsychiatric in EGPA; renal, neuropsychiatric and cardiovascular in MPA; gastrointestinal in PAN; peripheral vascular in TAK; none in GCA. Individual damage items that differed significantly between vasculitides and comparators are presented in Table 1.

**Conclusion:** In the first 6 months after diagnosis, patients with all forms of vasculitis (apart from GCA) develop more damage than patients with comparator conditions. This study suggests that these damage patterns, involving several body systems, are relevant measures of outcome that are characteristic of patients with vasculitis.

**Disclosure statement:** R.A.L. has received research funding from Chemocentryx, GSK, Nordic and Medimmune and honoraria from Roche and UCB. All other authors have declared no conflicts of interest.

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**276 Table 1. VDI items significantly more frequent in vasculitides than comparators**

<table>
<thead>
<tr>
<th>GPA (n = 384, n (%))</th>
<th>GPA comparator (n = 364, n (%))</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal blockage/chronic discharge/crusting</td>
<td>111 (28)</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>88 (22)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Estimated/measured GFR :&lt;0.50%</td>
<td>60 (15)</td>
<td>13 (4)</td>
</tr>
<tr>
<td>Proteinuria :&lt;0.5 g/24 h</td>
<td>42 (11)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Chronic sinusitis/radiological damage</td>
<td>40 (10)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>38 (10)</td>
<td>14 (4)</td>
</tr>
<tr>
<td>Nasal bridge collapse/septal perforation</td>
<td>30 (8)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>Osteoporosis/vertebral collapse</td>
<td>15 (4)</td>
<td>5 (1)</td>
</tr>
<tr>
<td><strong>EGPA (n = 106, n (%))</strong></td>
<td><strong>EGPA comparator (n = 134, n (%))</strong></td>
<td><strong>P-value</strong></td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>59 (56)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Chronic asthma</td>
<td>47 (44)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Nasal blockage/chronic discharge/crusting</td>
<td>17 (16)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Chronic sinusitis/radiological damage</td>
<td>15 (14)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>8 (8)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5 (5)</td>
<td>0</td>
</tr>
<tr>
<td>Proteinuria :&lt;0.5 g/24 h</td>
<td>4 (4)</td>
<td>0</td>
</tr>
<tr>
<td><strong>MPA (n = 158, n (%))</strong></td>
<td><strong>MPA comparator (n = 185, n (%))</strong></td>
<td><strong>P-value</strong></td>
</tr>
<tr>
<td>Estimated/measured GFR :&lt;0.50%</td>
<td>60 (38)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>Proteinuria :&lt;0.5 g/24 h</td>
<td>45 (28)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>26 (16)</td>
<td>11 (6)</td>
</tr>
<tr>
<td>Diastolic blood pressure &gt;95 mmHg or requiring antihypertensive treatment</td>
<td>20 (13)</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Osteoporosis/vertebral collapse</td>
<td>17 (11)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>10 (8)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Nasal blockage/chronic discharge/crusting</td>
<td>8 (6)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Cataract</td>
<td>6 (4)</td>
<td>0</td>
</tr>
<tr>
<td><strong>PAN (n = 39, n (%))</strong></td>
<td><strong>PAN comparator (n = 54, n (%))</strong></td>
<td><strong>P-value</strong></td>
</tr>
<tr>
<td>Peripheral neuropathy</td>
<td>13 (33)</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Gut infarction/resection</td>
<td>6 (15)</td>
<td>0</td>
</tr>
<tr>
<td><strong>TAK (n = 93, n (%))</strong></td>
<td><strong>TAK comparator (n = 34, n (%))</strong></td>
<td><strong>P-value</strong></td>
</tr>
<tr>
<td>Claudication &gt;3 months</td>
<td>44 (47)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Major vessel stenosis</td>
<td>42 (45)</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Absent pulses in one limb</td>
<td>41 (44)</td>
<td>4 (12)</td>
</tr>
<tr>
<td><strong>GCA (n = 453, n (%))</strong></td>
<td><strong>GCA comparator (n = 127, n (%))</strong></td>
<td><strong>P-value</strong></td>
</tr>
<tr>
<td>Diabetes</td>
<td>30 (7)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Osteoporosis/vertebral collapse</td>
<td>26 (56)</td>
<td>0</td>
</tr>
</tbody>
</table>

Some of the comparators were used for analyses with more than one type of vasculitis. *P*-value was calculated using chi-squared test or Fisher’s exact test. *Non-significant after Benjamini-Hochberg correction for multiple comparisons with false discovery rate of 0.25 and total number of variables 64.
277 USING THE BIRMINGHAM VASCULITIS ACTIVITY SCORE AS A SCREENING TOOL IN PATIENTS WITH SUSPECTED VASCULITIS

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1Rheumatology, University of Cagliari, Messina, Italy, 2Nuﬃeld Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford University, Oxford, UK, 3Internal Medicine, Jagiellonian University, Krakow, Poland, 4School of Medicine and Dentistry, James Cook University, Cairns, QLD, Australia, 5Rheumatology, University of Pennsylvania, Philadelphia, PA, USA and 9Rheumatology, Ipswich Hospital, University of East Anglia, Ipswich, UK

Background: The BVAS is validated to assess disease activity in systemic vasculitis, but has not been widely tested in conditions mimicking vasculitis. We aimed to explore its potential utility in screening patients with suspected vasculitis.

Methods: We analysed data from the ACR/EULAR Diagnostic and Classification Criteria in Vasculitis Study (DCVAS), using the submitting physician’s diagnosis (recorded certainty ≤75%) as the gold standard, with predetermined criteria to identify appropriate comparators for each vasculitis. Overall BVAS score and frequency of individual items were evaluated in the ANCA-associated vasculitides (AAVs), comprising granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA); polyclonal gammapathy (PNG); polyclonal gammapathy nodosa (PNG); GCA; Takayasu arteritis (TAK) and their comparator conditions.

Results: A total of 1122 patients with vasculitis and 487 comparators were analysed. The BVAS score (median [interquartile range]) was signiﬁcantly higher (P < 0.0001) in patients with each type of AAV vs comparators: GPA 19 (12–25) vs 11 (8–17); EGPA 18 (12–26) vs 11 (8–17); MPA 19 (15–24) vs 11 (5–17). Between 5 and 12 individual BVAS items were found signiﬁcantly more frequently in each of these vasculitides than their comparators, including bloody nasal discharge/nasal crusts, pulmonary infiltrate, proteinuria or haematuria for GPA; pulmonary inﬁltrate, wheeze, sensory peripheral neuropathy, mononeuritis multiplex, heart involvement with pericarditis, ischaemic pain and cardiomyopathy or congestive failure for EGPA; fever, bloody nasal discharge/nasal crusts, pulmonary inﬁltrate, proteinuria, haematuria and renal function abnormalities for MPA. These items were used to develop classiﬁcation trees (Table 1) with the following overall performance in terms of sensitivity/specificity: GPA 82%/81%, EGPA 83%/94%, MPA 71%/83%. We further analysed the performance of the trees for the subgroup of patients in whom ANCA was tested and found no additional advantage of ANCA testing. For PAN, GCA and TAK there was no signiﬁcant difference in BVAS score compared with comparators, and few or no BVAS items were discriminative.

Conclusion: BVAS consists of several items highly speciﬁc for GPA, EGPA and MPA, from which we have developed classiﬁcation trees that can facilitate accurate and systematic clinical screening of patients with suspected AAV. However, BVAS is not effective in distinguishing PAN, GCA or TAK from comparator conditions.

Disclosure statement: R.A.L. has received research funding from ChemoCentryx, GSK, Nordic and Medimmune and honoraria from Roche and UCB. All other authors have declared no conﬂicts of interest.

278 ANALYSIS OF A TERTIARY CENTRE LARGE VESSEL VASCULITIS COHORT IDENTIFIES MYOCARDITIS AS A RARE LIFE-THREATENING PRESENTATION

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1Rheumatology and 2Radiology, Imperial College Healthcare NHS Trust, London, UK

Background: Cardiac involvement in large vessel vasculitis (LVV) is an important cause of morbidity and mortality, particularly in Takayasu arteritis (TA). Cardiac failure is typically secondary to uncontrolled arterial hypertension or ischaemic heart disease, which occurs as a consequence of coronary arteritis or premature atherosclerosis. Pulmonary hypertension and ascending aortic dilatation with valve failure represent additional serious cardiovascular complications. However, cardiac failure secondary to myocarditis is rarely reported.

Methods: The Imperial College Healthcare NHS Trust LVV database was retrospectively reviewed to identify those patients with cardiac involvement in large vessel vasculitis (LVV) is an important cause of morbidity and mortality, particularly in Takayasu arteritis (TA). Cardiac failure is typically secondary to uncontrolled arterial hypertension or ischaemic heart disease, which occurs as a consequence of coronary arteritis or premature atherosclerosis. Pulmonary hypertension and ascending aortic dilatation with valve failure represent additional serious cardiovascular complications. However, cardiac failure secondary to myocarditis is rarely reported.

Methods: The Imperial College Healthcare NHS Trust LVV database was retrospectively reviewed to identify those patients with cardiac involvement in large vessel vasculitis (LVV) is an important cause of morbidity and mortality, particularly in Takayasu arteritis (TA). Cardiac failure is typically secondary to uncontrolled arterial hypertension or ischaemic heart disease, which occurs as a consequence of coronary arteritis or premature atherosclerosis. Pulmonary hypertension and ascending aortic dilatation with valve failure represent additional serious cardiovascular complications. However, cardiac failure secondary to myocarditis is rarely reported.

Disclosure statement: R.A.L. has received research funding from ChemoCentryx, GSK, Nordic and Medimmune and honoraria from Roche and UCB. All other authors have declared no conﬂicts of interest.

Table 1. Performance of classification trees for GPA, EGPA and MPA

Classification tree for GPA

<table>
<thead>
<tr>
<th>Clinical pattern</th>
<th>GPA correctly classified as GPA, %</th>
<th>GPA comparator incorrectly classified as GPA, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A, +, B, +</td>
<td>39</td>
<td>2</td>
</tr>
<tr>
<td>A, +, B, C</td>
<td>17</td>
<td>5</td>
</tr>
<tr>
<td>A, +, B, D, +</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>A, +, B, D, E, +</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>A, +, B, G, E</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Classification tree for EGPA

<table>
<thead>
<tr>
<th>Clinical pattern</th>
<th>EGPA correctly classified as EGPA, %</th>
<th>EGPA comparator incorrectly classified as EGPA, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>H, +, I, +</td>
<td>46</td>
<td>2</td>
</tr>
<tr>
<td>H, +, I, J</td>
<td>27</td>
<td>2</td>
</tr>
<tr>
<td>H, +, I, K</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>H, +, I, K</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Classification tree for MPA

<table>
<thead>
<tr>
<th>Clinical pattern</th>
<th>MPA correctly classified as MPA, %</th>
<th>MPA comparator incorrectly classified as MPA, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>L, +, M</td>
<td>34</td>
<td>7</td>
</tr>
<tr>
<td>L, +, M, N, O</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>L, +, N, O</td>
<td>19</td>
<td>7</td>
</tr>
</tbody>
</table>

BVAS items used in classification trees: (A) bloody nasal discharge/nasal crusts; (B) proteinuria or haematuria; (C) other skin vasculitis (livedo racemose/reticularis, skin nodules); (D) conductive or sensori neural hearing loss; (E) paranasal sinus involvement; (F) arthropathic arthritis; (G) pulmonary nodules or cavities; (H) peripheral eosinophilia (included as an extra item); (I) mononeuritis multiplex; (J) wheeze; (K) pericarditis, ischaemic cardiac pain, cardiomyopathy or congestive cardiac failure; (L) proteinuria or haematuria or creatinine >125 µmol/l or an increase in serum creatinine >30% or decrease in clearance >25%; (M) pulmonary infiltrate; (N) mononeuritis multiplex or sensory peripheral neuropathy; (O) fever >38°C. Present (+); absent (−).
involvement at presentation. Cases presenting with cardiac failure were enumerated and the diagnosis, cardiac presentation, imaging studies and subsequent medical and surgical management of patients suspected of having myocarditis at presentation were reviewed in detail.

Results: The LVV cohort included 139 patients with TA and 24 patients with GCA. In total, 16 patients presented with cardiac failure without a history of ischaemic coronary heart disease: 14 (87.5%) had TA and 2 (12.5%) GCA. The four patients (25%) with myocarditis at presentation (three females with TA and one male with GCA) represented 2.5% of the total LVV cohort. A diagnosis of myocarditis was established by transthoracic echocardiography (TTE), cardiac MRI (CMRI) and troponin analysis. CMRI assessment was reproducible, allowing identification, quantification and surveillance of functional abnormalities. Myocardial oedema, a marker of inflammation in active disease, was assessed using T2 sequences. A late gadolinium sequence was used as a marker of inflammatory tissue damage, as evidenced by a patchy, non-ischaemic pattern of enhancement. In three patients, prednisolone (1 mg/kg) and monthly pulsed CYC (15 mg/kg) were prescribed. In one young woman, CYC treatment with GCA) represented 2.5% of the total LVV cohort. A diagnosis of myocarditis at presentation (three females with TA and one male (87.5%) had TA and 2 (12.5%) GCA. The four patients (25%) with myocarditis at presentation were reviewed in detail.

Conclusion: Clinically significant myocarditis in LVV remains a rare presentation. High-resolution non-invasive imaging offers early detection and a diagnostic alternative when the current gold standard myocardial biopsy is considered high risk. Treatment with CYC and prednisolone is associated with resolution in myocardial enhancement and clinically important improvements in cardiac symptoms and LVEF.

Disclosure statement: The authors have declared no conflicts of interest.

280 A POPULATION-BASED DESCRIPTIVE ANALYSIS OF SHORT-TERM CO-MORBIDITIES IN GRANULOMATOSIS WITH POLYANGIITIS

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1Epidemiology Group, 2Chronic Diseases Research Group and 3Medical Sciences, University of Aberdeen, Aberdeen, UK

Background: Existing research suggests that granulomatosis with polyangiitis (GPA) patients face an increased burden of co-morbidities in the short term. However, much of the supporting evidence comes from unrepresentative study settings (e.g. secondary care) mostly focusing on a single group of co-morbid conditions. This study is the first to use a population-based primary care dataset to compare the burden of short-term co-morbidities in GPA patients and the general population.

Methods: Data were extracted from the Primary Care Clinical Informatics Unit Research (PCCIUR) database, a general practice (GP) database covering approximately one-third of Scottish GPs. Read codes (clinical information coding system used by UK GPs) identified GPA patients. Five general population patients (i.e. non-GPA patients) were matched to each GPA patient by age, sex and GP. Information on demographics and diagnosis of commonly recognized co-morbidities was extracted for both cohorts. A co-morbidity was defined as an event that is not directly related to the clinical course of GPA. Co-morbid events diagnosed prior to the date of diagnosis of GPA (same date was used for non-GPA patients) were excluded from the analysis. Conditional logistic regression was used to compare the occurrence of selected co-morbid conditions in both cohorts. Odds ratios (ORs) and 95% CIs for the associations are reported.

Results: A total of 265 GPA patients (52.6% female) were identified in the PCCIUR database. The median age at diagnosis was 59 years (interquartile range (IQR) 48–68). GPA and non-GPA cohorts were followed up for a median of 7.88 years (IQR 4.29–12.61). ORs and 95% CIs for the occurrence of co-morbidities are summarized in Table 1.

Conclusion: Patients after a GPA diagnosis are more likely than the general population to have cataracts, hypertension, osteoporosis, thromboembolic disorder and type II diabetes. Interestingly, the occurrence of cancer and cardiovascular disease in GPA patients was not elevated, possibly indicating that these co-morbidities do not contribute to the short-term co-morbidity burden. The awareness and prompt management of short-term co-morbidities is crucial for improving the overall prognosis of GPA patients.

Disclosure statement: The authors have declared no conflicts of interest.

280 Table 1. Occurrence of co-morbidities in GPA patients compared with the general population

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>1.42 (0.80, 2.53)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>1.32 (0.85, 2.07)</td>
</tr>
<tr>
<td>Cataracts</td>
<td>2.14 (1.16, 3.96)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3.10 (2.15, 4.47)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>3.51 (1.99, 6.19)</td>
</tr>
<tr>
<td>Thromboembolic disorder</td>
<td>3.94 (1.95, 7.86)</td>
</tr>
<tr>
<td>Type II diabetes</td>
<td>2.18 (1.28, 3.76)</td>
</tr>
</tbody>
</table>

The non-GPA cohort was used as the reference group.

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279 HONEY ARE YOU DRUNK?

Philip P. Stapleton, Sanyanti Pattapola and Bhaskar Dasgupta

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Background: A 48-year old woman with a history of left retinal artery occlusion 15 years prior and brain injury 25 years prior with right frontal brain lesion/infarct attributed to a traffic accident met her husband in Egypt for a holiday. On arrival she appeared a little sleepy, confused and atatic and he assumed that she had taken a sleeping tablet with or without alcohol, as she was nervous about flying. With persistence of her symptoms for 5 days they discontinued their holiday and returned to the UK, where she was taken to hospital and referred to the stroke team. Following evaluation, she initially improved and was commenced on simvastatin and clopidogrel, but returned after 4 weeks with worsening symptoms.

Methods: Examination revealed ataxic gait, vertigo and mild slurred speech without focal limb weakness. Blood and urine tests with ECG, carotid Dopplers and brain MRI/magnetic resonance angiography (MRA) studies were requested with repeat MRI and cerebral angiogram at 4 weeks when she developed worsening symptoms.

Results: Cardiac studies and CT of chest, abdomen and pelvis were unremarkable. All blood and immunologic tests were reassuring. Injection screen was negative for tuberculosis, HIV, syphilis, CMV, EBV, HSV, hepatitis B and C and Borrelia. Lumber puncture showed normal cerebrospinal fluid opening pressure, clear colourless fluid without malignant cells on cytology and negative HSV screen. MRA indicated patent common, internal carotid and vertebral arteries of good calibre. Brain MRI highlighted corpus callosum lesions.

Conclusion: The differential diagnosis included embolic phenomena, encephalitis, vasculitis, hereditary stroke and neoplastic lesions. A multidisciplinary team review of case history, laboratory and imaging studies concluded with a diagnosis of Susac’s syndrome from the history of encephalopathy, sensorineural deafness and branch retinal artery occlusion with characteristic MRI supratentorial lesions with predilection for the corpus callousum. Treatment was i.v. methylprednisolone with conversion to tapering oral prednisolone and 66% CRI of CYC. With treatment, the patient’s Montreal Cognitive Assessment (MoCA) improved from 12/30 to 16/30 on prednisolone and then to 25/30 after three cycles of CYC. Audiology indicated 80% recovery. Susac’s syndrome is a rare disorder characterized by a triad of acute or subacute encephalopathy, partial or complete occlusion of the branch retinal artery and inner ear disease with hearing loss, most notably. With a presentation such as with our patient, differential diagnosis is broad. On exclusion of common causes, rare syndromes such as Susac’s should be considered, with prompt treatment to offset further complications. Our patient’s history and presentation with characteristic MRI brain findings confirmed our diagnosis. This case highlights the value of a multidisciplinary review for complex presentations, particularly in patients with a medical history that suggests a more commonly encountered condition.

Disclosure statement: The authors have declared no conflicts of interest.
281 RESEARCH PRIORITY SETTING IN VASCULITIS
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1Health Sciences School, 2Norwich Medical School, University of East Anglia, Norwich and 3Research Office, Vasculitis UK, Matlock, UK

Background: Vasculitis UK (VUK; a national patient support group for vasculitis) wanted to develop a research strategy and wished to find out from their membership the members’ research priorities for funding.

Methods: A postal questionnaire survey and an e-mail survey of the members of VUK was undertaken. A survey questionnaire was developed and participants were asked to rank 18 areas of possible research from most important to least important. Details of diagnosis, gender, age and role (i.e. patient, care, health professional or researcher) were collected. The survey was distributed electronically to members of VUK via email with a link to the survey (using SurveyMonkey software). Members were also sent a copy of the questionnaire with the regular quarterly newsletter. Members were requested not to complete both the electronic and paper versions of the questionnaire. The link to the survey was also made available via social media networks. The survey was also sent to health professionals known to have an interest in vasculitis via the UKIVAS and Lockwood club databases. The preliminary results were also presented to a patients’ symposium.

Results: There were 354 respondents; 72% were female, the median age was 67 years (range 13–89); 78% were patients, ~80% of respondents were members of VUK and ~10% were members of other groups including the Lauren Currie Twilight Trust and a local support group. Granulomatosis with polyangiitis (GPA) was the most frequent diagnosis, affecting nearly 50% of respondents, followed by eosinophilic granulomatosis with polyangiitis (Churg–Strauss) at 12% and microscopic polyangiitis (MPA) at 6%. The top four priorities were disease diagnosis, new treatments, causes of vasculitis and education of health professionals. The role of exercise, financial impact on patients, epidemiology and health economics were ranked lowest. Comparing the ranking of the patients with the health professionals and researchers showed very little difference in their priorities. The attendees at the patient symposium overwhelmingly concurred with the results of the ranking exercise.

Conclusion: There is agreement between patients, caregivers, health professionals and researchers in setting research priorities in vasculitis. The majority of responses came from patients with GPA, which reflects the background of VUK. This information will be used to inform a research strategy for VUK.

Disclosure statement: J.M. has received honoraria from AbbVie and Bristol-Myers Squibb. All other authors have declared no conflicts of interest.

282 A SINGLE-CENTRE EXPERIENCE OF 52 CASES OF LARGE VESSEL VASCULITIS: PRESENTATION, DIAGNOSIS, IMAGING, HISTOLOGY, TREATMENT AND OUTCOME TIMES
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Background: Large vessel vasculitis (LVV) is an uncommon yet important diagnosis because of the significant morbidity and mortality of untreated disease.

Methods: We performed a retrospective analysis from case records of 52 patients with LVV seen atSoutheastern University Hospital since 2010 that looked at presentation, diagnosis, imaging, histology, treatment and outcomes.

Results: Nineteen patients had GCA (36.5%), 8 had PMR (15%), 3 had GCA and PMR (6%), 15 had LUV only (29%), 5 had retinopathic fibrosis (RF5%) (9%), 1 had RA and 1 had sarcoidosis. Thirty-two presented with constitutional (61.5%), 17 with cranial (32.6%), 11 with polymyalgia (21%) and 4 with abdominal symptoms (7.5%); 6 had limb claudication (11.5%), while 13 had other symptoms (25%) such as back pain or arthritis. Vascular US findings were analysed in 30 cases diagnosed with GCA and/or PMR. Seven had a positive US (23.3%), 7 had a negative US (23.3%) and the procedure was not done in 16 (53.3%) (US was not routine in 2010). In the same subgroup, six (53.3%) had positive temporal artery biopsy (TAB), five (18.6%) had a negative TAB and TAB was not performed in one. FDG-PET scan was done in all cases. The aorta was the most common vessel (48%) in which PET showed increased FDG uptake, followed by the axillary (12.6%), subclavian (10.1%), brachial (5.3%), vertebral (1.2%), carotid (1.2%) and iliac (1.2%) arteries. Twelve patients were treated with prednisolone only (22.6%), 5 with one DMARD only (9.4%), 18 with prednisolone and one DMARD (33.9%) (MTX or LEF), 2 with prednisolone and two DMARDs (3.7%), 1 with two DMARDs (1.8%), 5 with prednisolone and one or two biologics (9.4%), 6 with prednisolone and DMARDs (one and biologic (11.5%) and 3 were on no medications (6.6%). Nineteen showed complete response to treatment (absence of symptoms and normal inflammatory markers). Eleven (21.5%) had active disease (symptomatic with raised inflammatory markers) and 21 (41.1%) showed partial response (symptomatic or with raised inflammatory markers).

Conclusion: Our experience shows that LVV is common in the context of GCA, PMR (suggesting a common link between the two) and RF, but can present on its own with constitutional symptoms. The diagnosis of LVV has increased with increased use of FDG-PET imaging, which shows that the aorta and upper limb vessels are most commonly involved. TAB was positive in 72.7% of patients with GCA with LVV. The most common presentations were with constitutional symptoms followed by cranial and polyarthralgia (polymyalgia). The majority were treated with prednisolone/prednisolone plus DMARDs (LEF or MTX) and showed complete or partial response to treatment. Biologics (tacrolimus/rituximab) plus prednisolone (with or without LEF) were required in the most severe cases.

Disclosure statement: B.D. has received consulting fees from Roche, GSK, Servier and Mundipharma and research funding from NAPP. All other authors have declared no conflicts of interest.

283 VASCULAR ENDOTHELIAL GROWTH FACTOR AS AN AID TO DIAGNOSIS OF GIANT CELL ARTERITIS
Nicola Goodfellow1, Julien Mortel1, Alberto Floris1, Surjeet Singh2, Andrew Hutchings3, Shauna Masters1, Yashika Sharma1, Vanshika Sharma1, Shaifali Jain1, Afse Sabokbar1, Raashid A. Lugman1 and the TABUL Investigators
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Background: GCA is a common vasculitis with significant risk of blindness. Although temporal artery biopsy (TAB) is currently performed for diagnosis, the sensitivity can be as low as 39%; US is emerging as a more effective and cost-effective test. Vascular endothelial growth factor (VEGF) is present in inflamed arterial wall in GCA and elevated circulating levels have been reported in GCA compared with controls. We sought to evaluate the performance of VEGF as a diagnostic tool for GCA, which is less invasive than TAB and cheaper than TAB or US.

Methods: We used samples from patients recruited to a large multicentre study comparing TAB with US for diagnosis of suspected GCA. We randomly selected 26 patients with TAB-positive GCA and 26 controls (negative TAB and final diagnosis not GCA). Most patients were receiving high doses of glucocorticoid therapy at recruitment. The serum VEGF concentration was measured at weeks 0, 2 and 26 by ELISA (Quantikine, R&D Systems, Minneapolis, MN, USA). Week 0 values were plotted on a receiver operating characteristic (ROC) curve to identify the most effective cut-off for an abnormal result. Sections of TAB were stained by immunohistochemistry for VEGF expression (polyclonal rabbit anti-human VEGF, AbCam).

Results: Patients were significantly older than controls [mean age 76 years (∼4.73) vs 66 (±4.73); P = 0.003] but had similar gender (62% females each). The mean baseline VEGF concentration was 873 pg/ml (95% CI 631, 1110) in GCA vs 470 pg/ml (95% CI 328, 625) in controls (P = 0.017). This difference between groups was not observed at any other time point. The area under the ROC curve for VEGF concentration at week 0 was 0.73. The optimal cut-off was 713 pg/ml, providing a sensitivity of 65% and a specificity of 88%. These values compare favourably with reported performance of other available tests such as ESR and CRP (sensitivity 86% and 84%; specificity 30% and 29%, respectively), TAB (sensitivity 40%, specificity 100%) and US (sensitivity 54%, specificity 81%). VEGF expression by immunohis-tochemistry in TAB sections from three patients with GCA was higher than in two controls, implying that VEGF is upregulated in GCA and may signal locally to drive the vasculitic process. Furthermore, serum VEGF concentration appears to reflect the severity of the temporal artery, therefore measuring serum VEGF concentration is a valid surrogate for local inflammation.

Conclusion: In this study, serum VEGF was a useful test to support a diagnosis of GCA. Further studies will evaluate this in a larger cohort of suspected cases of GCA. We can explore the effectiveness and cost-effectiveness of measuring VEGF alone or in combination with clinical assessment and other diagnostic tests for GCA. VEGF could potentially be effective as a prognostic marker or as a therapeutic target.
Disclosure statement: N.G. is an employee of the National Institute for Health Research. R.L. has received research funding from Chemocentryx, GSK, Nordic and Medimmune and honoraria from Roche and UCB. All other authors have declared no conflicts of interest.

284 DIFFERENCES IN EARLY DAMAGE PATTERNS IN VARIOUS FORMS OF PRIMARY SYSTEMIC VASCULITIS

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Background: Immunosuppressive therapy has substantially reduced the mortality of systemic vasculitides, which are chronic conditions associated with long-term damage. We aimed to compare and contrast early damage patterns in patients with different forms of vasculitis using the Vasculitis Damage Index (VDI).

Methods: We compared patterns of damage among patients with eight forms of primary vasculitis using data from the ACR/EULAR Diagnosis and Classification Criteria in Vasculitis Study (DCVAS), which recruits patients within 2 years of onset of disease. The VDI was evaluated at least 6 months after diagnosis.

Results: We examined the pattern of damage in 453 patients with GCA (median age 74 years [interquartile range (IQR) 12], male:female ratio 153:150), 395 with granulomatosis with polyangiitis (GPA; age 56 years [IQR 27], male:female ratio 199:196), 158 with microscopic polyangiitis (MPA; age 65 years [IQR 17], male:female ratio 70:88), 106 with eosinophilic granulomatosis with polyangiitis (EGPA; age 58 years [IQR 21], male:female ratio 58:48), 93 with Takayasu arteritis (TAK; age 46 years [IQR 30], male:female ratio 49:30), 42 with Behcet's disease (BD; age 33 years [IQR 11], male:female ratio 22:30) and 39 with polyarteritis nodosa (PAN; age 52 years [IQR 27], male:female ratio 22:17). The VDI [at a mean of 241 days (s.o. 143) after diagnosis] was categorized as low in IgAV and GCA [median VDI 0 (range 0–7)]; intermediate in PAN, GPA and BD [median VDI 1 (range 0–8)] and high in MPA, TAK and EGPA [median VDI 2 (range 0–11)]. The most frequent VDI systems involved per disease group compared with the correlated data set alpha to P < 0.001; MPA: kidneys (53%, P < 0.001); TAK: peripheral vessels (73%, P < 0.001); GPA: auditory (23%, P < 0.001); EGPA: lungs (58%, P < 0.001); TAK: peripheral vessels (73%, P < 0.001); IgAV: kidneys (17%, P < 0.001); BD: skin/mucosa (56%, P < 0.001); PAN: neurological (36%, P < 0.001). The most frequent individual VDI items recorded are shown in Table 1.

Conclusion: Damage occurred early in all systemic vasculitides studied. EGPA and TAK were associated with the highest levels of damage; IgAV and GCA had the lowest levels. These patterns could serve as a basis for evaluating the impact of new or existing therapies on outcomes in vasculitis.

Disclosure statement: R.A.L. has received research funding from Chemocentryx, GSK, Nordic and Medimmune and honoraria from Roche and UCB. All other authors have declared no conflicts of interest.

285 RELATIONS BETWEEN JOINT PROPRIOCEPTION AND MOVEMENT IN PATIENTS WITH AND WITHOUT JOINT HYPERMOBILITY SYNDROME

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Background: Joint hypermobility syndrome (JHS) is associated with poor proprioception, but studies have been limited to the shoulder, finger and knee, without consideration of associations between joints in the body. Therefore the aim was to evaluate associations of proprioception in four joints: shoulder, elbow, knee and ankle, to understand if their relationships differed between those without JHS.

Methods: A convenience sample of 20 women with and without clinically diagnosed JHS was recruited. Participants self-reported their dominant limb (writing hand, kicking foot), joint hypermobility (Beighton score) and physical activity level (International Physical Activity Questionnaire).

Proprioception was assessed using a passive joint angle reproduction (JAR) protocol. JAR measures the ability of participants to replicate a target angle, with the error between the final observed angle and target angle recorded (positive represents overshooting; negative represents undershooting). There were eight dominant limb JAR measures—four joints (shoulder, elbow, knee and ankle), with movements to flexion and extension; the order of testing was randomized. Each JAR measure included three trials. Independent t-tests evaluated demographics and JAR errors between groups. Pearson’s correlations evaluated associations of JAR errors and were tested for between-group differences. A Bonferroni adjustment for the correlated data set alpha to P ≤ 0.027.

Disclosure statement: All authors have declared no conflicts of interest.

284 Table 1. The three most frequent items of damage recorded for each vasculitis 6 months after diagnosis

<table>
<thead>
<tr>
<th>Item</th>
<th>Frequency, %</th>
<th>P-value compared with all other forms of vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCA (n = 453)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Visual impairment</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Blindness, one eye</td>
<td>8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. Diabetes</td>
<td>7</td>
<td>0.028</td>
</tr>
<tr>
<td>Granulomatosis with polyangiitis (n = 395)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Nasal discharge/crusts</td>
<td>29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Hearing loss</td>
<td>22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. eGFR &lt;50%</td>
<td>15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Microscopic polyangiitis (n = 158)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. eGFR &lt;50%</td>
<td>38</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Proteinuria &gt;0.5 g/24 h</td>
<td>28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. Peripheral neuropathy</td>
<td>16</td>
<td>0.007</td>
</tr>
<tr>
<td>1. Peripheral neuropathy</td>
<td>56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Chronic asthma</td>
<td>44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. Chronic breathlessness</td>
<td>20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Takayasu arteritis (n = 93)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Claudication</td>
<td>47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Major vessel stenosis</td>
<td>45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. Absent pulses, one limb</td>
<td>44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IgA vasculitis (n = 86)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Proteinuria &gt;0.5 g/24 h</td>
<td>16</td>
<td>0.004</td>
</tr>
<tr>
<td>2. Cutaneous ulcers</td>
<td>5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. Osteoporosis</td>
<td>9</td>
<td>0.460</td>
</tr>
<tr>
<td>Behcet’s disease (n = 42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Mouth ulcers</td>
<td>52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Visual impairment</td>
<td>17</td>
<td>0.002</td>
</tr>
<tr>
<td>3. Cataract</td>
<td>9</td>
<td>0.048</td>
</tr>
<tr>
<td>Polyarteritis nodosa (n = 39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Peripheral neuropathy</td>
<td>33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2. Ulcer</td>
<td>15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3. Cutaneous ulcers</td>
<td>8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

eGFR: estimated glomerular filtration rate.
Background: Joint hypermobility syndrome (JHS) is associated with poor prognosis and are associated with interstitial lung disease (ILD) in suspected connective tissue disease, especially myositis. Jo-1 is the most common of a group of autoantibodies called antisynthetase antibodies. We describe the clinical relationship between Jo-1 in a retrospective cohort study of patients tested for extractable nuclear antigens (ENA).

Methods: All ENA tests done between January 2013 and December 2014 in our hospital were identified. Testing is sequential: samples are first screened and testing of ENA subtypes only performed on screen-positive samples using a commercial assay (Inova Diagnostics; positive if >20 AU/ml). Clinical data from positive patients was extracted from electronic records in 2015, allowing a minimum of 6 months follow-up. ENA-negative patients, selected randomly, served as controls.

Results: A total of 4014 samples from 3584 patients were tested for ENA. The first sample tested, chronologically, was designated the test extension, elbow flexion and ankle dorsiflexion (Table 1). Flexion-extension correlations were high and statistically significant in those with JHS. Correlations between joints (e.g. shoulder-extension to knee extension) were also significant and high in participants with JPS (not shown; r = 0.49–0.79), while those without tended to have weaker non-significant correlations (r = 0.09–0.53).

Conclusion: Jo-1 seropositivity is rare in a teaching hospital population checked for ENA autoantibodies. Relatively few patients designated positive by a commercial assay had myositis and the frequency of ILD was similar in controls and positive patients. Our findings challenge the notion that there is a strong relationship between Jo-1, ILD and myositis when applied to a broad range of hospital patients.

Disclosure statement: The authors have declared no conflicts of interest.

286 JO-1: INTERSTITIAL LUNG DISEASE, MYOSITIS AND ME—DIAGNOSTIC RELATIONS

Ferial Mall1, Emma Derrett-Smith1, Tim Plant2 and Paresh Jobanputra1
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Background: Jo-1 autoantibodies are widely believed to indicate a poor prognosis and are associated with interstitial lung disease (ILD) in suspected connective tissue disease, especially myositis. Jo-1 is the most common of a group of autoantibodies called antisynthetase antibodies. We describe the clinical relationship between Jo-1 in a retrospective cohort study of patients tested for extractable nuclear antigens (ENA).

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Disclosure statement: The authors have declared no conflicts of interest.

286 Table 1. Demographics and JAR mean error

<table>
<thead>
<tr>
<th>Demographics</th>
<th>JHS (n = 20)</th>
<th>Control (n = 20)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (s.d.), years</td>
<td>32.5 (2.8)</td>
<td>26.4 (2.0)</td>
<td>0.043</td>
</tr>
<tr>
<td>BMI, mean (s.d.), kg/m²</td>
<td>26.6 (4.9)</td>
<td>25.3 (2.9)</td>
<td>0.239</td>
</tr>
<tr>
<td>Physical activity (MET), mean (s.d.), min/week</td>
<td>7040 (6485)</td>
<td>4812 (1033)</td>
<td>0.257</td>
</tr>
<tr>
<td>Beighton score, mean (s.d.)</td>
<td>6.2 (1.0)</td>
<td>1.2 (1.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

MET: Metabolic Equivalent of Task.

Conclusion: Jo-1 seropositivity is rare in a teaching hospital population checked for ENA autoantibodies. Relatively few patients designated positive by a commercial assay had myositis and the frequency of ILD was similar in controls and positive patients. Our findings challenge the notion that there is a strong relationship between Jo-1, ILD and myositis when applied to a broad range of hospital patients.

Disclosure statement: The authors have declared no conflicts of interest.

286 Table 1. Demographics and clinical characteristics of Jo-1-positive patients vs controls

<table>
<thead>
<tr>
<th>Jo-1 positive (n = 40)</th>
<th>Controls (n = 80)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), years</td>
<td>53 (19–88)</td>
<td>52 (17–87)</td>
</tr>
<tr>
<td>Sex (female), %</td>
<td>70</td>
<td>79</td>
</tr>
<tr>
<td>Dead, %</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>Current or previous malignancy, %</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>RF, %</td>
<td>17.5</td>
<td>6.3</td>
</tr>
<tr>
<td>Inflammatory arthritis, %</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Clinical myositis diagnosis, %</td>
<td>5</td>
<td>1.3</td>
</tr>
<tr>
<td>CKP &gt;1000, %</td>
<td>5</td>
<td>1.3</td>
</tr>
<tr>
<td>Intestinal lung disease, %</td>
<td>13</td>
<td>6</td>
</tr>
</tbody>
</table>

Other serology:

| ANA (1:100), n/ν (%) | 18/38 (47.4) | 22/79 (27.8) | 0.06 |
| RF, n/ν (%) | 8/25 (32) | 12/4 (27.3) | 0.78 |
| CCP, n/ν (%) | 0/16 (5) | 3/33 (9.1) | 0.54 |
| Anti-dsDNA (Crithidia positive), % | 7.5 | 1.3 | 0.11 |
| Scl70, % | 7.5 | 0 | — |
| SSA/Ro, % | 10 | 0 | — |
| SSB/La, % | 10 | 0 | — |
| RNP, % | 10 | 0 | — |

1Fisher’s exact test, two-tailed. 2Statistical analyses were not done on these comparisons since, by definition, controls were negative for ENA antibodies.

287 PROPRIOCEPTION AND LAXITY IN PATIENTS WITH JOINT HYPERMOBILITY SYNDROME WITH AND WITHOUT KNEE INSTABILITY

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Applied Health Research, Glasgow Caledonian University, Glasgow, UK

Background: Joint hypermobility syndrome (JHS) is associated with poor proprioception, is commonly known to affect joint laxity and is linked to reports of joint instability. However, the associations of joint proprioception to proprioception and instability in JHS are unclear. Therefore the aim of this study was to investigate the relationship of knee joint instability to knee proprioception and to frontal plane knee laxity in patients with JHS.

Methods: Data from 44 female participants with JHS [mean age 32.5 years (s.d. 7.6) and 20 age- and gender-matched healthy controls [mean age 33.1 years (s.d. 7.6)] were collected. JHS participants were divided into two subgroups: no knee instability (JHS-NI, no self-reported knee instability, n = 22) and knee instability (JHS-I, self-reported knee instability, n = 22). The knee test was the most symptomatic for participants with JHS and the dominant limb for control participants. There were three knee proprioception tests: passive motion sense (PMS), passive position sense (PPS) and active position sense (APS). PMS evaluates the ability to detect joint movement at 0.3/°sec, while the position sense measures the ability to replicate a joint angle. Knee laxity in the frontal plane was measured
applying a 7.7 Nm abduction/adduction moment and measuring the resulting joint rotation. Analysis of variance with Tukey’s post hoc test evaluated differences in proprioception and laxity and Pearson’s correlations evaluated associations between measures. Alpha was set to \( P < 0.05 \).

**Results:** The mean PMS detection angle in controls, JHS-NI and JHS-I was 1.19° (s.e. 0.82), 2.02° (s.e. 1.27) and 2.37° (s.e. 1.98), respectively. JHS-I showed a significantly higher detection angle relative to controls (\( P = 0.028 \)), with no significant differences noted between JHS-NI and controls or JHS-I. The absolute mean PPS error angle for controls, JHS-NI and JHS-I was 4.31° (s.e. 3.14), 6.89° (s.e. 2.40) and 7.79° (s.e. 3.24), respectively. Both JHS-NI and JHS-I had a higher angle error compared with the control group (\( P = 0.016 \) and \( P = 0.001 \), respectively); there were no significant differences between the JHS-NI and JHS-I groups. The absolute mean APS error angle for controls, JHS-NI and JHS-I was 3.50° (s.e. 1.04), 4.55° (s.e. 1.92) and 4.67° (s.e. 1.50), respectively. JHS-I showed significantly higher knee laxity relative to controls (\( P = 0.045 \)), with no significant differences noted between JHS-NI and controls or JHS-I. Laxity in the frontal plane showed no correlations with PMS (\( P = 0.267–0.702 \)), PPS (\( P = 0.203–0.310 \)) or APS (\( P = 0.102–0.324 \)) in any of the tested groups.

**Conclusion:** Those with JHS regardless of the presence of instability have poor PPS. In those with JHS, poor PMS and extreme levels of knee laxity appear to be independently related to the presence of knee instability. These results suggest that improvements to improved PMS may reduce episodes of knee instability in patients with JHS.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 288 UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE: A 122-PATIENT AUDIT FOCUSING ON INITIAL DIAGNOSIS AND CHANGES OVER TIME

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**Background:** The diagnosis of undifferentiated connective tissue disease (UCTD) has raised controversy over the years regarding making the diagnosis, evolution and prognosis. Le Roy et al. in 1980 and most recently Mosca et al. in 2014 proposed classification criteria for UCTD, but confusion still exists regarding making the diagnosis of UCTD, the evolution and prognosis of the syndrome and how the patient should be followed up over time.

**Methods:** This was a retrospective study of patients followed up in a specialist clinic in a tertiary referral centre (University College London Hospitals) with a diagnosis of UCTD, focusing on clinical and serological features, treatment, follow-up and disease evolution over time.

**Results:** A total of 121 patients were included in the study: 83% were females, the mean age at disease onset was 39 years (range 20–80) and the patients were followed up for at least 1 year (mean 12 years [range 1–40]). Seventy-eight per cent of these patients had a stable diagnosis of UCTD, while in 22% the diagnosis changed over time: 9% evolved into a specific CTD—4 SLE, 3 SS, 1 RA, 1 SSc and 1 antiphospholipid syndrome—7% had a change of diagnosis from a specific CTD to UCTD, 4% evolved into an overlap syndrome and 2% of the patients were no longer diagnosed as having any CTD at the end of the study. The most prevalent manifestations were joint pain (arthralgia/arthritis) in 89% of the patients, fatigue in 80%, RP in 63% and skin rashes in 49% and sicca symptoms in 45%. Lung involvement was observed in 11% of the patients, of which 8% had a non-specific interstitial pneumonia (NSIP) and 3% had a usual interstitial pneumonia (UIP) pattern. Thirty-six per cent of patients were noted to have associated gastro-oesophageal reflux disease. Serological features included positive ANA in 98%, anti-SSA in 53%, anti-Ro in 25%, anti-Ru in 25% and hypocomplementemia in 19% of the patients. Seven percent of the patients did not require any treatment for their UCTD, but the majority of patients were treated with HCQ only (75%) and the rest with other immunosuppressants/immunomodulators.

**Conclusion:** In our study, the majority of patients initially diagnosed with UCTD kept this diagnosis over time, but 13% of patients evolved to a defined CTD or an overlap syndrome and in 2% of patients the symptoms and serological features eventually resolved. Although UCTD is often mild, significant major organ involvement such as interstitial lung disease can occur, as well as evolution to a defined CTD or overlap syndrome. This should guide follow-up of these patients in clinic.

**Disclosure statement:** R.I. has received research funding from the EULAR scientific training bursary. The other author has declared no conflicts of interest.

### 289 A CYTOKINE-MEDIATED BIOLOGICAL BASIS FOR FATIGUE IN PRIMARY SJÖGREN’S SYNDROME

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**Background:** Fatigue is a common and problematic symptom in many chronic diseases including primary SS (pSS). Although the pathophysiological basis of fatigue is not fully understood and no biomarkers have yet been identified, emerging data implicates inflammatory pathways and immune dysregulation as potential mechanistic components. The aim of this study was to investigate the relationship between cytokine levels and patient-reported levels of fatigue, using pSS as an example of a chronic inflammatory condition.

**Methods:** Blood levels of 22 cytokines were measured in 161 patients with pSS from the UK Primary Sjögren’s Syndrome Registry (UKPSSR) and 28 healthy, non-fatigued controls. Patient-reported scores for fatigue were evaluated, classified according to severity, and compared with cytokine levels using Wilcoxon test. Logistic regression was used to determine the most important predictors of fatigue levels.

**Results:** Thirteen cytokines were significantly higher in pSS patients compared with healthy controls, with \( P < 0.001 \) for eight of these. Levels of four pro-inflammatory cytokines—IP-10 (\( P = 0.019 \)), TNF-α (\( P = 0.046 \)), LT-α (\( P = 0.034 \)) and INF-γ (\( P = 0.020 \))—decreased with increasing fatigue in the pSS cases, showing a negative correlation with the following r-values: IP-10, −0.2190; TNF-α, −0.1273; INF-γ, −0.1950 and LT-α, −0.0808. Serum levels of IFN-γ and IP-10 and pain and depression scores were the best predictors of fatigue level, with correct predictions of fatigue level in 67% of cases when these four variables were used.

**Conclusion:** Four pro-inflammatory cytokines decrease as fatigue level increases in pSS patients. Research into anti-inflammatory pathways and cytokines may be insightful in understanding the pathophysiological basis of fatigue. Cytokines, pain and depression appear to be the most powerful predictors of fatigue. Further study is required to characterize the complex biochemical cascades underlying fatigue in pSS and other chronic conditions, as well as the influence of potential clinical confounding factors such as pain and depression.

**Disclosure statement:** The authors have declared no conflicts of interest.

### 290 THE BURDEN OF SYSTEMIC DISEASE IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME

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**Background:** A high proportion of patients with SS have systemic features at some point in the course of their condition, with the highest prevalence historically reported in the anti-Ro/La-positive group. We reviewed our own well-characterized cohort of patients with primary SS to determine the frequency of clinically significant systemic features.

**Methods:** We undertook a retrospective case note review to determine the prevalence of significant systemic associations. All patients satisfied the American-European Consensus Group (AECG) criteria and were either Ro antibody positive and/or had a positive minor salivary gland biopsy.

**Results:** The cohort included a total of 245 patients and was comprised of 164 Ro+ (13 males, 151 females) and 81 Ro- but lip biopsy-positive patients (7 males, 74 females). Systemic disease was reported in 81 (55.5%) of the antibody-positive and 44 (54%) of the antibody-negative group. Some patients had more than one systemic complication. The prevalence of thyroid disease, lung involvement, liver disease, renal involvement, coeliac disease and osteoporosis were similar in both patient populations (see Table 1). Subacute cutaneous lupus (SCLE), immune thrombocytopaenia (ITP), myositis, monoclonal gammapathy of uncertain significance (MIGUS), lymphoma, corneal melt and renal stones were seen only in the antibody-positive group. However, neurological disease was observed.
in nine (11.1%) of the antibody-negative group but only six (3.7%) of the antibody-positive group.

Conclusion: Overall similar proportions of the antibody-negative and positive group had systemic complications. Certain conditions, most notably, SCLE, ITP, MGUS and lymphoma were seen only in the antibody-positive group. Interestingly, neurological complications were observed more frequently in the antibody-negative group. This study suggests that systemic complications are just as likely to affect antibody-positive as antibody-negative patients with SS. This would imply that all patients with SS warrant active treatment.

Disclosure statement: The authors have declared no conflicts of interest.

290 Table 1. Prevalence of systemic disease in SS patients

<table>
<thead>
<tr>
<th>Systemic feature</th>
<th>Re/La+, n (%)</th>
<th>Re/La-, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCLE</td>
<td>12 (7.3)</td>
<td>0</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>26 (15.8)</td>
<td>13 (16)</td>
</tr>
<tr>
<td>Lung disease</td>
<td>11 (6.7)</td>
<td>3 (3.7)</td>
</tr>
<tr>
<td>Liver disease</td>
<td>4 (2.4)</td>
<td>2 (2.4)</td>
</tr>
<tr>
<td>Neurological disease</td>
<td>6 (3.7)</td>
<td>9 (11.1)</td>
</tr>
<tr>
<td>ITD</td>
<td>2 (1.8)</td>
<td>0</td>
</tr>
<tr>
<td>Renal involvement</td>
<td>8 (4.9)</td>
<td>4 (4.9)</td>
</tr>
<tr>
<td>Renal stones</td>
<td>6 (3.7)</td>
<td>0</td>
</tr>
<tr>
<td>APL antibodies</td>
<td>6 (3.7)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>4 (2.4)</td>
<td>2 (2.5)</td>
</tr>
<tr>
<td>B12 deficiency</td>
<td>5 (3.0)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>Mysitis</td>
<td>2 (1.2)</td>
<td>0</td>
</tr>
<tr>
<td>Myasthenia gravis</td>
<td>1 (0.6)</td>
<td>1 (1.2)</td>
</tr>
<tr>
<td>MGUS</td>
<td>4 (2.4)</td>
<td>0</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>13 (7.9)</td>
<td>8 (9.9)</td>
</tr>
<tr>
<td>Myositis</td>
<td>1 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td>Corneal melt</td>
<td>1 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td>Chronic B cell leukaemia</td>
<td>0</td>
<td>1 (1.2)</td>
</tr>
</tbody>
</table>


291 COPING IS AN IMPORTANT OUTCOME THAT DOES NOT CORRELATE WITH HEALTH STATUS IN FIBROMYALGIA

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Background: FM has a significant impact on daily and psychosocial functions. Management can be challenging and consists of pharmacological and non-pharmacological treatments. How patients adapt and manage their illness as reflected by coping is an important outcome. Yet the effect of coping in FM remains largely unexplored. The aim of this study was to identify factors that impact FM outcome, measured by the Revised Fibromyalgia Impact Questionnaire (FIQR), and whether health status correlates with coping.

Methods: This was a cross-sectional survey of FM patients attending the nurse-led FM clinic in secondary care. Demographic data, visual analogue scales (VASs) for pain severity, fatigue severity, good days per week, patient self-questionnaires completed (including the Hospital Anxiety and Depression Scale (HADS), Revised Fibromyalgia Impact Questionnaire (FIQR)) and patients’ perspective of the level of health professional support were collected. Non-parametric inferential statistics (Pearson correlation for continuous, r-test for binary and analysis of variance for categorical data) were used, followed by forward stepwise multivariable linear regression to identify the three most significant predictors.

Results: Sixty-six patients (58 females, 8 males) participated in the study. The average age was 49.18 years (s.d. 11.62). The mean duration of symptoms was 15.21 years (s.d. 11.58). Sixty-six patients were 62.43 (s.d. 14.49), HADS-anxiety 12.08 (s.d. 3.78) and HADS-depression 9.36 (s.d. 4.12); 35 and 18 patients, respectively, had anxiety and depression scores >11. Eighteen patients were on amitriptyline, 7 on pregabalin, 3 on duloxetine and 5 on duloxetine. The mean number of good days per week was 1.73 (s.d. 1.48). Forty-two patients were unemployed and 47 patients reported having family support. The following factors were found to predict patients’ willingness to start treatment: fatigue VAS (P = 0.045), increasing age (P = 0.001), current employment (P < 0.005) and lack of family support (P = 0.023). Patients with high scores of HADS-depression were more likely to decline treatment (P = 0.007). Satisfaction with health care professional support, pain, number of good days per week, education and marital status were not predictive of willingness to start treatment. Following forward stepwise multivariable linear regression, the strongest correlations were found for older age, followed by negative correlations for HADS-depression and family support. Pharmacological treatment was declined by 42%. The main reasons for declining treatment were concerns about adverse effects (75%), ineffectiveness (21.5%) and both adverse effects and ineffectiveness (3.5%).

Conclusion: In patients suffering from FM the decision to start pharmacological treatment is influenced by a combination of clinical and psychosocial factors and medication beliefs. Poor uptake and adherence to medications will result in a poorer outcome. Adopting a multidimensional assessment and addressing severe depression may help inform better treatment plans and improve clinical outcome.

Disclosure statement: The authors have declared no conflicts of interest.

Poster viewing III

i180 Thursday 28 April 2016

POSTER VIEWING III

292 DETERMINANTS INFLUENCING PATIENT DECISION TO START PHARMACOLOGICAL TREATMENT IN FIBROMYALGIA

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Background: FM is a chronic disorder characterized by widespread pain, fatigue and unrefreshing sleep. Pharmacological and non-pharmacological treatments are often used to target specific symptoms. Several studies have shown the effectiveness of pharmacological treatment, including tricyclic antidepressants, duloxetine, pregabalin and gabapentin. However, many patients decline treatment and less than half of new users adhere to treatment. The willingness to start medication is a unexplored and yet very important aspect of management, as it directly influences outcome. The aim of this study was to identify determinants that influence patients’ willingness to start pharmacological therapy.

Methods: Sixty-six consecutive patients attending the nurse-led FM clinic in secondary care were recruited. Demographic data, visual analogue scales (VASs) for pain severity, fatigue severity, good days per week, patient self-questionnaires completed (including the Hospital Anxiety and Depression Scale (HADS), Revised Fibromyalgia Impact Questionnaire (FIQR)) and patients’ perspective of the level of health professional support were collected. Non-parametric inferential statistics (Pearson correlation for continuous, r-test for binary and analysis of variance for categorical data) were used, followed by forward stepwise multivariable linear regression to identify the three most significant predictors.

Results: Sixty-six patients (58 females, 8 males) participated in the study. The average age was 49.18 years (s.d. 11.62). The mean duration of symptoms was 15.21 years (s.d. 11.58). The mean FIQR was 62.43 (s.d. 14.49), HADS-anxiety 12.08 (s.d. 3.78) and HADS-depression 9.36 (s.d. 4.12); 35 and 18 patients, respectively, had anxiety and depression scores >11. Eighteen patients were on amitriptyline, 7 on pregabalin, 3 on duloxetine and 5 on duloxetine. The mean number of good days per week was 1.73 (s.d. 1.48). Forty-two patients were unemployed and 47 patients reported having family support. The following factors were found to predict patients’ willingness to start treatment: fatigue VAS (P = 0.045), increasing age (P = 0.001), current employment (P < 0.005) and lack of family support (P = 0.023). Patients with high scores of HADS-depression were more likely to decline treatment (P = 0.007). Satisfaction with health care professional support, pain, number of good days per week, education and marital status were not predictive of willingness to start treatment. Following forward stepwise multivariable linear regression, the strongest correlations were found for older age, followed by negative correlations for HADS-depression and family support. Pharmacological treatment was declined by 42%. The main reasons for declining treatment were concerns about adverse effects (75%), ineffectiveness (21.5%) and both adverse effects and ineffectiveness (3.5%).

Conclusion: In patients suffering from FM the decision to start pharmacological treatment is influenced by a combination of clinical and psychosocial factors and medication beliefs. Poor uptake and adherence to medications will result in a poorer outcome. Adopting a multidimensional assessment and addressing severe depression may help inform better treatment plans and improve clinical outcome.

Disclosure statement: The authors have declared no conflicts of interest.
Non-restorative sleep is a characteristic symptom of FM. A number of studies have reported abnormalities of sleep architecture on polysomnography (PSG). Alpha wave intrusion during delta wave sleep has been frequently reported in FM. However, alpha/ delta sleep has also been reported in other conditions, including depression and non-depressed patients with chronic fatigue. We have undertaken PSG in patients with FM and compared the findings with patients with OA who complained of sleep disturbance and a group of normal healthy control (NHC) subjects in order to determine if there are specific abnormalities of sleep architecture in FM.

Methods: We studied 19 newly diagnosed FM patients [mean age 41 years (range 19–58)], 17 patients with OA [mean age 46 years (range 19–63)] who had localized joint pain and sleep disturbance and 10 NHCs [mean age 38 years (range 23–61)]. All participants were female. The diagnosis was confirmed by a consultant rheumatologist. None of the patients were being treated for anxiety or depression and none had taken any antidepressant, psychoactive or sedative drugs for at least 2 weeks prior to analysis. Digital PSG was conducted in the patients' home on 2 consecutive nights using an Embla A10 unit ambulatory recorder. Each night of data was imported into Somnologica 5.1 then viewed and scored on a computer in 30 sec epochs by a trained sleep researcher. Arousals were computed automatically by the system. Spectral analysis of four channels was employed using open source software. Each frequency band was decomposed and power averaged over the whole night of sleep.

Results: There was no significant difference in total sleep time in the three groups, but sleep efficiency was significantly worse in FM and OA (P = 0.025). Sleep stage transitions (SSTs) were significantly increased in FM and OA (P = 0.019), with a marked increase in SSTs per hour (P = 0.002) compared with NHCs. There was no significant difference between FM and OA. Results of spectral analysis found an increase in alpha waves during stage 3 (delta wave) sleep in both FM and OA compared with NHCs, but without any difference between FM and OA. There was a numerical increase in spindle frequency during non-REM sleep compared with NHCs, more in FM than OA, but wide variation (1.12 ± 0.06, 0.98 ± 0.39, 0.61 ± 0.27 m/s).

Conclusion: Alpha/delta sleep in FM is not specific and is found with a similar density in patients with OA who have disturbed sleep. There is a trend towards an increase in spindle frequency in FM compared with OA and NHCs. Non-restorative sleep may be a result of an abnormal rate of SSTs, with frequent fluctuation between light and deep sleep.

Disclosure statement: The authors have declared no conflicts of interest.

Early replacement of vitamin D in vitamin D-deficient fibromyalgia patients improves reported pain and number of tender points

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Background: FM is a persistent and debilitating disorder. It can impose heavy economic burdens on society as well as on the patient. Recent research has found that low vitamin D levels are common among people with FM.

Methods: We investigated the correlation between pain duration, vitamin D levels and improvement in pain scores following vitamin D replacement in FM patients who are vitamin D deficient. Thirty patients with a diagnosis of FM according to ACR criteria and vitamin D deficiency without any co-morbidities and not on any analgesics were included in this study and prospectively followed up. The duration of pain, number of tender points, pain severity on the patient global health score and vitamin D levels were recorded at the beginning of the study. The patients received vitamin D supplementation. Vitamin D levels, the number of tender points and pain severity on the patient global health score were measured after 3 months.

Results: Patients did not have statistically significant differences in co-morbidities and were not on analgesia at baseline or during the follow-up period. There was a female predominance of 83.3% vs 67.7% male. Inflammatory markers were normal. Vitamin D replacement led to an improvement in the number of tender points in all 30 patients. The patient global health pain score also improved in 28 patients after vitamin D replacement. Three patients reported complete resolution of symptoms. The longer duration of pain before detection of vitamin D deficiency and subsequent commencement of oral vitamin D supplementation, the poorer the reduction in pain. Pain in young patients improved more following vitamin D replacement compared with older individuals. The severity of vitamin D deficiency at baseline was not associated with improvement of pain scores following vitamin D replacement. Pain duration and the percentage reduction in tender points showed there was a strong negative correlation between the two variables (r = −0.813, n = 30, P < 0.001), with longer pain duration associated with a lower percentage reduction in tender points and a lower percentage reduction in pain score (r = −0.670, n = 30, P < 0.001). Patient age and the percentage reduction in tender points showed that there was strong negative correlation between the two variables (r = −0.725, n = 30, P < 0.001), with younger patients being associated with a higher percentage reduction in tender points and a higher percentage reduction in pain score (r = −0.668, n = 30, P < 0.001). Mann–Whitney U test showed a significant difference in the percentage reduction of tender points of patients with pain duration of <15 months (mean difference 22.07, n = 15) vs pain duration of >15 months (mean difference 8.93, n = 15) (U = 14.00, z = −4.10, P < 0.001, r = 0.75).

Conclusion: Vitamin D deficiency in patients with FM is associated with worse symptoms. Early recognition of vitamin D deficiency and prompt replacement, especially in young patients, results in significant improvement of pain and can even lead to complete resolution of symptoms.

Disclosure statement: The authors have declared no conflicts of interest.
All the e-posters can be accessed via the e-poster site www.rheum2016eposters.org, and the 2016 conference app.

**E-POSTERS**

**BHPR: AUDIT AND CLINICAL EVALUATION**

**E01** A SURVEY OF PATIENT-REPORTED EXPERIENCE, PATIENT-REPORTED OUTCOME AND WORK IN PATIENTS SEEN IN RHEUMATOLOGY NURSE-LED CLINICS ON BEHALF OF THE WEST MIDLANDS RHEUMATOLOGY NURSE SPECIALIST NETWORK (WMRNSN)

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Modality Partnership Community Rheumatology Service

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Disclosure statement: The author has declared no conflict of interest.

**E02** PHARMACOLOGICAL MANAGEMENT OF RAYNAUD PHENOMENON IN A DISTRICT GENERAL HOSPITAL: AN AUDIT

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Rheumatology, New Cross Hospital, Wolverhampton, UK

Disclosure statement: The authors have declared no conflicts of interest.

**E03** DOCUMENTING CONSENT FOR INTRA-ARTICULAR INJECTIONS: QUALITY IMPROVEMENT THROUGH CLINICAL AUDIT

Laura R. Newton1,2, Muditha Samaranayaka3, Sabrina Juman2, Sarah Skeoch1, Audrey Low3, Paul Sanders1 and Pippa Watson1

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Disclosure statement: The authors have declared no conflicts of interest.

**E04** INITIAL RESULTS FROM A COMBINED RHEUMATOLOGY/DERMATOLOGY CONNECTIVE TISSUE DISEASE CLINIC IN BELFAST

Louise McDonald

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Disclosure statement: The author has declared no conflicts of interest.

**E05** REFERRAL PATTERNS FOR PATIENTS ATTENDING AN AUTOIMMUNE RHEUMATIC DISEASE CLINIC IN CENTRAL LONDON

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1Internal Medicine, Hospital Pedro Hispano, Matosinhos, Portugal, 2Rheumatology, Hospital Son Llàtzer, Palma de Mallorca, Spain, 3Rheumatology Research, University College Hospitals, London, UK

Disclosure statement: The authors have declared no conflicts of interest.

**E06** AUDIT OF THE USE OF RITUXIMAB IN THE TREATMENT OF RHEUMATOID ARTHRITIS AT UNIVERSITY COLLEGE LONDON HOSPITAL

Benjamin J. Langridge, Hibaq Ibrahim, Maria Leandro and Samantha Moore

Rheumatology, University College Hospital, London, UK

Disclosure statement: The authors have declared no conflicts of interest.

**E07** BIOLOGIC PRESCRIBING AMONG RHEUMATOLOGISTS IN LONDON: A SURVEY OF CURRENT TRENDS

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Disclosure statement: The authors have declared no conflicts of interest.

**BHPR RESEARCH: QUANTITATIVE**

**E08** FACTORS INFLUENCING PATIENTS' PARTICIPATION IN RHEUMATOLOGY RESEARCH STUDIES: EXPERIENCE FROM A SINGLE ACADEMIC CENTRE

Mumtaz Khan, Ian Bruce and Benjamin Parker

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Disclosure statement: The authors have declared no conflicts of interest.

**CASE REPORTS**

**E09** CASE OF INFLAMMATORY MYOPATHY WITH UNUSUAL DIAGNOSIS

Ganesh Kasavkar, Aijl Menon and Erin Vermaak

Rheumatology, Haywood Hospital, Stoke on Trent, UK

Disclosure statement: The authors have declared no conflicts of interest.

**E10** RECURRENT SKIN INFECTIONS IN A PATIENT WITH RHEUMATOID ARTHRITIS CAUSED BY PANTON-VALENTINE LEUKOCIDIN-PRODUCING STAPHYLOCOCCUS AUREUS

Fazal Sheikh1, Yasmeen Ahmad2 and Sarang Chitale2

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Disclosure statement: The authors have declared no conflicts of interest.
E11 GOLIMUMAB-INDUCED DERMATOPATHIC LYMPHADENOPATHY: A CURIOUS SIDE EFFECT OF GOLIMUMAB?
Rabia Yakooob1, Tom Fielman2, Lucy Knight3 and Sandeep Dahiya1
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Disclosure statement: The authors have declared no conflicts of interest.

E12 TWO CASES OF GIANT CELL ARTERITIS FOLLOWING HEAD TRAUMA, A NEW RISK FACTOR?
Shahryar Hadavi, Asad Khan, Fiona Hayes and Bhaskar Dasgupta
Rheumatology, Southend University Hospital NHS Foundation Trust, Southend, UK

Disclosure statement: The authors have declared no conflicts of interest.

E13 A CASE OF AA AMYLOIDOSIS SECONDARY TO PSORIATIC MUTILINS
Jennifer Christie and Abdel Salih
Rheumatology, Warrington Hospital, Warrington, UK

Disclosure statement: The authors have declared no conflicts of interest.

E14 GIANT CELL ARTERITIS AND VISUAL LOSS
Asanka Nugalayadda and Anupama Nandagudi
Rheumatology, Basildon and Thurrock University Hospital, Basildon, UK

Disclosure statement: The authors have declared no conflicts of interest.

E15 MYOCARDIAL INFARCTION AFTER RITUXIMAB IN ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS
David J. T. McCormick and Wing H. Yau
Rheumatology, Altnagelvin Area Hospital, Londonderry, UK

Disclosure statement: The authors have declared no conflicts of interest.

E16 ISORETINOIN-ASSOCIATED SACROILIITIS, HYPEROSTOSIS AND ENTHESOPATHY
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E17 NOT THE USUAL SUSPECTS—A CASE OF CHOLESTATIC HEPATITIS
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E18 A CASE OF PROFOUND ARTHRALGIA AND MYALGIA IN A WELL-CONTROLLED RHEUMATOID ARTHRITIS PATIENT
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E19 A PATIENT WITH ADULT-ONSET STILL’S DISEASE WITH AN INCREASED CHLAMYDIA PNEUMONIAE ANTIBODY TITRE
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E20 GOUT IN ASSOCIATION WITH PRIMARY HYPERPARATHYROIDISM
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E21 A CASE OF BILATERAL SENSORINEURAL SYMPTOMATIC HEARING LOSS IN A PATIENT WITH SUSPECTED SYSTEMIC LUPUS ERYTHEMATOSUS
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E22 EOSINOPHILIC POLYANGIITIS PRESENTING WITH TEMPORAL ARTERY ANEURYSM
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E23 SAME OLD SAME OLD SARCOID
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E24 BIOLOGIC AGENTS IN RHEUMATOID ARTHRITIS: ARE WE GETTING PARANOID?
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E26 FRAGILITY FRACTURES ARE ASSOCIATED WITH A SHORTER BODY HABITUS: RESULTS OF A LARGE OBSERVATIONAL COHORT

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E27 LOWER LIMB OSTEOARTHRITIS MAY NOT IMPEDE PHYSICAL ACTIVITY AT LOW IMPACTS: THE HERTFORDSHIRE COHORT STUDY

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E32 A SYSTEMATIC REVIEW OF ECONOMIC EVALUATIONS OF CONSERVATIVE THERAPIES FOR CHRONIC MUSCULOSKELETAL CONDITIONS OF THE LOWER EXTREMITY

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**OSTEOPOROSIS AND METABOLIC BONE DISEASE**

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Ercan Yuruk\(^1\), Dominic O’Donovan\(^2\) and Damodar Makkuni\(^1\)

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Disclosure statement: The authors have declared no conflicts of interest.

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E58 THE EFFECTS OF INFLIXIMAB ON THE PHASE LEVEL OF ANTI-CYCLIC CITRULLINATED PEPTIDE AND RHEUMATOID FACTOR IN A SAMPLE OF IRAQI PATIENTS WITH RHEUMATOID ARTHRITIS
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Disclosure statement: The authors have declared no conflicts of interest.

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**E64 A PILOT PROJECT ON THE USE OF A METHOTREXATE PATIENT INFORMATION FILM FOR DISEASE-MODIFYING ANTI-RHEUMATIC DRUG COUNSELLING**

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Disclosure statement: The authors have declared no conflicts of interest.

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**E66 AUDIT AND RE-AUDIT OF HEPATITIS B SCREENING IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH RITUXIMAB**

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E71 COMPARISON BETWEEN SLEEP, PAIN, FATIGUE AND MOOD IN FIBROMYALGIA AND OSTEOARTHRITIS

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Disclosure statement: The authors have declared no conflicts of interest.

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E73 EFFECT OF INFlixIMAB ON DEPRESSION DISORDER IN A SAMPLE OF IRAQI PATIENTS WITH ANKYLOSING Spondylitis at Baghdad teaching hospital

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E74 HEARING LOSS IN ANKYLOSING SPONDYLITIS

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E75 AUDIT OF PERIPHERAL PSORIATIC ARTHRITIS

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E76 MANAGEMENT OF PSORIATIC ARTHRITIS IN EAST OF ENGLAND

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E77 A RETROSPECTIVE CASE SERIES OF TEMPORAL ARTERY BIOPSIES FOR DIAGNOSIS OF TEMPORAL ARTERITIS

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