Dear Reader,

We are happy to present the thirteenth issue of the ‘Press Review and Journal Club’ newsletter that is a part of the EULAR School of Rheumatology (ESOR) educational initiative, the EULAR–EMEUNET Journal Club. In this issue you will find an overview of relevant articles published in top rheumatology journals and in major internal medicine journals. In this newsletter, we once again included articles published electronically in the period of December 2020 through March 2021 to bring you the latest updates in the field. The article selection includes translational and clinical research papers, sorted by the journals they were published in. In case you want to read the article in more detail, you can access it directly through a hyperlink. Among the selected articles, one has been chosen by our Twitter account subscribers to be discussed in a few weeks in an online Twitter Journal Club. Additionally, the ‘EMEUNET Paper of the Month’ has been selected by a popular vote through an online survey circulated among the rheumatology community. For the latter, a video interview with the first author explaining the main findings of the paper will be available on our YouTube channel.

The Journal Club aims to bring together rheumatologists, clinical researchers, basic scientists, and anyone else who might be interested in the topic, to participate in an online, lively discussion. These ‘meetings’ take place on Twitter at pre-specified times and dates; the next is planned for May 19th at 8:00 PM GMT (9:00 PM CET). Details on the selected article and the Journal Club you can find on page 3 of this issue as well as in the Twitter account of the EULAR–EMEUNET Journal Club.

We hope that you will enjoy reading this newsletter and look forward to ’seeing’ you soon at our Twitter JC meeting!

Javier Rodríguez Carrio, Aurélie Najm, Polona Zigon, Elena Nikipherou, Richard Conway, Paul Studenic, Alessia Alunno, Mikhail Protopopov, Maria Sokolova, Mary Lucy Marques, James Bluet, Edoardo Prediletto and Deshiré Alpizar-Rodriguez on behalf of the EULAR EMEUNET Journal Club team
The article for the next EULAR−EMEUNET Journal Club edition was determined by the public vote conducted between 30.04.2021 and 07.05.2021 in our Twitter account @EULAR_JC. The winner article with 37.7% of votes is:

Jon T Giles, Jesper Reinholdt, Felipe Andrade, Maximilian F Konig

**Associations of Antibodies Targeting Periodontal Pathogens With Subclinical Coronary, Carotid, and Peripheral Arterial Atherosclerosis in Rheumatoid Arthritis**

*Arthritis Rheumatol.* 2021 Apr;73(4):568-575 ([link](https://doi.org/10.1002/art.41171))

The association of cardiovascular disease (CVD) and rheumatoid arthritis (RA) is well known, and periodontal disease is associated with both CVD and RA, so a link is suggested between the two. Authors investigated the contribution of periodontal pathogens to CVD in RA. Coronary artery calcification (CAC), carotid intima-media thickness and plaque, and ankle-brachial index were explored in 197 RA patients by computed tomography, ultrasound, and Doppler ultrasound, respectively. Sera were assayed for antibodies against typical periodontal pathogens, associations of periodontitis atherosclerosis were explored using generalized linear models. Adjusting for relevant confounders and reported tooth loss, the mean CAC score was 90% higher in patients having antibodies against typical periodontal pathogens compared to those without; such seropositivity was significantly associated with all other assessed measures of atherosclerosis except carotid plaque, suggesting a role of periodontal disease in the development of CVD in RA.

The online Journal Club will take place on:

**May 19th, 2021 at 8:00PM GMT (9:00PM CET)**  
- duration 1 hour -

Follow the accounts @EULAR_JC, @eular_org and @EMEUNET

Use the hashtag #EULARJC to follow and join the discussion
Stefano Alivernini, Barbara Tolusso, Marco Gessi, Maria Rita Gigante, Alice Mannocci, Luca Petricca, Simone Perniola, Clara Di Mario, Laura Bui, Anna Laura Fedele, Annunziata Capacci, Dario Bruno, Giusy Peluso, Giuseppe La Torre, Francesco Federico, Gianfranco Ferraccioli, Elisa Gresese

Synovial tissue derived characteristics are included in a nomogram for the prediction of treatment response in naïve Rheumatoid Arthritis.


The authors explored the performance of the synovitis assessment using the Krenn synovitis score (KSS; histologic semiquantitative score assessing three features: enlargement of lining cell layer, cellular density of synovial stroma and leukocytic infiltrate) in patients with treatment-naïve rheumatoid arthritis (RA) further treated using the treat-to-target strategy for baseline diagnostic and treatment response prediction in a cohort of 1015 patients (545 – RA, 470 – other types of arthritis) who underwent ultrasound (US)-guided knee synovial tissue (ST) biopsy. The KSS distribution and synovial inflammation composition were contingent on disease duration and US scores in RA and other chronic inflammatory joint diseases. Baseline KSS directly correlated with DAS28 and could be used as a predictor of early DAS remission achievement. Out of the 3 variables composing the KSS, patients with treatment-naïve RA achieving DAS-remission at 6 months showed significantly lower synovial hyperplasia (1.47±0.11), stromal density (1.49±0.09) and inflammatory infiltrate scores (1.33±0.10) at baseline than patients not achieving DAS-remission at 6 months (1.79±0.08, p=0.01; 1.83±0.07, p=0.02 and 1.65±0.07, p=0.02, accordingly). The KSS was also related to autoantibody positivity in treatment-naïve RA. On logistic regression, having a very early onset RA, not having high disease activity and having a KSS<5 at baseline, were synergistic factors of DAS-remission achievement at 6 months and a nomogram integrating baseline clinical and histological characteristics of naïve RA enabled to predict up to 81.7% of probability to achieve 6 months DAS-remission.

Explore this paper in greater detail through an exclusive interview with the first author

Interview available on the [EMEUNET Tube](https://www.emeunet.com) soon!

The EMEUNET Paper of the Month is selected by an online vote of selected articles from each of the rheumatology journal contributions.

Watch out for our next poll!
Baraliakos et al. (doi:10.1136/annrheumdis-2020-218808) presented the results of the MAXIMISE Study, a phase 3b, double-blind, placebo-controlled 52-week trial designed to evaluate the efficacy of secukinumab in the management of axial manifestations of psoriatic arthritis (PsA). Patients were randomly assigned to either 300 or 150 mg of secukinumab or placebo. Both secukinumab dosages significantly improved ASAS20 response versus placebo at week 12 (63% and 66% vs 31% placebo). Using a logistic regression model after multiple imputation, OR for reaching ASAS20 response comparing 300 mg and 150 mg versus placebo (95% CI) were 3.8 (2.4 to 6.1) and 4.4 (2.7 to 7.0); p<0.0001. Combe et al. (doi:10.1136/annrheumdis-2020-219214) presented the results of a 52-week, multicentre, double-blind, placebo-controlled trial evaluating the efficacy and safety of filgotinib (100mg/200 mg: FIL100 and FIL200) versus placebo (through week 24) or adalimumab (40mg SC biweekly) in patients with active rheumatoid arthritis (RA) with stable weekly methotrexate (MTX). The proportion of patients (n=1755) achieving ACR20 at week 12 was significantly higher for FIL200 (76.6%) and FIL100 (69.8%) versus placebo (49.9%; treatment difference (95% CI), 26.7% (20.6% to 32.8%) and 19.9% (13.6% to 26.2%), respectively; both p<0.001). Filgotinib was superior to placebo in secondary endpoints assessing RA signs and symptoms, physical function and structural damage. FIL200 (but not FIL100) was non-inferior to adalimumab in achieving DAS28 ≤3.2 at week 12 (p<0.001). Safety profile was comparable among active treatment arms. Reid et al. (doi:10.1136/annrheumdis-2020-219727) aimed at investigating how genetics influence the risk of smoking-related systemic lupus erythematosus (SLE) manifestations. The interaction between smoking and the STAT4 risk allele resulted in further increase in the risk of myocardial infarction (MI) (OR 2.14; 95% CI 1.01 to 4.62) and nephritis (OR 1.53; 95% CI 1.08 to 2.17), with 54% (MI) and 34% (nephritis) of the risk attributable to the interaction. the IL12A rs564799 risk allele displayed association with MI in both cohorts (OR 1.53; 95% CI 1.01 to 2.31 and OR 2.15; 95% CI 1.08 to 4.26, respectively). Adamichou et al. (doi:10.1136/annrheumdis-2020-219069) applied machine learning in well-characterised patient data sets to develop an algorithm that can aid SLE diagnosis. Using Least Absolute Shrinkage and Selection Operator-logistic regression to select covariates, the model with the best performance included 14 clinical and serological variably weighted features. This model can produce individualised SLE risk probabilities: unlikely, possible, likely and definite SLE. Operating the model as binary (lupus/not-lupus), an excellent accuracy was found (94.8%) for identifying SLE, and high sensitivity for early disease (93.8%), nephritis (97.9%), neuropsychiatric (91.8%) and severe SLE requiring immunosuppressives/biologics (96.4%). This was converted into a scoring system (SLE Risk Probability Index; score >7 has 94.2% accuracy).
Mary is a Portuguese rheumatologist currently being a PhD applicant at Leiden University Medical Center, Leiden, The Netherlands. Her main research interests include clinical aspects, imaging and epidemiology of inflammatory arthritis (especially spondyloarthritis). Mary is a member of the Newsletter Sub-Committee.

James is a senior clinical lecturer, honorary consultant and co-deputy director of the MSc Clinical Rheumatology at the University of Manchester, UK, with an interest in strategies to improve treatment response in Rheumatoid Arthritis (RA). In 2015 he completed his PhD investigating methotrexate adherence in RA and methotrexate-pneumonitis. James is a member of the Newsletter Sub-Committee.

Smeele et al. (doi:10.1136/annrheumdis-2020-219547) aimed to determine the feasibility of the modern treat-to-target (T2T) approach and tumour necrosis factor inhibitors (TNFi) prescription in patients with rheumatoid arthritis (RA) wishing to conceive or who are pregnant. Results of the Preconception Counseling in Active RA (PreCARA) cohort (309 patients) were compared with results of the Pregnancy-induced Amelioration of RA (PARA) study, a historic reference cohort on RA during pregnancy. In the PreCARA cohort, 47.3% of the patients used TNFi at any time during pregnancy. Mean disease activity in the PreCARA cohort was lower than in the reference cohort (PreCARA: 75.4% were in low disease activity (LDA) or remission before pregnancy increasing to 90.4% in the third trimester; PARA: 33.2% and 47.3%, respectively, p<0.001), showing that LDA and remission are attainable goals during pregnancy. Ross et al. (doi: 10.1136/annrheumdis-2020-218439) have developed human-specific plasmacytoid dendritic cells (pDC) models to identify their role in inflammation and fibrosis, as well as attenuation of pDC function with BDCA2-targeting in scleroderma (SSc). RNAseq showed that TLR9-induced activation of human pDC goes beyond type I interferon (IFN) secretion, which is functionally inactivated by BDCA2-targeting, and BDCA2-targeting of pDC can completely suppress in vitro skin IFN-induced response, providing direct evidence supporting the development of attenuation of pDC function as a therapeutic application for SSc. Macfarlane et al. (doi/10.1136/annrheumdis-2020-219091) tested whether cognitive–behavioural therapy (CBT) can prevent the onset of chronic widespread pain (CWP) among adults at high risk. In a population-based randomised controlled prevention trial including 825 patients, participants received either usual care (UC) or a short course of telephone CBT (tCBT). The primary outcome was CWP onset at 12 months. A short course of tCBT did not prevent the onset of CWP in adults at high risk (tCBT: 18.0% vs UC: 17.5%; OR 1.05; 95% CI 0.75 to 1.48), but improved quality of life and was cost-effective (EQ-5D-5L utility score mean difference 0.024 (95% CI 0.009 to 0.040)); 0.023 (95% CI 0.007 to 0.039) more quality-adjusted life-years at an additional cost of £42.30 (95% CI –£451.19 to £597.90), yielding an incremental cost-effectiveness ratio of £1828). Li et al. (doi/10.1136/annrheumdis-2020-218460) aimed to identify novel autoantibodies and verify their diagnostic performance in ACPA-negative RA based on protein microarray technology. A total of 1011 sera from 559 RA patients (276 ACPA-positive), 239 disease controls and 213 healthy controls were collected and sampled on two sequential microarrays and ELISA and western blot (WB) detection, for novel autoantibodies discovery, validation and verification, respectively. Anti-PTX3 and anti-DUSP11 autoantibodies were found as newly identified biomarkers for diagnosis of ACPA-negative RA; their combination showed a sensitivity of 38.0% and a specificity of 88.72%, regardless of ACPA status.
In the prospective observational NOR-Gout study, Uhlig et al. (doi:10.1136/rmdopen-2020-001628) aimed at applying urate lowering treatment (ULT) combined with individual nurse-led information about gout to achieve target serum urate (sUA) (<360 μmol/L), and to identify predictors of achieving it. Of 211 patients, 186 completed the 12-month study. Mean sUA levels decreased from baseline 500 to 311 μmol/L at 12 months; 86% achieved the target. Alcohol use at least weekly vs less frequently (OR 0.14; 95% CI 0.04 to 0.55) and beliefs in overuse of medicines (OR per unit 0.77; 95% CI 0.62 to 0.94) decreased the likelihood of reaching the target, while higher self-efficacy for arthritis symptoms (OR 1.49 per 10 units; 95% CI 1.09 to 2.05) increased it. A post-hoc analysis of two phase 3 trials by Giles et al. (doi:10.1136/rmdopen-2020-001486) explored the impact of body mass index (BMI) on tofacitinib efficacy/safety in active psoriatic arthritis (PsA). In 710 patients, tofacitinib demonstrated higher efficacy response rates at month 3, compared with placebo, regardless of baseline BMI. However, ACR20/50/70 response rates, enthesitis resolution rates and changes from baseline in quality of life/function (month 3) were reduced if baseline BMI ≥35 kg/m² vs lower BMIs. Safety was generally comparable across BMI categories. Duarte et al. (doi:10.1136/rmdopen-2020-001539) aimed to separately assess the psychometric properties of each of the seven numeric rating scales (NRS) of the rheumatoid arthritis (RA) impact of disease questionnaire RAID. In 671 patients with established RA, the NRS correlated moderately to strongly with the respective external instrument of reference (r=0.62 to 0.81), showing good to excellent reliability (ICC: 0.5 to 0.90) and responsiveness (SRM: 0.93 to 1.82). In a cohort study of patients referred with dry syndrome (DS) for a suspicion of Sjögren’s syndrome (SS) who underwent salivary gland ultrasound (SGUS), Al Tabaa et al. (doi:10.1136/rmdopen-2020-001503) aimed to evaluate the relevance of SGUS in the SS diagnostic algorithm. Of 269 patients, 77 were classified as SS and 192 as non-Sjögren’s DS (NSDS). SGUS abnormalities were common in patients with SS vs NSDS (p<0.0001): 51% vs 8% for a SGUS score ≥2. A SGUS score ≥2 had: specificity (Sp)=91%, sensitivity (Se)=57%, positive/negative predictive value (PPV/NPV)=72%/82% for SS diagnosis. The SGUS’s characteristics in SSA-negative patients were similar to the whole population (Se=42%, Sp=91%, PPV=42%, NPV=92%) and could help to avoid labial salivary gland biopsy. López-Medina et al. (doi.org/10.1136/rmdopen-2020-001450) described peripheral features in all subtypes of spondyloarthritis (SpA) in a worldwide cross-sectional study ASAS-PerSpA study (4465 patients). 78% have ever had ≥1 peripheral musculoskeletal manifestation; 57% had peripheral joint disease, 44% had enthesitis and 15% had dactylitis. Results suggest that all peripheral features can be found in all subtypes of SpA, and that differences are quantitative rather than qualitative.
Rusman et al. (doi: 10.1002/art.41607) tested the efficacy of 16-week treatment with etanercept (ETN) in 80 patients with suspected non-radiographic axial spondyloarthritis (nr-axSpA). At 16 weeks, there was no significant difference in the percentage of patients achieving ASAS20 response between the ETN group (16.7%) and the placebo group (11.1%, relative risk 0.7, 95% CI 0.2 to 2.2, p=0.5). The authors concluded that in patients with clinically suspected nr-axSpA with high disease activity but without positive findings on SI joint MRI and/or elevated CRP level, treatment with ETN is not effective. Barturen et al. (doi: 10.1002/art.41610) applied integrative analysis to 955 patients with 7 different systemic autoimmune diseases (SADs) and to 267 healthy controls to understand if they could be grouped into a molecularly-defined stratification. Authors reported that patients with SADs could be stratified into three stable disease clusters (“inflammatory”, “lymphoid”, and “interferon”) with specific molecular patterns differentiating different molecular disease mechanisms. Amkreutz et al. (doi: 10.1002/art.41623) investigated the relation between autoantibodies and bone mineral density in patients with rheumatoid arthritis (RA). Dual X-ray absorptiometry (DXA) of lumbar spine (LS) and left hip (LH) was performed in 408 Dutch and 198 Swedish early RA-patients during five and ten years of follow-up, respectively. ACPAs were associated with a significantly lower baseline LH BMD, with an estimated marginal mean BMD 0.92 (95% CI 0.91 to 0.93) versus 0.95 (95% CI 0.93 to 0.97) g/cm², p=0.01, but not with greater BMD loss over time in treated RA-patients. ACPA alone did not appear to contribute to bone loss after disease onset when disease activity was well managed. Yokota et al. (doi/10.1002/art.41666) reported characterization and function of human TNFα and IL-6-induced osteoclasts using peripheral blood collected from patients with RA and healthy donors. The stimulation promoted NF-ATc1 expression, while the NF-AT and JAK inhibitors prevented TNFα and IL-6-induced osteoclast formation, while expression of IL-1β, TNFα, IL-12p40, and MMP-3 was significantly increased in TNFα and IL-6-induced osteoclasts, but not in osteoclasts. Sepriano et al. (doi.org/10.1002/art.41667) investigated how TNF inhibitors (TNFi) impact spinal radiographic progression (SRP) in a 10 years prospective cohort (ALBERTA FORCAST) of 314 patients with axial spondyloarthritis (axSpA) and whether this was coupled to their effect on inflammation. A gradient was seen for the effect of Ankylosing Spondylitis Disease Activity Score (ASDAS) at every start of a 2 years intervals (t) on the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at t+1 (end of the interval, interaction p-value 0.10), with a higher progression in patients never treated with TNFi [β (95% CI): 0.41 (0.13; 0.68)] compared to those continuously treated [0.16 (0.00;0.31)]. Authors concluded that TNFi reduce SRP in these patients which might be partially uncoupled from their effects on ASDAS.
Lamacchia et al. (doi.org/10.1093) reported the detection of circulating highly expanded (HEC) T-cell clones in genetically at-risk individuals for rheumatoid arthritis (RA), also defined as first-degree relatives of RA patients (RA-FDR)) before the clinical onset of the disease. They used next-generation sequencing from whole blood samples of RA-FDR (at three different pre-clinical stages) and of matched RA patients (n = 20/group). Absolute number of HEC was significantly higher in established RA patients (mean 4.65) and tended to be higher in symptomatic RA-FDR (mean 3.4) compared with asymptomatic RA-FDR (mean 1.55, p=0.003 and p=0.07; respectively). A common complication of Microscopic polyangiitis (MPA), interstitial lung disease (ILD) has been investigated in 49 patients with anti-neutrophil cytoplasmic antibody (ANCA)+ MPA and 10 healthy controls (32 MPA patients also presenting ILD) by Matsuda et al. (doi.org/10.1093) in order to assess serum biomarkers diagnostic and predictive performance. C–C motif chemokine ligand 2 (CCL2) serum levels were significantly higher in the MPA-ILD group than those of the MPA group (327.6 pg/ml, 95% CI 296.8 to 461.6) vs [249.1 pg/ml, 95%CI 188.5 to 319.5, p=0.0024], was related to increased fibrosis, and colocalized at an immunohistochemical level with CD68/CD163 macrophages. Gomez Hernandez et al. (doi.org/10.1093) collected saliva from 11 children diagnosed with Sjögren’s syndrome (SS) prior to age 18 years and 16 normal healthy children to assess the presence of 105 chemokines, cytokines and biomarkers (CCBMs) associated with lymphocyte and mononuclear cell functions. 43 CCBMs (40.9%, with 8 not previously reported) differed in children with SS from those in healthy study controls (p<0.05) and could differentiate the two groups (p<0.05). Elevated CCBMs in Ingenuity Pathway Analysis (IPA) annotations were associated with autoimmune diseases and with leukocytes functions. In order to evaluate the risk of severe infection and infection-related mortality among patients with newly diagnosed systemic lupus erythematosus (SLE) Zhao et al. (doi.org/10.109) investigated age- and gender- matched cohort (5,169 SLE/ 25,845 non-SLE) for a follow-up of 18 years. SLE patients had an increased risk of a greater total number of severe infections with crude RR of 3.24 (95%CI 3.06 to 3.43) and adjusted RR of 2.07 (95%CI 1.82 to 2.36). Authors concluded that SLE was associated with increased risks of first severe infection (1.8-fold), a greater total number of severe infections (2.1-fold) and infection-related mortality (1.6-fold). Oliveira et al. (doi.org/10.1093) investigated the role of Neutrophil extracellular traps (NETs) in individuals with periodontitis and RA and its association with clinical parameters. Individuals with early RA (n = 24), had a higher concentration of NETs in saliva and plasma than individuals with established RA (n = 64) or without RA (n = 76). Worse periodontal clinical parameters, RA onset and RA activity were significantly associated with circulating NETs.
Novella-Navarro et al. (doi: 10.1186/s13075-020-02354-1) explored the proportion of rheumatoid arthritis (RA) patients who fail to respond to multiple biologic DMARDs and aimed to identify baseline features that may predict multiple biologic DMARD failure from a prospective observational cohort single-centre study. A total of 41 out of 402 patients (10%) experienced multiple biologic DMARD failure. Baseline predictors of multiple biologic DMARD failure included joint erosions (OR 3.26; 95%CI 1.18 to 9.00), higher baseline DAS28 (OR 2.29; 95% CI 1.39 to 3.76), younger age (OR 0.95; 95%CI 0.90 to 0.99) and change in DAS28 ≤1.2 six months after commencing the first biologic DMARD (OR 11.12; 95% CI 3.34 to 26.82). Thomas et al. (doi: 10.1186/s13075-021-02452-8) investigated the incidence and risk factors for serious infections in patients with ANCA-associated vasculitides (AAV) in a real-world setting. The authors performed a retrospective analysis in three Greek tertiary referral centres over a 30 year period (1990-2020), including 162 patients with a follow-up period of 891 patient-years. Overall, 67 patients developed a serious infection with an incidence rate of 7.5/100 patient-years. Most of the serious infections occurred during the first year after diagnosis (42%). Patients treated with plasma exchange/dialysis (OR = 3.16, 95% CI 1.001 to 9.96) and those who had a higher Birmingham Vasculitis Activity Score (BVAS) at diagnosis (OR = 1.11; 95% CI 1.01 to 1.21) were more likely to develop a serious infection. Treatment with cyclophosphamide as induction or relapse therapy was associated with a higher serious infection incidence rate compared to rituximab (19.34 vs. 11.34/100 patient-years). Bywell et al. (doi: 10.1186/s13075-020-02391-w) examined patient preferences for second-line therapies in RA using a survey and discrete choice experiment. The authors recruited 358 patients, the study demonstrated a preference for treatment effectiveness, route of administration or severe side effects to be the most important attributes. Tablets and injections were preferred over an intravenous infusion. Nowell et al. (doi: 10.1186/s13075-021-02430-0) conducted a study recruiting 253 participants to the ArthritisPower registry who were invited to select which PRO was important to track via an app over 3 months to establish which patient reported outcomes (PRO) were most important for patients with inflammatory and non-inflammatory musculoskeletal diseases. The most important PRO for tracking via an app were the PRO Measurement Information System (PROMIS) fatigue (79%), physical function (66%), pain intensity (49%), pain interference (50%), duration of morning stiffness (54%) and sleep disturbance (56%). Xu et al. (doi: 10.1186/s13075-021-02458-2) used the data from the UK Biobank samples containing samples of 452,264 White British individuals, including 37,782 osteoarthritis (OA) patients, identified 5 candidate genes and 6 gene ontology terms related to hand OA, which may help to uncover the pathogenesis of hand OA.
Wong et al. (doi:10.1002/acr.24593) assessed the presence of depression and/or anxiety in 743 patients with psoriatic arthritis (PsA) using three definitions, identifying a significant share of PsA patients having a depression depending on a definition (44.54%, 48.99% and 28.4%). A total of 337 patients (45.36%) failed to achieve sustained minimal disease activity (MDA). The presence of depression/anxiety by the 3 definitions was associated with reduced probability of achieving sustained MDA, (OR=0.30, 95%CI 0.22 to 0.39; OR=0.34, 95%CI 0.26 to 0.45; OR=0.47, 95%CI 0.35 to 0.65, accordingly). Strait et al. (doi:10.1002/acr.24602) characterized the representation of dark skin colour in 1,043 images of patients with rheumatic diseases across four major rheumatology training resources. Dark skin was underrepresented in rheumatology educational materials when compared with the USA population (13.4% vs 20.6%, p<0.001). Tselios et al. (doi: 10.1002/acr.24592) compared the complete renal response rates in systemic lupus erythematosus (SLE) patients treated with medium versus high initial prednisone dose. Patients with new-onset lupus nephritis (LN) and standard immunosuppressive treatment were followed for at least 12 months, medium (≤30mg/day) and high (≥40mg/day) prednisone dose groups were matched based on the baseline differences using propensity score. High prednisone dose patients (n=103, mean 48.6±12.3 mg/day) achieved better rates of complete response compared to the medium dose group (n=103, mean dose 24.2±4.6 mg/day), 61.8% vs. 38.2%, p=0.024, at 12 months, respectively. Cumulative glucocorticoid dose was comparable. Complete remission rates were higher in high prednisone dose patients at two (67.8% vs. 39%, p=0.002) and three years (64.9% vs. 49.1%, p=0.025) after LN diagnosis. Foeldvari et al. (doi:10.1002/acr.24609) demonstrated significant differences between diffuse and limited cutaneous juvenile systemic sclerosis (jSSc) patients. A total of 150 patients were enrolled in a cohort across 42 academic institutions. Patients with diffuse cutaneous jSSc (n=108) had a more globally severe disease by Physician Global Assessment, VAS 0-100 (median 37.5 versus 20.0; p=0.002) and more pulmonary involvement (49% vs. 31%; p=0.045) than limited cutaneous jSSc, while patients with limited cutaneous jSSc (n=42) had more frequent cardiac involvement (17% vs. 2%, p=0.002). Patients with overlap features (17%) had an unexpected higher frequency of interstitial lung disease (61 vs. 40%, p=0.048). Tveter et al. (doi.org/10.1002/acr.24543) assessed the short-term effects of multimodal occupational therapy on pain and hand function in a randomized controlled trial including 180 patients with carpometacarpal joint (CMC1) osteoarthritis (OA). Compared to usual treatment, occupational therapy yielded significantly improved pain at rest by VAS 0-10 (−1.4, 95%CI −0.7 to −2.0), pain following grip strength (−1.1, 95%CI −0.5 to −1.7), as well as other outcomes.
Fuller et al. (doi:10.1016/j.semarthrit.2020.09.021) generated a list of outcome domains to inform the development of an Outcome Measures in Rheumatology (OMERACT) Core Domain set for calcium pyrophosphate deposition disease (CPPD) during semi-structured qualitative interviews by 28 patients, 6 caregivers, 7 HCPs and 1 stakeholder. Jaremko et al. (doi: 10.1016/j.semarthrit.2021.03.009) performed a preliminary study to validate a volumetric quantitative measurement (VQM) of hip effusions by manual versus automated artificial intelligence (AI) techniques. Two radiologist evaluated 358 hip MRIs, including 93 hip osteoarthritis subjects and an AI tool computed automatically joint fluid volumes. Manual VQM had excellent inter-observer reliability (ICC 0.96). AI versus the mean of 2 human readers predicted hip fluid volumes with ICC 0.86 at baseline and ICC 0.58 baseline versus week 8. Using an AI tool to automatically quantify hip joint fluid volume is highly feasible for clinical application. Jud et al. (doi: 10.1016/j.semarthrit.2020.11.003) investigated the prevalence and prognostic factors for aortic dilatation (AD) in giant cell arteritis (GCA). The study included 144 GCA patients and 115 controls. GCA patients developed more frequently AD of the ascending and thoracic descending aorta compared to controls (OR 2.60, 95%CI 1.19 to 5.67 and OR 3.65, 95%CI 1.48 to 8.97, respectively). Factors associated with AD were higher percentages of circulating CD3+/CD4+ cells (OR 1.10, 95% CI 1.03 to 1.17), higher CD4/CD8 ratio (OR 1.31, 95% CI 1.03 to 1.66) and polymyalgia rheumatica (OR 3.11, 95% CI 1.10 to 8.81). During follow-up, no GCA patient required surgical aortic repair or suffered aortic rupture or dissection. Choi et al. (doi: 10.1016/j.semarthrit.2021.03.014) conducted a nationwide study in Korea to evaluate the risk of cancer in patients with ANCA-associated vasculitis (AAV). A total of 1,982 patients diagnosed with AAV were identified using an insurance database. The patients and controls with no history of AAV or cancer were matched 1:4 by propensity scores. The overall incidence of cancer during 11 years of follow up was higher among patients with AAV than in controls (HR 1.32, 95% CI 1.08 to 1.61). Age, male sex, AAV subtype, and cyclophosphamide use were significantly associated with cancer risk. Feld et al. (doi/10.1016/j.semarthrit.2021.03.007) explored the presence and progression of radiographic sacroiliitis in a psoriatic arthritis cohort. Axial disease defined as unilateral sacroiliitis of ≤ Grade 2 was detected in 612/1354 patients (45%), 35% fulfilled the modified New York criteria for ankylosing spondylitis (AS). Radiographic progression of unilateral sacroiliitis of ≤ Grade 2 was assessed in 154 patients, 80 (52%) progressed to AS within 5.5 years. At baseline, progressors were diagnosed at a younger age (35.6 vs. 38.9, p = 0.05), had less degenerative disc disease (OR = 0.47, p = 0.02), worse peripheral radiographic damage (OR=1.02, p = 0.03) and worse psoriasis (OR = 1.09, p = 0.01) compared to non-progressors.
Beck et al. (doi:10.1056/NEJMoa2026834) screened the exomes and genomes of 1477 persons with undiagnosed recurrent fevers and/or systemic inflammation and 1083 affected by atypical, unclassified disorders. Somatic mutations affecting methionine-41 in UBA1, a gene encoding the ubiquitinating-activating enzyme 1 that initiates ubiquitylation, were identified in 25 men. These men had a late-onset, treatment refractory inflammatory syndrome with associated hematologic abnormalities, such as cytopenias, characteristic vacuoles in myeloid and erythroid precursors cells. This disorder was named the VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic). In a retrospective cohort study compared 177 patients with autoimmune diseases and a history of lung cancer with a control group of 219 patients without autoimmune diseases venous thromboembolic events, Jacob et al. (doi: 10.1001/jamanetworkopen.2020.29917) reported that patients with autoimmune diseases experienced no difference in overall survival (log-rank P=0.69), despite that fewer patients with autoimmune diseases received the standard of care than controls (126 (69.5%) vs 213 (95.3%), respectively; p<0.001). Gohir et al. (doi: 10.1001/jamanetworkopen.2021.0012) performed a randomized clinical trial including individuals aged 45 years or older with a diagnosis of knee osteoarthritis to compare the effect of an internet-based treatment vs routine self-management. At a 6-week follow-up, the intervention group showed a greater pain score reduction than the control group (between-group difference in NRS: −1.5, 95%CI −2.2 to −0.8). Friščić et al (doi.org/10.1016/j.immuni.2021.03.003) investigated (both in a mice models and in humans) the cellular mechanism behind remission and persistence of rheumatoid arthritis (RA) specifically on synovial fibroblasts (SFs). Authors reported an inflammation-mediated priming of this synovial tissue residents cells and also that repeatedly stimulated primed synovial fibroblasts (SFs) were more aggressive in term of migration, invasiveness and osteoclastogenesis. This priming relies on intracellular complement C3 - and C3a receptor – activation and together with an induced metabolic shift, SF are prevented from activation-induced senescence, they have enhanced NLRP3 inflammasome activity, and in consequence sensitizes tissue for inflammation. Bannier-Hélaouët et al (doi.org/10.1016/j.stem.2021.02.024) reported the establishment of a long-term 3D organoid culture conditions for mouse and human lacrimal gland, that recapitulate morphological and transcriptional features of lacrimal ducts. Trough CRISPR-Cas9-mediated genome editing the gene Pax6 has been revealed as the central actor in the regulation of eye development. Furthermore, single cell analysis have allowed the creation of an atlas highlighting the heterogeneity of the lacrimal glands. Finally, they investigated the process of tear secretion in response to neurotransmitter using lacrimal glands organoids as models (also in orthopic transplantation).
Mary is a Portuguese rheumatologist currently being a PhD applicant at Leiden University Medical Center, Leiden, The Netherlands. Her main research interests include clinical aspects, imaging and epidemiology of inflammatory arthritis (especially spondyloarthritis). Mary is a member of the Newsletter Sub-Committee.

James is a senior clinical lecturer, honorary consultant and co-deputy director of the MSc Clinical Rheumatology at the University of Manchester, UK, with an interest in strategies to improve treatment response in Rheumatoid Arthritis (RA). In 2015 he completed his PhD investigating methotrexate adherence in RA and methotrexate-pneumonitis. James is a member of the Newsletter Sub-Committee.

Liu et al. (J Rheum doi: 10.3899/jrheum.200354) evaluated levels of physical activity and attitudes towards exercise in patients with axial spondyloarthritis (axSpA) and peripheral spondyloarthritis (pSpA) in a USA population (n=264). US physical activity recommendations were met in 49% of those with axSpA and 41% with pSpA. In general, the attitudes and beliefs toward exercise and its perceived benefits were similar. The median score (scale 0-100) for general attitude toward regular exercise was 81.0 for axSpA and 88.0 pSpA. Participants with axSpA had higher concerns of joint injuries than pSpA (scale 0-100, 34.5 vs. 20) and spent less time undertaking light/moderate activities (βadj =1.94 min/week, 95% CI -2.96 to -0.93, −1.05 min/week, 95% CI -2.12 to 0.02, respectively). Tselios et al. (J Rheum doi: 10.3899/jrheum.200161) assessed factors associated with rapid progression within 3 years to end stage kidney disease in patients with lupus nephritis (LN) enrolled at The University of Toronto Lupus Clinic since 2008. Patients were required to have LN with a normal or mildly impaired renal function at baseline and require dialysis or eGFR<15/mL/min/1.73m2 within 3 years of diagnosis. Ten patients fulfilled the criteria, 50% had LN histopathologic class IV at diagnosis and poor compliance was associated with LN progression. Atukorala et al. (Scand J Rheumatol doi: 10.1080/03009742.2020.1829035) examined which factors may predict knee osteoarthritis (OA) flares using a web-based longitudinal study of 313 patients. A number of risk factors were associated with knee OA flare including older age, years of OA, BMI and knee buckling. The final model had an AUC of 0.73 (95% CI 0.67 to 0.80). Katz et al. (J Rheum doi: 10.3899/jrheum.191068) challenged the central sensitisation theory in fibromyalgia (FM) by investigating whether tenderness and intramuscular pressure in the trapezii of patients with FM (n=108) was higher compared to controls (n=30) in participants recruited in the USA. Muscle pressure (33 vs. 12 p<0.001), pain (6.7 vs. 1.4 p<0.001) and tenderness (2.1 vs. 0.5 p<0.001) were significantly higher in FM compared to controls. FM patients were more tender than controls based on both dolorimetry (p<0.001) and digital palpation (p<0.001). Migliore et al. (Ther Adv Musculoskel Dis doi: 10.1177/1759720X211002682) undertook a Bayesian network meta-analysis to assess the efficacy of cycling to a second TNFi compared to switching to a biologic/targeted synthetic DMARD with a different mechanism of action. Nine randomised controlled trials and 16 observational studies were included. Using a fixed-effect model switching to a different mechanism of action was the better treatment strategy (0.99 probability) for an improvement in ACR50 (OR 1.35; 95% CI 0.96 to 1.81) and a lower rate of treatment withdrawal (OR 0.53; 95% CI 0.40 to 0.68). The Bayesian network meta-analysis demonstrated a 68% probability that switching mechanism of action is better than cycling for DAS28 remission.
Alunno et al. (doi:10.1136/annrheumdis-2020-219724) presented EULAR points to consider on pathophysiology and use of immunomodulatory therapies in COVID-19. Two overarching principles (OAs) and fourteen points to consider (PtCs) were developed. OAs highlight the heterogeneous clinical spectrum of SARS-CoV-2 infection and the need of a multifaceted approach to target the different pathophysiological mechanisms. PtCs 1–6 encompass the pathophysiology of SARS-CoV-2 including immune response, endothelial dysfunction and biomarkers. PtCs 7–14 focus on the management of SARS-CoV-2 infection with immunomodulators. Curtis et al. (doi:10.1002/art.41734) presented the ACR guidance for COVID-19 vaccination in patients with rheumatic and musculoskeletal diseases (RMDs). Despite a paucity of direct evidence, 74 draft guidance statements were developed by the task force to provide guidance for use of the COVID-19 vaccines in RMD patients and to offer recommendations regarding the use and timing of immunomodulatory therapies around the time of vaccination. Mikuls et al. (doi:10.1002/art.41596) published the ACR guidance for the management of patients with RMDs during the COVID-19 Pandemic to promote optimal care. Connolly et al. (doi: 10.1136/annrheumdis-2021-220231) presented data on the safety of the SARS-CoV-2 mRNA vaccines in patients with RMDs, studying 325 participants with RMDs who received the SARS-COV-2 mRNA vaccines 51% Pfizer/BioNTech and 49% Moderna) between 17 December 2020 and 11 February 2021. The most common diagnoses were inflammatory arthritis (IA) (38%), systemic lupus erythematosus (SLE) (28%) and overlap connective tissue disease (CTD) (19%). Local symptoms including pain, swelling and erythema were reported by 89%. Systemic symptoms were reported by 69%. There was one case of PCR-confirmed SARS-CoV-2 and one diagnosis of peripheral neuropathy during follow-up. Boyarsky et al. (doi: 10.1136/annrheumdis-2021-220289) explored the response on SARS-CoV-2 mRNA vaccines in 123 patients with RMDs (IA: 28%, SLE: 20%, Sjogren’s syndrome: 13%, overlap-CTD: 29%) who received their first SARS-CoV-2 vaccination dose between 8 January 2021 and 12 February 2021. At a median (IQR) of 22 (18-26) days after the first vaccine dose, 74% (95%CI 65 to 81%) had a detectable anti-RBD antibody response. Younger participants appeared more likely to develop an antibody response (p=0.06). Patients treated with mycophenolate or rituximab were less likely to develop it (p=0.001 and p=0.04, respectively). Mageau et al. (doi: 10.1136/annrheumdis-2021-220010) used the French healthcare database system to identify SLE patients hospitalized with SARS-CoV-2 infection, identifying 1411 patients, including 293 (17%) in ICU. Interestingly, the overall mortality rate was lower in SLE/COVID-19+ inpatients as compared with the total population admitted for SARS-CoV-2 infection in France during the same period (9.5% vs 15.7%, p<0.0001). Campochiaro et al. (doi:10.1136/annrheumdis-2020-219811) explored the acceptance of COVID-19 vaccine in 202 patients with RMDs by a monocentric comparative survey, of whom 162 (80.2%) declared to be willing to receive COVID-19 vaccine.
EULAR continues to provide valuable content and guidance for clinicians and patients with Rheumatic Musculoskeletal Diseases (RMDs) around the world during the COVID-19 pandemic.

Access the EULAR COVID-19 Repository for clinicians - a dedicated space for clinicians and patients where all COVID-related resources and guidelines are concentrated.

- EULAR guidelines:
  - COVID-19 Clinic visit guidelines
  - EULAR provisional recommendations for the management of rheumatic and musculoskeletal diseases in the context of SARS-CoV-2
  - Factors associated with COVID-19-related death in people with rheumatic diseases
  - Plain Language Summaries of the COVID-19 Global Rheumatology Alliance

- EULAR - COVID-19 Reporting database for rheumatologists and other clinicians.
  - The EULAR - COVID-19 Database is a European pediatric and adult database to report on outcomes of COVID-19 in patients with RMDs. It has been updated with Module 2 – reports on cases of vaccination against SARS-CoV-2 of patients with RMDs are now being collected. The page also contains national registries.

- Information on vaccination against SARS-CoV-2 in patients with RMDs:
  - EULAR December 2020 View points on SARS-CoV-2 vaccination in patients with RMDs by Prof. Johannes Bijlsma.
  - EULAR PARE Webinar on COVID-19 and vaccination in RMD patients: What we know so far

The EULAR points to consider on pathophysiology and use of immunomodulatory therapies in COVID-19 have been published in Annals of Rheumatic Diseases. They summarize information that has been gathered so far on available treatment options and pathogenic mechanisms in COVID-19, based on published studies. These are the points to consider for finding optimal management options in patients with SARS-CoV-2 infection.
UPCOMING EULAR WEBINARS

EULAR Sonography Webinar 2021
Teaser for the EULAR Sonography Course 2022

Date & Time: Friday, 28 May 2021, 14:00 – 15:15 CEST

Description: This webinar will focus on the concept on how to learn ultrasound through the EULAR Sonography Courses (3-level, TTT, Paediatric) and on the importance of the successful achievement of the EULAR Competency assessment in MSUS. It will highlight the information on what to except in the EULAR Sonography Courses in 2022 and how to deal with the obliged pause in the ultrasound learning due to the pandemic period.

Target audience: This webinar is targeting physicians with interest in the EULAR Sonography Courses (Basic, Intermediate, Advanced, TTT & PEAD).

Scientific Organisers: Maria Antonietta D´Agostino (Italy and France)

Speakers: Esperanza Naredo (Spain), George AW Bruyn (Netherlands), Lene Terslev (Denmark), Maria Antonietta D´Agostino (Italy and France), Peter Mandl (Austria), Silvia Magni Manzoni (Italy), Wolfgang Schmidt (Germany)

Program: available online

Venue: Online, esor.eular.org

Course fee: Free of charge

Registration: You will need to login to your EULAR School of Rheumatology account to register. If you do not have a School account, you will need to create one before registering. After you have logged in, click on the "Enrol me" button to register for the webinar.
UPCOMING EDUCATIONAL EVENTS

**MAY 2021**

*Australian Rheumatology Association Annual Scientific Meeting*
- When and Where: 21-23 May 2021, Sydney, Australia (Hybrid Event)
- Website: [https://www.araconference.com/](https://www.araconference.com/)

*12th International Congress on Autoimmunity*
- When and Where: 28 May – 1 Jun 2021, Virtual Event
- Website: [https://autoimmunity.kenes.com/](https://autoimmunity.kenes.com/)

**JUNE 2021**

*EULAR 2021*
- When and Where: 2-5 Jun 2021, Virtual Event
- Website: [https://congress.eular.org/index.cfm](https://congress.eular.org/index.cfm)

*Federation of Clinical Immunology Societies (FoCIS) Annual Meeting 2021*
- When and Where: 8-11 Jun 2021, Virtual Event
- Website: [https://www.focisnet.org/meetings/focis-2021/](https://www.focisnet.org/meetings/focis-2021/)

*European Society of Musculoskeletal Radiology (ESSR) Congress 2021*
- When and Where: 10-12 Jun 2021, Virtual Event
- Website: [https://www.essr.org/congress/essr-2021/](https://www.essr.org/congress/essr-2021/)

*5th World Immune Regulation Meeting*
- When and Where: 30 June - 3 Jul 2021, Virtual Event
- Website: [http://www.wirm.ch/](http://www.wirm.ch/)

*6th World Psoriasis & Psoriatic Arthritis Conference*
- When and Where: 30 Jun - 3 Jun 2021, Virtual Event
- Website: [https://www.ifpaworldconference.com/](https://www.ifpaworldconference.com/)

**JULY 2021**

*Ten Topics in Rheumatology*
- Website: [http://tentopics.com/](http://tentopics.com/)

*10th AFLAR Congress*
- When and Where: 21-24 Jul 2021, Mombasa, Kenya
- Website: [https://aflar.net/](https://aflar.net/)

*1st PAFLAR Congress*
- When and Where: 28-30 Jul 2021, Virtual Event
- Website: [https://paflar.org/2021-paflar-congress/](https://paflar.org/2021-paflar-congress/)
EULAR 2021 virtual again

June 2nd – 5th, 2021

EULAR has decided to hold the EULAR 2021 Congress virtually again to protect everyone's health and safety. For more information, read the message by the EULAR President Ian McInnes.

The EULAR European Congress of Rheumatology comprises the major event in the calendar of world rheumatology. The **EULAR 2021 Virtual Congress** will address a wide range of topics including clinical, translational and basic science. Sessions dedicated to People with Arthritis and Rheumatism in Europe (PARE), Health Professionals in Rheumatology (HPR) will feature prominently.

**Registration for the EULAR Virtual CONGRESS is now open**

**View the EULAR 2021 Congress Scientific Programme (web version)**

**Final programme (PDF)**
Experts at EULAR offer hands-on advice for scientists investigating rheumatic and musculoskeletal diseases (RDMs) helping them optimise their research.

How does it work?

1. Select your support area and describe your needs in a short online form
2. Get matched with an experienced scientist
3. Obtain up to 10 hours of free consultation
4. Share your feedback upon service completion

Support Areas
• Clinical Research
• Translational Research

Service Examples:
✓ Study design
✓ Research reporting
✓ Statistical methods
✓ Data collection and analysis
✓ Ethical and regulatory issues
✓ Patient involvement
✓ Sampling strategy
✓ Access to patient and human materials
✓ Access to equipment and technologies

The EULAR Virtual Research Centre (VRC)
The EULAR Research Consultation Service is offered through the EULAR Virtual Research Centre under the umbrella of EULAR Research. It is available for researchers based in EULAR-affiliated countries. For more information, please visit the EULAR VRC web-page.
All over Europe, COVID-19 cases have been rapidly increasing again. This has mainly been driven by the younger population. @EMEUNET has started the social media campaign: #wearamask. The aim of this is to raise awareness for the need to wear a mask and follow social distancing to slow the infection rate of COVID-19 and “flatten the curve”. Through our social media channels, we are spreading the message, especially to the younger population, to slow down the infection rates and therefore protecting vulnerable groups like elderly people and people with RMD’s and to reduce the amount of hospitalized COVID-19 patients. Therefore, EMEUNET is posting pictures and videos of its members wearing a mask and sharing important messages of who they are wanting to protect. We encourage all of you to join in! Share your photos and messages marking them with the #wearamask hashtag, and do not forget to endorse the @EMEUNET Twitter or @EMEUNET Facebook account!

Check out a message from our Chair Felice Rivellese on our Youtube channel!
SHARE YOUR IDEAS!

Over the years EMEUNET has developed several projects covering different topics and areas of interest. However, we always appreciate any suggestions and welcome new ideas to expand on what we currently offer to EMEUNET members (What Is New), interviews and review of other EMEUNET activities.

For additional suggestions and ideas, just write down some lines to summarize your proposal and send it either via email at emeunet@eular.ch or through our website (http://emeunet.eular.org/contact_us.cfm). Don’t forget to provide your contacts so we can come back to you for additional details!

More information about EMEUNET can be found at http://emeunet.eular.org

Where to listen:

Anchor  Apple Podcasts  Breaker  Google Podcasts  Overcast  Pocket Casts  Radio Public  Spotify

SHARE YOUR IDEAS!

EMEUNET PODCASTS!

Are you too busy to read the whole Newsletter? Do you want to keep updated about the main EMEUNET activities and save time?

With our Podcasts, you can get updated while on the go, with extracts of the recent newsletters, highlights of the most recent publications in the field of Rheumatology, selected for you by EMEUNET members (What Is New), interviews and review of other EMEUNET activities.

Where to listen:

Anchor  Apple Podcasts  Breaker  Google Podcasts  Overcast  Pocket Casts  Radio Public  Spotify

MAY 2021