Congress Review

Review of the European Alliance of Associations for Rheumatology (EULAR) 2021 Virtual Congress

Location: EULAR 2021 virtual congress

Date: 2nd–5th June 2021

Citation: EMJ Rheumatol. 2021;8[1]:12-24. Congress Review.

Virtual again... once more the European Alliance of Associations for Rheumatology (EULAR) took the decision to hold their prestigious annual conference online in the face of the continuing COVID-19 pandemic. Originally organised to be hosted in Paris, France, the online conditions were no sanction to the congress as EULAR perfectly demonstrated rapid and effective adaptation to the 'new normal' of virtual congresses and online learning. The meeting resumed its full agenda and provided a seamless platform for all attendees to engage in sessions and meetings.

The Opening Plenary Session was given by Iain McInnes, EULAR President, who welcomed the virtual audience to EULAR 2021 and shared the objective of EULAR: "We seek to deliver world-class education, to provide penetrating and effective advocacy to our political classes, to offer empathetic and comprehensive support to patients, and to sustain the research efforts that will ultimately lead to cures for people with rheumatic diseases." He went on to introduce keynote speaker Mark Pollock, who gave an inspiring talk on building resilience against trials and tribulations as he, as a blind person, sadly fell and sustained an injury causing him to become permanently paralysed. "You have a decision to be a soloist or a collaborative person. Being blind and paralysed is a big challenge for the quality of life," shared Pollock. This challenge led him to collaborate with the 'Project Walk' paralysis recovery centre. "We should always build on resilience and collaborate. An attitude that is important to the world of people working together in fighting rheumatic diseases... The really big breakthroughs happen when we decide to be collaborators."

The highlights from the exciting and extraordinary 2021 Scientific Programme were delivered by Loreto Carmona, EULAR 2021 Scientific Programme Chair, one of the global leaders in clinical and epidemiological rheumatology research and the person responsible for orchestrating the programme. The Scientific Programme

"We seek to deliver world-class education, to provide penetrating and effective advocacy to our political classes, to offer empathetic and comprehensive support to patients, and to sustain the research efforts that will ultimately lead to cures for people with rheumatic diseases."

was rich in diversity. It included debate sessions on topics such as remote rheumatology and publication ethics; 'innovation stations' on topics such as 'fake news', drug development with a team from the European Medicines Agency (EMA), and new techniques for research on rheumatoid arthritis and spondyloarthritis, and lesser-known conditions such as Lyme disease; and workshops for practical skills. After laying out the programme, Carmona highlighted: "In each session of the congress, you will have something specifically for you. Please enjoy it."

McInnes then turned to Hendrik Schulze-Koops, Chair of the EULAR Abstract Committee, who presented the EULAR Abstract Awards. Schulze-Koops commended the success of science in spite of the pandemic: "It is wonderful to have seen so many contributions from people all over the world that work hard on rheumatology research and contribute to the success of EULAR. We had more than 3,000 abstracts submitted to the EULAR meeting, which were then divided into categories and scored by more than 100 people." Abstracts could be submitted under poster presentations, poster tours, and selected presented abstracts. The abstract categories were The Future in Rheumatology (for undergraduates), Health Professionals Rheumatology, People with Arthritis/Rheumatism in Europe (PARE), FOREUM, Basic Science, and Clinical Science, the winners for which included Giovanni Adami, Italy, whose abstract summary can be found in this journal issue.

Annamaria Iagnocco, EULAR President-Elect, shared her remarks on the future of EULAR and where she expects the direction of EULAR

to traverse under her upcoming leadership and guidance. "The RMD community has the potential to adapt to new challenges and to look into the future. The EULAR family is a team of people working together... In 2022 we will celebrate our 75th anniversary in Copenhagen, Denmark."

Awards were bestowed upon those who have shown astounding commitment to the discipline, whether in research, clinical science, or activities in EULAR. The winners of the Meritorious Awards were Maxime Dougas, France, and Josef Smolen, Austria, who Iagnocco praised for serving rheumatology in national and international prestigious roles. Honorary Membership Awards were given to Rikke Helene Moe, Norway, and Dieter Wiek, Germany, who have shown outstanding loyalty in achieving the objectives of EULAR. Finally, the Edgar Stene Prize was awarded to a person with rheumatic or musculoskeletal disease who had submitted the best essay describing their individual experience of living with their condition. Stine Björk Brondum Jefsen, Aarhus, Denmark, was awarded the 2021 prize for her essay 'On an equal footing'.

The EULAR President delivered the Closing Remarks, beaming with delight about the successes and collaboration exhibited by EULAR this past year: "We are proud of what EULAR had become: a global network for progression in rheumatology with as of this year an international research centre and new statues. The EULAR family is a fusion of physicians, healthcare professionals, patient [representatives] and the EULAR secretariat. Together with one goal: to improve the lives of people with rheumatic diseases." ■

"The really big breakthroughs happen when we decide to be collaborators."

EULAR 2021 REVIEWED →

"This variant leads to the overexpression of MUC5B which causes the development of pulmonary fibrosis and is the leading genetic risk factor for causing RA-ILD"

Rheumatoid Arthritis and Interstitial Lung Disease Linked by Genetic Variant

THE INFLAMMATORY autoimmune disease rheumatoid arthritis (RA) causes pain, swelling, and stiffness in the joints. RA inflammation also affects other body systems and can lead to fatigue. Interstitial lung disease (ILD) affects up to 10% of patients diagnosed with RA and is one of the main causes of death in these patients. A cohort study involving a biomedical database of 250,000 individuals in Finland, presented at EULAR 2021 showed that people with a *MUC5B* gene variant have a substantial lifetime risk of ILD, which in turn leads to an increase in morbidity. These collected data are significant and could assist healthcare professionals in identifying patients diagnosed with RA with a high chance of developing ILD.

The *MUC5B* gene regulates the protein mucin, which play an important role in the body's natural defence of infection. The promoter variant called rs35705950 is a variant of the *MUC5B* gene and has an allele frequency of 0.1 in the Finnish population; this variant leads to overexpression of *MUC5B,* which causes the development of pulmonary fibrosis and is the leading genetic risk factor for RA-ILD. Antti Palomäki and team utilised the FinnGen biobank samples, which contain up to 46 years of follow-up genetic data nationwide, to report the risk developing RA-ILD in patients diagnosed with RA by identifying the carriers of *MUC5B* promoter variant.

The results showed that of 248,400 people, 5,534 had been diagnosed with RA and 178 of these (3.2%) had developed RA-ILD. The *MUC5B* promoter variant was a strong biomarker, demonstrating high risk of developing ILD in patients diagnosed with RA. Of patients diagnosed with RA and carrying the *MUC5B* promoter variant, 14.5% had a lifetime risk at age 80 of developing ILD, compared with 5.2% of non-carriers. Additionally, in the general population of people without RA, *MUC5B* promoter carriers and non-carriers had risks of developing ILD of 3.9% and 1.3%, respectively. The researchers found that the risk variance became apparent at the age of 65. Male patients diagnosed with RA and carriers of *MUC5B* promoter variant were the highest-risk group, with 18.5% risk of developing ILD compared with 8.5% of non-carriers. ■

Study Suggests No Link to Increased Risk of Serious Infections with New Disease-Modifying Anti-rheumatic Drugs

RHEUMATOID arthritis (RA) in elderly patients is mainly associated with significant risk of serious infections. Certain anti-rheumatic treatments have been linked to higher risk of infections compared to others; however, the degree of these links is yet to be decided. A prospective, observational cohort study, carried out in Germany and presented at EULAR 2021, addressed the connection between a new class of anti-rheumatic drugs and its association with higher infection rates.

Biologic disease-modifying anti-rheumatic drugs (bDMARDs) and JAK inhibitors (JAKi), were the two new classes of drugs studied to assess their effects in elderly patients diagnosed with RA. The results of this Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) study were presented by Strangfeld and colleagues at the congress this year. The investigation enrolled 2,274 patients diagnosed with RA over the age of 70 years to start a new DMARD treatment following an ineffective use of a conventional synthetic treatment (csDMARD).

A total of 626 serious infections were noted in 425 of the enrolled patients. The observed data showed that serious infections were more prevalent in patients receiving csDMARDs compared to bDMARDs or JAKi; however, these data were not statistically significant, as serious infections were related to other underlying causes such as the use of glucocorticoids, increased disease activity, and other medical conditions such as diabetes, chronic pulmonary disease, and kidney disease. Increased physical capacity in the enrolled patients was linked to a decrease in the risk of serious infections. Overall, the results demonstrated that bDMARDs and JAKi treatments were not associated with increased risk of serious infection in elderly patients diagnosed with RA over 70 years old. ■

"the results demonstrated that bDMARDs and JAKi treatments were not associated with increased risk of serious infection in elderly patients diagnosed with RA over 70 years old."

Effectiveness and Safety of Faecal Microbiota Transplantation for Active Peripheral Psoriatic Arthritis

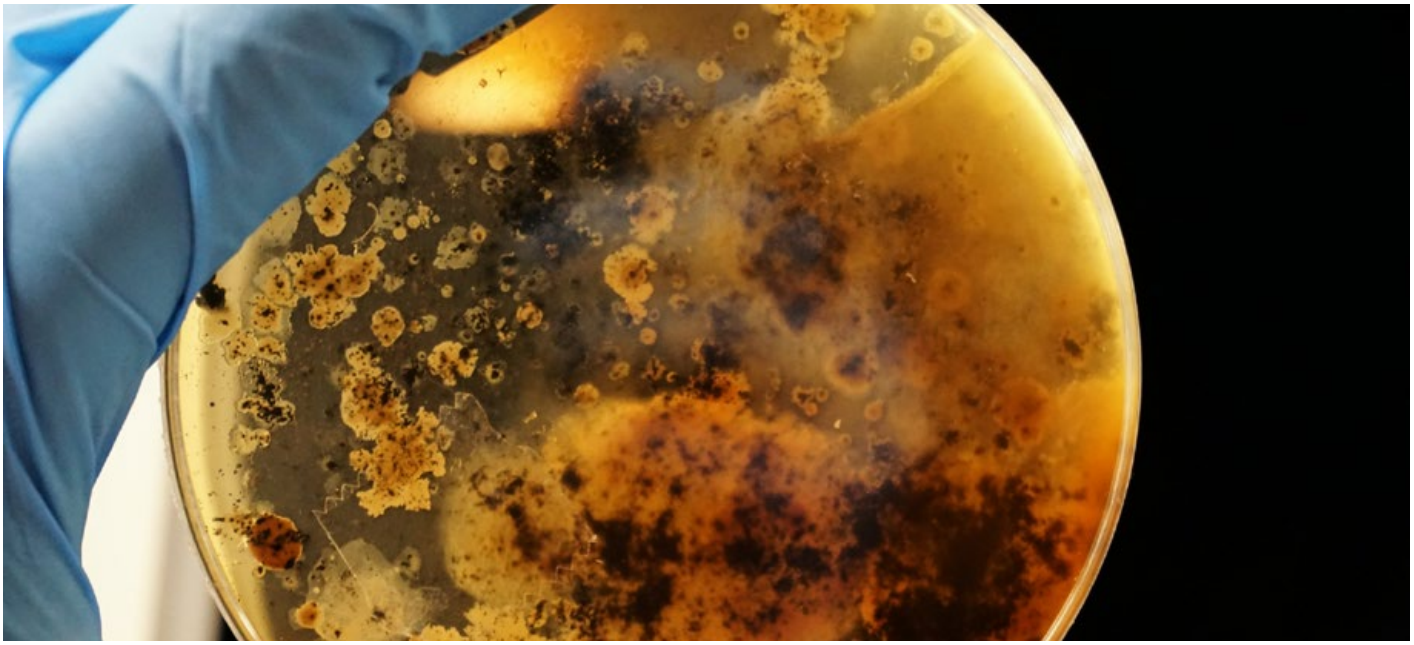
TARGETING gut dysbiosis and restoring microbiome homeostasis through the use of faecal microbiota transplantation (FMT) has been suggested as a novel therapeutic strategy for the management of extraintestinal inflammatory disorders; however, causality remains to be established. For this reason, Maja Skov Kragsnaes, Department of Rheumatology, Odense University Hospital, Denmark, and colleagues conducted a double-blind, parallel-group, sham-controlled superiority trial to evaluate the efficacy and safety of FMT in psoriatic arthritis (PsA), and shared their findings at EULAR 2021.

"Overall, the research findings clearly illustrate that FMT was inferior to sham in treating immune-mediated active peripheral PsA."

In this proof-of-concept study, 31 adult patients with active peripheral PsA (defined as ≥3 swollen joints) were randomly assigned, despite ongoing treatment with methotrexate, to receive either gastroscopic-guided FMT or sham transplantation into the duodenum. The transplants (50 g faeces) came from one of four healthy, thoroughly screened, anonymous stool donors. The primary end-point was the proportion of patients experiencing treatment failure (e.g., requiring treatment intensification) during the 26-week trial period. The first key secondary end-point was change in Health Assessment Questionnaire Disability Index (HAQ-DI) score from baseline to Week 26. Safety was also monitored throughout the trial.

Treatment failure occurred more frequently in the FMT group than in the sham group (60% versus 19%, respectively; risk ratio: 3.20; 95% confidence interval: 1.06–9.62; p=0.018). Similarly, during the course of the entire observation period the rate of treatment failure was statistically significantly higher in the FMT group compared with the sham group. Improvement in HAQ-DI score also differed between groups (0.07 and 0.30 for FMT and sham, respectively; p=0.031). Neither FMT nor sham appeared to result in serious adverse events.

Overall, the research findings illustrate that FMT was inferior to sham in treating immune-mediated active peripheral PsA. ■



"...analysis confirmed the significant relationship between TNFi use for 12 or more months in the previous interval and progression of the sacroiliitis sum score"

Tumour Necrosis Factor Inhibitors and Disease Progression in Patients with Spondyloarthritis

SACROILIITIS, characterised by inflammation of the sacroiliac joints, is a primary manifestation of axial spondyloarthritis (axSpA). Observational cohort studies have revealed that there is a low but detectable level of radiographic sacroiliitis progression, which may impact the function of patients with axSpA. Recent data showed that a longer duration of tumour necrosis factor inhibitor (TNFi) treatment delays spinal progression in axSpA; however, there is no clear consensus regarding the effect of TNFi usage on radiographic progression in sacroiliac joints. Therefore, Murat Torgutalp, Division of Gastroenterology, Infectious Diseases and Rheumatology, Charité – Universitätsmedizin Berlin, Germany, and colleagues investigated the longitudinal association between the progression of radiographic sacroiliitis and TNFi therapy in patients with early axSpA, sharing their findings at EULAR 2021.

In total, 301 patients (166 with non-radiographic axSpA and 135 with radiographic axSpA) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in the analysis. Two trained central readers scored the radiographs according to modified New York criteria. If both scored an image as definitive radiographic sacroiliitis, the patient was classified as having radiographic axSpA; the mean of both readers was used to calculate the sacroiliac sum score. Analysis focused on the association between TNFi use (previous and current) and radiographic sacroiliitis progression, defined as the change in sacroiliitis sum score over 2 years.

At baseline, 3% of patients (n=9) were treated with a TNFi and 28.9% of patients (n=87) received at least one TNFi during the entire follow-up period. Receiving ≥12 months of TNFi in the previous interval was associated with a lower progression of the sacroiliitis sum score compared to not receiving TNFi in the previous interval. This was not recorded in patients who received TNFi for longer than 12 months in the 2-year interval. Adjusted multivariable longitudinal generalised estimating equations analysis confirmed the significant relationship between TNFi use for 12 or more months in the previous interval and progression of the sacroiliitis sum score.

In conclusion, TNFi therapy was associated with slowing of the progression of radiographic sacroiliitis in patients with axSpA. This effect became apparent 2–4 years after initiation of the treatment. ■

A EULAR Framework and Task Force for Gender Equity

GENDER equity was one of the topics centre stage at EULAR 2021, with the congress announcing its plans to accelerate gender-equitable career advancement in academic rheumatology through a framework and task force.

The EULAR Task Force on Gender Equity in Academic Rheumatology set out to establish how much of an unmet need there is for supporting female rheumatologists, healthcare professionals, and non-clinical scientists in academic rheumatology. Once understanding the extent of the unmet need, the objective was to develop a framework and address the demand through EULAR and Emerging EULAR Network (EMEUNET).

EULAR collected possible interventions to accelerate gender-equitable career advancement in academic rheumatology through the following actions: expert opinion from the multi-disciplinary Task Force was acquired, survey data from EULAR scientific member society leaders were analysed, a narrative review of the relevant literature was studied, and EULAR, EMEUNET, and EULAR Executive Committee members were consulted. The interventions were subsequently ranked from 1 to 5 by Task Force members in order of perceived priority: 1 = very low; 5 = very high.

A framework containing 29 possible interventions was composed and covered six thematic areas: 1) EULAR policies; 2) advocacy and communication; 3) the EULAR congress and the associated symposia; 4) training courses; 5) peer/mentoring support; and 6) EULAR funding. The framework that was formulated gives structured interventions for advancing gender-equitable career progression in the field of academic rheumatology. ■

"The framework that was formulated gives structured interventions for advancing gender-equitable career progression in the field of academic rheumatology."

"The study showed that in a group of patients with rheumatic diseases, the spread of SARS-CoV-2 infection is greater than what has been previously observed through swab diagnosis."

True COVID-19 Spread and Prevalence is Greater than Currently Observed

TRUE prevalence and spread of COVID-19 is much greater than what is being recorded, because current statistics are only based on swab-diagnosed COVID-19 cases. Data shared at EULAR 2021 from Lombardy, Italy, reported that the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is still unknown and is much greater than observed because of the high proportion of subclinical infection, but is consistent with a healthy population.

The data were published as part of the EULAR 2021 poster presentations and are part of the MAINSTREAM project, a seroprevalence cross-sectional study performed by Ennio Giulio Favalli, Gaetano Pini Institute, Milan, Italy, and colleagues between 4th May and 16th June 2020 to evaluate the prevalence of anti-SARS-CoV-2 antibodies in a large cohort of patients with rheumatoid arthritis or spondylarthritis. Individuals in the study cohort were being treated with biological or targeted synthetic disease-modifying anti-rheumatic drugs and lived in Lombardy, a COVID-19 high-endemic area of Italy. Individuals (n=300) were tested for IgA, IgG, and IgM antibodies against three viral antigens: the receptor-binding domain, nucleoprotein, and spike protein. The data were then compared to the region's healthy population. The participants completed a questionnaire regarding the symptoms consistent with COVID-19, comorbidities, and risk factors.

In total, 65% of the participants had rheumatoid arthritis, 23% had psoriatic arthritis, and 21% had ankylosing spondylitis. The main therapy used for treatment were TNF inhibitors (57%), followed by abatacept (20%), IL-6 (11%), and JAK inhibitors (5%). Four out of the 300 individuals had been previously diagnosed with COVID-19 by a nasopharyngeal swab test.

On evaluation of Ig titres, 13.3%, 9%, and 13.6% of patients were positive for IgA, IgG, and IgM, respectively, and there was no significant difference when compared to the healthy population. Fifty-five percent of the patients who were seropositive were asymptomatic, 19.6% had major symptoms, 16% had minor symptoms, and 7% were hospitalised, however, no intensive care unit admissions or deaths were recorded. The titres of IgA, IgG, and IgM to the virus receptor-binding domain were higher in patients with both major and minor symptoms, compared to patients who were asymptomatic. In regard to age, sex, rheumatic diagnosis, and treatment, no differences were found between seronegative and seropositive patients.

The study showed that in a group of patients with rheumatic diseases, the spread of SARS-CoV-2 infection is greater than what has been previously observed through swab diagnosis. The rheumatic diseases and the ongoing therapies did not appear to have any impact on antibody positivity. ■

Uveitis Drug Withdrawal Studied in Children with Arthritis

EMERGING evidence during EULAR 2021 has highlighted risk of uveitis in patients being treated for juvenile idiopathic arthritis (JIA), specifically upon withdrawal of disease-modifying anti-rheumatic drugs (DMARD). This complication can have serious, lasting implications upon vision, leading to blindness if uncontrolled, and occurs frequently as a stand-alone condition in close to 20% of children with JIA.

EULAR 2021 gave the opportunity to Jens Klotsche and his colleagues to share an alarming risk profile they identified, involving children discontinued from DMARDs in extended oligoarthritis and rheumatoid factor-negative polyarthritis categories of JIA. The German Biologics in Pediatric Rheumatology (BiKeR) registry and Juvenile arthritis Methotrexate/Biologics long-term Observation (JuMBO) study provided data for analysis, presenting 2,041 children and stating adverse uveitis events during treatment and after removal of DMARDs.

Etanercept was taken in just over half (58%) of the children included, alongside 635 patients using methotrexate monotherapy (31%) and adalimumab (10%). Critical findings demonstrated children with uveitis had a lower age at JIA onset in comparison to patients without. Recurrent uveitis events were reported in 93 children, to a total of 142 events; for 27 of these children it was an incident reported during follow-up, 19 of which were flare-ups after the age of 18.

In the first 24 months after discontinuation, uveitis events were significantly more frequent, and in the first 3 months after DMARD removal. A notable finding was that children with a methotrexate dose of ≤10 mg/m^2 had a higher likelihood for uveitis events. The study Findings that uveitis relapses are common, and patients who stop DMARDs are at risk, are expected to promote regular uveitis screening after treatment is withdrawn. Sharing these findings at EULAR 2021 will help raise awareness among rheumatologists and ophthalmologists, in an event aiming to improve treatment, prevention and rehabilitation of rheumatic and muskuloskeletal diseases. However, it should be acknowledged this is the first prospective study to look at this relationship. ■

"Findings that uveitis relapses are common, and patients who stop DMARDs are at risk, are expected to promote regular uveitis screening after treatment is withdrawn."

Air Pollution and Passive Smoking Linked to Arthritis

ANALYSES of increasing evidence of associations between air pollution, passive exposure to smoking, and risk of developing rheumatoid arthritis (RA) were shared at EULAR 2021. Based on a large female population in France, the first study's findings offered insight into how future initiatives might combat the widespread influence of RA. Previous literature has shown active smoking to be the most reproducible risk factor for RA. A second study in Italy investigated air pollution levels that exhibit associations with failure of biologic therapy.

During EULAR 2021, Nguyen and colleagues explained their selection of a large prospective cohort of healthy females in their French study, examining 79,806 profiles, of which 698 cases of RA were identified. Looking at the whole population, 13.5% were exposed to passive smoking as children, 53.6% as adults, and 8.25% to both. They drew the conclusion that passive smoking in childhood and adulthood was positively associated with risk of RA, particularly among female patients who had never smoked themselves. These results suggest smoking by-products, via either active or passive inhalation, could generate autoimmunity towards antigens involved in RA pathogenesis. It should be considered that the conclusions drawn are limited to a female population, but future directives will build on the findings of the current study, given that RA is more common in female than male patients.

"Authors concluded environmental air pollution a determinant of poor response to biologic treatment, based on their findings future action should decrease fossil fuel emissions to benefit the persistence rate of therapies."

EULAR 2021 discussion progressed to a study by Adami and colleagues, investigating links between the lungs and inflammatory arthritis. To examine the association between concentration of air pollutants and biologic drug retention rates in people with chronic inflammatory arthritis, they conducted a case cross-over study involving 1,286 patients in Verona, Italy.

Of the cohort, 1,286 had chronic inflammatory arthritis, and the authors found an exposure-dependent relationship between air pollutants and markers of inflammation in patients of this sub-category. At the European Union's health protection limit for pollution (30 µg/m^3) there was a 38% higher risk of having altered C-factory smoke reactive protein levels. The authors concluded that environmental air pollution was a determinant of poor response to biologic treatment; based on their findings, future action should decrease fossil fuel emissions to benefit the persistence rate of therapies. ■

Increased Risk of COVID-19 in Inflammatory Joint Disease

AT EULAR 2021, population-based data shared by Vivekanantham and Bower examined the association between rheumatoid arthritis (RA) and diagnosis, hospitalisation, and death related to COVID-19. Amidst the pandemic, the findings were of great interest to people with inflammatory diseases, who may have higher risk of severe outcomes with the virus. Results from Spain suggest individuals with RA have increased risk of COVID-19 diagnosis and hospitalisation compared to the general population, while a database in Sweden found that the risk of severe infection was increased amongst patients with inflammatory joint diseases.

The first studied section included 80% of the population of Catalonia, with information linked to regional hospital figures between March and May 2020, to a total of 5,586,565 participants. Of this population, 16,344 had RA and exhibited a positive association with COVID-19 diagnosis and hospitalisation. It should be acknowledged that in this Spanish study the authors did not find any association between RA and worsening diagnosis to hospitalisation, or hospitalisation to death. Future studies will address factors linking RA and COVID-19, including comorbidities, underlying RA activity, and immunosuppressive medications.

The Swedish database studied mortality and risk of severe COVID-19 in 110,567 people with varying chronic inflammatory joint diseases, comparing this subset with 484,277 of the general population. Analysing admissions to hospital and deaths, the absolute risk of death from any cause in 2020 was observed to peak in mid-April. This peak was higher than that of 2015-2019, but the relative risk of death against the general population remained similar. In those with inflammatory joint disease, Bower shared that risk of hospitalisation, admission to intensive care, and death due to COVID-19 was 0.3%, 0.03%, and 0.07% respectively.

The studies discussed at EULAR 2021 bring forward crucial findings that may prove useful foundations for investigating the complex relationship between inflammation and infectious disease, specifically COVID-19. ■

"Results from Spain suggest individuals with RA have increased risk of COVID-19 diagnosis and hospitalisation compared to the general population, while a database in Sweden found that the risks of severe infection was increased amongst patients with inflammatory joint diseases."