Tuesday 1 May 2012, 09.00 – 10.30

BSR AND BHPR ORAL PRESENTATION OF ABSTRACTS

ORAL ABSTRACTS 1: SPONDYLOARTHROPATHIES

O1. DETECTING AXIAL SPONDYLOARTHRITIS AMONGST PRIMARY CARE BACK PAIN REFERRALS

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Background: Inflammatory back pain (IBP) is an early feature of ankylosing spondylitis (AS) and its detection offers the prospect of early diagnosis of AS. However, since back pain is very common but only a very small minority of back pain sufferers have ASpA or AS, screening of back pain sufferers for AS is problematic. In early disease radiographs are often normal so that fulfilment of diagnostic criteria for AS is impossible though a diagnosis of axial SpA can be made if MRI evidence of sacroiliitis is present. This pilot study was designed to indicate whether a cost-effective pick up rate for ASpA/early AS could be achieved by identifying adults with IBP stratified on the basis of age.
Methods: Patients aged between 18 and 45 years who were referred to a hospital physiotherapy service with back pain of more than 3 months duration were assessed for IBP. All were asked to complete a questionnaire based on the Berlin IBP criteria. Those who fulfilled IBP criteria were also asked to complete a second short questionnaire enquiring about SpA comorbidities, to have a blood test for HLA-B27 and CRP level and to undergo an MRI scan of the sacroiliac joints. This was a limited scan, using STIR, diffusion-weighted, T1 and T2 sequences of the sacroiliac joints to minimize time in the scanner and cost. The study was funded by a research grant from Abbott Laboratories Ltd.
Results: 50 sequential patients agreed to participate in the study and completed the IBP questionnaire. Of these 27 (54%) fulfilled criteria for IBP. Of these, 2 patients reported a history of an SpA comorbidity - 1 psoriasis; 1 ulcerative colitis - and 3 reported a family history of an SpA comorbidity - 2 psoriasis; 1 Crohn's disease. 4 were HLA-B27 positive, though results were not available for 7. Two patients had marginally raised CRP levels (6, 10 -NR $\leq$ 5).

19 agreed to undergo MRI scanning of the sacroiliac joints and lumbar spine; 4 scans were abnormal, showing evidence of bilateral sacroiliitis on STIR sequences. In all cases the changes met ASAS criteria but were limited. Of these 4 patients 3 were HLA-B27 positive but none gave a personal or family history of an SpA-associated comorbidity and all had normal CRP levels.
Conclusions: This was a pilot study yielding only limited conclusions. However, it is clear that:

- Screening of patients referred for physiotherapy for IBP is straightforward, inexpensive and quick.
- It appears that IBP is more prevalent in young adults than overall population data suggest so that targeting this population may be efficient.
- IBP questionnaires could be administered routinely during a physiotherapy assessment.
- HLA-B27 testing in this group of patients with IBP is a suitable screening tool.
- The sacroiliac joint changes identified were mild and their prognostic significance is not yet clear so that the value of early screening needs further evaluation.

Disclosure statement: C.H. received research funding for this study from Abbott. A.K. received research funding for this study, and speaker and consultancy fees, from Abbott. All other authors have declared no conflicts of interest.

O2. VALIDATION OF A SCREENING QUESTIONNAIRE FOR AXIAL SPONDYLOARTHRITIS IN A UK POPULATION

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Background: Ankylosing spondylitis (AS) is difficult to diagnose early in the disease course, leading to delayed diagnosis and poor patient outcomes. Previous attempts to screen populations for AS have focused on features of inflammatory back pain (IBP), but in practice such tools lack sensitivity. In this study we devised and validated a screening questionnaire in 3 patient groups: patients with definite AS, patients with sacroiliitis and patients with mechanical back pain, with a view to using this approach in population studies.
Methods: Participants were patients aged 18-60 treated in the rheumatology department. Three groups were identified from clinic letters and radiology imaging results: those with AS meeting the modified New York criteria (mNYC), those with MRI sacroiliitis not meeting mNYC (i.e. early axial SpA) and those with a 'mechanical' diagnosis and degenerative spinal or disc pathology on MRI. Participants were asked to complete and return a 14 question survey combining IBP criteria with family history and comorbidities. Differences in responses were analysed using Chi-squared and Fisher's exact tests.
Results: Questionnaires were sent to 100 AS patients (83 replies, 76 analysed), 95 sacroiliitis (SI) patients (59 replies, 46 analysed) and 100 mechanical pain patients (68 replies, 68 analysed). SI patients were significantly younger than the other groups (mean age 40.4 years (95% CI 37.0, 43.7) vs 46.9 (44.7, 49.1) for AS and 45.9 (43.8, 48.0) for mechanical). Mechanical patients were significantly more likely to be female (31% male vs AS 55% and SI 61%, χ^2 $p = 0.002$). Mean disease duration was 20.3 years (95% CI 18.0, 22.6) for AS and 7.39 (5.6, 9.2) for SI. Sacroiliac joint radiographs were reported by 2 radiologists with weighted kappa 0.49 (95% CI 0.36, 0.62). Agreement between the 2 MRI readers was measured using intra-class correlation ($ICC = 0.71$, $p < 0.001$). AS and sacroiliitis patients differed only in frequency of iritis and inflammatory bowel disease and were considered together. Insidious onset ($p = 0.252$), alternating buttock pain ($p = 0.229$) and waking in the second half of the night ($p = 0.180$) did not discriminate between those with inflammatory and mechanical pain. Binary logistic regression was used to develop a model differentiating inflammatory from mechanical pain. The final model of male sex, symptom onset by age 33, no radiation of pain, pain improves as day goes on, pain increases with rest and personal history of iritis correctly classified 86% of cases with Nagelkerke R^2 0.486. By assigning 1 point for each feature present a numerical score was calculated and a ROC curve constructed (area under curve 0.911 (95% CI 0.87, 0.96)). A score $\geq$3 has sensitivity 75.6% and specificity 87.9%.
Conclusions: We have developed a model that performs well at differentiating patients with established AS and non-radiographic sacroiliitis from those with mechanical back pain. This will now be used in a primary care prevalence study.
Disclosure statement: K.G. received research grants from Pfizer and Abbott, attended an MSD conference, and is on the advisory board of UCB. L.H. received a research grant and honoraria from Pfizer. All other authors have declared no conflicts of interest.

O3. THE PREVALENCE AND BURDEN OF ANKYLOSING SPONDYLITIS IN EUROPE: A SYSTEMATIC REVIEW

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Background: For effective provision of health-care, knowledge of disease distribution is paramount. Although Ankylosing Spondylitis (AS) prevalence is reported, it is often derived from small-scale

population studies and may vary considerably by geography. To date, there has been no attempt to collate these estimates and establish a single European prevalence of AS. Thus the current study aimed to determine, in Europe: (a) the prevalence of AS, and (b) to estimate the overall number of AS patients.

Methods: A systematic literature search was conducted in September 2011 across 5 databases including Medline and Embase using a set of 8 search terms. This search string consisted of both MeSH terms and text words including, Ankylosing Spondylitis, Spondyloarthropathies and Prevalence. The search was limited to English but was not limited by date. Data was extracted on prevalence and 95% confidence intervals. Where the latter was not presented, these were calculated from data in the paper. From this the median prevalence for Europe was computed. Firstly this was applied to the European population, as per the sum of the most recent censuses for each country (www.who.int/en/) to estimate the overall burden of AS. A separate European estimate was obtained based on census data and country-specific prevalence, or, when this information was missing, prevalence in neighbouring countries. Thirdly, a final estimate was made, as above, but where country specific prevalence was missing, using prevalence from countries with similar HLAB27 prevalence [1].

Results: 5,024 articles were identified during the initial literature search, of which 361 were considered potentially relevant based on article titles. On removing duplicates, reviews, non European studies and those with insufficient data, 14 articles were eligible, providing data from 11 countries. Prevalence varied from 9 per 10,000 (8.9–9.1) in the Czech Republic, to 49 per 10,000 (22–77) in Turkey. Separately, one paper from Germany reported a prevalence of 86 per 10,000, but was excluded due to major methodological differences compared to the other studies. The median AS prevalence in Europe was 23.5 per 10,000 equating to 1.63 million individuals.

The alternative methods of computing burden of AS in Europe yielded estimates of 1.65 and 1.71 million patients respectively, giving a mean (across all 3 methods) of 1.66 million.

Conclusions: This study presents a AS prevalence estimate for the whole of Europe by collating all available data published to date and is the first study to estimate the current burden of AS. Further sensitivity analysis, using slightly different assumptions for countries with no prevalence data, result in remarkably similar estimates of the total population, with a mean of 1.66 million patients. With costs of new therapies and impact on work disability, this represents a considerable burden on health services.

Disclosure statement: G.J. received research grants and speaker fees from Abbott, and research grants from Pfizer. G.M. received research grants from Abbott and Pfizer. All other authors have declared no conflicts of interest.

1. Cavalli-Sforza LL. The History and Geography of Human Genes 1994.

O4. WORK DISABILITY IN ESTABLISHED PSORIATIC ARTHRITIS: A CROSS-SECTIONAL STUDY USING THE WORK PRODUCTIVITY ACTIVITY INDEX

William Tillett[1], Deepak Jadon[1], Dinny Wallis[1], Luisa Costa[1], Nicola Waldron[1], Nina Griffith[1], Charlotte Cavill[2], Eleanor Korendowych[1], Corinne de Vries[2] and Neil McHugh[1,2]
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Background: There is increasing awareness that work disability (WD) is an important outcome measure in arthritis. The burden of WD in Rheumatoid arthritis (RA), Ankylosing spondylitis (AS) and Psoriasis (PsO) is well established however the data in psoriatic arthritis (PsA) is sparse and there is no well validated outcome measure. The Work Productivity Activity Index- Specific Health Questionnaire (WPAI-SHP) has been used to measure WD in PsO and AS. We set out to explore the feasibility and construct validity of the WPAI-SHP in PsA.

Methods: This cross sectional study was undertaken as part of the Long term Outcomes in Psoriatic Study II (LOPAS II). 380 patients with PsA were sent the following questionnaires by post in January 2011; Health Assessment Questionnaire (HAQ-DI- physical function), Patient Global (PtG), EuroQol (EQ5D- quality of life), Dermatology Life Quality Index (DLQI- skin-specific quality of life), FACIT-fatigue (Fatigue), WPAI-SHP (WD) and an additional work questionnaire. The WPAI-SHP is comprised of six questions and reports WD as percentages of; absenteeism (work time missed), presenteeism (impairment at work/ reduced effectiveness) and productivity loss (overall work impairment/ absenteeism plus presenteeism). Correlations were explored using Spearman correlation coefficients (cc).

Results: 270 (71%) participants responded, 50% male, mean age 58yrs (standard deviation- SD 17.2), mean PsA duration 17yrs (SD 10.6). 70% of respondents were of UK working age (18-65yrs), of these 80% (179) were in work. Of those not working 23% were not working because of their PsA, 21% were off work for other reasons and 56% were retired. Of the 179 respondents in work absenteeism, presenteeism and productivity loss were 4.7%, 21.1% and 24.0% respectively, median PtG 2.0 (Interquartile range-IQR 1.0), median Pain VAS 2.3 (IQR 3.3), median HAQ-DI 0.5 (IQR 1.1), median EQ5D 0.73 (IQR 0.17), median DLQI 2.0 (IQR 3.0) and median FACIT fatigue 40.0 (IQR 17.7) Correlations of WD with these outcomes are reported in Table 1. Presenteeism and productivity loss both show strong correlation with the PtG, HAQ-DI, EQ5D and FACIT-fatigue. WD was not correlated with type of work, age, sex, PsA duration, the presence of erosive disease or spinal disease.

Conclusions: There are significant levels of unemployment due to PsA in those of working age as well as high levels of presenteeism and productivity loss in those who remain at work. The WPAI was found to be feasible and correlation with measures of physical function, quality of life and fatigue provides initial evidence for the construct validity of the WPAI in PsA.

TABLE 1 Spearman correlations between WPAI-SHP and health status outcomes

	Patient global	Pain VAS	HAQ DI	EQ5Dindex	DLQI	FACIT-fatigue
Absenteeism	0.16	0.13	0.36*	−0.24*	−0.1	−0.24*
Presenteeism	0.56*	0.43*	0.61*	−0.64*	0.26*	−0.64*
Productivity loss	0.56*	0.43*	0.66*	−0.65*	0.15	−0.64*

*$p < 0.01$.

Disclosure statement: W.T. received a research grant from Abbott. All other authors have declared no conflicts of interest.

O5. INFLUENCE OF LEFLUNOMIDE ON THE LEVELS OF MATRIX METALLOPROTEINASE-3 AND PYRIDINOLINE IN PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Conventional laboratory markers of inflammation (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)) at PsA correlate with the severity of lesions of the musculoskeletal system worth than in rheumatoid arthritis. This greatly complicates the paraclinical assessment of the efficiency of treatment and degree of destructive changes in connective tissue (DCT) in the PsA, especially when short-termed observations are provided. This study is aimed to evaluate the impact of Leflunomide (Lef) alone and in combination with Methotrexate (MTX) or Sulfasalazine (SS) on the clinical activity and level of MMP-3 and PYR in PsA patients (pts).

Methods: The study involved 63 PsA pts with peripheral arthritis. 32 pts were receiving Lef alone and 31 - Lef in addition to MTX (19) or SS (13). Response was evaluated according to PsARC criteria, Health Assessment Questionnaire (HAQ), DAS and DAS CRP. Serum levels of MMP-3 and PYR were conducted at baseline and after 3 months of the treatment.

Results: After 3 months the decrease of MMP-3 (19.6%) and PYR (8.6%) levels was observed. The changes were more striking in the group of PsARC responders (65% of pts): levels of MMP-3 decreased by 28.6%, PYR - by 10.9%, and accompanied by decreased the number of swollen and tender joints - by 72.6% and 63.1%, HAQ - by 37.8%, ESR and CRP - by 20.6% and 11%, DAS and DAS CRP - by 38.2% and 10.7%. The changes of PYR and MMP-3 in the group of non-responders were not significant. Prior to treatment the levels of MMP-3 and PYR in PsARC responders were 18.2 ± 8.80 ng/ml and 2.11 ± 0.67 nmol/l and were higher compared with non-responders by 18.9% and 7.6% (both $p < 0,01$). Reduction of MMP-3 after treatment was significantly greater in pts receiving Lef in addition to MTX or SS - 24.4% vs 13.0% in pts receiving Lef alone. Statistical differences in the dynamics of PYR, ESR and CRP between patients treated with Lef in addition to MTX or SS and Lef alone were not registered. Changes in MMP-3 level positively correlated with the dynamics of the number of swollen joints ($r = 0.29$, $p < 0.03$) and duration of morning stiffness ($r = 0.52$, $p < 0.001$), while the dynamics of the other laboratory parameters (ESR, CRP, PYR) was not correlated with the changes of clinical parameters or MMP-3.

Conclusions: Significant reduction in levels of MMP-3 and PYR under the influence of treatment shows the ability of Lef to lower levels of inflammation and bone destruction in pts with PsA. Among the laboratory markers of inflammation and DCT only the dynamics of

MMP-3 levels correlates with the changes in arthritis activity and confirmes the higher efficacy of Lef in addition to MTX or SS vs Lef alone and in the best way shows the differences between the PsARC responders and non-responders. This suggests that MMP-3 may be acceptable laboratory marker for assessing anti-inflammatory/anti-destructive action of DMARDs in PsA pts in short-term observations.
Disclosure statement: All authors have declared no conflicts of interest.

O6. EVALUATION OF EFFICACY AND SAFETY OF SECUKINUMAB IN THE TREATMENT OF PATIENTS WITH MODERATE-TO-SEVERE ANKYLOSING SPONDYLITIS

Paul Emery[1], Dominique Baeten[2], Joachim Sieper[3], Jurgen Braun[4], D. van der Heijde[5], Iain McInnes[6], Jaap Van Laar[7], R. Landewe[8], Bryan P. Wordsworth[9], Jurgen Wollenhaupt[10], Herbert Kellner[11], I. Paramarta[2], Arthur Bertolino[1,2], Andrew M. Wright[1,3] and Wolfgang Hueber[1,2]
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Background: The current proof of concept study explored the efficacy and safety of secukinumab (AIN457), a fully human monoclonal antibody, for targeted IL-17A blockade as a novel therapeutic strategy in the treatment of moderate-to-severe ankylosing spondylitis (AS).
Methods: A2209 (NCT00809159) is a 28-week (wk), double blind, placebo controlled study. 30 patients with active AS were randomized (4:1) to receive two i. v. infusions of secukinumab 10 mg/kg or placebo, given 3 weeks apart. Primary endpoint was the proportion of patients achieving the Assessment of SpondyloArthritis international Society (ASAS) 20 response at wk 6. A Bayesian method for the primary endpoint analysis was applied and included historical placebo information from 8 representative AS trials. Final data will be presented.
Results: Demographics and baseline characteristics were comparable between groups. Five patients (3 on placebo and 2 on secukinumab) discontinued the study prior to the primary endpoint analysis (wk 6), mostly due to unsatisfactory therapeutic effect. After randomization, efficacy data of one patient was not available due to a protocol violation. At wk 6, 14/23 (61%) secukinumab-treated patients achieved ASAS20 responses versus 1/6 (17%) placebo-treated patients (probability of positive treatment difference = 99.8%; 95% credible interval 11.5%, 56.3%). At wk 6, 30% secukinumab-treated patients achieved ASAS40 response and 35% achieved ASAS5/6 response. Mean BASDAI in secukinumab-treated patients was reduced by 1.8 (individual reductions ranging from 5.6 to −0.8) at wk 6. ASAS response rates were greatest at the primary endpoint at wk 6, and declined thereafter up to end of study at wk 28, consistent with the preliminary dose regimen of only two doses of 10 mg/kg given at days 1 and 22, as chosen for this proof-of-concept study. Post-hoc analyses of subgroups showed superior response rates with TNFi naive patients (11/13; 85%) compared to TNFi pre-exposed patients (3/10; 30%). PK profile for secukinumab was as expected for an IgG1 therapeutic antibody and similar to the profiles seen in other indications. The incidence of adverse events was similar to those observed in previous secukinumab studies. Overall, 30 infections (22 mild, 7 moderate, 1 severe) were reported in 18 patients. Two SAEs (placebo: blood pressure increased; secukinumab: subcutaneous abscess) and no death were reported in this study.
Conclusions: The primary endpoint of this study was met, as secukinumab induced ASAS20 responses were significantly higher than placebo at wk 6. No early safety signals were noted in this study population. Data presented here suggest that secukinumab may be useful for the treatment of active ankylosing spondylitis and thereby warrant larger long term studies on safety and efficacy.
Disclosure statement: D.B. received grants and research support from Abbott, Pfizer and Centocor. A.B. was formerly employed by Novartis. J.B. is a consultant to VirtualScopics. P.E. is a consultant to Merck, Pfizer, Roche, Abbott, Bristol-Myers Squibb, Lilly and Takeda. W.H. is an emloyee of Novartis. R.L. received grants and research support from Amgen, Abbott, Centocor, Schering, Pfizer, Wyeth and UCB, and is a consultant to Amgen, Abbott, Centocor, Schering, Pfizer, Wyeth, UCB, Merck and Roche. I.M. received grants and research support from Merck, Roche, Pfizer and Bristol-Myers Squibb. J.S. received grants and research support from Pfizer, Merck, Abbott, sanofi-aventis and Bristol-Myers Squibb, and is a member of the speakers bureaus of Pfizer, Merck, Abbott, sanofi-aventis and Bristol-Myers Squibb. D.V. received grants and research support from Abbott, Amgen, Bristol-Myers Squibb, Centocor, Chugai, Merck, Novartis, Pfizer, Roche, sanofi-aventis, Schering-Plough, UCB and Wyeth, and is a consultant to Abbott, Bristol-Myers Squibb, Centocor, Chugai, Merck, Novartis, Pfizer, Roche, sanofi-aventis, Schering-Plough, UCB and Wyeth. J.V. received grants and research support from Roche, is a consultant to Roche, and is a member of Roche's speakers bureau. B.W. is a member of the speakers bureaus of Abbott and Merck. A.W. is an employee of Novartis. All other authors have declared no conflicts of interest.

Tuesday 1 May 2012, 11.30 – 13.00

BSR AND BHPR ORAL PRESENTATION OF ABSTRACTS

ORAL ABSTRACTS 2: IMAGING

O7. HAND OSTEOARTHRITIS PAIN HAS PERIPHERAL AND CENTRAL COMPONENTS DEMONSTRATED BY ALGOMETER SCORES AND FUNCTIONAL MRI

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Background: Hand osteoarthritis (OA) is a prevalent condition typified by chronic pain and reduced function. We hypothesized that hand OA subjects have enhanced sensitivity and firing of peripheral nociceptors in the hand, thereby potentiating chronic pain. In this study we aimed to: 1. evaluate the characteristics of local pain in hand OA; 2. assess if central sensitization contributes to pain perception in our hand OA cohort.
Methods: Participants with proximal and distal interphalangeal joint (PIP and DIP) hand OA and controls were recruited ($n = 13$ per group with 780 hand joints assessed in total). Clinical scores including VAS (visual analogue score), HAQ (health assessment questionnaire), Kellgren-Lawrence (K-L) scores for radiological severity and pain thresholds using algometers (Wagner, USA) were measured. Central brain pain processing was tested with a standardized finger flexion-extension (FFE) task which reproduced pain in hand OA subjects but not controls. Functional MRI (fMRI) was performed with a 1.5T GE scanner (General Electric Systems, Milwaukee, USA) during the FFE task. Activation of brain regions was evaluated using FMRIB software (www.fmrib.ox.ac.uk/fsl). Grouped data analysis with a z-statistic threshold of 2.3 and multiple comparisons correction at $p < 0.05$ was used.
Results: Hand OA participants reported pain despite 92% taking oral analgesics. The mean VAS in the hand OA group was $59.31\,mm \pm 8.19$ compared with $4.00\,mm \pm 1.89$ in controls. The hand OA cohort had higher HAQ scores than controls ($p < 0.0001$) showing significant functional impairment. Objective pain measures by algometer in 30 hand joint regions per subject showed significantly lower pain thresholds in the OA group versus controls ($p < 0.0001$). Radiological changes occurred mainly in the PIP/DIP joints, as demonstrated by a K-L score of 3-4 in 17.3% of all DIP and PIP joints assessed in comparison to only 3% of CMC joints and 0.27% of MCP joints. In our functional MRI analysis, the results of the mean group activation signal thresholded to statistical significance ($p < 0.05$) demonstrated increased activation of the thalamus, cingulate gyrus, frontal and somatosensory cortex in the hand OA group. The regions activated in hand OA subjects are all recognized regions of brain pain processing. In contrast, activation in the control group was only observed in the motor cortex, as would be expected with the FFE task, but not in other brain regions associated with pain processing.
Conclusions: Hand OA subjects have lower pain thresholds globally in their hands compared with controls, demonstrated by algometer scores which showed low pain thresholds even in hand joints where radiological severity was low. Our fMRI data also demonstrate evidence of central sensitization in our cohort of hand OA subjects. We therefore conclude that algometers and functional neuroimaging measure distinct components of hand OA pain and are useful biomarkers of disease.
Disclosure statement: All authors have declared no conflicts of interest.

O8. ULTRASOUND FEATURES OF OSTEOPHYTES AND CARTILAGE THICKNESS AT THE KNEE ARE ASSOCIATED WITH PAIN AND FUNCTIONAL IMPAIRMENT: THE NEWCASTLE THOUSAND FAMILIES STUDY

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Background: Previous studies have shown contradictory results for the association of structural changes of osteoarthritis (OA) on imaging with clinical symptoms. We performed a comparison of ultrasound features of knee OA with clinical symptoms among members of the Newcastle Thousand Families birth cohort.
Methods: Participants from the cohort aged 63 years (born in May-June 1947), had both knees scanned by a trained musculoskeletal sonographer. Ultrasound protocols were derived from EULAR guidelines. Knee osteophytes (yes/no), minimum femoral cartilage thickness in right knee (mm) and effusion >4 mm (yes/no) were recorded. These data were analysed in relation to pain, stiffness and function in the lower limbs as reported by participants using the WOMAC questionnaire. Each of the three WOMAC subscales was subdivided in to four categories of severity. Logistic and linear regression was used to calculate the association of features of knee OA with clinical symptoms. Adjustment for potential confounders such as BMI, sex and presence of knee effusion was also performed.
Results: 311 participants were scanned; 55% women, mean BMI was $27.9\,kg/m^2$ ($sd = 4.9$). Prevalence of knee osteophytes was 30%, mean right knee minimum femoral cartilage thickness was 1.47 mm; prevalence of knee effusions was 22%. Those in the highest category of pain had an OR of 4.42 for osteophytes (95% CI 2.17, 8.98) when compared to those without knee pain. Similarly, those with severe stiffness had an OR of 4.21 (95% CI 2.01, 8.83) and those with physical dysfunction had an OR of 4.15 (95% CI 1.96, 8.80) for knee osteophytes when compared to those with no symptoms. These estimates were reduced in magnitude but remained statistically significant after adjustment for BMI and sex. Minimum cartilage thickness was associated with pain (adjusted co-efficient -0.11; 95% CI -0.20, -0.01) and reduced physical function (adjusted co-efficient -0.13; 95% CI -0.24, -0.02) but not stiffness; when comparing those in the most severe symptom category with those without symptoms. Knee effusion had no association with any of the three subscales of the WOMAC questionnaire.
Conclusions: This is the first study to compare ultrasound features of OA with clinical symptoms in a population based cohort. The presence of knee osteophytes had a positive association with pain, stiffness and functional impairment. Femoral cartilage thickness in the knee had an inverse association with pain and functional impairment. However, there was no association of knee effusion with pain, stiffness or function. The associations of ultrasound detected osteophytes and cartilage thickness with clinical symptoms improve our understanding of the relationship between symptoms and structural changes in knee OA, which is strong. This also demonstrates the potential utility of ultrasound in prospective population based epidemiological studies of OA as well as in clinical practice.
Disclosure statement: All authors have declared no conflicts of interest.

O9. THE DIAGNOSTIC UTILITY OF SALIVARY GLAND ULTRASOUND FOR THE INVESTIGATION OF SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (PSS) is a chronic multi-system condition characterized by oral and ocular dryness, musculoskeletal pain and fatigue. Although xerostomia is a cardinal symptom of Sjögren's Syndrome, it can also be caused by medications, radiotherapy, various other medical conditions or idiopathic.

An imaging technique that can reliably discriminate PSS-related xerostomia and oral dryness due to other conditions will be invaluable in the diagnosis of PSS.

Traditional techniques for salivary imaging such as sialography or scintiscans involve exposure to radiation, invasive and can be uncomfortable for patients. In this study, we present our experience

of using salivary gland ultrasound in the assessment of patients presenting with a dry mouth or suspected PSS.

Methods: 200 patients who had attended the Department of Dental and Maxillofacial Radiology, Newcastle Dental Hospital between May 2010 and May 2011 for ultrasound investigation were identified using the hospital's electronic patient administration system. 74 out of the 200 imaging requests were for patients presenting with 'dry mouth', 'xerostomia' or suspected Sjögren's Syndrome. The medical records including the final diagnosis, clinical history and laboratory data of these patients were reviewed. All patients underwent ultrasound examination of the major salivary glands using a standardized approach performed by one of the two co-authors (IM and AC). Parotid and submandibular glands were assessed for gland echogenicity,(normal or presence of hypoechoic foci), fibrosis running through parenchyma, gland demarcation and presence of lymph nodes. Vascularity changes within enlarged (>1 cm) lymph nodes were also assessed for aberrant blood flow patterns.

Results: Of the 74 patients who have undergone salivary gland ultrasound for xerostomia or suspected PSS, 34 patients have a final diagnosis of PSS, of whom 29 also had positive ultrasound features of SS.

Statistical analysis of the data captured demonstrates a sensitivity of 0.906, specificity of 0.881, with positive and negative predictive values as 0.853 and 0.925 respectively.

Gland appearances of the Sjögren's patient were multiple hypoechoic foci, marked fibrosis through the parenchyma and indistinct gland margins, although the severity of each of these factors can vary considerably between patients.

Conclusions: Ultrasound is a useful imaging technique for the evaluation of parenchymal change within the major salivary glands. It has been found to be a specific, effective, non-invasive and relatively cost-effective investigation, involving no ionizing radiation and with no obvious complications. However, further work is required to assess the specificity and sensitivity of the modality in the assessment of this complex clinical problem.

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

O10. LONG-TERM RADIOGRAPHIC OUTCOME IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH GOLIMUMAB: 104 WEEK RESULTS FROM THE GO-REVEAL STUDY

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Background: Golimumab (GLM), a human monoclonal anti-TNFα antibody administered as every 4 weeks subcutaneous injections demonstrated long-term clinical efficacy and acceptable safety through wk104. The effect of GLM on inhibition of progression of structural damage PsA pts has been shown through wk52. Week 104 radiographic results are being reported now.

Methods: Adult PsA pts with ≥3 swollen & ≥3 tender joints (SJC/TJC) were randomized to receive SC placebo (PBO) or GLM 50 mg or 100 mg q4 wks. At wk16, pts with <10% improvement in SJC/TJC's entered early escape (EE) in a double-blinded manner to GLM 50 mg (PBO pts) or GLM 100 mg (GLM 50 mg pts). All pts randomized to PBO received GLM 50 mg from wk24 through wk104. Pts on GLM 50 mg could be dose-escalated based on the investigator's judgment to GLM 100 mg after unblinding at wk52. Radiographs of the hands and feet were read at wks 0, 52, and 104. Erosions and joint space narrowing were evaluated by two independent readers unaware of treatment and image time sequence using the van der Heijde-Sharp (vdH-S) method modified for PsA. Data were analysed based on randomized groups (analyses for PBO group includes pts who qualified for EE, crossed-over to GLM 50 mg and pts were dose-escalated from GLM 50 mg to GLM 100 mg; GLM 50 mg group includes pts who qualified for EE and pts who were dose-escalated to GLM 100 mg; GLM 100 mg group includes pts who qualified for EE). Due to lack of adequate control arm, no statistical comparisons were performed at wk52 or wk104.

Results: 405 pts were enrolled. Mean age was 46–48 yrs, median SJC/TJC's were 12–14/22–24, HAQ scores were 1.0–1.1, CRP levels were 0.6 mg/dL, and mean (median) total vdH-S scores were 16.34–22.99 (9.00–10.50). Change from baseline to wk52 in total scores were [mean + SD (median, IQR)]: 0.10 + 1.88 (0.00 [0.00, 0.50]), −0.30 + 1.65 (0.00 [-0.50, 0.00]), and −0.35 + 1.70 (0.00 [0.00, 0.00]) for the PBO, GLM50mg, and GLM100 mg groups, respectively. Change from wk52 to wk104 in total score were: −0.03 + 1.59 (0.00 [0.00, 0.00]), −0.10 + 0.10 (0.00 [0.00, 0.00]), and 0.02 + 0.71 (0.00 [0.00, 0.00]), respectively. Change from baseline to wk104 in total score were: 0.08 + 3.19 (0.00 [-0.50, 0.50]), −0.39 + 2.04 (0.00 [-0.90, 0.00]), and −0.32 + 1.873 (0.00 [-0.50, 0.00]), respectively.

Conclusions: GLM 50 mg and 100 mg treated patients with active PsA showed no to minimal evidence of radiographic disease progression through wk104.

Disclosure statement: A.B. is an employee of Janssen. C.C. is an investigator for Janssen. D.G. is an investigator for Janssen. N.G. is an employee of Janssen. A.K. is an investigator for Janssen. G.K. is an investigator for Janssen. I.M. is an investigator for Janssen. P.M. is an investigator for Janssen. D.V. is an investigator for Janssen. W.X. is an employee of Janssen. All other authors have declared no conflicts of interest.

O11. EARLY EFFECT OF SECUKINUMAB IN REDUCING SPINAL INFLAMMATION AS DETECTED BY MAGNETIC RESONANCE IMAGING IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Secukinumab, a fully human IgG1k anti-IL17A monoclonal antibody, showed significant improvement of clinical signs and symptoms of ankylosing spondylitis (AS). Here, we evaluated the clinical effects of secukinumab (10 mg/kg i.v.) on spinal inflammation, as detected by magnetic resonance imaging (MRI) in patients with AS.

Methods: A2209 (NCT00809159) is a 28-week double blind, placebo controlled study. 30 patients with active AS were randomized (4:1) to receive two i. v. infusions of secukinumab 10 mg/kg or placebo, given 3 weeks apart. Primary endpoint was the proportion of patients achieving Assessment of SpondyloArthritis international Society (ASAS) 20 response at week 6. Sagittal MRI of the spine was performed including T1- and short tau inversion recovery (STIR) sequences at baseline (BL), week 6 and week 28. Images were analysed by an independent reader, who was blinded to treatment allocation and chronology of images, using the Berlin modification of the AS spinal MRI (ASspiMRI-a) scoring system. Changes between baseline and follow-up in each treatment arm were evaluated by Wilcoxon signed-rank test.

Results: 27 patients (22 secukinumab; 5 placebo) had evaluable MR images at baseline. Due to early discontinuation, 2 patients on placebo at week 6 and 6 patients on secukinumab at week 28 were not analysed for MRI. At week 6, a higher proportion of patients achieved ASAS20 response with secukinumab versus placebo (61% [n = 14/23] vs. 17% [n = 1/6]). Improvement in mean Berlin MRI scores with secukinumab was seen as early as week 6 and sustained up to week 28 versus placebo (BL: 9.2, wk6: 6.7, wk28: 5.7 vs. BL: 20.6, wk 6: 21.0, wk28: 19). Early improvements at week 6 were especially noted in patients with higher baseline scores. Only minor changes were seen in patients on placebo.

Conclusions: Results of this study suggest that treatment with only 2 infusions of secukinumab substantially reduces spinal inflammation as detected by MRI. MRI score improvements were seen as early as week 6 and sustained up to week 28. Results are consistent with MRI findings obtained in previous AS trials with TNF blockers. These results support that secukinumab may be a potential treatment for patients with active AS.

Disclosure statement: D.B. received grants and research support from Abbott, Pfizer and Centocor. P.E. is a consultant to Merck, Pfizer, Roche, Abbott, Bristol-Myers Squibb, Lilly and Takeda. S.G. is an employee of Novartis. W.H. is an employee of Novartis. R.L. received grants and research support from Amgen, Abbott, Centocor, Schering, Pfizer, Wyeth and UCB, and is a consultant to Amgen, Abbott, Centocor, Schering, Pfizer, Wyeth, UCB, Merck and Roche. D.L. is an employee of Novartis. I.M. received grants and research support from Merck, Roche, Pfizer and Bristol-Myers Squibb. J.S. received grants and research support from Pfizer, Merck, Abbott, sanofi-aventis and Bristol-Myers Squibb, and is a member of the speakers bureaus of Roche, Pfizer, Merck, Abbott, sanofi-aventis and Bristol-Myers Squibb. D.V. received grants and research support from Abbott Laboratories, Amgen, Bristol-Myers Squibb, Centocor, Chugai, Merck, Novartis, Pfizer, Roche, sanofi-aventis, Schering-Plough, UCB and Wyeth, and is a consultant to Abbott, Amgen, Bristol-Myers Squibb, Centocor, Chugai, Merck, Novartis, Pfizer, sanofi-aventis, Schering-Plough, UCB and Wyeth. B.W. is a member of the speakers bureaus of Abbott and Merck. A.W. is an employee of Novartis. All other authors have declared no conflicts of interest.

O12. TOCILIZUMAB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE ASSOCIATED WITH EARLY REDUCTIONS IN TISSUE INFLAMMATION: 12 WEEK RESULTS FROM A MAGNETIC RESONANCE IMAGING SUBSTUDY OF A RANDOMIZED CONTROLLED TRIAL

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Background: Tocilizumab (TCZ) monotherapy is superior to methotrexate (MTX) in achieving clinical reduction of disease activity in rheumatoid arthritis (RA). A 24 wk interim analysis of the phase 3b ACT-RAY study showed no additional clinical benefit from adding MTX to TCZ vs TCZ + placebo (PBO). This analysis describes magnetic resonance imaging (MRI) measures of synovitis (SYN), osteitis (OST), & erosion (ERO) through wk 12 after therapy initiation.

Methods: In the ACT-RAY study, RA patients (pts) with inadequate response to MTX were randomized to continue stable MTX or receive PBO, both in combination with TCZ 8 mg/kg IV every 4 wks. In a substudy of this trial (N = 63), 0.2T extremity MRI of one hand (metacarpophalangeal joints 1-5) & wrist was acquired at baseline (BL) & wks 2, 12, & 52. Change in scores from BL through wk 12 for the TCZ + MTX & TCZ + PBO groups are compared to evaluate early effects of treatment on joint inflammation.

Results: Both groups showed high disease severity & burden at BL (Table). By wk 2, decreases in SYN & OST were observed & became statistically significant in both gps by wk 12. There were no significant changes from BL in mean ERO. In the PBO group, BL OST scores were higher. The proportion of patients who experienced improvements (≥ Smallest Detectable Change (SDC)) for both SYN & OST was higher in the PBO group than in the MTX gp. Similar pt numbers experienced ERO progression vs regression in each group (Table). No pt in the TCZ + PBO group & only 1 (3.3%) patient in the TCZ + MTX group developed a newly eroded bone.

Conclusions: MRI data demonstrate that TCZ is associated with early suppression of SYN and OST, with no mean increase in ERO score through wk 12. Continuation of MTX in combination with TCZ or switching to TCZ monotherapy are equally beneficial for early suppression of joint inflammation. TCZ monotherapy may be an appropriate option for pts intolerant or unwilling/unable to take MTX.

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TABLE Mean values and SDC-based classification of RAMRIS scores

	TCZ + MTX (n = 31)					TCZ + PBO (n = 32)				
Mean RAMRIS Score	BL (n = 31)	Wk 2 (n = 31)	BL to wk2 Δ (95% CI) (n = 31)	Wk 12 (n = 30)	BL to wk 12 Δ (95% CI) (n = 30)	BL (n = 32)	Wk 2 (n = 32)	BL to wk2 Δ (95% CI) (n = 32)	Wk 12 (n = 29)	BL to wk 12 Δ (95% CI) (n = 29)
SYN	7.2	7.1	−0.1 (−0.5,0.3)	6.3	−0.9* (−1.6,-0.2)	7.4	6.5	−0.9# (−1.5,−0.4)	5.7	−1.9** (−2.8,-1.0)
OST	7.8	7.6	−0.2* (−1.3,0.9)	4.4	−3.6# (−6.5,-0.7)	11.1	10.3	−0.7 (−1.8,0.3)	5.5	−5.1* (−8.6,−1.6)
ERO	19.4	19.4	0.0 (−0.4,0.5)	19.2	−0.3 (−1.2, 0.6)	16.0	16.2	0.2 (−0.0, 0.5)	16.6	0.0 (−0.6,0.6)

Δ Change, *P ≤ 0.01, #P ≤ 0.001, **P ≤ 0.0001. Wilcoxon signed rank test for no change from BL within group. Percentile interval: 95% CI of mean change from BL within group.

	TCZ + MTX (n = 30) n (%)		TCZ + PBO (n = 29) n (%)	
Classification derived from SDC* at week 12	Regressors (change ≤-SDC)	Progressors (change ≥ SDC)	Regressors (change ≤-SDC)	Progressors (change ≥ SDC)
SYN	7 (23.3)	1 (3.3)	11 (37.9)	0
OST	6 (20.0)	0	9 (31.0)	1 (3.4)
ERO	3 (10.0)	2 (6.7)	3 (10.3)	2 (6.9)

* SDC values at wk 12: SYN 1.71, OST 4.27, ERO 1.51

Tuesday 1 May 2012, 14.00 – 16.00

BSR AND BHPR PLENARY ABSTRACTS

BSR AND BHPR PLENARY ABSTRACTS

PA1. EPIDEMIOLOGY OF SPORTING INJURIES AMONG ELITE SOCCER PLAYERS: A LONGITUDINAL STUDY

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Background: Effective preventive strategies against musculoskeletal injuries among elite athletes require knowledge of their incidence and risk factors. We report a three year longitudinal register-based study of sporting injuries among a cohort of soccer players registered at a single professional club.
Methods: Data were maintained on all musculoskeletal sporting injuries sustained among all 272 elite players registered over the three year period 2007-10, at a single professional football club. Players were included from schoolboy (under-12), scholars (16-18), development (18-21) and first team (16+ years) squads, over the study period. Data included the date, type, severity and impact of injuries.
Results: 477 injury episodes were experienced by 131 players over the observation period (incidence 48.2% per year of follow-up; first team 65.2%; development 10.4%; scholar 21.4%; and schoolboy 71.4%). Multiple injuries in the same player were frequent at all ages. The most frequent injuries occurred at the ankle (16%), knee (14.8%), as well as muscular strains of the four major lower limb muscle groups (27.9%). At the ankle, ligamentous strains accounted for 53% of the injuries; at the knee, the corresponding proportion of ligamentous injury was 35%. Similar proportions and grades of injury were observed in training and match situations; however, there was a significant ($p < 0.05$) excess of injuries in the last quarter of training periods. In a logistic regression model, significant determinants of injury severity included tissue (ligament v muscular OR 7.5; 95%CI 3.3-16.9); site (knee OR 15.5; 95%CI 2.9-82.9); and direct trauma (OR 3.3; 95%CI 1.5-7.3). Activities significantly ($p < 0.05$) associated with injury severity included changing direction, tackling, landing from a jump and collision.
Conclusions: Musculoskeletal injury is frequent among elite soccer players and become apparent at early stages of post-pubertal development (schoolboy, development squad) as well as among senior team players. Injuries cluster in individuals at all age groups studied, and are often limit further participation. Strategies to reduce such injuries need to focus on both the mechanism of trauma, as well as individual susceptibility. The injury database developed for this study will provide a basis for future evaluation of such strategies.
Disclosure statement: All authors have declared no conflicts of interest.

PA2. EPRATUZUMAB DEMONSTRATES CLINICALLY MEANINGFUL IMPROVEMENTS IN PATIENTS WITH MODERATE-TO-SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM EMBLEM™, A PHASE IIB STUDY

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Background: Epratuzumab (Emab) is a novel, humanized, anti-CD22 monoclonal antibody under development for the treatment of active SLE. The 12-wk, multicentre, Phase IIb, randomized, double-blind, placebo-controlled study (NCT00624351) discussed here was designed to evaluate the efficacy and safety of Emab in SLE, and identify an optimal dose and regimen for further studies.
Methods: Pts with moderate/severe SLE (≥1 BILAG 2004 A or ≥2 Bs) were randomized to 1 of 6 intravenous regimens: placebo (PBO: standard of care) or cumulative dose (cd) Emab (200, 800, 2400 or 3600 mg in equal divided doses using 2 every other wk [EOW] infusions or 2400 mg cd as 4 equal infusions 1 wk apart). Both 2400 mg cd groups (1200 mg EOW and 600 mg weekly) were also combined for analysis. Concomitant oral corticosteroids/immunosuppressives were to be stable before first infusion and during the study. Primary endpoint was a combined responder index of clinical disease activity at wk 12, defined as reduction of all baseline BILAG A to B/C/D and BILAG B to C/D in all body systems, no BILAG worsening in other organ systems, and no deterioration in SLEDAI or PGA, with no increase in corticosteroids/immunosuppressives over baseline.
Results: At baseline, in the entire population ($N = 227$) mean age was 38.8 years, 94% were female, 78% Caucasian; with high disease activity (70% with ≥1 BILAG A, mean total scores: BILAG 15.2, SLEDAI 14.8). At wk 12, compared with the responder rate in the PBO group (21.1%), responder rates were statistically greater in the Emab 600-mg weekly (2400 mg cd) (45.9%; $p = 0.03$) and 2400-mg combined groups (43.2%; $p = 0.02$); and showed clinically meaningful improvement in the 1200-mg EOW (2400 mg cd) group (Table 1). By wk 12, 18.9% of pts in both 2400-mg cd groups achieved enhanced BILAG improvement (improvement of all body systems to BILAG C or better on consecutive visits, with no worsening) vs 13.2% in placebo. Emab was well tolerated with an incidence of serious adverse events and infusion reactions similar to PBO.
Conclusions: Emab cd 2400 mg demonstrated clinically meaningful improvements in disease activity in pts with moderately to severely active SLE at 12 wks, with responder rates twice those of PBO ($p = 0.02$ to $p = 0.07$). Results validate the combined index emphasizing BILAG and support Phase III trials of Emab in SLE.
Disclosure statement: A.B. is an employee of UCB. C.G. received consultancy fees from UCB, Roche, Genentech and Aspreva Pharmaceuticals/Vifor Pharma, and grant/research support from Aspreva Pharmaceuticals/Vifor Pharma. K.K. received grant/research support from UCB, MedImmune, Genentech and NovoNordisk, and consultancy fees from UCB, MedImmune, Genentech, NovoNordisk, Zymogenetics and MerckSerono. B.K. is an employee of UCB. M.P. received grant/research support from UCB, and is a consultant to UCB. V.S. received consultancy fees from UCB. D.W. received consultancy fees from UCB, Genetech, MedImmune, HGS, NovoNordisk and BMS. All other authors have declared no conflicts of interest.

TABLE 1.

		Emab cd 200 mg	Emab cd 800 mg	Emab cd 2400 mg	Emab cd 2400 mg	Emab cd 2400 mg	Emab cd 3600 mg
	PBO (n = 38)	100 mg EOW (n = 39)	400 mg EOW (n = 38)	600 mg weekly (n = 37*)	1200 mg EOW (n = 37)	Combined group (n = 74)	1800 mg EOW (n = 38)
Responders n (%)	8 (21.1)	12 (30.8)	10 (26.3)	17 (45.9)	15 (40.5)	32 (43.2)	9 (23.7)
		1.7 (0.6-4.7)	1.3 (0.5-3.9)	3.2 (1.1-8.8) p = 0.03**	2.6 (0.9-7.1) p = 0.07**	2.9 (1.2-7.1) p = 0.02**	1.2 (0.4-3.4)

* 2 pts randomized but never received drug; ** p values not adjusted for multiple comparisons

PA3. WILL I WASTE YOUR TIME? DELAYS IN SEEKING HELP FOR RA FLARES

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Background: Anecdotal evidence suggests that patients vary in how long they wait before seeking medical help for an RA flare. The aim of this research is to explore why, and their tipping points for seeking help.
Methods: Q-Methodology: 29 RA patients sorted 23 statements (generated in previous qualitative interviews) about their help seeking behaviours when in a flare, across a forced distribution in ranked order of agreement. Data were analysed using centroid factor analysis with varimax rotation (i.e. the participants and not the items are the variables). Demographic and clinical data were collected and patients completed comments booklets about their rationale for sorting the statements.
Results: Consensus was reached on 9 statements and two factors were produced, which explained 51% of the study variance and accounted for 22 of the 29 participants. None of the Q-sorts were confounded (loading on more than one factor). A participant loading of 0.54 reached significance at $p < .01$.

Consensus: ''When I just don't know what to do anymore'': The top 3 of the 9 consensus statements are 'when the pain becomes too intense', 'when the Flare has gone on longer than expected' and 'when the symptoms become uncontrollable', suggesting these are the tipping points for seeking help.

Factor A: Definite Decision: ''It won't go away, so I won't wait'': Sixteen participants: mean disease duration 15.2yrs (SD 10.3), age 54.8yrs (SD 9.6), HAQ score 1.360 (SD 0.8), 69% female, 69% on biologic therapies.

These patients will seek help quickly when they are in a flare, they know that their medical team can help and that their flare won't go away on its own. They don't worry about wasting their own or the Rheumatologist's time and will not wait until their next scheduled appointment for help. Tipping points for seeking help for these patients are worries about long term damage to their joints, knowing their flare needs to be controlled by new medication and their quality of life being affected.

Factor B: Cautious Indecision: ''Lying down and not moving until it goes'': Six participants: mean disease duration 18.7yrs (SD 13.9), age 50.5yrs (SD 15.4), HAQ score 1.23 (SD 0.9) 67% female, 0% on biologic therapies.

These patients wait to contact the medical team when they are in a flare. They are reluctant to seek help as they hope the flare will go away on its own and do not believe it will last until they seek medical help. They don't like asking for help and worry about wasting the Rheumatologist's time. They may wait until their next scheduled appointment before seeking help and will try to manage their symptoms themselves. These patients need to be prompted by a friend or family member to seek help.
Conclusions: Whilst consensus indicates pain is a tipping point, for some patients a complex interaction of beliefs hinders their help-seeking behaviour. Health care professionals should be aware that some patients delay help-seeking due to fears of time wasting, thus potentially risking further damage.
Disclosure statement: All authors have declared no conflicts of interest.