management of pain due to inflammation, less is reported on pain despite inflammation control, with most such reports addressing rheumatoid arthritis (RA).

Objectives: To investigate the prevalence of pain despite inflammation control after start of a first anti-TNF therapy in psoriatic arthritis (PsA) patients and its relation to EULAR treatment response.

To test the feasibility of a network analysis approach to examine associations between clinical variables and mental health symptoms in RA.

Methods: PsA patients starting a first anti-TNF therapy 2004-2010 were identified in the prospective, observational South Swedish Arthritis Group register (n= 352, 48% women), with mean age 47 years and mean disease duration 10 years. At anti-TNF start, 63% of patients had ongoing methotrexate and 68% were on any conventional DMARD(s). Based on the patient acceptable symptom state (PASS) 1, unacceptable pain was defined as >40 mm on a Visual Analogue Scale (VAS) of pain (scale 0-100 mm), and concomitant inflammation control (as in earlier RA studies) was captured through CRP<10 mg/L, 2 in combination with <1 swollen joint (of 28). 3 Assessments were performed at baseline, 1.5, 3, 6 and 12 months after anti-TNF start. Furthermore, analyses were conducted in relation to EULAR treatment response after 3 months (good, moderate, no response). Differences in pain measures between treatment response groups were estimated by logistic regression.

Results: At start of a first anti-TNF therapy, 84.5% of PsA patients reported unacceptable pain, which declined to 42.9% after 3 months and then remained stable during the rest of the study period, being 39.5% at 12 months (Figure 1A). In contrast, the fraction showing unacceptable pain despite inflammation control was largely unchanged over the study period (24.0 % at treatment start, 26.7% at 3 months and 26.2% at 12 months). Unacceptable pain at 3 months was strongly related to EULAR 3-month response (23.7% of good responders vs. 70.8% of non-responders; p<0.001), whereas for unacceptable pain despite inflammation control the relation was less pronounced (19.3% of EULAR good responders vs 37.5% of non-responders, p=0.016). Among EULAR good responders, unacceptable pain despite inflammation control constituted 81% of all unacceptable pain at 3 months (Figure 1B).

* VAS pain>40 mm. ** VAS pain>40 mm+CRP<10+Swollen joints<1 (constituting a subset and thus included in unacceptable pain).
§ p<0.05 vs. unacceptable pain despite inflammation control in no response, § p<0.05 vs. unacceptable pain in moderate response,
¶ p<0.05 vs unacceptable pain in no response.

Conclusion: A considerable proportion of PsA patients starting their first biological treatment reported unacceptable pain throughout the first treatment year. Among EULAR good responders non-inflammatory pain made up more than 4/5 of this pain load at 3 months, indicating insufficient effects of biologics on a subset of patients with inflammation-independent pain, and strongly warrants alternative treatment strategies in affected patients.

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OP0113

HISTOLOGICAL AND MOLECULAR PORTRAIT OF THE SYNOVIAL TISSUE IN EARLY TREATMENT-NAÏVE PSORIATIC ARTHRITIS IN COMPARISON WITH RHEUMATOID ARTHRITIS

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Background: Psoriatic Arthritis (PsA) and Rheumatoid Arthritis (RA) are autoimmune joint diseases characterised by chronic inflammation of the synovial tissue (ST). It has been previously suggested that PsA-ST has less marked hyperplasia of the synovial lining and fewer infiltrating T/B cells in comparison with RA. However, several confounders such as treatment, disease duration, sampling techniques and predominance of large joints samples may have influenced these findings.

Objectives: To compare the synovial features of PsA/RA at the beginning of the disease process and prior to any treatment for defining their histological/molecular individual characteristics, and to correlate the histological pattern with clinical parameters.

Methods: 183 consecutive treatment-naïve patients with <12 months symptoms and active synovitis of at least one joint were enrolled into the Pathobiology of Early Arthritis Cohort (PEAC) at the Barts Health NHS Trust, and underwent a baseline US-guided synovial biopsy of an inflamed joint. ST inflammatory infiltrate was evaluated by semi-quantitative score (0-4) of the immunostaining for CD68 (macrophages), CD3 (T cells), CD20 (B cells) and CD138 (plasma cells). Patients were classified as: pauci-immune if CD68sublining (SL)<2 and/or CD3-CD20-CD138<1; diffuse-mixed if CD68SL≥2, CD20<2 or CD138<2; lymphoid-mixed if CD20≥2 or CD138≥2. RNA sequencing of the ST was performed on 93RA/15PsA patients.

Results: 39/183 patients were diagnosed with PsA (32 polyarticular, 7 oligoarticular) and 144/183 with RA (2010 ACR/EULAR criteria). Age was significantly lower in PsA patients. The comparison of the age-adjusted baseline variables showed: significantly higher number of tender and swollen joints in RA, but no significant differences between ESR, CRP and DAS28; higher US synovial thickening score of the biopsied joint in PsA, but comparable power-doppler. ST was obtained from small joints in 74.4% of PsA and 82% of RA. Histological comparison is summarised in Table 1 and 2. Only in RA, the pauci-immune phenotype associated with significantly lower ESR, CRP and DAS28 compared to lymphoid-mixed; this association was maintained in a subset of 26 RA patients age- and gender-matched with the PsA population. Transcriptomic profiling showed that PsA-ST has significantly higher expression of the skin fibroblasts, eosinophils and neutrophils cellular gene modules. Genes significantly up regulated in PsA clustered in neutrophil recruitment/enrichment, cell migration and cytoskeleton remodeling modules.

	PsA (n=37)	RA (n=125)	p value
CD3	0.9 (1)	1.7 (1.3)	0.0045*
CD20	0.8 (1.1)	1.4 (1.5)	0.03*
CD68L	1.5 (1.3)	1.8 (1.2)	0.16
CD68SL	1.8 (1.2)	2.3 (1.2)	0.04*
CD138	0.8 (1.2)	1.4 (1.5)	0.02*

	PsA (n=37)	RA (n=125)	p value
Pauci-immune	16 (43.2%)	31 (24.8%)	0.056
Diffuse-Myeloid	12 (32.4%)	40 (32%)	
Lymphoid-Myeloid	9 (24.4%)	54 (43.2%)	

Conclusion: The identification of specific histological and molecular signatures characterising early-untreated PsA will help to better understand the disease pathogenesis and explore novel therapeutic targets.

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OP0114

MACHINE LEARNING TOOLS IDENTIFY PATIENT CLUSTERS AND SWOLLEN AND TENDER JOINT CORRELATION PATTERNS IN A LARGE DATABASE FROM THE SECUKINUMAB PSORIATIC ARTHRITIS CLINICAL DEVELOPMENT PROGRAM

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Background: Identifying patient phenotypes using machine-learning (ML) techniques amidst the variability and heterogeneity of the clinical manifestations of psoriatic arthritis (PsA) could be the first critical step towards better understanding of the disease eventually leading to individualized medicine.¹

Objectives: To identify distinct clusters of patients with PsA based on patients' tender joint (TJ) and swollen joint (SJ) counts and correlation patterns among TJ and SJ counts at baseline as captured in the secukinumab FUTURE trials program.

Methods: Pairwise correlations were explored among 76 SJ and 78 TJ measurements of >2,700 patients with PsA across 5 phase III studies with ~425,000 data entries at baseline and were visualized using heatmaps. Due to high correlations between SJs and corresponding TJs, a composite variable "swollen/tender joint count" was constructed for each joint. Hierarchical clustering was then performed on the composite using "1-correlation" as the dissimilarity metric and Ward's agglomeration method for pairwise grouping of joints. A dendrogram was used to visualize and assess the resulting joint groupings.

Results: The hierarchical clustering algorithm grouped the 78 individual joints into distinct and natural clusters (Figure 1A). At higher level of the dendrogram, the algorithm grouped separately all foot, larger (jaws, clavicles, ankles, hips, wrists, knees, shoulders, elbows), and hand joints. Cutting the dendrogram at 15 clusters separated all the joints into distinct groups; hand joints (distal and proximal phalanges, metacarpals and thumbs), and foot joints (distal and proximal phalanges, metatarsals and big toes). Similar clustering algorithms were explored to identify patient clusters at baseline with distinct swelling and tenderness patterns across the identified joint groups. High correlation between swelling/tenderness of the left and swelling/tenderness of the corresponding right joint was observed across all individual joints (Figure 1B); a high correlation was also observed between swelling and tenderness at all individual joints. More localized patterns showed that there is a gradual decrease in correlation (from highest to lowest) among TJs and SJs in adjacent vs non-adjacent fingers, which is evident from

grey-scale patterns (Figure 1C). Specifically, a gradual decrease in correlation between the swelling of 2nd distal interphalangeal joint and the tenderness of the 2nd-5th distal phalanges was noted.

Conclusion: Machine learning methodology confirmed a natural grouping of joints in patients with psoriatic arthritis based on baseline swelling and tenderness and revealed complex correlation patterns. Additional cluster analyses have demonstrated distinct patient clusters across the identified joint groups. Further investigating potential associations of other disease manifestations such as skin and nail involvement to define additional phenotypes may explain differences in disease pathogenesis and treatment outcomes.

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OP0115

GENERAL AND SEX-SPECIFIC PREDICTORS OF PSA AMONG PATIENTS WITH PSORIASIS

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Background: Risk prediction models in electronic health record (EHR) databases may assist in early identification of patients with psoriasis likely to develop psoriatic arthritis (PsA).¹ A better understanding of potential predictors and whether stratification by sex would be needed in building such algorithms is required.¹

Objectives: Examine general and sex-specific predictors of PsA in an EHR dataset among patients with psoriasis

Methods: A retrospective cohort study was performed within the OptumInsights EHR Database (United States) between 2006-2017. Patients with two or more ICD codes for psoriasis and ages 16-90 were identified. The outcome was PsA (defined by a single ICD code). Potential predictors, in particular comorbidities and infections, were also identified using ICD codes. Hazard ratios were calculated using Cox proportional hazards models between individual predictors and development of incident PsA in univariate models and those that were significant (p<0.1) were entered into a multivariable model. A final model was achieved using automated stepwise regression. Separate models were developed for each sex as some predictors (e.g., polycystic ovarian syndrome, prostatitis) are sex-specific.

Results: Among 215,386 patients with psoriasis, mean age was 50 (SD 15.6) and 55% were female. At index date (one year after date of first psoriasis code), 4.6% and 4.2% of patients had been prescribed a biologic therapy or oral therapy in the past year. Mean follow up time was 5.6 years (SD 2.8) and 4,288 patients developed incident PsA (incidence 3.5 cases/1,000 person years). Previously identified predictors were significant in univariate models (depression, fatigue, inflammatory bowel disease, uveitis, hyperlipidemia, fracture; data not shown due to space restrictions) but several new predictors were also identified (diabetes, hidradenitis suppurativa, celiac disease, irritable bowel syndrome, sepsis, post-traumatic stress disorder, anxiety, anemia) (Table). Automated regression identified subsets of these factors in multivariable models; these models differed by sex.

Conclusion: Predictors of developing PsA differed by sex but obesity, depression, and fatigue were statistically significant predictors in both groups. Infections were also associated with development of PsA but the type of infection differed by sex.

Figure 1. Summary of Results

A. Dendrogram of the hierarchical clustering of 78 joints; bottom-most "leaves" correspond to the individual joints. Cutting the dendrogram at 15 clusters (grey dashed horizontal line) results in the distinct joint groups ("branches") labeled below the dendrogram.
B. Correlation heatmaps depicting pairwise correlations of all 76 swollen joints and 78 tender joints.
C. Pairwise correlations between swollen finger joints of the right hand and corresponding tender joints; darker/lighter grey corresponds to higher/lower correlations.
TEN: tender; SWO: swollen; R: right; MCP: metacarpal; PIP: proximal; DIP: distal phalanges; numbers 1-5: fingers 1 (thumb) through 5 (little)