

Wednesday 2 May 2012, 09.15 – 10.45

**BSR AND BHPR ORAL PRESENTATION OF ABSTRACTS****ORAL ABSTRACTS 3: RA TREATMENT AND OUTCOMES****O13. VALIDATION OF JADAS IN ALL SUBTYPES OF JUVENILE IDIOPATHIC ARTHRITIS IN A CLINICAL SETTING**

Flora McErlane<sup>1,2</sup>, Michael W. Beresford<sup>1,3</sup>, Eileen M. Baidam<sup>3</sup>, Wendy Thomson<sup>2</sup>, Kimme Hyrich<sup>2</sup>, Alice Chieng<sup>7</sup>, Joyce Davidson<sup>5</sup>, Helen E. Foster<sup>4</sup>, Janet Gardner-Medwin<sup>5</sup>, Mark Lunt<sup>2</sup> and Lucy Wedderburn<sup>6</sup>

<sup>1</sup>Institute of Child Health, University of Liverpool, Liverpool, United Kingdom; <sup>2</sup>School of Translational Medicine, University of Manchester, Manchester, United Kingdom; <sup>3</sup>Paediatric Rheumatology, Alder Hey Children's Hospital, Liverpool, United Kingdom; <sup>4</sup>Rheumatology, Newcastle Medical School, Newcastle upon Tyne, United Kingdom; <sup>5</sup>Rheumatology, Royal Hospital for Sick Children, Glasgow, United Kingdom; <sup>6</sup>Rheumatology Unit, Institute of Child Health, London, United Kingdom; <sup>7</sup>Rheumatology, Royal Manchester Children's Hospital, Manchester, United Kingdom

**Background:** Juvenile Arthritis Disease Activity Score (JADAS) is a 4 variable composite disease activity (DA) score for JIA (including active 10, 27 or 71 joint count (AJC), physician global (PGA), parent/child global (PGE) and ESR). The validity of JADAS for all ILAR subtypes in the routine clinical setting is unknown. We investigated the construct validity of JADAS in the clinical setting in all subtypes of JIA through application to a prospective inception cohort of UK children presenting with new onset inflammatory arthritis.

**Methods:** JADAS 10, 27 and 71 were determined for all children in the Childhood Arthritis Prospective Study (CAPS) with complete data available at baseline. Correlation of JADAS 10, 27 and 71 with single DA markers was determined for all subtypes. All correlations were calculated using Spearman's rank statistic.

**Results:** 262/1238 visits had sufficient data for calculation of JADAS (1028 (83%) AJC, 744 (60%) PGA, 843 (68%) PGE and 459 (37%) ESR). Median age at disease onset was 6.0 years (IQR 2.6-10.4) and 64% were female. Correlation between JADAS 10, 27 and 71 approached 1 for all subtypes. Median JADAS 71 was 5.3 (IQR 2.2-10.1) with a significant difference between median JADAS scores between subtypes ( $p < 0.01$ ). Correlation of JADAS 71 with each single marker of DA was moderate to high in the total cohort (see Table 1). Overall, correlation with AJC, PGA and PGE was moderate to high and correlation with ESR, limited JC, parental pain and CHAQ was low to moderate in the individual subtypes. Correlation coefficients in the extended oligoarticular, rheumatoid factor negative and enthesitis related subtypes were interpreted with caution in view of low numbers.

**Conclusions:** This study adds to the body of evidence supporting the construct validity of JADAS. JADAS correlates with other measures of DA in all ILAR subtypes in the routine clinical setting. Given the high frequency of missing ESR data, it would be useful to assess the validity of JADAS without inclusion of the ESR.

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

**O14. HAS ORTHOPAEDIC INTERVENTION FOR RHEUMATOID ARTHRITIS CHANGED IN LINE WITH COMBINATION AND ANTI-TNF THERAPIES? AN EVALUATION OF JOINT SURGERY RATES AND PROGNOSTIC FACTORS IN TWO UK INCEPTION COHORTS (1986-2011)**

Elena Nikiphorou<sup>1</sup>, Lewis Carpenter<sup>2</sup>, Patrick Kiely<sup>3</sup>, David Walsh<sup>4</sup>, Josh Dixey<sup>5</sup> and Adam Young<sup>1</sup>

<sup>1</sup>Rheumatology, ERAS/ERAN, St Albans, United Kingdom; <sup>2</sup>Centre for Lifespan & Chronic Illness Research, University of Hertfordshire, Hatfield, United Kingdom; <sup>3</sup>Rheumatology, St George's Healthcare NHS Trust, London, United Kingdom; <sup>4</sup>Academic Rheumatology, Arthritis Research UK Pain Centre, University of Nottingham, Nottingham, United Kingdom; <sup>5</sup>Rheumatology, New Cross Hospital, Wolverhampton, United Kingdom

**Background:** Orthopaedic surgery in RA is considered a surrogate marker for joint destruction. It has been postulated that the need for orthopaedic surgery would be reduced with greater use of more intense therapies for RA. We were able to examine this proposal in two UK multicentre inception cohorts conducted between 1986 & 2011.

**Methods:** The Early RA Study (ERAS) recruited from 1986-1999 ( $n=1465$ ), the Early RA Network (ERAN) from 2002 ( $n=1236$ ). Symptom onset to baseline was median 6 months in both and time to 1st DMARD was median 2 & 1 month respectively. Standardized clinical, laboratory and x-ray measures were performed yearly in both cohorts. Disease-modifying, steroid and biologic therapies reflected conventional practice and guidelines of the time frames examined. Source data of all orthopaedic interventions included clinical datasets (patient report and medical records from 1986), which were validated with Hospital Episode Statistics (HES from 1997) and the National Joint Registry (NJR from 2002). Length of follow up was based on the National Death Registry.

**Results:** In ERAS 558 patients (38%) had 1287 orthopaedic procedures over a maximum of 25 years follow up. 18.5% had major (e.g. total joint replacements), 16% had intermediate (e.g. wrist synovectomy, forefoot arthroplasty), and 17% minor (e.g. carpal tunnel release). In ERAN (max 9 years follow up) 216 patients (17.5%) had 326 procedures, 7% major, 3.4% intermediate, 9% minor. Graphic displays will show that secular declines in combined major/intermediate surgical rates were seen from 1987-2011 (18 to 16 per 1000 patients/year), coinciding with use of more intensive combination and biologic therapies. Declines were mainly in intermediate type surgery of wrist, hands and feet (8 to 6 per 1000 patients/year) and not in total joint replacements (mainly hip & knee). Risk factors were also different for the two surgical groups. In univariate analysis, women had increased risk for intermediate surgery only (odds ratio 3.2, CI 2.21-4.7). Baseline and 1year DAS, HAQ, ESR, Haemoglobin(HB) and erosions all predicted 5 & 10 year major and intermediate surgery (ORs all significant around 1.5-2). Low HB predicted a subgroup who had multiple joint surgery by 5 & 10years (OR 2.6, CI 1.5-4.4 and OR 3.0, CI 2.1-4.4 respectively). In Cox regression, sex, onset age and erosions predicted intermediate surgery, and sex, onset age and HB predicted major surgery.

**Conclusions:** Orthopaedic surgery is an important and common outcome in RA by 10 years, not often reported and difficult to predict. Only hand/foot surgery rates showed a consistent decline from 1986-2011, suggesting a different pathology or response to therapy between large and small joint destructive processes. HB does not normally

TABLE 1 Spearman's correlation between JADAS 71 and single markers DA by ILAR subtype

ILAR Subtype	Systemic onset JIA	Persistent oligo JIA	Extended oligo JIA	Rheumatoid factor neg JIA	Rheumatoid factor pos JIA	Enthesitis related JIA	Psoriatic JIA	Undifferentiated JIA	Unknown subtype	Total cohort
Number of children	23	111	12	57	7	9	19	7	17	262
AJC	0.54	0.67	0.53	0.75	0.53	0.34	0.59	0.81	0.37	0.59
PGA	0.63	0.69	0.25	0.73	0.14	0.05	0.50	0.83	0.56	0.64
PGE	0.51	0.68	0.83	0.61	0.41	0.69	0.71	0.9	0.48	0.61
ESR	0.28	0.31	0.35	0.4	0.6	0.85	0.43	0.7	0.5	0.53
Limited 71 JC	0.29	0.51	0.23	0.37	0.14	-0.12	0.4	0.81	0.45	0.41
Parental pain	0.23	0.62	0.03	0.57	0.41	0.69	0.7	0.79	0.42	0.53
Childhood health assessment questionnaire	0.25	0.57	-0.07	0.36	-0.47	0.84	0.37	0.8	0.66	0.47

perform well as a predictor of outcome in RA, but did for orthopaedic intervention.

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

#### O15. PREDICTING RESPONSES TO ANTI-TNF $\alpha$ THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS USING METABOLOMIC ANALYSIS OF URINE

Sabrina R. Kapoor<sup>1,2</sup>, Andrew Filer<sup>1,3</sup>, Martin Fitzpatrick<sup>1</sup>, Benjamin A. Fisher<sup>5</sup>, Peter C. Taylor<sup>4</sup>, Christopher Buckley<sup>1,2</sup>, Iain McInnes<sup>5</sup>, Karim Raza<sup>1,2</sup> and Stephen P. Young<sup>1</sup>

<sup>1</sup>Rheumatology Research Group, University of Birmingham, Birmingham, United Kingdom; <sup>2</sup>Rheumatology, University of Birmingham and Sandwell & West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom; <sup>3</sup>Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom; <sup>4</sup>Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom; <sup>5</sup>Rheumatology, Imperial College, London, United Kingdom; <sup>6</sup>Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom

**Background:** Anti-TNF $\alpha$  therapies are highly effective in the treatment of rheumatoid arthritis (RA) but a significant proportion of patients have an inadequate response. Given the important role of TNF $\alpha$  in regulating systemic and localized metabolism, we sought to determine if the metabolic profile of patients prior to therapy could be used to predict responses to anti-TNF $\alpha$  agents.

**Methods:** Urine was collected from 16 patients with RA before and during therapy with infliximab or etanercept as part of a multicentre study. All patients were female and the mean age was 51.5. 14 patients were positive for rheumatoid factor and 14 for the anti-CCP antibody. All patients had a DAS28 > 4 at baseline. Urine metabolic profiles were assessed using NMR spectroscopy. The relationship between metabolic profiles and clinical outcomes was assessed (using partial least square discriminant analysis (PLSDA), Galgo and PLS-R analysis) and relevant metabolites were identified (using metabolite databases and Chemomix).

**Results:** Baseline urine metabolic profiles were able to discriminate between RA patients who did (7 patients) or did not (9 patients) have a good response to anti-TNF $\alpha$  therapy according to EULAR criteria with a sensitivity of 85.9% and specificity of 85.7% with several metabolites (in particular citrate, creatinine and cresol) contributing. There was a significant correlation between baseline metabolic profiles in the urine samples and the extent of change in DAS 28 (PLS-R analysis  $p=0.04$ ). In patients with RA who responded to TNF $\alpha$  antagonists, a good response to therapy was associated with changes in the following urinary metabolites: erythritol, phenylacetic acid, cresol, propionic acid, methylamine, citrate, hippuric acid and creatinine. Urine samples were also available for 20 patients with psoriatic arthritis (PsA). Similar metabolites were identified in the urine samples of the patients with PsA that responded to TNF $\alpha$  antagonists. We were unable to study the ability of baseline urinary metabolite profiles to predict response in PsA as all but one of the PsA patients responded according to predefined criteria.

**Conclusions:** There are clear differences in the metabolic profiles of baseline urine samples of RA patients who go on to respond well

to anti-TNF $\alpha$  therapy. This may be relevant in the development of clinically useful predictive strategies.

**Disclosure statement:** C.B, B.F, I.M., P.T.: Merck provided funding for the clinical study (but not for the metabolomic analysis reported here). All other authors have declared no conflicts of interest.

#### O16. DOUBLE-BLIND STUDY OF TOCILIZUMAB + METHOTREXATE VERSUS TOCILIZUMAB + PLACEBO IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS DESPITE PRIOR METHOTREXATE: PROGRESSION OF STRUCTURAL DAMAGE, QUALITY OF LIFE AND PHYSICAL FUNCTION AT 24 WEEKS

Maxime Dougados<sup>1</sup>, Karsten Kisse<sup>2</sup>, Howard Amital<sup>3</sup>, Philip Conaghan<sup>4</sup>, Emilio Martin-Mola<sup>5</sup>, Evgeny Nasonov<sup>6</sup>, Georg Schett<sup>7</sup>, Orrin Troum<sup>8</sup>, Tiina Veldi<sup>9</sup>, Corrado Bernasconi<sup>2</sup> and Tom Huizinga<sup>10</sup>

<sup>1</sup>Rheumatology, Paris-Descartes University, Cochin Hospital, Paris, France; <sup>2</sup>Roche, F. Hoffmann-La Roche Ltd, Basel, Switzerland; <sup>3</sup>Rheumatology, Sheba Medical Center, Tel-Hashomer, Israel; <sup>4</sup>NIHR-Leeds Biomedical Research Unit, University of Leeds, Leeds, United Kingdom; <sup>5</sup>Rheumatology, Hospital Universitario La Paz, Madrid, Spain; <sup>6</sup>Rheumatology, Institute of Rheumatology, Moscow, Russian Federation; <sup>7</sup>Department of Internal Medicine, Institute for Clinical Immunology, University of Erlangen-Nuremberg, Erlangen, Germany; <sup>8</sup>Rheumatology, Keck School of Medicine, University of Southern California, Santa Monica, California, United States of America; <sup>9</sup>Rheumatology, East-Tallinn Central Hospital, Tallinn, Estonia; <sup>10</sup>Rheumatology, Leiden University Medical Center, Leiden, Netherlands

**Background:** Tocilizumab(TCZ) monotherapy is superior to methotrexate (MTX) in achieving clinical reduction of disease activity in rheumatoid arthritis (RA). This analysis of data from phase 3b ACT-RAY assesses outcomes in terms of progression of structural damage, quality of life(QoL), & physical function.

**Methods:** In ACT-RAY, patients(pts)on MTX were randomized to continue MTX with addition of TCZ 8mg/kg every 4 wks or placebo (PBO) + TCZ. The primary endpoint was Disease Activity Score in 28 joints(DAS28) remission rate[RR] at 24 wks. Radiographs of the hand & feet were taken at baseline (BL) & wk24 & were scored by independent readers blinded to treatment allocation, clinical response, & sequence of X-rays. QoL was assessed by HAQ-DI & RAQoL.

**Results:** Of 556 pts randomized, 92%(n=512;TCZ + MTX = 260; TCZ + PBO = 252) completed 24 wks. Mean baseline characteristics were similar for both gps (female, 80.3%;age, 53.3yrs; RA duration, 8.2 yrs; DAS28,6.35)except for radiographic scores (Table). DAS28 RR was 40.4% & 34.8% in TCZ + MTX & TCZ + PBO gps, respectively (P=NS). ACR20/50/70/90 response rates were 72%/45%/25%/6%(TCZ + MTX)& 71%/41%/26%/5%(TCZ + PBO)(all P=NS). Progression of structural damage was low (Table 1). BL characteristics did not affect outcomes. HAQ-DI & RAQoL improved significantly from BL, with no differences between gps (Table 1). Rates per 100 pt-yrs of serious adverse events (SAEs) & serious infections were 21 & 6 for TCZ + MTX & 18 & 6 for TCZ + PBO. AE-related discontinuations & dose modifications occurred in 3.9% & 27.4% of TCZ + MTX & 2.9% & 18.5% of TCZ + PBO pts, respectively. ALT elevations >60 U/L were observed in 16% and 6% of TCZ + MTX & TCZ + PBO pts.

TABLE 1 Radiographic & QoL results at week 24

Genant-modified Sharp Score (GSS), mean (SD)	TCZ + MTX N=277	TCZ + PBO N=276	Between-group difference (95% CI)
Total GSS			
. Baseline	30.4 (31.8)	37.1 (40.5)	
. Baseline annualized progression rate	3.71	4.47	
. Change from baseline	0.08 (1.88) P=0.3304*	0.22 (1.11) P=0.3304*	-0.13 (-0.39, 0.13)
JSN Score			
. Baseline	14.7 (17.3)	17.7 (21.7)	
. Change from baseline	0.08 (1.49) P=0.8235*	0.11 (0.70) P=0.8235*	-0.02 (-0.22, 0.17)
. Erosion Score Baseline	15.7 (15.4)	19.4 (19.8)	
. Change from baseline	-0.01 (0.79) P=0.0871*	0.11 (0.63) P=0.0871*	-0.11 (-0.23, 0.02)
No progression in GSS (patients with changes = 0), n (%)			
. Total GSS	181 (65.3)	162 (58.7)	P=0.0871†
. JSN Score	218 (78.7)	203 (73.6)	P=0.1319†
. Erosion Score	190 (68.6)	179 (64.9)	P=0.3317†
QoL data Change from baseline, mean (SD)			
. HAQ-DI	0.56 (0.67)	-0.55 (0.53)	P=0.9323‡
. RAQoL	-5.97 (7.95)	-5.19 (7.06)	P=0.3080‡

\*P-values are for between-group differences in adjusted means (change from baseline to week 24) from the analysis of covariance. †P-values are for between-group differences (two-sided Cochran-Mantel-Haenszel test stratified for region and baseline DAS28). ‡P-values are for between-group differences (two-sided Wilcoxon rank-sum test of no difference between the 2 treatment groups in change from baseline).

**Conclusions:** TCZ+MTX was not clinically superior to TCZ monotherapy based on DAS28 remission rates and other efficacy endpoints. There was near-complete arrest of progression of structural damage and significant improvement in QoL with both treatments. Safety data confirm previous findings.

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

#### O17. SECUKINUMAB TREATMENT PROVIDES SUSTAINED RESPONSE OVER ONE YEAR IN PATIENTS WITH RHEUMATOID ARTHRITIS

Patrick Durez<sup>1</sup>, Mark C. Genovese<sup>2</sup>, Hanno B. Richards<sup>3</sup>, Jerzy Supronik<sup>4</sup>, Eva Dokoupilova<sup>5</sup>, Jacob A. Aelion<sup>6</sup>, Sang-Heon Lee<sup>7</sup>, Christine E. Coddling<sup>8</sup>, Herbert Kellner<sup>9</sup>, Takashi Ikawa<sup>10</sup>, Sophie Hugot<sup>3</sup>, Gregory Ligozio<sup>11</sup> and Shephard Mpofu<sup>3</sup>

<sup>1</sup>Rheumatology, Université Catholique de Louvain, Louvain, Belgium;

<sup>2</sup>Immunology and Rheumatology, Stanford University, Palo Alto, California, United States of America; <sup>3</sup>Integrated Hospital Care,

Novartis Pharma AG, Basel, Switzerland; <sup>4</sup>Department of Medicine, NZOZ Centrum Medyczne Artur Racewicz, Bialystok, Poland;

<sup>5</sup>Department of Medicine, Medical Plus, Uherske Hradiste, Czech Republic; <sup>6</sup>Department of Medicine, Arthritis Clinic, Jackson,

Tennessee, United States of America; <sup>7</sup>Internal Medicine, Konkuk University Medical Center, Seoul, Republic of Korea; <sup>8</sup>Rheumatology & Internal Medicine, Health Research of Oklahoma, Oklahoma,

United States of America; <sup>9</sup>Rheumatology, Centre for Inflammatory Joint Diseases, Munich, Germany; <sup>10</sup>Department of Medicine,

Kobe-Konan Yamate Clinic, Kobe, Japan; <sup>11</sup>Integrated Hospital Care, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey,

United States of America

**Background:** In a proof-of-concept study, secukinumab showed rapid and significant improvement of signs and symptoms in rheumatoid arthritis (RA) patients relative to placebo. We assessed efficacy and safety of secukinumab in RA patients despite stable methotrexate (MTX) up to Week (wk) 52.

**Methods:** Adult RA patients (n=237) on MTX were randomized equally to receive monthly s.c injections of secukinumab 25 mg, 75 mg, 150 mg, 300 mg or placebo. After wk16, responders on secukinumab remained on the same dose whereas doses were escalated in non-responders at wk20 (except patients initially on 300 mg who remained on the same dose). All placebo patients were switched to secukinumab 150 mg. Patients were followed up to wk52. Primary endpoint was the proportion of patients achieving American College of Rheumatology (ACR) 20 at wk16.

**Results:** Demographics and baseline characteristics were comparable across all groups. At wk16 ACR20 responders were higher with secukinumab 75 mg, 150 mg and 300 mg vs placebo (47%, 47% and 54% vs. 36%) but did not reach statistical significance. Responders on secukinumab at wk 16 maintained their ACR responses through wk52; for the 25 mg, 75 mg, 150 mg, 300 mg cohorts ACR20 responses were 67%, 57%, 90% and 71%, respectively. Highest responses in ACR50/70 responses at wk24 and wk52 were seen in patients who remained on secukinumab 150 mg for the entire study (wk24: ACR50=50%, ACR70=20%; wk52: ACR50=55%, ACR70=40%). DAS28-CRP reductions were sustained up to wk52 in responders on secukinumab 150 mg along with improvement in HAQ scores (-0.6=wk24 vs -0.8=wk52) and EULAR remission rates (DAS28-CRP ≤ 2.6: 30% = wk24 vs 40% = wk52). Non-responders did not gain much additional efficacy benefit after dose escalation as assessed by ACR20/50/70 and DAS28-CRP. The overall rates of AEs from wk20 - 60 were comparable to those observed up to wk20 (60-70%) and most AEs were mild to moderate in severity and did not lead to study discontinuation. Between wk 20 - 60 the rate of infections was 31.9% with six infections reported as SAEs. A total of 28 SAEs were reported in 21 patients. In this period, three malignancies and no deaths were reported.

**Conclusions:** The primary efficacy endpoint was not achieved in this study. ACR20 responders at wk16 showed sustained improvement of

efficacy through wk52 with highest efficacy in patients who remained on 150 mg throughout the study. DAS28-CRP and HAQ scores improved through week 52 in responders who remained on secukinumab 150 mg. There were no safety signals with secukinumab related to specific organ class and the rate and frequency of AEs remained stable over time with no unexpected safety findings.

**Disclosure statement:** P.D. received research grants from Abbott, Roche, Schering-Plough and Wyeth, and is a member of the speakers bureaus of Abbott, Centocor, Roche, Schering-Plough, UCB and Wyeth. M.G. received research grants and consultancy fees from Novartis. S.H. is an employee of, and holds stock, stock options or bond holdings in, Novartis. G.L. is an employee of Novartis. S.M. is an employee of, and holds stock, stock options or bond holdings in, Novartis. H.R. is an employee of Novartis. All other authors have declared no conflicts of interest.

#### O18. WITHDRAWAL OF ADALIMUMAB IN EARLY RHEUMATOID ARTHRITIS PATIENTS WHO ATTAINED STABLE LOW DISEASE ACTIVITY WITH ADALIMUMAB PLUS METHOTREXATE: RESULTS OF A PHASE 4, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Arthur Kavanaugh<sup>1</sup>, Paul Emery<sup>2</sup>, Roy Fleischmann<sup>3</sup>, Ronald Van Vollenhoven<sup>4</sup>, Karel Pavelka<sup>5</sup>, Patrick Durez<sup>6</sup>, Benoît Guérette<sup>7</sup>, Sourav Santra<sup>8</sup>, Laura Redden<sup>8</sup>, Hartmut Kupper<sup>9</sup> and Josef S. Smolen<sup>10</sup>

<sup>1</sup>Division of Rheumatology, Allergy and Immunology, University of California, San Diego, La Jolla, California, United States of America;

<sup>2</sup>Department of Rheumatology, Leeds Teaching Hospital, Leeds, United Kingdom; <sup>3</sup>Department of Rheumatology, University of Texas

Southwestern, Dallas, Texas, United States of America; <sup>4</sup>Department of Rheumatology, The Karolinska Institute, Stockholm, Sweden;

<sup>5</sup>Department of Rheumatology, Charles University, Prague, Czech Republic; <sup>6</sup>Department of Rheumatology, Université Catholique de

Louvain, Louvain, Belgium; <sup>7</sup>GPRD, Abbott, Rungis, France; <sup>8</sup>GPRD, Abbott, Abbott Park, Illinois, United States of America; <sup>9</sup>GPRD,

Abbott, Ludwigshafen, Germany; <sup>10</sup>Department of Rheumatology, Medical University of Vienna and Hietzing Hospital, Vienna, Austria

**Background:** Treatment with adalimumab (ADA)+methotrexate (MTX) has been shown to be effective in inducing low disease activity (LDA) or remission in early, active, MTX-naïve RA pts. This study assessed outcomes after 52 weeks of double-blind withdrawal or continuation of ADA in early RA pts who achieved a stable LDA target (DAS28 <3.2 at wks 22 & 26) with initial ADA+MTX.

**Methods:** MTX-naïve pts ≥18 years old with RA <1 year and DAS28(CRP) > 3.2, ESR ≥ 28 mm/hr or CRP ≥ 1.5 mg/dL, and either >1 erosion, RF+, or anti-CCP+ were randomized to ADA+MTX (n=515) or PBO+MTX (n=517) for 26 wks (Period 1, P1). Pts who achieved the stable LDA target were re-randomized to continue ADA+MTX [ADA+MTX(R)→ADA+MTX] or have ADA withdrawn [ADA+MTX(R)→PBO+MTX] for an additional 52 wks (P2). Clinical, radiographic, and functional outcomes were evaluated. Logistic regression was used to determine baseline (BL) predictors of stable composite outcomes (DAS28 < 2.6 or SDAI ≤ 3.3, and HAQ < 0.5, and ΔmTSS ≤ 0.5 from wks 52-78) in ADA+MTX(R)→PBO+MTX pts. Pts were monitored for adverse events (AEs).

**Results:** Of 466 ADA+MTX pts completing P1, 207 (44%) achieved the stable LDA target and were re-randomized to ADA+MTX(R)→PBO+MTX (n=102) or ADA+MTX(R)→ADA+MTX (n=105). Mean BL characteristics were similar for the two groups (RA duration 3.9 mos, DAS28 5.9/5.7, CRP 28.4/23.5 mg/L, TJC68 25.5/23.3, SJC66 16.4/15.4, HAQ 1.62/1.39, and mTSS 12.2/10.8). Outcomes at wk 78 were generally comparable, although significantly more ADA+MTX(R)→ADA+MTX pts achieved higher levels of disease control, and numerically fewer pts had radiographic progression (Table). Only lower BL HAQ predicted achieving stable composite outcomes from wks 52-78 (P < .01) in ADA+MTX(R)→PBO+MTX pts. AEs [n (%)] in 863 pts with any ADA exposure: SAEs, 106 (12.3); serious infections, 35 (4.1); malignancies, 11 (1.3) including

TABLE 1. Outcomes at Week 78 (LOCF unless otherwise specified)

Treatment group	ACR20/50/70, %	DAS28 <3.2, %	DAS28 <2.6, %	SDAI ≤11, %	SDAI ≤3.3, %	ΔmTSS ≤0.5, %*	mean ΔmTSS*	mean HAQ
ADA + MTX(R)→PBO + MTX	94/80/65	81	66	84	51	81	0.3	0.35
ADA + MTX(R)→ADA + MTX	95/89/77	91	86	92	62	89	0.1	0.33
P value	.72/11/.05	.04	.001	.07	.1	.06	.69	.66

\* Multiple imputation.

nonmelanoma skin cancer, 4 (0.5); opportunistic infections (excluding TB), 8 (0.9); confirmed TB, 4 (0.5); deaths, 9 (1.0).

**Conclusions:** Most MTX-naïve pts with early, active RA who achieved stable LDA after 26 wks of ADA+MTX treatment maintained good clinical, radiographic, and functional responses through wk 78 upon removal of ADA. Lower HAQ at BL predicted stable disease remission, normal function, and no radiographic progression. More pts who remained on ADA+MTX achieved higher levels of disease control compared with pts who had ADA removed, suggesting that certain pts may benefit from continued ADA+MTX therapy.

**Disclosure statement:** P.D. is a member of the speakers bureau of BMS. P.E. is a consultant to Abbott, Merck, Pfizer, Roche and BMS.

R.F. received grant/research support from, and was a consultant to, Abbott. B.G. is an employee of, and possible stock/option holder in, Abbott. A.K. is a consultant to Abbott. H.K. is an employee of, and possible stock/option holder in, Abbott. K.P. is a member of the speakers bureaus of Abbott, Roche, MSD and BMS. L.R. is an employee of, and possible stock/option holder in, Abbott. S.S. is an employee of, and possible stock/option holder in, Abbott. J.S. received grant/research support, and is a consultant to, Abbott. R.V. received research support from, and is a consultant to, Abbott, Glaxo SmithKline, Merck, Pfizer, Roche and UCB. All other authors have declared no conflicts of interest.



Wednesday 2 May 2012, 11.45 – 13.15

# BSR AND BHPR ORAL PRESENTATION OF ABSTRACTS

## ORAL ABSTRACTS 4: BHPR

### O19. THE IMPACT OF PAIN ON SUCCESSFUL AGEING

Ross Wilkie<sup>1</sup>, Abdelouahid Tajar<sup>2</sup> and John McBeth<sup>1</sup>

<sup>1</sup>Keele University, Keele, United Kingdom; <sup>2</sup>Centre for Statistics in Medicine, Oxford University, Oxford, United Kingdom



**Background:** With population ageing there is a growing drive to promote a healthier old age and ways to age successfully. Successful ageing is a multi-faceted state, which involves preservation of biomedical, physical, psychosocial and lay components to enable cognitive, physical and mental well-being, social participation and quality of life. Musculoskeletal pain is common in older adults and is considered as a stressor which impacts on a number of body functions. This is the first longitudinal study to investigate the relationship between musculoskeletal pain and successful ageing in the general population.

**Methods:** Population-based prospective cohort study of adults aged 50 years and over, the North Staffordshire Osteoarthritis project was conducted. Subjects were those who had completed questionnaires at baseline, 3 and 6-year follow-ups. Based on their reports of pain, subjects (n=2949) were classified into those reporting no, regional and widespread pain (ACR criteria). Using published methodology a 33-item successful ageing index (SA) was constructed by summing the number of deficits across biological, psychological and functional domains. SA scores were calculated for each subject at baseline, 3 and 6 years by dividing the number of deficits by the total number of potential deficits and was expressed as a score from 0 to 100. Linear regression models were used to test the association between SA in each time point and pain status at baseline. Mixed modelling was used to explore the longitudinal trends in SA across six years; pain was included as a time varying variable to examine the impact of change in pain status on SA. These associations were then adjusted for potential confounders: gender, education and baseline social networks, use of analgesia and diagnoses of chronic musculoskeletal conditions (osteoarthritis and inflammatory arthropathies).

**Results:** Median age of subjects was 61 (IQR: 55 to 67). 54% were female. At baseline 834 (28.7%) had no pain, 1296 (44.5%) had regional pain and 780 (26.8%) had widespread pain. Baseline regional and widespread pain were associated with higher SA scores at all three time points ( $p < 0.05$ ); those with widespread pain had the highest scores. Increasing pain was associated with increasing SA scores over time; an increase from none to regional and regional to widespread pain resulted in a 19% and 17% increase in SA scores respectively. An increase from none to widespread lead to a 40% increase in SA score. Adjustment for diagnosed musculoskeletal conditions and analgesic use had little effect on the impact of pain on increasing SA scores.

**Conclusions:** The results indicate that pain has a significant adverse affect on successful ageing. At baseline, individuals with regional and widespread pain had accumulated significantly more signs of less successful ageing than those with no pain. The longitudinal results indicate that increasing pain significantly accelerates the rate of less successful ageing, independent of diagnoses and analgesia.

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

### O20. FOREFOOT BURSAE ARE A PROGNOSTIC INDICATOR OF DISABLING FOOT COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS OF A PROSPECTIVE THREE-YEAR STUDY

Lindsey S. Hooper<sup>1,2</sup>, Catherine J. Bowen<sup>1,2</sup>, Lucy Gates<sup>1,2</sup>, David Culliford<sup>1</sup>, Christopher J. Edwards<sup>1,2</sup> and Nigel K. Arden<sup>2,3</sup>

<sup>1</sup>Faculty of Health Sciences, University of Southampton, Southampton, United Kingdom; <sup>2</sup>Rheumatology, Southampton University Hospitals NHS Trust, Southampton, United Kingdom;

<sup>3</sup>Nuffield Department of Orthopaedics, Rheumatology and



Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom

**Background:** Foot complications represent a significant burden to patients with RA in terms of pain, but also because of the disabling nature of impaired mobility. There is limited evidence to suggest which patients may go on to experience the greatest burden of disability and what factors may be clinically relevant treatment targets in the prevention and management of such cases. Thus, the study aim was to determine the natural history of foot related disability in patients with RA. A secondary aim was to identify potential explanatory variables either associated with or predictive of disabling foot complications in patients with RA.

**Methods:** Patients with RA were consecutively, prospectively recruited from a Southampton rheumatology outpatient clinic. Data collection was completed at baseline (N = 149), one-year (n = 120) and three-year follow-up (n = 60). Patient-reported disabling foot complications were evaluated using the two subscales of the Foot Impairment Score; foot impairment/footwear restriction (FISIF) & activity limitation/participation restriction (FISAP), and a visual analogue scale of overall wellbeing. Explanatory variables investigated included ultrasound detectable forefoot pathology and markers of disease activity. The main statistical methods used were multiple linear regression and tests of linear association (Pearson's Correlation coefficient; PCC).

**Results:** Overall patient-reported disabling foot complications were highly prevalent across all time points (Table 1). Changes in foot impairment and activity limitation were significantly associated with fluctuations in disease activity (FISIF: DAS28-ESR PCC = 0.455,  $p = 0.000$ ; ESR PCC = -0.356,  $p = 0.008$ , FISAP: DAS28-ESR PCC = 0.433,  $p = 0.001$ ; ESR PCC = -0.439,  $p = 0.001$ ), and approaching a significant association with changes in forefoot bursae (FISIF: PCC = 0.255,  $p = 0.063$ ; FISAP: PCC = 0.255,  $p = 0.063$ ). Disease duration and forefoot bursae prevalence were identified as significant prognostic indicators of foot impairment ( $p = 0.009$ ,  $p = 0.012$  respectively), explaining 16% of score variability in the final regression model ( $R^2 = 0.16$ ). Disease duration, forefoot bursae and erosion prevalence were identified as significant prognostic indicators of activity limitation ( $p = 0.006$ ,  $p = 0.019$ ,  $p = 0.002$ , respectively), explaining 35% of score variability in the final regression model ( $R^2 = 0.35$ ). No factors were identified as significant predictors of overall wellbeing.

**Conclusions:** Forefoot bursae are both predictive of and associated with patient reported disabling foot complications longitudinally, and may represent a relevant treatment target and prognostic indicator of long term foot health.

TABLE 1. Longitudinal changes in patient-reported disabling foot complications

	BASELINE Mean, (SD), Range	YEAR ONE Mean,(SD), Range	YEAR THREE Mean,(SD), Range
FISIF	10.7 (4.8), 0-20	10.4 (5.1), 0-20	10.4 (5.1), 0-20
FISAP	16.9 (10.3), 0-29	17.3 (9.9), 0-30	17.4 (9.8), 0-30

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

### O21. THE CONTINUING PROFESSIONAL DEVELOPMENT FOR HEALTH PROFESSIONALS WORKING WITHIN MUSCULOSKELETAL SERVICES: A NATIONAL UK SURVEY

Jo Adams<sup>1</sup>, Sarah Ryan<sup>2</sup>, Hannah Haywood<sup>1</sup> and Helen Pain<sup>1</sup>

<sup>1</sup>Faculty of Health Sciences, University of Southampton, Southampton, United Kingdom; <sup>2</sup>Staffordshire Rheumatology Centre, Haywood Hospital, Stoke-on-Trent, United Kingdom

**Background:** Musculoskeletal health care professionals have expressed concern at the increased difficulties in undertaking continuing professional development (CPD). CPD includes 'a wide range of learning activities through which professionals maintain and develop throughout their career to ensure that they retain their capacity to practise safely, effectively and legally within their evolving scope of practice'. It is conducted to 'provide the best possible care for patients' and can include formal or informal activities. CPD is a



requirement in many countries for nurses and AHPs, although recommendations for the time spent on CPD varies, from no specific time requirements for UK AHPs to 35 hours over three years for UK Nurses.

**Methods:** This electronic survey explored the current UK status of CPD, for nurses and AHPs working in musculoskeletal services. It formed the second phase of a two part research project funded by Arthritis Research UK. The first phase used three focus groups and two telephone conference calls to explore patients, clinicians and managers experiences of CPD within MSK services. These findings informed the content and development of this electronic questionnaire survey. The survey was designed using Question Mark Perception, administered from the University of Southampton and distributed via professional bodies and BHPR. Results were collected online and analysed in SPSS PASW 17 using frequency data and  $\chi^2$  analyses.

**Results:** 354 responses were analysed, (51.7% physiotherapists; 30.2% occupational therapists; 9.9% podiatrists; 7.3% nurses; 0.9% other). 63.8% of responders worked exclusively in the NHS. 81% worked in England, 14% in Scotland; 4% in Wales and 2% in Northern Ireland. 84% of respondents had more than five years' experience working with patients who have musculoskeletal conditions.

The most frequent reported reasons for undertaking CPD was to improve patient care (56%) maintenance of clinical skills (37%) and to stay up to date (28%). The majority of respondents reported that their organization was supportive of CPD activities and in applying new knowledge to practice (86%) however, the most frequently reported barriers to CPD included lack of funding (78%) and within this group 24% reported no available CPD funding. 68% reported having too many other tasks including meeting productivity targets and 42% reported that they could only "sometimes or never" secure CPD study leave. There were no statistically significant differences in seniority level nor employment sector in accessing CPD opportunities.

**Conclusions:** The results indicate that despite the organizational support for CPD respondents faced substantial challenges accessing CPD when under pressure to achieve productivity targets, with little assistance in terms of funding. This discrepancy may indicate that greater support is required for musculoskeletal nurses' and AHPs' CPD needs.

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

#### O22. DEBRIDEMENT OF PAINFUL FOREFOOT PLANTAR CALLOSITIES IN RHEUMATOID ARTHRITIS: THE CARROT RANDOMIZED CONTROLLED TRIAL



Heidi J. Siddle<sup>1,2</sup>, Anthony C. Redmond<sup>1</sup>, Robin Waxman<sup>1</sup>, Abigail R. Dagg<sup>3</sup>, Begonya Alcacer-Pitarch<sup>1</sup>, Richard A. Wilkins<sup>1</sup> and Philip S. Helliwell<sup>1</sup>

<sup>1</sup>Division of Musculoskeletal Disease, University of Leeds, Leeds, United Kingdom; <sup>2</sup>Foot Health Department, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; <sup>3</sup>Podiatry Department, The Mid Yorkshire Hospitals NHS Trust, Wakefield, United Kingdom

**Background:** Foot pain is common in rheumatoid arthritis (RA). Symptoms often occur, due to hard callus arising as a result of increased pressure over the plantar metatarsal head. Sharp scalpel debridement of painful plantar callosities is a standard treatment to relieve discomfort but it carries risks of haemorrhage, ulceration and introduction of infection. Furthermore, debridement is rarely the sole course of treatment; functional orthotic therapy and footwear advice/provision may also be used. Recently, the short-term benefits of callus reduction for people with RA were called into question.

**Methods:** 65 patients with RA and presenting with painful forefoot plantar callosities for the first time were randomized to receive one of two treatment protocols. The treatment arm comprised regular debridement of painful forefoot plantar callosities in conjunction with mechanical interventions (e.g. orthoses, footwear) while the control arm comprised mechanical interventions alone. The primary outcome was a reduction in pain on a 100 mm visual analogue scale. Secondary outcomes included health status (Leeds Foot Impact Scale, a disease-specific scale for measuring the impact of foot disease in 2 domains: impairment/footwear (LFIS<sub>F</sub>) and activity/participation (LFIS<sub>AP</sub>)), ambulatory function (velocity measured by GAITrite) and complication rates (ulceration, infection). Patients were followed up for 18 months.

**Results:** The mean baseline and 18 month follow-up pain scores were 40.8 and 22.3, respectively, for the treatment group and 53.4 and 34.0, respectively, for the control group. There was no difference between groups in the primary outcome of pain, allowing for differences in baseline scores ( $F=1.2$ ,  $p=ns$ ). Mean baseline and follow-up GAITrite velocity scores were 90.1 and 89.8 cm/sec for the treatment group and 85.7 and 88.5 cm/sec for the control group. In the treatment

group, mean baseline LFIS<sub>F</sub> score was 12.2 and follow-up was 11.3, mean baseline LFIS<sub>AP</sub>, was 15.3 and follow-up was 15.7. In the control group, mean baseline LFIS<sub>F</sub> score was 14.1 and follow-up was 13.2, mean baseline LFIS<sub>AP</sub>, was 18.0 and follow-up was 16.1. Secondary outcomes of health status and ambulatory function also showed no differences between groups. Complication rates were infrequent in both groups.

**Conclusions:** Sharp scalpel debridement of painful forefoot plantar callosities in conjunction with mechanical interventions in RA reduced pain, but the effect was no different from the use of mechanical interventions alone. The long-term outcomes were consistent with previous study findings and further question the efficacy of sharp scalpel debridement of painful forefoot plantar callosities in people with RA.

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

#### O23. PSYCHOLOGICAL WELL-BEING IN EARLY RHEUMATOID ARTHRITIS: FINDINGS FROM THE EARLY RHEUMATOID ARTHRITIS NETWORK



Sam Norton<sup>1</sup>, Patrick Kiely<sup>3</sup>, David Walsh<sup>4</sup>, Richard Williams<sup>5</sup> and Adam Young<sup>2</sup>

<sup>1</sup>Institute of Public Health, University of Cambridge, Cambridge, United Kingdom; <sup>2</sup>Rheumatology Department, City Hospital, St Albans, United Kingdom; <sup>3</sup>Department of Rheumatology, St George's Healthcare NHS Trust, London, United Kingdom; <sup>4</sup>Department of Rheumatology, Sherwood Forest Hospitals NHS Foundation Trust, Nottingham, United Kingdom; <sup>5</sup>Department of Rheumatology, Hereford Hospitals NHS Trust, Hereford, United Kingdom

**Background:** Psychological well-being in rheumatoid arthritis is known to be reduced compared to the general population. The aim of this study is to examine longitudinal changes in psychological well-being, normed against the general population, in a large sample of patients with recent onset RA. Factors related to psychological well-being at presentation and changes in psychological well-being over 5 years are assessed.

**Methods:** Data are from the Early Rheumatoid Arthritis Network (ERAN), a prospective observational cohort recruiting DMARD naïve patients at presentation from 21 centres in the UK and Ireland. In total, 1235 patients were recruited between 2002 and September 2011. Patients were re-assessed after 3-6 months, 12 months and then yearly. Psychological well-being was assessed using the SF36 Mental Health scale (SF36-MH). Scores on the SF36-MH scales were normed against the UK general population (mean = 50, SD = 10). Mixed effects models, incorporating random effects for the baseline level of distress and linear change, were used to model changes in SF36-MH scores over the first 5 years of follow-up.

**Results:** Mean age at onset was 57.1 years and 68% were female. At presentation to the rheumatologist the mean normed SF36-MH scores was 46.6 (SD = 11.1). Indicating psychological well-being to be significantly reduced compared to the general population ( $t(955) = -9.27$ , Cohen's disease =  $-0.33$ ,  $p < .001$ ). Younger age ( $b = .09$ ,  $p < .001$ ), higher baseline CRP ( $b = .89$ ,  $p = .009$ ), worse baseline functional disability (HAQ;  $-2.10$ ,  $p < .001$ ), and worse baseline SF36 Vitality score ( $b = .45$ ,  $p < .001$ ) were all significantly related to worse baseline SF36-MH score in multivariate analysis. On average, psychological well-being improved by .50 units per year ( $z = 3.90$ ,  $p < .001$ ). By 3 years SF36-MH scores were not significantly reduced compared to the general population (mean = 49.0,  $t(415) = -1.70$ , Cohen's disease =  $-0.10$ ,  $p = .091$ ). Significant heterogeneity was observed in the rate of change across individuals ( $z = 2.49$ ,  $p = .013$ ). Improvements in psychological well-being were attenuated by higher baseline BMI ( $b = -.04$ ,  $p = .046$ ) and increased age ( $b = -.02$ ,  $p = .022$ ). Greater improvements in psychological well-being were seen in individuals with low baseline SF36 Vitality scores ( $b = -.05$ ,  $p = .001$ ), providing some indication of regression to the mean.

**Conclusions:** Psychological well-being in early RA, prior to the use of disease-modifying therapy, is reduced compared to the general population. Over time psychological well-being normalizes, taking longer in those with high BMI and increased age.

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

**O24. HEALTH PROFESSIONALS' PERCEPTIONS OF THE EFFECTS OF EXERCISE ON JOINT HEALTH IN RHEUMATOID ARTHRITIS PATIENTS II: A FOLLOW-UP FOCUS GROUP STUDY**



Serena Halls<sup>1</sup>, Rebecca-Jane Law<sup>1</sup>, Jeremy Jones<sup>1,2</sup>, David Markland<sup>1</sup>, Peter Maddison<sup>1</sup> and Jeanette Thom<sup>1</sup>

<sup>1</sup>School of Sport, Health and Exercise Sciences, Bangor University, Bangor, United Kingdom; <sup>2</sup>Rheumatology, Betsi Cadwaladr University Health Board, Bangor, United Kingdom

**Background:** Exercise is important in the management of RA. Our research has indicated that RA patients perceive health professionals (HPs) lack certainty and clarity about exercise in RA management and its relationship to joint damage (Law et al., 2010). Furthermore, our questionnaire study of rheumatology HPs suggested that perceptions of HPs and patients are not congruent (Halls et al., 2011). We therefore set out to further explore HPs' perceptions regarding the effects of exercise on joint health in RA patients' using focus groups.

**Methods:** Four moderated focus groups were conducted with multidisciplinary teams (MDTs) of rheumatology HPs (n = 24; 19 females, 5 males; 5 rheumatologists, 8 nurses, 5 physiotherapists, 4 occupational therapists, 2 other HPs; age: 30 - 60 years; duration working with RA: 3 - 32 years) from across the North-West United Kingdom. The main questions addressed included: (i) What are your thoughts about exercise and joint health in your RA patients? (ii) What do you tell your RA patients about exercise? and (iii) Why do the perceptions of patients and HPs differ? Focus group recordings were transcribed verbatim and transcripts were analysed using framework analysis. Discussion with three associated researchers consolidated validation at different stages of analysis.

**Results:** Focus group analysis identified twenty one constructs and five themes as factors relating to HPs' perceptions of exercise and joint health in their RA patients. The five emergent themes were: 'Exercise is beneficial', 'Concerns about damage to joints', 'Patients have barriers to exercise', 'HP knowledge differs' and 'Patients may think service delivery is vague'.

**Conclusions:** HPs articulated acute awareness of the benefits and importance of exercise for RA patients. Concerns regarding exercise, particularly weight-bearing exercise, were expressed explicitly, as well as indirectly, which could lead to confusion for RA patients. The perceived lack of a solid evidence base was highlighted as a reason for these concerns. Moreover, the complexity of RA treatment and management was felt to negatively impact the likelihood of exercise prescription. When managing RA, HPs provide individualized care and promote self-management. These issues may explain why patients perceive their MDTs lack certainty and clarity about exercise in RA management and its relationship to joint damage. Further research is warranted to address the uncertainties of HPs regarding exercise and joint health.

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

recently diagnosed (<15 months) SLE patients from 30 centres across 11 countries since 2000. Baseline and annual assessments record clinical, laboratory and therapeutic data according to a standardized protocol. MetS was defined according to the 2009 Consensus Statement from the International Diabetes Federation which requires any 3 of the following 5 criteria to be met: elevated race-specific waist circumference (MetS WC); elevated triglycerides or on specific therapy (MetS TG); reduced HDL-cholesterol or on specific therapy (MetS HDL); elevated blood pressure or on specific therapy (MetS BP); elevated fasting glucose or diabetes mellitus (MetS Glucose).

**Results:** To date 1686 patients have been recruited of whom 1506 (89.3%) were female and the mean (SD) age at enrolment was 35.2 (13.4) years old. 45.1% of patients were Caucasian, 16.1% were of African backgrounds and 15.2% were Hispanic. Mean (SD) prednisolone dose was 24.1 (16.8) mg at enrolment, 24.4 (19.8) mg at year 1 and 16.2 (15.5) mg at year 2. Of the 1494 (86.6%) patients with sufficient data to determine their MetS status at enrolment 245 (16%) had MetS, falling to 193/1065 (12.6%) at year 1 and 207/894 (13.5%) at year 2. Of the 720 patients with complete MetS data over the first 2 years, 526 (73%) never developed MetS, 84 (12.1%) had MetS on at least 2 occasions and 31 (4.4%) had MetS at every visit. Table 1 shows the prevalence of each MetS component over time in those with MetS data. Whilst the prevalence of elevated waist circumference and blood pressure remains stable, the prevalence of both elevated glucose and triglycerides fell over time.

**Conclusions:** MetS was common in this cohort of young, predominantly female, patients with recently diagnosed SLE. Overall, 27% had MetS on at least 1 occasion during the first 2 years of follow-up. Certain components of MetS vary over time in SLE patients and may be more responsive to changes in inflammatory disease burden and exposure to therapy.

TABLE 1. MetS phenotype over time

	Enrolment (%) Total n = 1494	Year 1 (%) Total n = 1065	Year 2 (%) Total n = 894
MetS IDF 2009	16	12.6	13.5
MetS WC	48.4	50.8	49.3
MetS BP	46.0	48.5	50.6
MetS TG	46.1	36.8	39.2
MetS HDL	59.1	54.6	55.3
MetS Glucose	20.2	14.1	13.4

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

**O26. NITRATED NUCLEOSOME LEVELS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: ASSOCIATIONS WITH ETHNICITY, AUTOANTIBODY STATUS AND ETHNICITY**

Sara C. Croca<sup>1</sup>, Charis Pericleous<sup>1</sup>, Harry Yong<sup>1</sup>, David Isenberg<sup>1</sup>, Ian Giles<sup>1</sup>, Anisur Rahman<sup>1</sup> and Yiannis Ioannou<sup>1</sup>

<sup>1</sup>Rheumatology, University College London, London, United Kingdom

**Background:** Many different autoantibodies have been described in patients with SLE and serological assays have concentrated mainly on measuring autoantibody levels. Measuring levels of modified autoantigens may also be valuable. Nucleosomes from apoptotic debris are known to play a key role in pathogenesis of SLE, especially lupus nephritis. Nitration of histones within nucleosomes may be enhanced in patients with SLE by the presence of increased serum levels of reactive nitrogen species characteristic of inflammatory states. We developed a novel assay for measuring serum nitrated nucleosome (NN) levels. Here we report on results of this assay in patients with SLE and associations with ethnicity, autoantibody profile and measures of disease activity in patients with SLE.

**Methods:** Multiple stored serum samples (mean 8 per patient) from a cohort of 49 patients with SLE were tested. The samples had been obtained over a mean (SD) follow-up period of 89 (46) months. NN levels were measured using a novel capture ELISA: serum added to a streptavidin plate pre-coated with a biotinylated anti-nitrotyrosine antibody followed by detection with a rabbit anti-histone-3 antibody and then an anti-rabbit IgG HRP conjugated antibody. OD values were converted to standard absorbance units (AU) by comparison to a positive control sample loaded on every plate. The mean absorbance value for each of the patients was calculated. Univariate analysis was used to investigate association between these levels and age, gender, ethnicity, disease duration, autoantibody status and disease activity. For all samples where data were available, we obtained anti-dsDNA and complement C3 levels and disease activity from a matching date and from the previous 3 assessments if these had occurred in the preceding 12 months. Using the British Isles Lupus Assessment Group (BILAG) index, we categorized the samples by disease activity as

**ORAL ABSTRACT 5: CONNECTIVE TISSUE DISEASES**

**O25. VARIABILITY IN THE PHENOTYPE OF METABOLIC SYNDROME OVER TIME IN A MULTICENTRE INTERNATIONAL INCEPTION COHORT OF PATIENTS WITH SLE**

Ben Parker<sup>1</sup>, Murray B. Urowitz<sup>3</sup>, Dafna D. Gladman<sup>3</sup> and Ian Bruce<sup>1,2</sup>, on Behalf of the SLICC Registry<sup>3</sup>

<sup>1</sup>Arthritis Research UK Epidemiology Unit, University of Manchester, Manchester, United Kingdom; <sup>2</sup>Kellgren Centre for Rheumatology, Manchester Royal Infirmary, Manchester, United Kingdom; <sup>3</sup>Centre for Prognosis Studies, Toronto Western Hospital, Toronto, Ontario, Canada

**Background:** The metabolic syndrome (MetS) is a clustering of metabolic abnormalities associated with an increased risk of developing diabetes and atherosclerosis. MetS may also contribute to the increased cardiovascular risk seen in SLE. We examined the prevalence and phenotype of MetS over the first 2 years of follow-up in a multicentre international inception cohort of patients with SLE.

**Methods:** The Systemic Lupus International Collaborating Clinics Registry for Atherosclerosis (SLICC-RAS) inception cohort enrolled



follows. Current activity (on the date of the sample) was defined as high if global BILAG score was  $\geq 5$  and low if it was  $< 5$ . Disease activity over the most recent 4 assessments was characterized as persistently low activity (all systems BILAG C, D or E) or persistently moderate-high activity (A or  $\geq 1$  B in any BILAG system on at least 2/4 occasions). 90% of all samples fell into one of those two categories and the rest were excluded. Anti-dsDNA was defined as high or normal based on a cut-off of 50 IU/ml. C3 was defined as low or normal based on a cut-off of 0.9 g/l.

Results: The assay yielded reproducible results with an intra and inter-plate coefficient of variation of  $< 10\%$ . The mean age of the patients was 36 years (SD 13) and 81% were female. 23 were Caucasian, 18 Afro-Caribbean (A-C) and 8 other ethnicities. 17 patients had no NN at any time-point. In the other 34 patients, NN levels varied over time (mean 32.4 AU; SD 62.2; min 0; max 270.4). Age, gender and disease duration were not associated with NN level. A-C patients had significantly higher NN than other ethnic groups ( $p = 0.03$ ). Anti-Sm positivity was strongly associated with higher NN levels. Mean NN was 103.5 AU in anti-Sm positive and 7.75 AU in anti-Sm negative patients ( $p < 0.0001$ ). The apparent effect of ethnicity may be mediated via anti-Sm positivity since A-C patients were significantly more likely than other ethnic groups to be anti-Sm positive ( $p = 0.04$ ) and within the A-C group, anti-Sm positive patients had significantly higher NN levels than anti-Sm negative patients ( $p = 0.0004$ ). There was no relationship between NN levels and positivity for anti-La, anti-Ro, anti-RNP or antiphospholipid antibodies.

As shown in table 1, higher NN levels were significantly associated with current and persistently high activity, low C3 and high anti-dsDNA. In addition, we categorized the samples in terms of activity in individual systems. The highest mean NN levels were seen in patients with neuropsychiatric flares ( $n = 18$ , NN = 54.9) and general flares ( $n = 31$ , NN = 50.3) whereas the lowest were seen in those with mucocutaneous ( $n = 41$ , NN = 26.2) and cardiovascular ( $n = 13$ , NN = 23.2) flares.

**Conclusion:** NN were found in the serum of 65% of patients with SLE. Anti-Sm positivity and Afro-Caribbean ethnicity were associated with significantly higher NN levels. High NN levels were also associated with high disease activity, high anti-dsDNA and low complement. In addition, flares in different organ systems may be associated with different levels of NN.

TABLE 1.

	Number of samples (n)	Mean (SD) NN level	p-value (high vs. low)
Persistently moderate-high activity	188	40.50 (51.7)	0.038
Persistently low activity	154	24.8 (72.3)	
BILAG $< 5$	204	25.6 (57.3)	0.045
BILAG $\geq 5$	171	37.9 (69.3)	
Anti-dsDNA			
High ( $> 50$ IU/ml)	171	29.0 (48.1)	0.035
Normal ( $\leq 50$ IU/ml)	177	21.9 (38.6)	
C3			
Normal ( $\geq 0.9$ g/l)	207	20.8 (40.6)	$< 0.0001$
Low ( $< 0.9$ g/l)	138	31.6 (47.0)	

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

#### 027. IS THERE AN ASSOCIATION BETWEEN WARFARIN AND SURVIVAL IN SSC-PAH PATIENTS TREATED WITH FIRST-LINE BOSENTAN MONOTHERAPY?

Clare E. Warrell<sup>1</sup>, David Dobarro<sup>1</sup>, Clive Handler<sup>1</sup>, Christopher P. Denton<sup>2</sup>, Benjamin E. Schreiber<sup>1</sup> and John G. Coghlan<sup>1</sup>  
<sup>1</sup>Pulmonary Hypertension, Royal Free Hampstead NHS Trust, London, United Kingdom; <sup>2</sup>Rheumatology, Royal Free Hampstead NHS Trust and UCL Medical School, London, United Kingdom

**Background:** Bosentan monotherapy is a commonly used first line therapy in systemic sclerosis associated pulmonary arterial hypertension (SSc-PAH) but there is limited data on survival in this rare patient group. Some case series have suggested a possible survival benefit in patients with idiopathic pulmonary arterial hypertension who are treated with warfarin, however little is known about its effect in patients with SSc-PAH. By studying a well defined patient cohort treated with the same PH-specific therapy, we hoped to identify whether warfarin treatment was associated with improved survival.

**Methods:** A retrospective analysis of consecutive patients with newly diagnosed SSc-PAH at a large regional centre from 2003-July 2010. Inclusion criteria were: systemic sclerosis and treatment naïve PAH (mPAP  $\geq 25$  mmHg, PCWP  $\leq 15$ ) when starting bosentan monotherapy. Patients with evidence of significant interstitial lung disease on imaging (HRCT) or lung function tests (FVC  $< 70\%$ ) were excluded. Survival

distributions were measured using Cox-Mantel log rank test. Kaplan-Meier survival estimates were used to investigate the influence of variables on survival.

**Results:** 125 patients were identified. The mean age was 63 (range 23-85) and 88% were female (ratio F:M 7.3:1). Disease subtype was LcSSc in 116 patients (93%) and DcSSc in 9 patients (7%). Mean haemodynamic values at initial right heart catheterization were mPAP 40 mmHg and PVR 580 dyns.s.cm-5.

Univariate cox regression analysis showed the following factors were not associated with survival: gender ( $p = 0.377$ ), age ( $p = 0.086$ ), disease type ( $p = 0.138$ ), baseline NTproBNP ( $p = 0.527$ ), six-minute-walking distance ( $p = 0.114$ ), mPAP ( $p = 0.273$ ), PVR ( $p = 0.538$ ), immunosuppressant therapy ( $p = 0.473$ ) and WHO functional class ( $p = 0.081$ ). Warfarin treatment was the only factor found to have a significant association with better survival (HR 0.43  $p = 0.009$  95%CI 0.23-0.81).

On multivariate analysis after adjustment for age, disease subtype, gender and WHO functional class warfarin remained the only significant prognostic factor (HR 0.50  $p = 0.048$  95%CI 0.026-0.99). Kaplan-Meier survival estimates showed that warfarin was associated with a improved survival (Log-rank  $p = 0.0068$ ).

**Conclusions:** We present a novel finding, that warfarin treatment is associated with a dramatically improved survival in SSc-PAH patients treated with first line bosentan monotherapy. The benefits associated with warfarin may be due to unmeasured confounders, its effect on the disease or interactions between the drugs. Ideally, a randomized controlled trial is required to investigate with the association is causal.

**Disclosure statement:** J.C. has received staff support, consultancy fees, lecture fees and research grants from Actelion, GSK, Pfizer, and consultancy fees and lecture fees from Bayer and Ely Lilly. C.D. has received speaker fees from Pfizer, Actelion and GSK, and consultation and research grants from Pfizer and Actelion. C.H. has received education and travel grants from Actelion and. B.S. has received educational and travel grants from Actelion and GSK, and speaker fees from Actelion. All other authors have declared no conflicts of interest.

#### 028. ANTI-EIF2 IS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS

Zoe E. Betteridge<sup>1,2</sup>, Felix Woodhead<sup>8,3</sup>, Christopher Bunn<sup>4</sup>, Christopher P. Denton<sup>5</sup>, David Abraham<sup>4</sup>, Sujal Desai<sup>6</sup>, Roland du Bois<sup>7</sup>, Athol Wells<sup>3</sup> and Neil McHugh<sup>1,2</sup>  
<sup>1</sup>Bath Institute for Rheumatic Diseases, University of Bath, Bath, United Kingdom; <sup>2</sup>Rheumatology, Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom; <sup>3</sup>National Heart and Lung Institute, Imperial College, London, United Kingdom; <sup>4</sup>Department of Immunology, Royal Free Hospital, London, United Kingdom; <sup>5</sup>Centre for Rheumatology, Royal Free Hospital, London, United Kingdom; <sup>6</sup>Department of Radiology, Kings College Hospital, London, United Kingdom; <sup>7</sup>Medicine, National Jewish Health, Denver, Colorado, United States of America; <sup>8</sup>Respiratory Medicine, University Hospitals Coventry and Warwickshire, Coventry, United Kingdom

**Background:** Positive anti-nuclear autoantibodies (ANAs) occur in 75-95% of Systemic Sclerosis (SSc) patients. The specific SSc autoantibodies (anti-centromere, anti-topoisomerase-1, anti-RNA polymerase III, anti-U3RNP, anti-U11/U12 RNP and anti-To/Th) have been shown to correlate with distinct clinical subsets of patients. Other SSc related autoantibodies (PmScl, Ku, Ro60, La and U1RNP) can be found in a variety of other connective tissue diseases and in SSc patients with overlap features. Despite this vast array of autoantibodies, there remains a group of SSc patients that still appear autoantibody negative. Here we report a new autoantibody in seven patients with SSc.

**Methods:** Serum and clinical data were collected from 379 patients with SSc investigated for interstitial lung disease and a separate 169 unselected SSc patients. Serum was also available from a control population consisting of 171 patients with other forms of connective tissue disease (dermatomyositis, polymyositis, systemic lupus erythematosus and rheumatoid arthritis), 141 patients with idiopathic interstitial lung disease and 88 healthy normal controls. All sera were tested by routine serological techniques followed by radiolabelled protein immunoprecipitation (IPP) for those samples negative for the most common SSc-related autoantibodies, anti-centromere, anti-topoisomerase 1 and anti-RNA polymerase III autoantibodies. Patients' sera that immunoprecipitated a novel 30kDa band were further analysed by indirect immunofluorescence and IPP using depleted cell extracts to establish a common reactivity. A combination of non-radiolabelled IPP and mass spectrometry (MS) was used to identify the novel autoantigen and findings were confirmed using both immunodepletion and IPP-western blotting using commercial antibodies.



**Results:** A novel autoantigen with an estimated molecular weight of 30kDa was recognized by 7 sera with SSc, 6 of whom had confirmed interstitial lung disease, and by no controls. The seventh novel autoantibody-positive patient did not have a chest CT but had a reduced pulmonary gas transfer. Six of the patients had diffuse cutaneous involvement and four had overlap features with other autoimmune diseases (two polymyositis and two RA). None of the seven sera contained other known autoantibodies. Immunodepletion experiments indicated that all seven serum samples immunoprecipitated the same autoantigen and MS analysis identified the novel autoantigen as EIF2 (Eukaryotic Initiation Factor 2). These findings were confirmed by both immunodepletion and immunoprecipitation western blotting using commercial anti-EIF2 antibodies.

**Conclusions:** We report a novel autoantibody (anti-EIF2) found in a small number of patients with SSc (approximately 1%) that appears to be specific for SSc / SSc-overlap and closely associated with the presence of interstitial lung disease. Our findings emphasize the close association between SSc and the development of disease-specific autoantibodies.

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

#### O29. OPTICAL COHERENCE TOMOGRAPHY VALIDATION: A NEW QUANTITATIVE IMAGING BIOMARKER FOR AFFECTED SKIN IN SCLERODERMA

Giuseppina Abignano<sup>1,2</sup>, Sibel Aydin<sup>1</sup>, Concepcion Castillo-Gallego<sup>1</sup>, Daniel Woods<sup>3</sup>, Adam Meekings<sup>3</sup>, Dennis McGonagle<sup>1</sup>, Paul Emery<sup>1</sup> and Francesco Del Galdo<sup>1</sup>

<sup>1</sup>Section of Musculoskeletal Diseases, Leeds Institute of Molecular Medicine, Leeds, United Kingdom; <sup>2</sup>Rheumatology Unit, Second University of Naples, Naples, Italy; <sup>3</sup>Michelson Diagnostics Ltd, Orpington, United Kingdom

**Background:** Skin involvement in systemic sclerosis (SSc) is often primary outcome in clinical trials but it is still orphan of a quantitative imaging technique. Optical Coherence Tomography (OCT) is an emerging imaging technology for clinical examination employing a low-intensity infra-red laser beam and providing high-contrast 2 mm deep skin images with a 4 micron resolution. The purpose of this study was to evaluate face validity of OCT in scleroderma.

**Methods:** Dorsal aspect of forearms was assessed in this study employing topical probe "VivoSight" (Michelson Diagnostics) and optics of Swept-source Fourier-Domain type with a laser wavelength of 1305 +/- 15 nm. A 4 mm area was scanned with 100 scans each of 4 micron thickness. Clinical skin involvement was determined using the modified Rodnan skin score (mRSS). The study included 5 forearms scored as "3", 5 scored as "0" and 5 from healthy controls. Matlab software was employed to calculate mean density of the scans. Haematoxylin-Eosin (H&E) staining was performed from forearm skin biopsy, within 1 cm of OCT scanned region, in two SSc patients.

**Results:** OCT images collected in healthy volunteers showed, consistently with published findings, a regular hyper-reflective border of the skin surface (4 micron) and a homogeneous hypo-reflective epidermal layer (60 micron). The papillary dermis was consistently visualized as hyper-reflective area compared to the adjacent epidermis allowing the visualization of the dermal-epidermal junction (DEJ). Mean Optical Density (OD) data showed that DEJ was a OD nadir region between 60 and 70 micron from the surface, the papillary dermis a high density region (OD range: 0.64-0.72; micron range: 60-100) and the reticular dermis had a OD ranging from 0.72 and 0.4. In contrast SSc affected tissues (mRSS=3) showed no DEJ and no increase in OD in the papillary dermis which appeared with a range density of 0.61-0.56. Interestingly the OD range of this area was almost normal in patients with mRSS=0 (OD=0.64-0.67). Validation with H&E staining of 2 SSc patients with mRSS=3 in the target region, confirmed the localization of the above mentioned density areas.

**Conclusions:** This is a proof-of-concept validation of face validity of OCT as quantitative imaging technique of scleroderma skin. Sensitivity to change ability of OCT is under evaluation to determine whether the technique could be used as outcome measure of skin involvement in SSc.

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

#### O30. THE CLINICAL RELEVANCE OF ANTI-RO52 AND ANTI-RO60 IN PATIENTS IN THE UNITED KINGDOM PRIMARY SJÖGREN'S SYNDROME REGISTRY (UKPSSR)

Josephine Vila<sup>2</sup>, Sheryl Mitchell<sup>2</sup>, Simon Bowman<sup>2</sup>, Elizabeth Price<sup>3</sup>, Colin T. Pease<sup>4</sup>, Paul Emery<sup>4</sup>, Jacqueline Andrews<sup>4</sup>,

Michele Bombardieri<sup>5</sup>, Nurhan Sutcliffe<sup>5</sup>, Constantino Pitzalis<sup>5</sup>, Peter Lanyon<sup>6</sup>, John Hunter<sup>7</sup>, Monica Gupta<sup>7</sup>, John McLaren<sup>8</sup>, Marian Regan<sup>9</sup>, Annie Cooper<sup>10</sup>, Ian Giles<sup>11</sup>, David Isenberg<sup>11</sup>, Saravanan Vadivelu<sup>1,2</sup>, David Coady<sup>1,3</sup>, Bridget Griffiths<sup>2</sup>, Dennis Lendrem<sup>2</sup>, Heather Foggo<sup>2</sup>, Jessica Tarn<sup>2</sup> and Wan-Fai Ng<sup>1</sup>  
<sup>1</sup>Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom; <sup>2</sup>Rheumatology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom; <sup>3</sup>Rheumatology, Great Western Hospitals NHS Foundation Trust, Swindon, United Kingdom; <sup>4</sup>Section of Musculoskeletal Disease, Leeds Institute of Molecular Medicine, University of Leeds, Leeds, United Kingdom; <sup>5</sup>Rheumatology, Barts and the London NHS Trust UK, London, United Kingdom; <sup>6</sup>Rheumatology, Nottingham University Hospital, Nottingham, United Kingdom; <sup>7</sup>Rheumatology, Gartnavel General Hospital, Glasgow, United Kingdom; <sup>8</sup>Rheumatology, NHS Fife, Whiteman's Brae Hospital, Kirkcaldy, United Kingdom; <sup>9</sup>Rheumatology, Royal Derby Hospital, Derby, United Kingdom; <sup>10</sup>Rheumatology, Royal Hampshire County Hospital, Winchester, United Kingdom; <sup>11</sup>Rheumatology, University College London Hospitals NHS Foundation Trust, London, United Kingdom; <sup>12</sup>Rheumatology, Queen Elizabeth Hospital, Gateshead, United Kingdom; <sup>13</sup>Rheumatology, Sunderland Royal Hospital, Sunderland, United Kingdom

**Background:** Primary Sjögren's syndrome (pSS) is a multi-system autoimmune disease. Anti-Ro is the most commonly associated antibody. This can be differentiated into two subtypes, anti-Ro52 and anti-Ro60, each specific to different antigens. Clinical associations of the subtypes remain controversial in pSS. The UKPSSR is a large national cohort and biobank of over 600 clinically well characterized patients with pSS. All data and samples have been collected prospectively using a standardized proforma as previously described [1], providing a unique opportunity to explore whether anti-Ro52 and anti-Ro60 are associated with distinct clinical manifestations in pSS.

**Methods:** Serum anti-Ro 52 and anti-Ro60 levels were measured using a high sensitivity Phadia assay on 314 UKPSSR patients as part of the interim analysis. Patients were stratified according to the presence of anti-Ro52 or anti-Ro60 and the relationship between these antibodies and clinical manifestations of pSS were examined. The EULAR Sjogren's syndrome disease activity index (ESSDAI) was used as the basis for stratification of involvement of different organs. Differences between groups were tested using Chi-squared and Mann Whitney U tests for categorical and non-parametrical data respectively.

**Results:** Anti-Ro52 was positive in 81% of patients and anti-Ro60 in 82%. 8 (2.5%) patients were positive for anti-Ro-52 but not anti-Ro-60, 10 (3.1%) patients were positive for anti-Ro-60 but not anti-Ro52, and 49 (15.6%) patients were negative for both antibodies. There was a significant association between anti-Ro52 and disease activity in the biological (RR=4.6, 95% CI: 2.3, 9.2; p<0.0001) and articular (RR=0.7, 95% CI: 0.5, 0.9; p=0.039) domains, abnormality of Schirmer's test (RR=1.6, 95% CI: 1.3, 2.1; p<0.0001) and salivary flow (RR=1.13, 95% CI: 1.0, 1.3; p=0.042). There was a significant association between anti-Ro60 and disease activity in the biological (RR=6.2, 95% CI: 2.7, 14.5; p<0.0001) and cutaneous (RR=6.9, 95% CI: 1.0, 49.3; p=0.037) domains and Schirmer's test (RR=1.4, 95% CI: 1.1, 1.7; p=0.0001). A negative anti-Ro52 was significantly associated with fatigue visual analogue scores (p=0.034). Positive anti-Ro60 was significantly associated an elevated overall ESSDAI score (p=0.030). There was no significant association between antibody status and raynauds, renal, haematological, central nervous system, peripheral nervous system, muscular, glandular, liver or lymph node involvement, symptom duration, age or sex.

**Conclusions:** The percentage of patients positive for both subtypes was similar in this cohort, in contrast to previous literature which showed a preponderance of anti-Ro52 in pSS. Anti-Ro-52 and anti-60 were associated with articular and cutaneous manifestations respectively. Positivity of either antibodies was associated with increased disease activity in the biological domains.

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

#### Reference

1. Ng WF et al. Rheumatology 2011;50:32-9.

Wednesday 2 May 2012, 14.45 – 16.15

# BSR AND BHPR ORAL PRESENTATION OF ABSTRACTS

## ORAL ABSTRACTS 6: PRIMARY CARE

### O31. AUDIT TO ASSESS GP AWARENESS AND DOCUMENTATION OF BIOLOGICS AND DMARDS IN PRIMARY CARE PATIENT RECORDS

Charlotte Goodhead<sup>1</sup>, Priya Shekar<sup>1</sup>, Clive Kelly<sup>1</sup>, Gail Francis<sup>1</sup>, Ann-Marie Bailey<sup>2</sup>, Lynsey Thompson<sup>1</sup> and Jennifer Hamilton<sup>1</sup>  
<sup>1</sup>Rheumatology, Queen Elizabeth Hospital Gateshead, Gateshead, United Kingdom; <sup>2</sup>South of Tyne and Wear Medicines Management, Sunderland Teaching Primary Care Trust, Sunderland, United Kingdom

**Background:** Drugs such as subcutaneous (sc) methotrexate and biologics used for the management of rheumatoid arthritis are usually hospital prescribed. A previous audit demonstrated biologic drugs were only documented in primary care EMIS records in 14/111 (13%) patients attending GP practices north of Tyne and Wear. It is vital that GPs are aware of such medications due to infection risk and drug interactions. Consequently a method for recording hospital prescribed medications on EMIS was developed along with a shared care agreement allowing GPs to prescribe sc methotrexate to stable self injecting patients.

**Methods:** All patients on biologic mono or combination therapy attending Gateshead Rheumatology service were identified (n=205), as well as patients receiving sc methotrexate in the community prescribed by GPs (n=56) and all patients currently attending the hospital methotrexate clinic or receiving hospital prescribed methotrexate via a homecare company (n=82). All GP practices were given instructions on registering hospital prescribed drugs on EMIS for existing patients and at initiation of biologic or sc methotrexate therapy for all those patients started after the EMIS guideline was launched. GPs were asked to opt into a shared care agreement for patients receiving sc methotrexate via a primary care BUPA prescription. Each GP practice was contacted and a receptionist asked to see whether the drug was listed on EMIS, or whether there was a note on the computer.

**Results:** 343 patients were identified. In total 73/205 (36%) of biologic drugs were listed on EMIS. Of those on biologic monotherapy 37/84 (44%) had the correct medication recorded on the patient's EMIS record. This compares with 35/121 (29%) of those on combination biologic therapy. 77/121 (64%) of the combination biologic group had only the DMARD registered, 1/121 (0.8%) had only the TNF registered and 8/121 (7%) no DMARDs listed at all. With regards to hospital prescribed sc methotrexate 55/82 (67%) GP practices were aware of prescription but 8 of those patients didn't have the drug recorded on EMIS. For those practices where prescribing had been transferred to the GP it was initially thought that the drug hadn't been registered in 10/56. On recontacting the practices it was discovered that the drug had been prescribed in 8/10 as metoject and in the other 2 cases the drug had been discontinued between the start of the audit and contacting the GP.

**Conclusions:** 100% of patients receiving sc methotrexate via a GP prescription have the medication correctly recorded on EMIS. This compares with less than 50% of those on hospital prescribed biologic drugs and 67% of those on hospital prescribed sc methotrexate. Although an improvement on the previous audit there is a continued clinical risk. Further work is underway to streamline communication between hospital and GP prescribing systems and to further refine the EMIS protocol for hospital prescribed drugs.

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

### O32. THE MRC PHYSIODIRECT TRIAL: A PRAGMATIC RANDOMIZED CONTROLLED TRIAL OF PHYSIODIRECT TELEPHONE ASSESSMENT AND ADVICE SERVICES VERSUS USUAL CARE FOR MUSCULOSKELETAL PROBLEMS

Chris Salisbury<sup>1</sup>, Nadine E. Foster<sup>2</sup>, Annette Bishop<sup>2</sup>, Jo Coast<sup>3</sup>, Angelo Franchini<sup>1</sup>, Jeanette Hall<sup>4</sup>, Sandra Hollinghurst<sup>1</sup>, Cherida Hopper<sup>1</sup>, Sean Grove<sup>4</sup>, Surinder Kaur<sup>1</sup> and Alan Montgomery<sup>1</sup>

<sup>1</sup>Academic Unit of Primary Health Care, University of Bristol, Bristol, United Kingdom; <sup>2</sup>Arthritis Research UK Primary Care Centre, Keele University, Keele, United Kingdom; <sup>3</sup>Department of Health Economics, University of Birmingham, Birmingham, United Kingdom; <sup>4</sup>MSK Outpatients, Bristol Community Health, Bristol, United Kingdom

**Background:** Patients with musculoskeletal problems referred by GPs for physiotherapy often experience long delays before treatment. Some physiotherapy services have introduced a treatment pathway called PhysioDirect, involving initial telephone assessment and advice, with written self-management and exercise advice sent by post. Patients are invited for face-to-face treatment only when necessary. Our hypothesis was that PhysioDirect would be equally clinically effective compared with usual care, but more cost-effective, with increased patient satisfaction and shorter waits for treatment.

**Methods:** Multi-centre pragmatic individually randomized trial comparing PhysioDirect versus usual care (patients join a waiting list and receive face-to-face care). PhysioDirect services were established in four PCTs. Adults with musculoskeletal problems, either self-referred for physiotherapy or referred from primary care, were invited to participate and randomized (by remote web-based allocation) to PhysioDirect or usual care. Outcome data were collected at baseline, 6 weeks and 6 months after randomization. Outcomes were collected by patient self-report and from medical records, blind to treatment allocation. The primary clinical outcome was SF36 PCS at 6 months; secondary outcomes included MYMOP, EQ5D, patient satisfaction, waiting times, time lost from work. Incremental cost-effectiveness was assessed using cost per QALY.

**Results:** 2256 patients were recruited and randomized (1513 PhysioDirect, 743 Usual Care). 1921 (85%) were followed up at 6 months. PhysioDirect and usual care were equally clinically effective on our primary outcome (difference in mean PCS -0.01, 95% CI -0.80 to 0.79) and using the MYMOP measure (-0.02, 95% CI -0.16 to 0.11). Time to first assessment was 7 days for PhysioDirect compared to 34 days for Usual Care. Overall satisfaction appeared to be very slightly higher amongst those offered usual care (3.8% which equates to 0.19 points on a 6 point scale) which may not be meaningful. NHS costs were similar in the two arms (PhysioDirect £196.43 versus usual care £189.19, difference in means £19.30 (-£37.60 to £76.19)) while QALYs gained were also similar (difference in means 0.007 (-0.003 to 0.016)). Patients in PhysioDirect had a small but earlier improvement in health status than those in the Usual Care, achieved at an insignificantly greater cost. Incremental cost per QALY gained was £2889.

**Conclusions:** A system of physiotherapy based on initial telephone and advice, offering face-to-face care only when necessary is equally clinically effective and broadly acceptable to patients compared with usual care. Although mean physiotherapy and total NHS costs were somewhat greater in PhysioDirect there was a gain in QALY compared to Usual Care due to more rapid improvement in patient outcomes.

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

### O33. FREQUENCY OF MUSCULOSKELETAL SYMPTOMS AND PRESENTING COMPLAINTS IN VIDEO-OBSERVED PRIMARY CARE CONSULTATIONS WITH PATIENTS AGED 45 AND OVER

Zoe Paskins<sup>1</sup>, Tom Sanders<sup>1</sup>, Peter R. Croft<sup>1</sup> and Andy B. Hassell<sup>1</sup>  
<sup>1</sup>Arthritis Research UK Primary Care Centre, Keele, United Kingdom

**Background:** Most literature relating to musculoskeletal consultations in primary care relies on data collected retrospectively by questioning either GP or patient, or by analysing READ code data. Collecting data using video recordings of consultations has the advantage of being more accurate, avoiding recall bias and coding bias, and also facilitates more in-depth study. This abstract reports early findings from a study of video recorded primary care consultations, which aims to explore the patterns of consultation in patients with musculoskeletal symptoms and to understand more about osteoarthritis (OA) consultations in particular.

**Methods:** With ethical approval, 5 GPs in 2 practices in Staffordshire have agreed and participated to date. In 2 half day surgeries per GP, patients aged 45 and over, attending routine consultations, were asked to consent to having their consultation video recorded and

TABLE 1.

Questionnaire results	n (%)	Viewed consultation		
		Actually discussed joint pain, n (%)	Diagnosis	Frequency
Total number of patients that reported having joint pain within last 7 days	37/75 (49.3)	17/37 (45.9)	See below	
Of those reporting joint pain, number who intended to discuss this with GP	23/37 (62.2)	15/23 (65.2)	OA None given, pending investigation None given, advice only Not musculoskeletal e.g. neurological, flu like illness RA Soft tissue Gout	2 <sup>a</sup> 3 3 3 2 2 <sup>a</sup> 1
Of those reporting joint pain, number who did not intend to discuss this with GP	14/37 (37.8)	2/14 (14.3)	OA Gout	1 1
Total number of patients that did not report joint pain within last 7 days	38/75 (50.7)	3/38 (7.9)	None given, advice only Soft tissue Malignancy	1 1 1
Total		20/75 (26.7)		

<sup>a</sup>One patient had two diagnoses.

complete a questionnaire regarding their demographics, symptoms and agenda for the consultation. The video recorded consultations were then viewed by ZP and actual symptoms discussed and diagnosis recorded.

**Results:** 71.4% of eligible patients agreed to participate. Of those participating, 42.7% were female and 57.3% male, with a mean age of 69 (range 45-91). Table 1 shows the number of patients that reported having joint pain, the proportions of these that intended to, and subsequently did discuss joint pain, along with the diagnosis.

**Conclusions:** The prevalence of joint pain in patients consulting their GPs has not been reported previously, and the data presented here, albeit from a small sample, suggests that 49.3% of these patients aged 45 and over are experiencing joint pain. Data from local GP databases suggests that 14% of consultations in this age group relate to musculoskeletal symptoms, yet the data from this study suggests a higher proportion (21.3%). Furthermore, this study highlights that a number of patients intend to discuss joint pain but do not ultimately raise this concern with the GP (10.6%).

Further aspects of this study which include qualitative analysis of the consultations and post consultation interviews with participants will provide a fuller picture of the pattern of consultation.

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

#### 034. DECIDING TO CONSULT THE GENERAL PRACTITIONER FOR SYMPTOMATIC OSTEOARTHRITIS: A CHOICE-BASED CONJOINT ANALYSIS STUDY

Domenica E. Coxon<sup>1</sup>, Martin Frisher<sup>2</sup>, Kelvin P. Jordan<sup>1</sup>, Clare Jinks<sup>1</sup> and George Peat<sup>1</sup>

<sup>1</sup>Arthritis Research UK Primary Care Centre, Keele University, Keele, United Kingdom; <sup>2</sup>Department of Medicines Management, Keele University, Keele, United Kingdom

**Background:** Symptomatic osteoarthritis (OA) is a major cause of disability. However, even among people with persistent, severe pain, many often do not consult their general practitioner (GP) about it over several years. Previous studies of the determinants of consultation for OA have focussed almost exclusively on patient characteristics and clinical need. Yet, given reports of patients' negative experiences and low expectations of healthcare services, their perceptions of what primary care has to offer will also be important. This study investigated the relative importance of service-related factors and clinical need factors in the decision to consult a GP for symptomatic OA.

**Methods:** The design was a partial-profile choice-based conjoint analysis study based on a cross-sectional survey using a single postal self-complete questionnaire. Adults aged 50 years and over with hip, knee, or hand pain were identified from an existing population cohort study. Eligible potential participants were sent a postal self-complete questionnaire containing 10 choice tasks, each presenting two scenarios based on a combination of three out of six selected attributes (pain characteristics, pain disruption to everyday life, other current health problems, assessment/investigations available, treatment options available, and GP attitude). Multinomial logit regression (main effects) was used to estimate the relative importance patients placed on each of the attributes. Results represent the aggregate difference between the maximum and minimum utilities, expressed as logits, for each attribute level. Latent class analysis was used to identify subgroups of respondents with similar preferences.

**Results:** 863 (74%) people responded (55% female) (mean age 70 years, range: 58-93). The most important determinant of the patient's decision to consult the GP for joint pain was the extent to which pain disrupted everyday life (1.10 logits). GP attitude (0.86) was

perceived to be more important than the available treatments (0.45) or assessment/investigations (0.48). The decision to consult the GP for joint pain was less influenced by other health problems (0.46) and episodes of more severe, unpredictable pain (0.16). Subgroups identified by latent class appeared to be based more on differences in the strength of preferences overall than to differences in the relative importance of attributes per se.

**Conclusions:** Service-related factors are as influential as the most important need-related determinant of consultation (i.e. disruption). Believing the GP would regard joint pain as 'part of the normal ageing process that one just has to accept' is a strong disincentive to seeking help, potentially outweighing other aspects of quality of care. Partial-profile conjoint methods are acceptable to respondents, well-completed, and can address attributes that are less accessible in traditional epidemiological designs.

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

#### 035. ARE RHEUMATOID ARTHRITIS PATIENTS SCREENED FOR CARDIOVASCULAR DISEASE IN PRIMARY CARE?

Helen L. Monk<sup>1</sup>, Sara Muller<sup>1</sup>, Christian Mallen<sup>1</sup> and Samantha L. Hider<sup>1</sup>

<sup>1</sup>Arthritis Research UK Primary Care Centre, Keele University, Keele, United Kingdom

**Background:** The association between rheumatoid arthritis (RA) and increased risk of cardiovascular disease (CVD) is well recognized, reflected in EULAR and BSR guidance recommending cardiovascular screening in RA. Whether this is translated into routine clinical practice in primary care is less clear. The aim of this study was to compare rates of primary care CVD screening amongst RA patients and age, gender and practice-matched controls to determine if the additional cardiovascular risk associated with RA is being recognized and managed appropriately.

**Methods:** This study was undertaken in two linked regional primary care databases: Consultations in Primary Care Archive (CiPCA) and Investigations in Primary Care Archive (IiPCA). All patients in the database with a diagnostic Read Code for RA between 2000 and 2008 and still registered with the practice in 2009 were identified and matched to 4 controls. CiPCA and IiPCA were searched for records of blood pressure, body weight, smoking status, glucose and cholesterol monitoring during 2009 in both cases and controls.

**Results:** 401 RA cases were identified and matched to 4 controls. Overall, the mean age was 58.7 years and 66% were female. No difference in screening between cases and controls was identified for blood pressure, body weight, cholesterol or glucose level. Increased screening for smoking status was apparent in RA patients (62% versus 67%) (95%CI 0.0%, 10.0%). The rate of screening for each risk factor was similar in males and females, but those aged over 65 years were more likely to be screened for any and for all risk factors ( $p < 0.0001$ ). 352 (88%) RA patients had screening for at least 1 CVD risk factor compared to 985 (82%) controls (difference: 5.8% (95%CI 1.4%, 9.2%). The proportion having a comprehensive CVD screen (all 5 risk factors) was low (cases 25% versus controls 26%) and similar in cases and controls ( $p = 0.648$ ).

**Conclusions:** Despite the well-known association between rheumatoid arthritis and cardiovascular disease such knowledge is not being translated into additional screening for people with rheumatoid arthritis. More emphasis needs to be placed on ensuring those with rheumatoid arthritis are actively screened for cardiovascular disease in primary care.

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

**O36. GOUT, ALLOPURINOL AND ERECTILE DYSFUNCTION: AN EPIDEMIOLOGICAL STUDY IN A PRIMARY CARE CONSULTATION DATABASE**

Edward Roddy<sup>1</sup>, Sara Muller<sup>1</sup>, Richard Hayward<sup>1</sup> and Christian Mallen<sup>1</sup>

<sup>1</sup>Arthritis Research UK Primary Care Centre, Stoke-on-Trent, United Kingdom

**Background:** Erectile dysfunction (ED) is prevalent in the general population, affecting 2% of men under 40 years rising to 86% of those aged over 80 years. Risk factors for ED are similar to those for gout and include diabetes mellitus, vascular disease, hypertension, obesity and alcohol use, raising the possibility that gout and ED are associated. Furthermore, impotence is described as a rare side-effect of allopurinol. However, no published epidemiological studies have explored possible associations between gout, allopurinol and ED. The objectives of this cross-sectional epidemiological study were to examine the association between ED and, firstly, gout and, secondly, allopurinol, adjusting for confounding co-morbidities and co-prescriptions.

**Methods:** Data were taken from a validated database of general practice records from nine practices in the UK covering 64,747 adults between 2001 and 2008. Men consulting for gout were identified via Read codes and each matched with four controls for age, practice and year of gout consultation. Consultations for ED, ischaemic heart disease (IHD), hypertension and diabetes mellitus were also identified via Read codes. Prescription of allopurinol, diuretics, anti-

hypertensives, H2 antagonists and anti-depressants were categorized according to British National Formulary codes and then identified in a linked prescription database. Unadjusted odds ratios (OR) were calculated between gout and ED and then adjusted for the presence of IHD, hypertension, diabetes mellitus, and prescription of diuretics, anti-hypertensives, H2 antagonists and anti-depressants, using logistic regression models. In gout cases only, the association between allopurinol prescription and ED was examined adjusting for the same potential confounders.

**Results:** 1292 men with gout were identified and successfully matched to four controls. Mean age was 59.9 years. IHD, hypertension, diabetes mellitus, and prescription of diuretics, anti-hypertensives, and H2 antagonists, but not anti-depressants, were more prevalent in gout cases than controls. 116 (9.0%) men with gout consulted with ED compared to 429 (8.3%) of controls (adjusted OR 0.97; 95%CI 0.78, 1.22).

Of those men who consulted with gout, 506 (39%) had received at least one prescription for allopurinol. Consultation with ED occurred in 65 (12.9%) men who received allopurinol and 51 (6.5%) who were not prescribed allopurinol (unadjusted OR 2.22; 95%CI 1.50, 3.28). This association remained significant after adjustment for IHD, hypertension, diabetes mellitus, and prescription of diuretics, anti-hypertensives, H2 antagonists and anti-depressants (OR 1.92; 95%CI 1.28, 2.87).

**Conclusions:** Gout per se is not associated with ED. However, allopurinol prescription is associated with ED after adjustment for multiple confounding co-morbidities and co-prescriptions. Prescribers should be aware of allopurinol as a cause of ED amongst men with gout.

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