

# Canadian Rheumatology Association Meeting Virtual Conference February 2–5, 2022

The 76th Annual Meeting of the Canadian Rheumatology Association was held virtually on February 2–5, 2022. The program consisted of presentations covering original research, symposia, awards, and lectures. Highlights of the meeting include the following 2022 Award Winners: Distinguished Rheumatologist, John G. Hanly and Lori B. Tucker; Distinguished Teacher-Educator, Stephen Aaron; Emerging Investigator, Jessica Widdifield; Ian Watson Award for the Best Abstract on SLE Research by a Trainee, Maher Banjari; Phil Rosen Award for the Best Abstract on Clinical or Epidemiology Research by a Trainee, Molly Dushnicky; Best Abstract by a Rheumatology Resident, Wen Qi; Best Abstract on Basic Science Research by a Trainee, Omar Cruz Correa; Best Abstract by a Post-Graduate Research Trainee, Holly Philpott; Best Abstract on Quality Care Initiatives in Rheumatology, Michael Zeeman; Best Abstract by a Medical Student, Samir Magdy Iskander; Best Abstract by an Undergraduate Student, Daniel Onwuka; Best Abstract by a Rheumatology Post-Graduate Research Trainee, Jennifer Lee; Best Abstract on Research by Young Faculty, Nancy Maltez; Best Abstract on Pediatric Research by Young Faculty, Chelsea DeCoste; Best Abstract on Spondyloarthritis Research, Vanessa Ocampo; Practice Reflection Award, Gold, Bailey Dyck. Lectures and other events included: Keynote Lecture by Grace Wright: Towards Equity: Is Everyone in the Rheum Paving the Path to Equity with Diversity?; State of the Art Lecture by Tuhina Neogi: Pain Across the Spectrum of Rheumatic Diseases; Dunlop-Dottridge Lecture by Simon Carrette: Vasculitis: What Have We Learned in the Past 50 Years?; and the Great Debate: Be it Resolved that the Rheumatology Healthcare Provider Is Responsible for Prescribing and Monitoring Physical Activity. Arguing for: Claire LeBlanc and Laura Passalent, and against: Arthur Bookman and Marie Clements-Baker. Topics including rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, Sjögren syndrome, psoriatic arthritis, spondyloarthritis, vasculitis, osteoarthritis, fibromyalgia, and their respective diagnoses, treatments, and outcomes are reflected in the abstracts, which we are pleased to publish in this issue of *The Journal of Rheumatology*.

# PODIUM PRESENTATIONS

## POD01

### Studying Clusters of Patients With Systemic Lupus Erythematosus (SLE) According to Cognitive Function, Self-reported Outcomes, Disease Activity, and Clusters Dynamic Over 1 Year

Ambika Gupta (University of Toronto, Toronto); Sindhu Johnson (Toronto Scleroderma Program, Mount Sinai Hospital; Division of Rheumatology, Toronto Western Hospital; Department of Medicine, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Kathleen Bingham (UHN, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto); Juan Diaz-Martinez (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto); Mahta Kakvan (Toronto Western Hospital, Toronto); Carmela Tartaglia (University Health Network, Toronto); Lesley Ruttan (University Health Network, Toronto); Joan Wither (Division of Genetics and Development, Krembil Research Institute; Division of Rheumatology, University Health Network; Department of Immunology, University of Toronto, Toronto); May Choi (University of Calgary, Calgary); Marvin Fritzier (University of Calgary, Calgary); Dennisse Bonilla (Toronto Western Research Institute, Toronto); Dorcas Beaton (University of Toronto/Institute for Work and Health, Toronto); Patricia Katz (University of California San Francisco, Professor of Medicine and Health Policy, Division of Rheumatology, Department of Medicine, San Francisco); Robin Green (University Health Network, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** Systemic lupus erythematosus (SLE) has a high prevalence of cognitive impairment (CI). Patient reported outcomes (PROs) capture patient perceptions of their health condition, health related quality of life (HRQoL) and other aspects. We aimed to determine if self-reported fatigue, anxiety, depression, perceived deficits questionnaire (PDQ-20), HRQoL, disease activity scores and cognitive neuro-battery (NB) cluster into distinct groups. We assessed if patients changed clusters at 1 year of follow-up.

**Methods:** This is a retrospective analysis of patients aged 18-65 years, who attended a single center (Jul 2016 – Mar 2019) and completed baseline and 1 year follow-up visits. Patients completed a comprehensive NB, Beck anxiety/depression, fatigue severity score (FSS), Short Form Health Survey (SF-36) physical (PCS) and mental scores (MCS), and the PDQ-20 (subjective cognitive function). Disease activity was assessed by SLEDAI-2K. Ward's method was used for clustering and Principal Component Analysis was used to confirm the number of clusters. Clusters were grouped based on symptom intensity, defined as those that had high, medium, and low PROs scores relative to one another. We assessed the stability and movement of clusters at 1 year.

**Results:** 142 patients were included, 89.4% comprised females. The mean age and SLE duration at enrolment were  $43.1 \pm 12.1$  and  $15.3 \pm 10.1$  years, respectively. Three clusters were found: Cluster 1 had low, Cluster 2 had

moderate, and Cluster 3 had high symptom intensity (Figure 1). In Cluster 3, the most severe scores for fatigue, depression, anxiety, PDQ-20, and SF-36 MCS were found. NB scores in Cluster 3 were similar to Cluster 2. SLEDAI-2K was similar in Clusters 1 and 3 and more active in Cluster 2. At 1 year follow-up, 49% of patients remained in their baseline cluster. Cluster 1 had the highest stability (77% of patients stayed in the same cluster), followed by Cluster 3 and Cluster 2 had the lowest stability. A minority of patients from Cluster 1 moved to Cluster 3 (19%). In Cluster 3, only 9% moved to Cluster 1.

**Conclusion:** Three distinct clusters of symptom intensity were found in SLE patients in association with cognitive function with Cluster 3 displaying the highest symptom severity and worse cognitive function versus Cluster 1 having the lowest symptom burden and better cognitive function. Patients remained in the same cluster at one year, particularly in Cluster 1 and Cluster 3, and there was a low tendency to move between these two Clusters.

## POD02

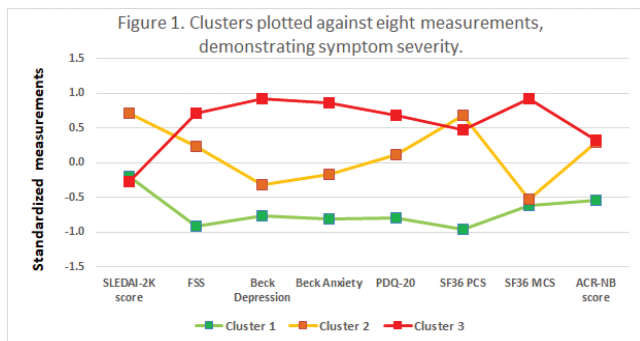
### Effectiveness of the Making it Work™ Program at Improving Absenteeism in Workers With Inflammatory Arthritis – Results of a Randomized Controlled Trial

Andre Luquini (University of British Columbia - Department of Experimental Medicine/Arthritis Research Canada, Richmond); Yufei Zheng (Arthritis Research Canada, Richmond); Hui Xie (Arthritis Research Canada/Faculty of Health Sciences at Simon Fraser University, Richmond); Catherine Backman (Rehab Sciences/Occupational Therapy, University of British Columbia, Richmond); Pamela Rogers (Arthritis Research Canada, Richmond); Alex Kwok (Arthritis Research Canada, Richmond); Astrid Knight (Arthritis Research Canada, Richmond); Monique Gignac (Institute for Work and Health, Dalla Lana School of Public Health, University of Toronto, Toronto); Dianne Mosher (University of Calgary, Calgary); Linda Li (Rehab Sciences/Physical Therapy, University of British Columbia, Arthritis Research Canada, Richmond); John Esdaile (University of British Columbia (Division of Rheumatology)/Arthritis Research Canada, Richmond); Carter Thorne (The Arthritis Program Research Group, Newmarket); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver)

**Objectives:** Despite advances in treatment, absenteeism remains a major problem for workers living with inflammatory arthritis (IA). We evaluated the effectiveness of the Making-it-Work™ (MIW) at preventing days missed from work and work interruptions.

**Methods:** A multi-center RCT evaluated the effectiveness of MIW at improving absenteeism over two years. Participants were recruited from rheumatologist practices, consumer organizations and arthritis programs, in three provinces, eligible if: diagnosis of IA, employed, age 18-59, and concerned about ability to work. Participants were randomized 1:1 to MIW or usual care plus printed material on workplace tips. MIW consists of five online self-learning modules and group meetings, individual vocational counseling and ergonomic assessments. Questionnaires were administered every 6 months. Outcomes were 1) number of sick days (occasional days missed from work and sick leaves < 2 months duration) per 100 workable-days; 2) work interruptions > 2 months duration per 100-days follow-up, and 3) the combined outcome (sick days plus work interruptions of any duration per 100-days follow-up). Intention-to-treat analysis using Beta-binomial logistic regression models were used to evaluate the intervention effects on the three absenteeism outcomes, accounting for the potential overdispersion in binomial outcomes. Odds ratios (OR) representing the intervention's effect on the daily risk of each absenteeism outcome, adjusting for baseline characteristics [age, sex, education, ethnicity, job type, RA duration, pain, disease activity (RADAI), fatigue, and physical function (HAQII)], 95% confidence intervals and Wald-tests were computed using robust standard errors accounting for potential model misspecifications. Analyses were conducted using STATA 16.

**Results:** A total of 564 participants were recruited, with 85% completing 2-year follow-up. Baseline characteristics were similar between groups.



| Beta binomial logistic regression model estimating the effect of the intervention on absenteeism |                          |          |                             |          |
|--------------------------------------------------------------------------------------------------|--------------------------|----------|-----------------------------|----------|
| Outcomes                                                                                         | Univariate Model (N=532) |          | Multivariable Model (N=525) |          |
|                                                                                                  | Odds Ratio (95%CI)       | P values | Odds Ratio (95%CI)          | P values |
| Sick Days per 100 workable days                                                                  | 0.79 (0.63, 0.97)        | 0.028    | 0.76 (0.61, 0.95)           | 0.014    |
| Work Interruptions > 2 months per 100 days of follow-up                                          | 0.70 (0.47, 1.02)        | 0.064    | 0.7 (0.46, 1.06)            | 0.09     |
| Combined per 100 days of follow-up                                                               | 0.74 (0.6, 0.91)         | 0.004    | 0.73 (0.59, 0.91)           | 0.005    |

Mean (SD) number of sick days were 2.7 (4.6) and 2.3 (4.3) per 100 workable days, for controls and MIW, respectively; and mean (SD) number of days of work interruptions were 10.5 (22) and 8.8 (21.2) per 100 days of follow-up, respectively. The intervention group had a 21% lower odds of taking sick days from work ( $P = 0.028$ ), a 30% lower odds of work interruptions ( $P = 0.064$ ), and a 26% lower odds of the combined outcome ( $P = 0.004$ ; Table).

**Conclusion:** Results of the RCT reveal that the program was effective at improving absenteeism by decreasing the odds of sick days and work interruptions, although the latter was of borderline statistical significance. Effectiveness at preventing long-term work disability will be assessed at 5 years. This program fills one of the most important unmet needs for people with inflammatory arthritis.

### POD03

#### Work Disability and Function in Systemic Lupus Erythematosus (SLE): Early Results of an Exploratory National Study

Behdin Nowrouzi-Kia (University of Toronto, Toronto); Antonio Avina-Zubieta (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Richmond); Mary Fox (York University, Toronto); William Shaw (UConn Health, Farmington); Maggie Ho (UHN, Toronto); Derek Haaland (Department of Medicine, McMaster University, Hamilton); Janet Pope (University of Western Ontario, London); Paul Fortin (Université Laval, CHU de Québec, Québec); Kathleen Bingham (UHN, Toronto); Nathalie Rozenbojm (University of Toronto Lupus Clinic, University Health Network, Toronto); Mark Matsos (McMaster University, Hamilton); Kimberly Legault (McMaster University, Hamilton); Konstantinos Tselios (University of Toronto, Toronto); Christine Peschken (University of Manitoba, Winnipeg); Jiandong Su (Toronto Western Hospital, Toronto); Jennifer Reynolds (University of British Columbia, Department of Medicine, Division of Rheumatology, Vancouver); Catherine Ivory (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto); Jorge Sanchez-Guerrero (Toronto Scleroderma Program, Division of Rheumatology, Toronto Western Hospital, University Health Network; Division of Rheumatology, Mount Sinai Hospital; University of Toronto, Toronto); Lily Lim (University of Manitoba, Winnipeg); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Patricia Katz (University of California San Francisco, Professor of Medicine and Health Policy, Division of Rheumatology, Department of Medicine, San Francisco); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** As a potentially severe disease with high morbidity, systemic lupus erythematosus (SLE) is associated with disability and functional impairment. We hypothesize that the creation of a functional profile will enhance our understanding of the impact of SLE on patients' everyday functioning, allowing us to optimize interdisciplinary interventions. In this study, we focus on work disability and function. The objective of the study was to create a functional profile of patients with SLE. A functional profile is defined as activities of daily living and those related to work functioning (eg, instrumental activities of daily living).

**Methods:** A self-administered questionnaire was used to collect data from patients at 10 Canadian centers (9 academic centers and one community center). Patients who consented were asked to complete the Work Role Functioning Questionnaire v2.0 (WRFQ), World Health Organization – Disability Assessment Schedule 2.0 (WHO-DAS), and the Beck Depression

Inventory (BDI-II). Descriptive statistics were obtained for demographic, clinical and functional outcomes. In this cross-sectional study, we report the results from the first 31 participants.

**Results:** Participants' mean age was  $41.3 \pm 12.0$  years. 90% were female, 51.6% Caucasian, 16.1% Black, 9.7% Chinese and 22.6% other races, with a mean SLE duration of  $15.5 \pm 10.9$  years. The total mean score for the WRFQ was  $73.8 \pm 24.8$ . The WRFQ subscale mean scores were also reported for work scheduling demands ( $66.4 \pm 36.0$ ), work output demands ( $75.7 \pm 26.5$ ), physical demands ( $71.6 \pm 29.5$ ), mental and social demands ( $73.5 \pm 25.2$ ) and flexibility demands ( $77.6 \pm 21.9$ ). The WHO-DAS 2.0 total mean score was  $27.5 \pm 12.2$ , representing approximately the 94.7th population percentile, meaning that only about 5.3% of the population score higher (more disabled) than our sample. Specifically, patients reported 'moderate to extreme' difficulty walking a long distance such as a kilometer (42.0%), getting dressed (22.6%) and taking care of household tasks (45.1%). The total score for the BDI-II was  $19.9 \pm 14.4$ , and 41.9% of patients reported scores  $\geq 22$ , suggesting moderate levels of depression.

**Conclusion:** The WRFQ total and subscale scores showed significant limitation among patients. Scores are comparable to a sample of patients diagnosed with cancer who returned to work for at least 12 hours per week. Quality of life was low, and rates of depression were high. We are actively recruiting patients at all 10 centers. It is anticipated that the creation of a first-ever functional profile of work disability will provide opportunities for a multidisciplinary team approach to deliver improved care and management of work disability and functional outcomes. Supported by a CIORA grant.

### POD04

#### Characteristics of Emergency Department and Urgent Care Center Use by Patients With Inflammatory Arthritis Conditions

Cheryl Barnabe (University of Calgary, Calgary); Patrick McLane (University of Alberta, Edmonton); Brian Holroyd (University of Alberta, Edmonton); Eddy Lang (University of Calgary, Calgary); Nadia Luca (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Steven Katz (University of Alberta, Edmonton); Joanne Homik (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Shanon McQuitty (Arthritis Research Canada, Vancouver); Eileen Davidson (Arthritis Research Canada, Richmond); Katie Lin (University of Calgary, Calgary); Kelsey Chomistek (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Meghan Elliott (University of Calgary, Calgary); Clare Hildebrandt (Calgary); Nazret Russon (Edmonton); Michelle Stasiuk (Calgary); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary)

**Objectives:** Persons with inflammatory arthritis (IA) conditions (Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Juvenile Idiopathic Arthritis (JIA), gout) face health system limitations in accessing appropriate ambulatory care; this may result in an otherwise avoidable visit to an emergency department (ED) or urgent care centre (UCC). Our objective was to describe the frequency of ED/UCC visits, patterns of use, acuity at presentation, and disposition by individuals with IA conditions.

**Methods:** Our estimates were based on population-based data hosted by Alberta Health. We applied validated case definitions to administrative data (years 2002-2018) to define prevalent RA, AS, PsA, JIA and gout cohorts based on physician claims or prior hospitalization for that type of IA. National Ambulatory Care Reporting System (NACRS) data (years 2008-2018) was analyzed to estimate ED/UCC use by individuals in these cohorts.

**Results:** In fiscal year 2017-2018 there were a total of 172,331 individuals meeting case definitions for IA conditions in Alberta. They had a total of 156,570 ED/UCC visits representing 6.8% of all ED/UCC usage in the province (see Table 1 for individual IA condition results). Approximately 1/3 of individuals with IA conditions accessed the ED/UCC (RA 37%,



| Inflammatory Arthritis Condition         | Rheumatoid Arthritis (n=4833) | Psoriatic Arthritis (n=4312) | Ankylosing Spondylitis (n=17481) | Juvenile Idiopathic Arthritis (n=1915) | Gout (n=9990) |
|------------------------------------------|-------------------------------|------------------------------|----------------------------------|----------------------------------------|---------------|
| Proportion of Cases Accessing ED/UCC (%) | 37.0                          | 46.2                         | 35.7                             | 34.0                                   | 33.5          |
| Visits per individual (mean, SD)         | 0.9 (1.1)                     | 1.3 (1.6)                    | 0.9 (1.3)                        | 0.8 (1.0)                              | 0.8 (1.5)     |
| CTAS 1 – resuscitation (%)               | 0.7                           | 0.8                          | 0.4                              | 0.1                                    | 0.8           |
| CTAS 2 – emergent (%)                    | 14.6                          | 16.3                         | 13.7                             | 15.3                                   | 15.6          |
| CTAS 3 – urgent (%)                      | 38.7                          | 37.8                         | 38.1                             | 38.0                                   | 37.9          |
| CTAS 4 – less urgent (%)                 | 30.8                          | 28.2                         | 32.0                             | 37.3                                   | 32.0          |
| CTAS 5 – nonurgent (%)                   | 11.6                          | 13.6                         | 10.7                             | 7.7                                    | 10.4          |
| Presentation 0800-1600 hours (%)         | 54.0                          | 50.7                         | 53.6                             | 45.5                                   | 55.7          |
| Presentation 1603-2200 hours (%)         | 28.9                          | 29.4                         | 30.0                             | 36.0                                   | 28.6          |
| Presentation 2201-0759 hours (%)         | 17.2                          | 20.0                         | 16.3                             | 18.5                                   | 17.7          |
| Weekday presentation (%)                 | 70.4                          | 70.6                         | 70.2                             | 68.8                                   | 70.3          |
| Length of Stay, minutes (median, IQR)    | 179 (86, 354)                 | 205 (89, 427)                | 158 (79, 309)                    | 140 (82, 241)                          | 181 (87, 371) |
| Return to ED/UCC within 72 hours         | 19.5                          | 22.8                         | 19.8                             | 16.0                                   | 18.8          |
| Admitted to hospital                     | 15.3                          | 17.3                         | 11.2                             | 6.0                                    | 17.3          |

Legend: ED = Emergency Department; UCC = Urgent Care Centre; SD = standard deviation; CTAS = Canadian Triage Acuity Score; IQR = Interquartile range

AS 36%, JIA 34%, Gout 34%) although this was more frequent in those with PsA (46%). PsA patients also had an increased frequency of visits per individual (mean 1.3) compared to RA and AS (each 0.9), and JIA and Gout (each 0.8). The majority of visits (38%) were triaged as urgent (Canadian Triage Acuity Scale = 3). Daytime presentation (08:00-16:00 hours) was the most common for all individuals (range 51-56% for RA, PsA, AS and gout, 46% for JIA) and those with JIA had the highest frequency of evening presentation (36%). ED/UCC visit rates were consistent over weekday and weekend/statutory holidays. The median length of stay ranged from 140 minutes for JIA to 205 minutes for PsA. Approximately 1/5 of all visits resulted in a return to ED/UCC within 72 hours, and admission rates varied (JIA 6%, AS 11%, RA 15%, PsA and gout 17%). Over the full 10-year analysis period, annual estimates were relatively stable with the exception of visits for gout which increased from 2.14% in fiscal year 2008-2009 (95% CI 2.13-2.16) to 3.62% in fiscal year 2017-2018 (95% CI 3.59-3.64) of overall provincial ED/UCC use.

**Conclusion:** This descriptive analysis provides an initial perspective of ED/UCC use by individuals with IA conditions and the opportunity to investigate reasons for this usage.

#### POD05

##### Does Patient Age Affect Surgical Appropriateness and Influence Surgeon Recommendations for Primary Total Knee Arthroplasty? A Cross-sectional Study of 2037 Patients.

Gillian Hawker (University of Toronto, Toronto); Eric Bohm (University of Manitoba, Winnipeg); Michael Dunbar (Dalhousie University, Halifax); Allyson Jones (University of Alberta, Edmonton); Tom Noseworthy (University of Calgary, Calgary); Deborah Marshall (University of Calgary, Calgary); BEST-Knee Study Team (Toronto)

**Objectives:** Rising total knee arthroplasty (TKA) rates in younger patients raises concern about appropriateness. We asked: Are younger individuals seeking consultation for TKA less likely to be appropriate and, controlling for appropriateness, more likely to be recommended for surgery?

**Methods:** This cross-sectional study was nested within a prospective cohort of knee osteoarthritis (OA) patients referred for TKA between 2014 and 2016 to centralized arthroplasty centers in Alberta, Canada. Pre-consultation, questionnaires assessed patients' TKA appropriateness (need: knee symptoms, prior treatment; readiness/willingness to undergo TKA; health status; expectations) and contextual factors (eg, employment). Post-consultation, surgeons confirmed study eligibility and reported their TKA recommendation. Using generalized estimating equations to control for clustering by surgeon, we assessed relationships between patient age (< 50, 50-59, ≥ 60 years) and TKA appropriateness and receipt of a surgeon TKA recommendation.

**Results:** Of 2,037 participants, 3.3% and 22.7% were < 50 and 50-59 years; 58.7% female, 35.5% employed. Compared to older participants, younger participants reported significantly worse knee symptoms, higher use of OA therapies, higher TKA readiness and similar willingness, but had higher BMI, were more likely to smoke and to consider ability to participate in vigorous activities, eg, sports, as very important TKA outcomes. TKA was offered to 1,500 individuals (73.6% overall; 52.2%, 71.0% and 75.4% for those < 50, 50-59 and ≥ 60 years, respectively). In multivariable analyses, the odds of receiving a TKA recommendation were higher with greater TKA

need and willingness, in non-smokers, and those who indicated improved ability to go upstairs and straighten the leg were very important TKA outcomes. Controlling for TKA appropriateness, patient age was not associated with surgeons' TKA recommendations.

**Conclusion:** Younger individuals with knee OA referred for TKA had similar or greater TKA need, readiness and willingness than older individuals, but were at higher risk for complications, eg, early revision. Incorporation of TKA appropriateness criteria into TKA decision-making may facilitate consideration of TKA benefits and risks in a growing population of young, obese individuals with knee OA.

#### POD06

##### Assessing the Relationship Between Health Outcomes and Ethnic Concentration in Patients With Childhood-onset Systemic Lupus Erythematosus

Ibrahim Mohamed (The Hospital for Sick Children, Brampton); Chelsea DeCoste (IWK Health Centre, Halifax); Lawrence Ng (University of Toronto, The Hospital for Sick Children, Toronto); Paris Moaf (The Hospital for Sick Children, Toronto); Hardil Bhatt (University of Toronto Faculty of Medicine, Toronto); Dragana Ostojic-Aitkens (The Hospital for Sick Children, Toronto); Bryan Maguire (The Hospital for Sick Children, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto); Deborah Levy (Division of Rheumatology, SickKids Hospital; Faculty of Medicine, University of Toronto, Toronto); Alene Toulany (The Hospital for Sick Children, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto)

**Objectives:** Adolescents with childhood-onset Systemic Lupus Erythematosus (cSLE) often face challenges in managing their disease and their mental health. There is sparse data on the effects of ethnic concentration, reflecting both new immigrants and visible minorities, on cSLE health outcomes. The objectives of this study were to examine the relationship between ethnic concentration of patients with cSLE and active disease, disease damage, and comorbid psychiatric diagnosis.

**Methods:** We conducted a retrospective cohort study of patients under 18 years old diagnosed with SLE meeting ACR/SLICC criteria and seen at the Lupus Clinic at SickKids between July 1, 2018, to July 1, 2020. Patient data was collected using the Epic electronic health record system, stored in RedCap, and analyzed using R/RStudio. The Ontario Marginalization Index is an area-based index used to display the differences in marginalization between geographical areas. Ethnic concentration, a dimension of the Ontario Marginalization Index, measures the concentration of new immigrants and visible minorities in an area. Ethnic concentration scores were generated using the full postal codes of patients and modeled as a continuous variable (range: -1.2 to 4.3). We performed multivariable logistic regression analysis to examine the associations of ethnic concentration with the presence of active disease (average SLEDAI-2K score > 4), disease damage (SLICC/ACR damage index > 0), and comorbid psychiatric diagnosis.

**Results:** 179 children (mean age 15.7 years and 83% female) were included (Table 1). Self-reported race/ethnicity was 45% Asian, 17% White, 16% Black, 8% Latin/Hispanic, 8% Arab/Middle Eastern, 2% Aboriginal, 1% Pacific Islander, and 2% declined response. 61% of the patients were in the fifth quintile of ethnic concentration (highest ethnic concentration) (Table 1). 29% had active disease, 19% had disease damage, and 21% had

**Table 1. Demographic and Clinical Characteristics of Pediatric Patients with cSLE (n=179).**

|                                              |                  |
|----------------------------------------------|------------------|
| Age, median (IQR)                            | 15.7 (13.7-16.9) |
| Female, n (%)                                | 149 (83%)        |
| Disease duration in years, median (IQR)      | 1.3 (0.0, 4.0)   |
| Ethnic concentration score, median (IQR)     | 1.2 (0.1, 1.9)   |
| <b>Ethnic concentration quintiles, n (%)</b> |                  |
| Quintile 1 (lowest ethnic concentration)     | 10 (6%)          |
| Quintile 2                                   | 8 (4%)           |
| Quintile 3                                   | 19 (11%)         |
| Quintile 4                                   | 33 (18%)         |
| Quintile 5 (highest ethnic concentration)    | 109 (61%)        |



at least one comorbid psychiatric diagnosis. The most common comorbid psychiatric diagnoses were mood (11%) and anxiety (12%) disorders. Multivariable logistic regression models did not show an association between ethnic concentration and active disease (OR = 1.12, 95% CI 0.79-1.59, P = 0.52) or disease damage (OR = 1.03, 95% CI 0.71-1.48, P = 0.88). Ethnic concentration was associated with a lower presence of psychiatric diagnosis (OR = 0.71, 95% CI 0.49-1.04, P = 0.08), although not statistically significant.

**Conclusion:** In this sample of patients with cSLE, higher ethnic concentration was associated with lower psychiatric diagnoses. Further research is required to investigate the relationship between ethnicity and psychiatric diagnoses to identify possible disparities in reporting or evaluating mental health illnesses among marginalized children.

#### POD07

##### The Long-term Cardiac Prognosis of Kawasaki Disease: Results From a Retrospective Matched Data Linkage Study

Jennifer Lee (University of Toronto, Toronto); Brian Feldman (The Hospital for Sick Children, Toronto); Brian McCrindle (SickKids, University of Toronto, Toronto); Ping Li (ICES, Toronto); Rae Yeung (The Hospital for Sick Children, Toronto); Jessica Widdifield (Sunnybrook Research Institute, ICES, University of Toronto, Toronto)

**Objectives:** To evaluate the risk of hypertension and other major adverse cardiac events (MACE) in individuals after Kawasaki disease (KD).

**Methods:** A retrospective matched data-linkage study was conducted. KD patients diagnosed at SickKids from 1991-2008 were linked to administrative databases to ascertain outcomes up until 2019. The risk for hypertension, mortality, and MACE were compared with general population comparators, matched on sex, age, year of cohort entry, ethnicity, and geographic region. Incidence rates (IR) per 1000 person-years (PY), incidence rate ratio (IRR), absolute risk increase (ARI), and cumulative incidence were calculated. Multivariable cause-specific hazard models were performed to determine if KD resulted in a difference in time to hypertension or MACE, adjusting for income and rurality. A multivariable cox model was performed to evaluate differences in survival. Within the KD group, the risk for hypertension, death, and MACE were compared according to KD subtype, sex, treatment resistance, and coronary artery aneurysms (CAA) status.

**Results:** 1,174 KD patients and 11,740 comparators were included. The IR of hypertension in the KD group [IR: 1.4/1000 PY (95% CI 0.9-2.0)] was significantly higher than the non-KD group [IR: 0.6/1000 PY (95% CI 0.5-0.7)] with an IRR estimate of 2.2 (95% CI 1.5-3.3). Similarly, IR for death [IRR: 2.4 (95% CI 1.2-4.7)] and MACE [IRR: 10.5 (95% CI 6.2-17.8)] were significantly increased in KD. The ARI for all outcomes remained low. Hypertension, death, and MACE had an ARI of 0.8 cases/1000 PY (95% CI 0.4-1.2), 0.3/1000 PY (95% CI 0.1-0.6), and 1.2/1000 PY (95% CI 0.8-1.7), respectively. The 28-year cumulative incidence for hypertension and MACE in the KD group was 3.8% (95% CI 2.5-5.5) and 1.2% (95% CI 0.6-2.4%), respectively. The 20-year survival probability in the KD group was 99.1% (95% CI 98.2-99.6%). Relative to comparators, KD patients had an increased risk for hypertension (aHR:2.2, 95% CI 1.5-3.4), death (aHR:2.5, 95% CI 1.3-5.0), and MACE (aHR:10.7, 95% CI 6.4-17.9). For hypertension and MACE, the aHR was highest following diagnosis and the excess risk diminished after 16 years and 13 years of follow-up, respectively. Hypertension risk was not statistically different according to subtype, CAA status, sex, or IVIG resistance. MACE risk was significantly associated with increased IVIG resistance (Log-Rank Test P < 0.0001) and presence of CAA (Log-Rank Test P < 0.0001).

**Conclusion:** In our study, KD was associated with an increased risk for hypertension, death and MACE. KD patients with CAA experienced the highest risk for MACE. For all cardiac outcomes, the increased risk was highest following diagnosis and the excess risk diminished as KD patients aged. However, overall prognosis remains favorable with low event rates. Best Abstract by a Rheumatology Post-Graduate Research Trainee Award.

#### POD08

##### Improvement in Overall Survival, Skin Fibrosis and Lung Function With Autologous Hematopoietic Stem Cell Transplantation in Systemic Sclerosis

Nancy Maltez (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Mianbo Wang (Lady Davis Institute for Medical Research, Montreal); George Wells (University of Ottawa Heart Institute, Ottawa); Peter Tugwell (University of Ottawa, Ottawa); Murray Baron (McGill University, Jewish General Hospital, Montreal); Zora Marjanovic (Hôpital Saint-Antoine, Paris); Pauline Lansiaux (Université de Paris, Paris); Dominique Farge (Université de Paris, Paris); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal)

**Objectives:** Systemic sclerosis (SSc) is a chronic disease characterized by vasculopathy, inflammation and fibrosis. Rheumatologists have limited options to effectively treat rapidly progressive disease. There is an important unmet medical need for disease modifying therapy for patients with SSc. Autologous hematopoietic stem cell transplantation (AHSCT) has been shown in randomized controlled trials and is well recognized to be an effective treatment for rapidly progressive SSc. However, there is a paucity of data pertaining to its performance as compared to real-world routine clinical practice. The objective of this study was to evaluate the effectiveness of AHSCT for SSc compared to conventional care used in routine clinical practice.

**Methods:** SSc patients from Canada and France who underwent AHSCT were compared to SSc patients who met criteria for AHSCT (as defined in the ASTIS trial) but received conventional care. The primary outcome was overall survival. Secondary outcomes included modified Rodnan skin score (mRSS), forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO). Baseline characteristics were compared using descriptive statistics. Overall survival for both groups was estimated by constructing Kaplan-Meier survival curves based on time to death. Measures of mRSS, FVC and DLCO were compared using linear regression models. Analyses were adjusted for baseline scores and incorporated stabilized inverse probability of treatment weights to account for confounding by indication. Propensity scores were estimated using logistic regression.

**Results:** 41 SSc patients who underwent AHSCT, and 85 patients treated with conventional care were compared. At baseline, mean mRSS was 25.0 (10.5) in the AHSCT group and 27.0 (8.0) in the conventional care group. Mean FVC and DLCO were 78.9 (17.5) and 55.2 (15.5) in the AHSCT group and 79.0 (20.2) and 62.0 (19.6) in the conventional care group, respectively. AHSCT was associated with improvement in overall survival (log-rank P = 0.115; Figure 1). In follow-up, the mRSS was lower with AHSCT compared to conventional care: 7.25 point between group difference at 12 months (P < 0.001), 6.41 points at 24 months (P ≤ 0.001) and 4.48 points at 36 months (P < 0.001). There was no statistically significant

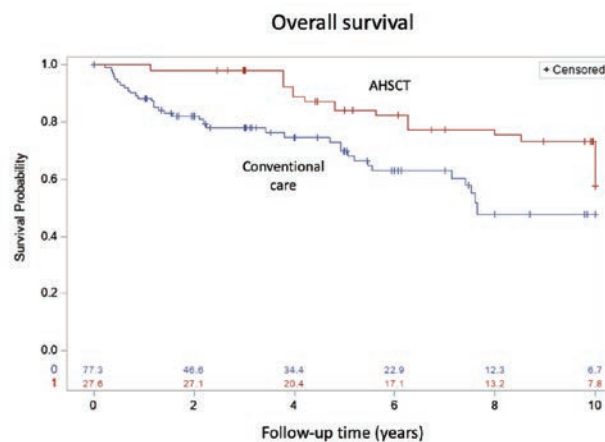


Figure 1: Kaplan-Meier survival estimates of overall survival adjusted for stabilized inverse probability of treatment weights.

difference in FVC between groups at 12 months but at 24 months, AHST was associated with a higher FVC (between group difference of 9.22 ( $P < 0.001$ )) but a lower DLCO (between group difference of -3.43 ( $P = 0.002$ )).

**Conclusion:** The present study provides crucial real-world long-term data pertaining to key clinical outcomes to support the use of AHST in patients with SSc. Best Abstract on Research by Young Faculty Award.

#### POD09

##### **Timing of Congenital Heart Block in Relation to Fetal Echocardiography in Anti-Ro/La Positive Pregnancies**

Nikola Wilk (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal); Mayssa Moukarzel (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Jessica Simoneau (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Wadi Mawad (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal); Gabriel Altit (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal)

**Objectives:** Current congenital heart block (CHB) screening method for anti-Ro/La-positive pregnancies with serial echocardiography often fail to identify early reversible cardiac dysfunction. Our objectives were to review timing of CHB occurrence in relation to fetal echocardiography in anti-Ro/La-positive pregnancies at our institution.

**Methods:** Using an electronic database, we identified all pregnancies referred for fetal echocardiogram between 2013 and 2021 at the McGill University Health Centre, with the following key words within the clinical indication field: "congenital heart block", "anti-Ro", "anti-La", "lupus", "SLE", "Sjogren", or "mixed connective tissue disease". We excluded pregnancies with a fetus exhibiting cardiac anatomical and/or genetic anomalies. Pregnancies were classified as follows: 1) those with positive anti-Ro/La antibodies, 2) those with a rheumatic disease with negative anti-Ro/La, and 3) control pregnancies identified from the same database without rheumatic disease nor autoantibodies.

**Results:** Out of 117 charts screened, 62 were included, with a total of 75 fetuses studied. The first group was composed of 47 fetuses; the second group was composed of 11 fetuses and the control group was composed of 17 fetuses. Patients with anti-Ro/La antibodies had substantially higher numbers of fetal echocardiograms (5.5 [standard deviation, SD 1.9] vs 2.7 [SD 1.6] vs 1.1 [SD 0.3]). Fives cases of CHB were identified in the first group, with the average gestational age at detection being 23.1 (SD 7.4) weeks, and none in the other 2 groups. Three cases (60%) of CHB were found during serial echocardiography in previously known anti-Ro/La-positive mothers at 19.0, 23.4 and 26.0 weeks, while two cases (40%) were referred at 20.0 and 23.9 gestational weeks for fetal echocardiogram with incidental finding of bradycardia after which they were tested for anti-Ro/La (and found positive). All CHB cases were complete when first detected and all except one were found on the initial fetal echocardiogram. Only one fetus reversed from a 3rd-degree atrioventricular block (AVB) to a 1st-degree AVB after receiving dexamethasone, while the other four fetuses remained in 3rd-degree AVB throughout their pregnancy.

**Conclusion:** We observed that most CHB were detected early during the pregnancy course (most often on the first fetal echocardiogram) and all were already 3rd-degree. Despite this, one fetus (out of five) reversed from 3rd to 1st-degree AVB after dexamethasone initiation. Our findings illustrate the need for further studies to identify an alternative diagnostic strategy more sensitive at detecting earlier reversible cardiac involvement in anti-Ro/La positive pregnancies.

#### POD10

##### **Polyarticular Arthritis Caused by Mutations in the ASAH1 Gene: Farber Disease Diagnostic Clues and Lessons From a Natural History Study**

Paul Dancey (Janeway Children's Hospital and Rehabilitation Centre, St. John's); John Mitchell (Montreal Children's Hospital, Montreal); Alexander Solyom (Aceragen, Basel); Kathleen Crosby (Aceragen, Durham)

**Objectives:** To further define the signs and symptoms of Farber disease, including joint disease, subcutaneous nodules, dysphonia, and osteolysis, which can lead to referral to rheumatology. To understand the clinical presentation of this rare disease to aid in clinical diagnosis and reduce diagnostic delay.

**Methods:** The Observational and Cross-Sectional Cohort Study of the Natural History and Phenotypic Spectrum of Farber Disease (NCT03233841) was the first systematic clinical study of the natural history of Farber disease, an ultra-rare lysosomal storage disorder caused by mutations in the ASAH1 gene. The study collected retrospective and prospective data, including patient demographics, clinical presentation, phenotype, diagnostic history, and patient reported outcomes.

**Results:** 45 patients with Farber disease (27 living, 18 deceased) who had or had not undergone hematopoietic stem cell transplant (HSCT) were enrolled from 16 centers in 9 countries. A cohort of 24 living non-HSCT patients were followed prospectively. The patients represented the broad phenotypic spectrum of Farber disease, from rapidly progressive (severe) to slowly progressive (attenuated). In patients whose data was available for analysis, the average age at enrollment was 7.2 years (range 1 to 28 years). The average age of onset of joint disease (arthritis and/or contractures) was 15 months (range 3 months to 7 years), of subcutaneous nodules was 13 months (range 3 months to 5 years), and of dysphonia was 13 months (range birth to 8 years). The average time from onset of symptoms to Farber disease diagnosis was 2 years (range < 1 to 12 years). At baseline, the mean number of joints affected with active arthritis was 11.3 (range 0-36) and the mean number affected with contractures was 18 (range 0-38). The Child Health Assessment Questionnaire Disability Index (CHAQ) ranging from 0 (no impairment) to 3 (unable to do) was high, with mean scores of 2.62-3.00 across visits.

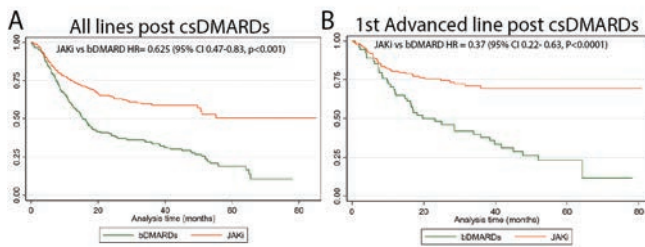
**Conclusion:** Data from the Farber disease natural history study further defined the cardinal symptoms, phenotypic spectrum, and high disease-related burden in patients with Farber disease. The early age of onset and large number of joints affected with arthritis or contractures confirms that patients with Farber disease can be misdiagnosed as JIA polyarthritis. Demographic information and numbers of patients enrolled indicate that Farber disease is likely not as rare as previously thought. ASAH1 genetic testing for patients referred to the rheumatology clinic with symptoms including polyarticular arthritis, subcutaneous nodules, or dysphonia, may shorten the time to diagnosis in patients with Farber disease.

#### POD11

##### **JAKi Inhibitors Have Higher Long-term Durability of Treatment in Rheumatoid Arthritis Compared to Other bDMARDs in a Real World Two-center Canadian Cohort Study**

Samir Iskander (University of Western Ontario, Schulich School of Medicine & Dentistry, London, Ontario); Karla Machlab (University of Western Ontario, Schulich School of Medicine & Dentistry, London); Jocelyn Chow (Newcastle University - School of Medical Education, Newcastle Upon Tyne); Sara Hewitt (St. Joseph's Health Care, London); Gabrielle Sraka (McMaster University, Hamilton); Tatiana Nevskaya (Rheumatology Research, St. Joseph's Health Care, London); Louise Vanderhoek (Rheumatology Research, St. Joseph's Health Care London, London); Jillian Bylsma (University of Western Ontario, Schulich School of Medicine & Dentistry, London); Elaine Soucy (Credit Valley Rheumatology, University of Toronto, Mississauga); Andrew Chow (Credit Valley Rheumatology, University of Toronto, Mississauga); Janet Pope (University of Western Ontario, London)

**Objectives:** Biological disease modifying anti-rheumatic drugs (bDMARDs) and Janus Kinase inhibitors (JAKi) are both recommended post conventional synthetic disease modifying anti-rheumatic drug (csDMARD) therapy failure in active rheumatoid arthritis (RA), but the data on long-term durability are limited. This study aims to compare dura-



bility and retention of JAKi vs other bDMARDs in a real-world database of 2 Canadian centers and identify factors associated with higher retention of treatment.

**Methods:** This was a two-center study of 333 adult RA patients (79.8% females, age  $60.76 \pm 11.98$  years, disease duration  $15.9 \pm 10.6$  years) failing multiple csDMARDs prior to initiating either bDMARDs (TNF inhibitors, abatacept, rituximab, tocilizumab) or JAKi, after June 2014 (when tofacitinib was approved in Canada). Durability and predictors of discontinuation were analyzed by Kaplan-Meier and Cox regression analyses.

**Results:** There were 539 treatment events (236 bDMARDs, 303 JAKi) and 272 Discontinuations. In a Cox proportional hazards model there was significantly better retention for JAKi, with a hazard ratio for treatment discontinuation of JAKi compared with bDMARDs of 0.625 (95% CI 0.47-0.83,  $P < 0.001$ ), adjusted for gender, age, disease duration, and line of therapy (Figure 1A). The greater durability of JAKi was more pronounced when only the first advanced line therapy after csDMARDs was analyzed (HR 0.37,  $P < 0.0001$  95% CI 0.22-0.63) adjusted for gender, age, and disease duration (Figure 1B). The analysis revealed better retention for both groups as first line advanced therapy compared to later lines of therapy. The HR of discontinuation 2nd line advanced therapy = 1.83 ( $P = 0.002$ , 95% CI 1.24-2.70) compared to 1st line therapy adjusted for class, duration of RA, age, gender. The HR of 3rd or higher the same model was 1.61 ( $P = 0.007$ , 95% CI 1.14-2.26). The most common reasons for discontinuation were inefficacy (63%) and side effects (20%). Subgroup analysis reveals no differences in discontinuation due to side effects between JAKi and bDMARDs (Cox HR 1.0006,  $P = 0.98$ ). However, JAKi were less likely to be discontinued due to inefficacy compared to bDMARDs (Cox HR 0.654,  $P = 0.029$ , 95% CI 0.45-0.96).

**Conclusion:** Clinical practice guidelines have placed bDMARDs equal to JAKi as post csDMARD failure therapy in active RA. This study demonstrates JAKis have greater durability compared to other bDMARDs regardless of gender, age, disease duration, and line of therapy. Therefore, JAKi may be considered as a preferable method of treatment post csDMARD failure in active RA. Best Abstract by a Medical Student Award.

#### POD12

##### Results From the 2020 Canadian Rheumatology Association's Workforce and Wellness Survey

Stephanie Kulhawy-Wibe (University of Calgary, Calgary); Jessica Widdifield (Sunnybrook Research Institute, ICES, University of Toronto, Toronto); Jennifer Lee (University of Toronto, Toronto); Carter Thorne (The Arthritis Program Research Group, Newmarket); Elaine Yacyshyn (Division of Rheumatology, University of Alberta, Edmonton); Michelle Bathish (McMaster University, Hamilton); Dana Jerome (Women's College Hospital, Toronto); Rachel Shupak (St. Michael's Hospital, Toronto); Konstantin Jilkine (University of Manitoba, Winnipeg); Jane Purvis (Peterborough); Justin Shamis (University of Toronto, Toronto); Janet Roberts (Division of Rheumatology, Dalhousie University, Dartmouth); Jason Kur (University of British Columbia, Vancouver); Jennifer Burt (Saint Clare Mercy Hospital, St. John's); Nicole Johnson (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Cheryl Barnabe (University of Calgary, Calgary); Nicole Spencer (University of Calgary, Calgary); Mark Harrison (University of British Columbia/Arthritis Research Canada, Vancouver);

Janet Pope (University of Western Ontario, London); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary)

**Objectives:** The Canadian Rheumatology Association (CRA) launched the Workforce and Wellness Survey to update the Canadian rheumatology workforce characteristics.

**Methods:** The survey was developed from the 2015 iteration and expanded to include additional aims. It consisted of 26 questions including demographic and practice information, pandemic impacts, and the Mini-Z questionnaire to assess burnout. After pilot testing by 8 rheumatologists, French and English survey versions were distributed to CRA members electronically between 10/14/2020 and 3/5/2021. The number of full-time equivalent (FTE) rheumatologists per 75,000 population was estimated from the median proportion of time in clinical practice multiplied by provincial rheumatologist numbers from the Canadian Medical Association (CMA).

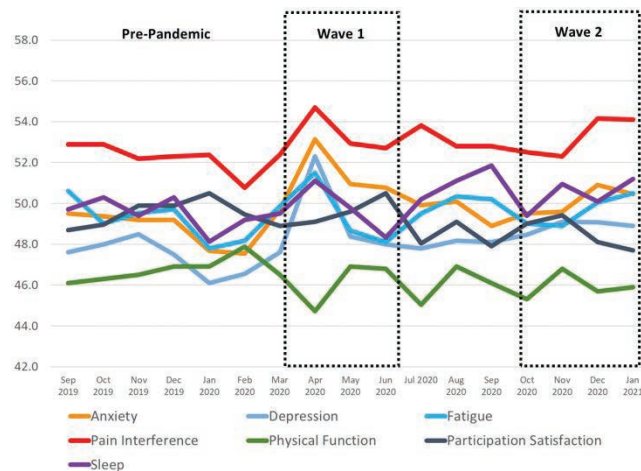
**Results:** Forty four percent (183/417) of the estimated practicing rheumatologists (149 adult; 34 pediatric) completed the survey. The median age was 47 years (IQR 40-60), 62% were female, and 28% planned to retire within the next 5-10 years. Respondents spent a median of 65% of their time in clinical practice, holding a median of 6 (IQR 3-7) half-day clinics, with 6 (IQR 4-12) new consultations and 40 (IQR 25-60) follow-ups seen per week. FTE rheumatologists per 75,000 ranged between 0 and 0.70 in each province/territory and 0.62 per 75,000 nationally. This represents a deficit of 1 to 78 FTE rheumatologists per province/territory and 194 FTE rheumatologists nationally to meet the CRA's workforce benchmark of 1 rheumatologist per 75,000 population. Approximately half of survey respondents reported burnout (51%). Women were at 2.86 increased odds of burnout. Older age was protective against burnout, with a decrease in odds of 0.95% per year of age. As a result of the pandemic, rheumatologists were more engaged in virtual care (97% increase). Despite holding the same number of half-day clinics per week, fewer new and follow-up patients were seen per week, and more time spent on clinical paperwork.

**Conclusion:** There is a shortage of rheumatologists in Canada. This shortage may be compounded by the threat of burnout to workforce retention and productivity. The pandemic has significantly impacted patient volume, likely affecting rheumatologist remuneration and contributing to delayed care. Strategies to address these workforce issues are urgently needed.

#### POD13

##### Riding Multiple Waves of Uncertainty: The Impact of COVID-19 on RA Patients in the Canadian Early Arthritis Cohort (CATCH)

Susan Bartlett (McGill University, Montreal); Orit Schieir (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Janet Pope (University of Western Ontario, London); Glen Hazlewood (University of Calgary, Calgary); Louis Bessette (Laval University, Quebec City); Gilles Boire (Université de Sherbrooke, Sherbrooke); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Edward Keystone (University of





Toronto, Toronto); Carol Hitchon (University of Manitoba, Winnipeg); Vivian Bykerk (Hospital for Special Surgery, New York); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

**Objectives:** During the COVID-19 pandemic, Canadians with RA faced considerable uncertainty due to greater risk of infection, hospitalization, changing access to RA medications, and very limited access to in-person RA care. We examined trends in perceived stress, physical, emotional, and social health prior to and during the first two waves of COVID-19 in adults with RA.

**Methods:** Data were from patients enrolled in CATCH who completed PROMIS-29 between 9/2019 and 1/2021. Descriptive statistics were calculated to evaluate changes in PROMIS-29 scores 6 months prior to, and during Wave 1 (March-June 2020) and Wave 2 (October-January 2021) of the COVID-19 pandemic.

**Results:** 858 visits were collected from 3/16/20 through 1/31/21 and compared with 956 pre-pandemic visits. Participants were mostly white (86%) women (72%) with a mean age of 55 years. Pre-pandemic, mean PROMIS-29 scores were in the normal range, with the lowest being Physical Function (46.7) and the highest Pain Interference (52.3). Monthly trends showed that impacts were greatest in April 2020 (Figure) where mean PROMIS-29 scores were meaningfully worse for all domains except Participation (mean D -0.4); the largest changes were in Depression (D+4.8) and Anxiety (D+4.2) (all  $P < 0.01$ ). Compared with pre-pandemic visits, by April higher proportions had moderate-severe Anxiety (12% vs 23%), Depression (11% vs 23%), Fatigue (18% vs 25%), Sleep Disturbance (10% vs 19%), Pain (23% vs 40%), Participation (15% vs 21%) and Disability (25% vs 34%) (all  $P < 0.05$ ). By July 2020, mean scores had improved for Depression (D -4.5), Anxiety (D -3.2), Fatigue (D -2.0) and Perceived Stress (D -0.7). The proportions of patients with moderate-severe symptoms ( $\geq 60$ ) were similar to pre-pandemic levels except Pain, Function, Participation, and Sleep where 29%, 34%, 21% and 17%, respectively continued to have moderate-severe impairments. Wave 2 scores were higher than pre-pandemic, but lower than Wave 1, with the largest changes in depression and anxiety. Mean RA-FQ increased peaking in April 2020 and Dec 2020-Jan 2021 (Figure). More patients had disease flares in April (45%) and December (35%) than in the pre-pandemic period.

**Conclusion:** In the initial waves of the pandemic, 1 in 3 Canadians with RA reported moderate-severe pain and disability, 1 in 4 had moderate-severe anxiety, depression and fatigue, and 1 in 5 had sleep disturbance and impaired participation. The largest changes were in anxiety and depression during both waves. While most symptoms resolved between waves, average impairment in physical function remained much higher 12 months into the pandemic.

#### POD14

##### Characteristics and Evolution of Patients With Difficult-to-treat Rheumatoid Arthritis

Wen Qi (CHU de Québec-Université Laval, Québec); Antoine Robert (CHU de Québec-Université Laval, Québec); Narcisse Singbo (Centre de recherche du CHU de Québec-Université Laval, Québec); Lucie Ratelle (CHU de Québec research centre, Québec); Louis Bessette (Laval University, Québec); Paul Fortin (Department of Rheumatology, CHU de

**Table 1. Significant variables in univariate analysis**

|                                           | Odds ratio (95% CI, p value)    |
|-------------------------------------------|---------------------------------|
| Chronic pain syndromes                    | 4.23 (2.22-8.06, $p < 0.0001$ ) |
| ESR at diagnosis (elevated <sup>1</sup> ) | 0.48 (0.28-0.83, $p = 0.0086$ ) |
| CPR at diagnosis (elevated <sup>1</sup> ) | 0.46 (0.25-0.86, $p = 0.0154$ ) |

<sup>1</sup>When compared to the normal reference range of the laboratory at which the test was done

Québec-Université Laval, Québec); Jacques Brown (Department of Rheumatology, CHU de Québec-Université Laval, Québec); Lactitia Michou (Department of Rheumatology, CHU de Québec-Université Laval, Québec)

**Objectives:** EULAR published a definition of difficult-to-treat rheumatoid arthritis (D2T-RA). The aim of this study was to identify characteristics of patients with D2T-RA and describe their evolution.

**Methods:** This is a retrospective study of the electronic medical records of all adults with RA, that meet the ACR/EULAR 2010 classification criteria, on at least one biologic or target synthetic DMARD (b/tsDMARD) at our hospital. According to the EULAR definition, the D2T-RA group must have failed  $\geq 2$  b/tsDMARDs and still have signs of active/progressive disease (such as a CDAI  $> 10$ ) after 3-6 months on treatment. The non-D2T group was defined as a low-disease activity (CDAI  $\leq 10$ ) for at least one year on 1 or 2 b/tsDMARD mechanisms of action (b/tsDMARD MOA). We compared the patients' characteristics, comorbidities, and disease activity at baseline and at any time a switch in b/tsDMARD occurred. Remission was defined as CDAI  $\leq 2.8$  and low-disease activity as CDAI 2.9-10. Descriptive statistics and proportions were calculated. Univariate analysis was performed. P-value less than 0.05 was considered statistically significant.

**Results:** Among the 403 patients, 99 (25%) were D2T-RA and 304 (75%) were non D2T-RA. Patients were predominantly women (D2T 80% versus non-D2T 77%,  $P = 0.558$ ). The mean age at inclusion was similar ( $65 \pm 12$  years versus  $61 \pm 10$  years, respectively,  $P = 0.062$ ). The D2T group received a median of 4 b/tsDMARDs (IQR = 3-6) with a median of 3 different MOA (IQR = 3-4). The non-D2T group was treated by a median of 1 b/tsDMARD (IQR = 1-2) with 1 MOA (IQR = 1-1). Patients with D2T-RA had a median disease duration of 36 months (IQR = 20-65) before meeting the EULAR definition. Chronic pain syndromes were associated with D2T-RA (Table 1). After a patient becomes D2T, the two b/tsDMARD MOA associated with the longest remission duration were Jak inhibitors ( $n = 35/99$ , 35%) and TNFi ( $n = 22/99$ , 22%). A no-response to the first TNFi did not predict a subsequent no-response to the second TNFi for the same D2T patient. Due to its retrospective nature, this study is subject to selection and information biases. A time-cohort bias could have given an advantage to RA treatments recently introduced.

**Conclusion:** Consistent with the findings from another study, chronic pain disorders seem more prevalent in D2T-RA, and they should carefully be assessed to avoid possible unnecessary switch. After a patient becomes D2T, Jak inhibitors may be considered in their treatment strategy. Best Abstract on Research by a Rheumatology Resident Award.

## POSTER TOURS

### TOUR01

#### Association of Antiphospholipid Antibodies With Thromboembolic Events and Severe Outcomes in COVID-19

Arielle Mendel (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Marvin Fritzler (University of Calgary, Calgary); Yvan St. Pierre (McGill University, Montreal); Joyce Rauch (Research Institute of the McGill University Health Centre, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal)

**Objectives:** The prognostic significance of antiphospholipid antibodies (aPL) in COVID-19 remains unclear. Within a large prospective cohort of individuals with and without COVID-19, our objective was to determine if aPL are associated with thromboembolic events and other severe outcomes.

**Methods:** Symptomatic individuals undergoing SARS-CoV-2 nasopharyngeal PCR testing at a Quebec tertiary center were enrolled in a prospective biobank cohort between March-July 2020. PCR results, demographics, medical history, hospitalization details and clinical outcomes were collected using a standard form. Subjects were classified as COVID+ ( $\geq 1$  positive PCR) or non-COVID (all PCR negative). Biobanked plasma (drawn day 0-7 after enrolment) was tested for anticardiolipin (aCL) IgM and IgG, anti-domain I of  $\beta 2$ -glycoprotein I (aD1 $\beta 2$ GP1) IgM and IgG, and anti-phosphatidylserine/prothrombin (aPS/PT) IgM and IgG (Inova Diagnostics, San Diego); and lupus anticoagulant (LAC; Precision BioLogic, Halifax) using manufacturers' cut-offs. Samples were also tested for SARS-CoV-2 IgM and IgG. We compared aPL prevalence (overall and subtypes) between COVID+ and non-COVID subjects. In hospitalized COVID+ patients, we performed multivariate logistic regressions evaluating aPL (and subtypes) and thromboembolic events (arterial and venous), as well as acute kidney injury (AKI), intensive care unit (ICU) stay, mechanical ventilation, and death, adjusting for age and sex.

**Results:** COVID+ (n = 291) and non-COVID (n = 365) subjects were similar in age and sex, but more COVID+ subjects were admitted to hospital (83% vs 61%) and had positive SARS-CoV-2 serology (70% vs 3%) compared to non-COVID subjects (Table 1). At baseline, 43% of COVID+ subjects were aPL+ versus 32% of non-COVID subjects (difference in proportion 11%; 95% CI 3-18). Among hospitalized patients with COVID+ (n = 241), having any aPL+ was independently associated with AKI (OR 1.9; 95% CI 1.1-3.3), ICU stay (OR 1.8; 95% CI 1.0-3.5), and mechanical ventilation (OR 3.7; 95% CI 1.7-7.8). Both aCL IgM and aCL IgG were independently associated with ICU stay and mechanical ventilation. We saw a strong trend for the association of aCL IgG with thrombotic events (OR 2.3; 95% CI 0.9-6.0), though the CI included the null value.

Table 1. Characteristics and aPL status of COVID+ and non-COVID subjects (n=656)

| Characteristic                                                        | COVID + subjects<br>n=291 | Non-COVID subjects<br>n=365 |
|-----------------------------------------------------------------------|---------------------------|-----------------------------|
| Age in years, mean (SD)                                               | 67 (18)                   | 64 (20)                     |
| Female sex, n (%)                                                     | 151 (52)                  | 183 (50)                    |
| Hospital admission, n (%)                                             | 241 (83)                  | 224 (61)                    |
| Prospective follow-up, mean days (SD)                                 | 70 (48)                   | 60 (51)                     |
| Positive SARS-CoV-2 serologies<br>IgM and/or IgG <sup>1</sup> , n (%) | 201/288 (70)              | 11/362 (3)                  |
| Antiphospholipid status, n (%)                                        |                           |                             |
| Any aPL                                                               | 123/289 (43)              | 116/361 (32)                |
| aCL IgM                                                               | 74/289 (26)               | 36/361 (10)                 |
| aCL IgG                                                               | 37/289 (13)               | 36/361 (10)                 |
| aD1 $\beta 2$ GP1 IgM                                                 | 18/289 (6)                | 20/359 (6)                  |
| aD1 $\beta 2$ GP1 IgG                                                 | 2/289 (1)                 | 3/359 (1)                   |
| aPS/PT IgM                                                            | 24/284 (8)                | 22/352 (6)                  |
| aPS/PT IgG                                                            | 17/284 (6)                | 18/352 (5)                  |
| LAC                                                                   | 9/214 (4)                 | 12/274 (4)                  |

Abbreviations : aPL, antiphospholipid antibody; aCL, anticardiolipin, aD1 $\beta 2$ GP1, anti-domain-1 of  $\beta 2$ -glycoprotein-1; aPS/PT, anti-phosphatidylserine/prothrombin; LAC, lupus anticoagulant  
<sup>1</sup>SARS-CoV-2 serologies were performed by Luminex xMAP SARS-CoV2 multi-antigen (IgG) and DiaSource COVID ELISA (IgM and IgG), with cutoffs according to manufacturers' recommendations

**Conclusion:** In this large prospective sample, > 40% of individuals with COVID-19 had aPL early in their clinical course. In hospitalized COVID-19 patients, aPL were associated with increased risk of severe outcomes, with a strong trend for association between aCL IgG and thrombotic events. Our findings suggest that aPL, in particular aCL, might be useful markers for risk stratification in COVID-19.

### TOUR02

#### Evaluating COVID-19 Vaccination in Patients With Systemic Lupus Erythematosus

Maher Banjari (University of Toronto, Toronto); Laura Whittall-Garcia (University Health Network, Toronto); Ghayda Aldabie (University of Toronto, Toronto); Ambika Gupta (University of Toronto, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto)

**Objectives:** To evaluate disease flare and post-vaccination reactions (reactogenicity) in patients with Systemic Lupus Erythematosus (SLE) following two-dose SARS-CoV-2 mRNA vaccination.

**Methods:** We conducted a prospective single-center observational study including patients with SLE who received an mRNA COVID-19 vaccination. Patients met the revised 1997 ACR classification criteria for SLE or had three criteria and a supportive biopsy (skin or kidney). Patients attending the Lupus Clinic are followed at regular intervals (every 2 to 6 months). At each follow-up visit, clinical, treatment, and laboratory information are collected according to a standard protocol, and SLEDAI-2K is calculated and recorded at every visit. For every patient included in the study the SLE activity status, treatment and laboratory data are collected from the closest visit prior to the vaccine and at 2-4 weeks after each dose.

**Results:** 39 SLE patients who received two-doses of SARS-CoV-2-mRNA vaccination between March 2nd and August 6th 2021 were included. Median age was 40 (20-63) with 90% females (n = 35), and 23% non-white (n = 9). Median disease duration was 11 years (1-37). 5 patients did not attend their second protocol visit following the second dose. 5 patients (12%) had a disease flare requiring treatment. Most of the flares consisted of arthritis (4/5). The fifth patient had biopsy proven skin vasculitis. Of the 4 male patients included in the study 2 patients had flares. Among patients who had flares, only one patient had an increase in the level of anti-dsDNA antibodies (from 5 to 15 IU/ml) and another patient had a decrease in her previously normal C3 following vaccination (1.02 to 0.89 g/L); both patients had arthritis. 3 out of 5 patients were treated with small dose prednisone and the other two were treated either by increasing the dose of Mycophenolate Mofetil (MMF) or non-steroidal anti-inflammatory drugs. The most frequently reported reactions post vaccination were pain at the injection site (PIS) (n = 18), headache (n = 6) and arthralgia (n = 6). Among patients reporting arthralgia, half of them were found to have clinical arthritis and required treatment. Most patients received Pfizer-BioNtech (n = 35) and 4 patients had Moderna. No allergic reactions or SARS-CoV-2 diagnoses were reported.

**Conclusion:** This small study suggests that SLE patients tolerated the vaccinations well with flares occurring in 12.8%. Patients should be assessed post vaccination to ensure that flares are treated promptly. Best Abstract on SLE Research by a Trainee - Ian Watson Award

### TOUR03

#### Safety and Immunogenicity of COVID-19 Vaccine in Immunosuppressed Adults With Autoimmune Diseases

Ines Colmegna (The Research Institute of the MUHC, Montreal); Mariana Useche (The Research Institute of the MUHC, Montreal); Emmanouil Rampakakis (JSS Medical Research Inc, Montreal); Nathalie Amiable (CHU de Québec-Université Laval Research Center, Québec); Emmanuelle Rollet-Labelle (CHU de Québec-Université Laval Research Center, Québec); Louis Besette (Laval University, Québec); Jo-Anne

Costa (CHU de Quebec Laval University, Quebec); Marc Dionne (CHU de Quebec Laval University, Quebec); Mary-Ann Fitzcharles (McGill University Health Centre, Montreal); Elizabeth Hazel (McGill University, Montreal); Deirdre McCormack (McGill University Health Center, Montreal); Laetitia Michou (Department of Rheumatology, CHU de Québec-Université Laval, Québec); Pantelis Panopalis (McGill University, Montreal); Marc-Andre Langlois (University of Ottawa, Ottawa); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Paul Fortin (Department of Rheumatology, CHU de Québec-Université Laval, Québec)

**Objectives:** Immunocompromised conditions or a history of autoimmune disease were exclusion criteria of the initial SARS-CoV-2 vaccines clinical trials. We assessed the safety and immunogenicity of the mRNA-1273 SARS-CoV-2 vaccine following a two-dose regimen in patients with rheumatic diseases.

**Methods:** We conducted a prospective, non-randomized, open label, comparative clinical trial (NCT04806113) at two academic centers in Canada. Trial participants were adults with either one of the following diagnoses (i) seropositive rheumatoid arthritis (RA) on stable treatment for  $\geq 3$  months (ii) systemic lupus erythematosus (SLE) on stable treatment with mycophenolate mofetil (MMF); (iii) other rheumatic disease receiving  $\geq 10$  mg of prednisone; or age/sex matched adults without rheumatic diseases (controls). The primary outcomes included solicited local and systemic reactogenicity adverse events (AEs) in the 7 days after each dose; and unsolicited AEs in the 28 days following each dose. As secondary outcome, we assessed the effects of age and treatment on seropositivity [presence of serum IgG antibody against SARS-CoV-2 spike protein (IgG-S) and its receptor binding domain (IgG-RBD)], measured at baseline and  $28 \pm 7$  days after each dose of the vaccine in a custom automated ELISA platform.

**Results:** We enrolled 220 participants including 131 RA, 23 SLE, 8 other rheumatic disease, and 58 controls. The mean age ( $\pm$  SD) was  $60.4 \pm 12.2$  and 72% were female. Local and systemic solicited AEs were more frequently reported after the 2nd dose (versus the first dose) in all subjects (94 vs 86.8%;  $\Delta = 7.2\%$ , 95% CI 2.8%-11.7%), with pain at the injection site being the most common. Swollen joints, following both vaccine doses, were more frequently reported by RA patients than controls (22.9 vs 3.4%;  $\Delta = 19.5\%$ , 95% CI 10.9%-28%); however, there was no increase in disease activity scores post-vaccination. After the 1st dose, seropositivity for both IgG-S and IgG-RBD was 100% in controls, but only 67.7% in RA, 34.8% in SLE, and 87.5% in other rheumatic diseases. After the 2nd dose, seropositivity for both IgG-S and IgG-RBD remained 100% in controls and increased to 88.5% in RA and 78.3% in SLE and persisted at 87.5% in other rheumatic diseases. People on rituximab (9 vs 88%,  $\Delta = -78.8\%$ , 95% CI -98.1% to -59.5%) or MMF (39 vs 58%,  $\Delta = -19.3\%$ , 95% CI -36.4% to -2.2%) had lower humoral responses than patients not on those drugs post-2 vaccine doses.

**Conclusion:** In this prospective study, the mRNA-1273 SARS-CoV-2 vaccine was not associated with severe disease flares. MMF and rituximab were associated with a reduction in vaccine-induced humoral responses.

#### TOUR04

##### **Nivolumab Associated Bone Pain and Hyperparathyroidism: A New Immune Related Adverse Event?**

Azin Rouhi (University of Alberta, Edmonton); Carrie Ye (Division of Rheumatology, University of Alberta, Edmonton)

**Background:** Immune checkpoint inhibitors (ICI) have shown great promise in the treatment of multiple malignancies. The use of ICIs has been associated with toxicities that are referred to as immune related adverse events (irAEs). Various toxicities, such as endocrinologic, rheumatologic, and neurologic irAEs have been observed. We report a case of bone pain and hyperparathyroidism that developed shortly after treatment with nivolumab. To our knowledge, this is the first case of hyperparathyroidism developing after ICI initiation.

**Case:** A 68-year-old male with malignant melanoma was assessed in the Rheumatology in Immuno-Oncology clinic at the Kaye Edmonton Clinic

in June 2021 for widespread arthralgias and bone pain that started in January 2021. There was no history of morning stiffness and physical exam revealed no evidence of joint effusions, tenderness or decreased range of motion. He was initially diagnosed with stage IIIc malignant melanoma in June 2020, for which he underwent tumor resection and was started on nivolumab in September 2020. He was noted to have persistent hypercalcemia, as high as 2.73 (normal range 2.1-2.6 mmol/L) dating back to October 2020. Calcium levels were last normal in September 2020. Serum albumin and creatinine remained within normal range. He was not on any medications that could contribute to hypercalcemia. On further investigation he was found to have paradoxically elevated parathyroid hormone (PTH) level of 7.1 pmol/L (normal range 1.4-6.8 pmol/L). Total Vitamin D level was 74 nmol/L (normal range 80-200), 24-hour urine calcium was normal at 3.8 mmol/day, with a calcium/creatinine clearance ratio of 0.01. PTH-related peptide was undetectable. Nuclear medicine scan and contrast enhanced CT were negative for parathyroid adenoma. The patient completed one year of ICI treatment with nivolumab in August 2021. Most recent calcium level in September 2021 was 2.66 mmol/L, although his bone pain was starting to improve.

**Conclusion:** We report a case of bone and joint pain likely secondary to hyperparathyroidism following treatment with nivolumab. Hyperparathyroidism has never been reported as an irAE in the literature. There have been rare cases of hyperparathyroidism associated with auto-antibodies against the calcium-sensing receptors (CaSR) with resulting hypercalcemia and often hypocalciuria. These patients frequently have other autoimmune endocrinopathies, such as Type 1 diabetes or Hashimoto's thyroiditis. In our patient, however, there was no evidence of hypocalciuria or other autoimmune endocrinopathies. Rheumatologists should be aware of potential immune-related endocrinopathies in patients on ICI that can present with non-inflammatory bone and joint pain.

#### TOUR05

##### **Beliefs and Concerns About RA Medications May Predict Influenza Vaccine Hesitancy: Results From the Canadian Early Arthritis Cohort (CATCH)**

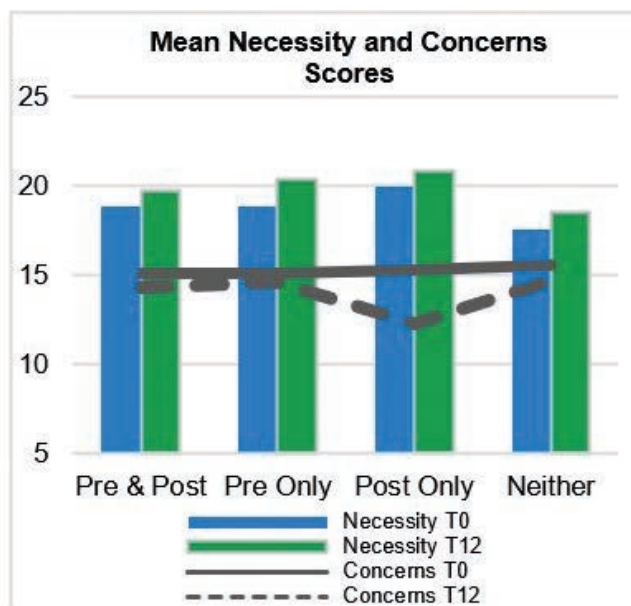
Viviane Ta (McGill, Montreal); Orit Schieir (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Vivian Bykerk (Hospital for Special Surgery, New York); Ines Colmegna (The Research Institute of the MUHC, Montreal); Carol Hitchon (University of Manitoba, Winnipeg); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Louis Bessette (Laval University, Quebec City); Glen Hazlewood (University of Calgary, Calgary); Edward Keystone (University of Toronto, Toronto); Gilles Boire (Université de Sherbrooke, Sherbrooke); Janet Pope (University of Western Ontario, London); Susan Bartlett (McGill University, Montreal)

**Objectives:** As adults with RA are at a higher risk for infections, including influenza and related complications, an annual influenza vaccination is recommended by CRA and others. Despite this, we recently showed that influenza vaccination coverage remains suboptimal in Canadian adults both in the year prior to (37%) and after (42%) a new diagnosis of RA. Here, we explore whether RA medication beliefs and concerns also may play a role in predicting influenza vaccine hesitancy.

**Methods:** We used data from RA patients enrolled in the Canadian Early Arthritis Cohort (CATCH) between September 2017 and February 2021 who had reported their vaccination status in the previous year and completed the Beliefs about Medicines questionnaire at enrolment. The BAMQ asks about beliefs related to the necessity of taking RA medications, as well as concerns. Clinical data was obtained from medical records. Multivariable logistic regression was used to examine the independent effects of Necessity beliefs, medication Concerns, and the Necessity-Concerns difference scores between vaccinated and non-vaccinated groups while controlling for socio-demographic and RA characteristics.

**Results:** At enrolment, participants (N = 405) were mostly white (80%) women (67%) with a mean (SD) age of 56 years and symptom duration





of 5 months. Among 233 patients with vaccination info available post-dx, 68% of those vaccinated post-dx reported having been vaccinated in the year prior to RA diagnosis. Post-diagnosis, participants vaccinated prior to diagnosis (OR 27.57; 95% CI 8.91-85.33), on advanced therapies (OR 6.57; 95% CI 1.70-25.39), and with a higher Necessity-Concerns Differential (OR 1.11; 95% CI 1.02-1.21) had a greater odds, while women (OR 0.24; 95% CI 0.08-0.67), minorities (OR 0.07; 95% CI 0.01-0.40), and smokers (OR 0.09; 95% CI 0.02-0.45) had a lower odds of influenza vaccination. Participants who were not vaccinated before developing RA but vaccinated in the year after diagnosis had lower mean Concerns and higher mean Necessity-Concerns differential scores compared to those vaccinated at both timepoints, only pre-diagnosis, or neither timepoint (Figure).

**Conclusion:** In Canadians with early RA, certain individual (male sex, non-white race, smoking, medication beliefs/concerns) and treatment characteristics (advanced therapeutics, prior vaccination) were associated with a greater likelihood of vaccination. Vaccine hesitancy was associated with a higher level of RA medications concerns and low necessity beliefs. Conversations about medication beliefs, concerns and vaccination history as part of the diagnostic workup may help increase influenza vaccine coverage.

#### TOUR06

##### The Relationship Between Disease Activity Measures and Work Productivity and Activity Impairment in Patients With Rheumatoid Arthritis in the Rheum4U Precision Health Registry Patient Cohort

Deborah Marshall (University of Calgary, Calgary); Namneet Sandhu (University of Calgary, Calgary); Susanne Benseler (Section of Rheumatology, Department of Pediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Marinka Twilt (University of Calgary, Calgary); Alexis Guigue (University of Calgary, Calgary); Inelda Gjata (University of Calgary, Calgary); Martina Stevenson (University of Calgary, Calgary); Dianne Mosher (University of Calgary, Calgary); Rheum4U Team (Calgary)

**Objectives:** To understand the association of work productivity and activity impairment and disease activity in patients with RA in the Rheum4U Precision Health Registry (PHR) at baseline. Affecting approximately 1% of Canadians, rheumatoid arthritis (RA) can lead to irreversible joint damage, functional disability, decreased work productivity, and loss of work. The Work Productivity and Activity Impairment (WPAI) questionnaire is a validated tool for assessing impairment in work productivity and daily activities and an indicator of health status in RA patients. Patient-reported outcomes and disease activity measures have been found to

correlate with work productivity and activity impairment using the WPAI questionnaire. Precision Health Registry (PHR) is a longitudinal study that uses a web-based platform, Rheum4U, to enroll patients with suspected or confirmed inflammatory arthritis and collects prospective data at two adult rheumatology clinics in Calgary, Alberta. By understanding the relationship between WPAI and disease activity measures in our PHR cohort, we will be better informed in supporting our goal of improving quality of care for our patients.

**Methods:** Participants complete WPAI at their baseline visit and every 6 months thereafter. Disease activity measures, CDAI and DAS28CRP, are automatically calculated incorporating patient reported outcomes, laboratory markers and physician captured data. Statistical significance was assessed using nonparametric tests.

**Results:** The PHR cohort consists of 965 participants. Of these, 681 (71%) had an RA diagnosis with 73% females and mean age of 54.69 years (SD 13.65). DAS28CRP and CDAI were available for 85% and 94% of RA participants, respectively. Baseline WPAI was completed by 648 (95%) RA participants, with 348 (54%) reporting employment. The non-employed group was found to have a higher median activity impairment (29% vs 15%,  $P < 0.001$ ) than the employed group. Looking specifically at the employed group, the median activity impairment was reportedly larger than the median work impairment (15% vs 10%,  $P < 0.001$ ). Both the activity and work impairment were found to positively correlate with disease categories, measured either using CDAI or DAS28CRP [Kendall's  $\tau = 0.32, 0.37, 0.38, 0.47, P < 0.001$ ]. For the employed group, absenteeism was 6% and presenteeism was 22%, on average. Similar to work impairment, presenteeism was found to increase with higher disease categories.

**Conclusion:** Disease activity measures positively correlated with work productivity and activity impairment. Additionally, presenteeism was more severe than absenteeism and activity impairment was greater than work impairment, for those employed. This suggests that patients are going to work but their disease activity impacts their work productivity and home life.

#### TOUR07

##### Physician and Patient Reported Effectiveness Outcomes Are Similar in Tofacitinib and TNF Inhibitors in Rheumatoid Arthritis Patients: Data from a Rheumatoid Arthritis Registry in Canada

Mohammad Movahedi (University Health Network, Toronto); Angela Cesta (University Health Network, Toronto); Xiuying Li (University Health Network, Toronto); Edward Keystone (University of Toronto, Toronto); Claire Bombardier (University of Toronto, Toronto); OBRI investigators (University Health Network, Toronto)

**Objectives:** Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment as an alternative option to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi). We aimed to evaluate physician and patient reported effectiveness outcomes in TNFi compared to TOFA, using real-world data from the Ontario Best Practices Research Initiative (OBRI).

**Methods:** RA patients enrolled in the OBRI initiating their TOFA or TNFi (Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab, and Biosimilars) between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Patients were required to have physician and patient reported effectiveness outcomes data available at treatment initiation and 6-month ( $\pm 2$  months) follow-up. These included clinical disease activity index (CDAI), rheumatoid arthritis disease activity index (RADAI), HAQ-DI, sleep problem, and anxiety/depression scores. Multiple imputation (Imputation Chained Equation,  $N = 20$ ) was used to deal with missing data for covariates at treatment initiation. To deal with confounding by indication, we estimated propensity scores for covariates with an absolute standard difference greater than 0.1 between the two treatment groups.

**Results:** A total of 419 patients were included. Of those, 226 were initiating a TNFi and 193 TOFA, and had a mean (SD) disease duration of 8.0 (8.7) and 12.6 (9.6) years, respectively. In the TNFi group, 81.9% were female

and mean age (SD) at treatment initiation was 56.6 (13.4) years. In the TOFA group, 85% were female and mean (SD) age at treatment initiation was 60.3 (11.2) years. The TNFi group was less likely to have prior biologic use (21.7%) compared to the TOFA group (67.9%). At treatment initiation, physical function measured by HAQ-DI was significantly lower in TNFi compared to the TOFA group (1.2 vs 1.4). The rate of CDAI LDA/remission at 6 months was 33.6% and 26.4% in TNFi and TOFA group, respectively. The generalized linear mixed models (GLMM) adjusting for propensity score quantile, showed that there was no significant difference in CDAI LDA/remission (ORs: 0.85, 95% CI 0.51, 1.43), RADAI ( $\beta$ -coefficient: 0.48, 95% CI -0.18, 1.14), HAQ-DI ( $\beta$ -coefficient: -0.01, 95% CI -0.18, 0.16), sleep problems ( $\beta$ -coefficient: -0.25, 95% CI -0.95, 0.45), and anxiety/depression scores ( $\beta$ -coefficient: 0.12, 95% CI -0.35, 0.58) between the two treatment groups (TOFA used as reference).

**Conclusion:** In this real-world data study, we found that, physician and patient reported effectiveness outcomes are similar in the TNFi and TOFA groups 6 months after treatment initiation in patients with RA.

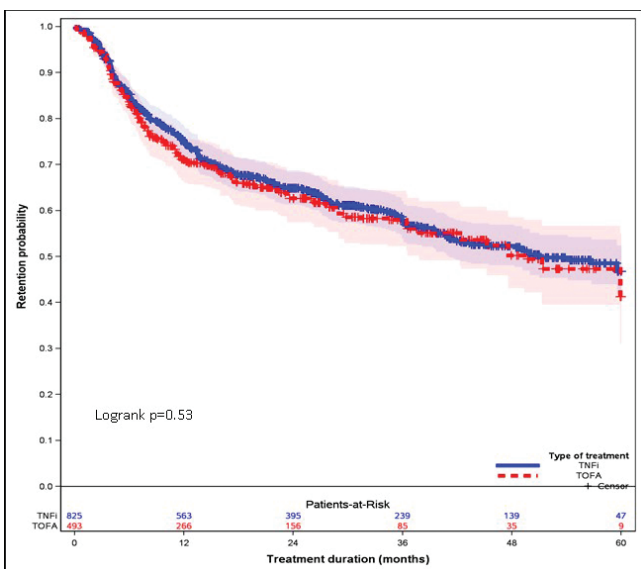
#### TOUR08

##### Discontinuation Rate of Tofacitinib Is Similar When Compared to TNF Inhibitors in Rheumatoid Arthritis Patients: Pooled Data From Two Rheumatoid Arthritis Registries in Canada

Mohammad Movahedi (University Health Network, Toronto); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal); Louis Coupal (Institut de Rhumatologie de Montréal, Montréal); Angela Cesta (University Health Network, Toronto); Xiuying Li (University Health Network, Toronto); Edward Keystone (University of Toronto, Toronto); Claire Bombardier (University of Toronto, Toronto); OBRI investigators (University Health Network, Toronto); Rhumadata investigators (Montreal)

**Objectives:** Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment as the first or an alternative option to biologic disease-modifying antirheumatic drugs (bDMARDs), including tumor necrosis factor inhibitors (TNFi). The similarity in retention of TNFi and TOFA was previously reported separately by the Ontario Best Practices Research Initiative (OBRI) and the Quebec cohort RHUMADATA. To increase the study power, we propose to evaluate the discontinuation rate (due to any reason) of TNFi compared to TOFA, using pooled data from both these registries.

**Methods:** RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA or TNFi between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Time to discontinuation was assessed using adjusted Kaplan-Meier (KM) survival and Cox regression



models. To deal with confounding by indication, we estimated propensity scores for covariates with a standard difference greater than 0.1. Models were then adjusted using stratification and inverse probability of treatment weight (IPTW) methods.

**Results:** A total of 1318 patients initiated TNFi (n = 825) or TOFA (n = 493) with mean (SD) disease duration of 8.9 (9.3) and 13.0 (10.1) years, respectively. In the TNFi group, 78.8% were female and mean age (SD) at treatment initiation was 57.6 (12.6) years. In the TOFA group, 84.6% were female and mean (SD) age at treatment initiation was 59.5 (11.5) years. The TNFi group was less likely to have prior biologic use (33.9%) than the TOFA group (66.9%). At treatment initiation, the mean (SD) CDAI was significantly (P < 0.05) lower in the TNFi group [20.0 (11.7)] compared to the TOFA group [22.1 (12.4)]. Physical function measured by HAQ-DI was also significantly lower (P < 0.05) in the TNFi compared to the TOFA group (1.2 vs 1.3). Over a mean follow-up of 23.2 months, discontinuation was reported in 309 (37.5%) and 182 (36.9%) of all TNFi and TOFA patients, respectively. After adjusting for propensity score deciles across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 0.96, 95% CI 0.78-1.18; P = 0.69). The results were similar for two propensity adjustment methods (Figure).

**Conclusion:** In this pooled real-world data study, we found that TNFi and TOFA retention is similar in patients with RA. In the next step we will analyze the data for specific reasons of discontinuation. We will also repeat analysis comparing discontinuation in the first users versus those after one or more biologic failure.

#### TOUR09

##### Prediction of Psoriatic Arthritis in Patients With Psoriasis Using DNA Methylation Profiles

Omar Cruz Correa (University Health Network, Toronto); Remy Pollock (University of Toronto Psoriatic Arthritis Program, Centre for Prognosis Studies in the Rheumatic Diseases, Krembil Research Institute, University Health Network, Toronto); Rohan Machhar (Toronto Western Hospital, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto)

**Objectives:** Psoriatic arthritis (PsA) is an immune-mediated inflammatory arthritis, associated with psoriasis, that significantly increases morbidity and may increase mortality risk. However, we currently lack the means of predicting which psoriasis patients will develop PsA, and a large number of patients remain undiagnosed. Regulation of gene expression through DNA methylation can be altered by stochastic events or environmental factors and can potentially trigger and maintain PsA pathophysiological processes. With this research, we identified DNA methylation changes that can predict which psoriasis patients will develop PsA at an early stage of the disease.

**Methods:** In a nested case-control study design, we obtained blood samples from 60 psoriasis patients that developed arthritis (converters) and 60 psoriasis patients that did not (biologic-naive, matched for age, sex, psoriasis duration and duration of follow-up). Genome-wide DNA methylation was assessed using Infinium Methylation EPIC BeadChips (Illumina, San Diego, CA, USA). Array data preprocessing, normalization and correction for technical sources of variation were performed in the R programming environment as recommended in the ChAMP package pipeline. Methylation differences between converters and non-converters were identified by a multivariate linear regression model including clinical covariates (age, sex, BMI, smoking) and conversion status using the Limma package. Predictive performance of methylation markers was assessed by developing machine learning classification models. Support vector machine models were trained using 75% of samples, keeping the other 25% as testing set for evaluating the prediction of conversion or non-conversion. Models were built using methylation data with and without the addition of clinical variables.

**Results:** We identified a set of 36 highly relevant methylation markers (with FDR-adjusted p-values lower than 0.05 and a minimum change in methylation of 0.05) found across 15 genes and several intergenic regions. Enrichment analysis of the 15 genes with highly relevant methylation

markers showed no significantly enriched functional pathways. A classification model using only these 36 markers correctly identified 28 out of 30 samples as converters or non-converters, achieving an accuracy of 93%. The addition of clinical information to DNA methylation data did not increase the performance of the classification models.

**Conclusion:** We identified a set of 36 highly significant methylation markers associated with the development of PsA in psoriasis patients. This work shows that DNA methylation patterns at an early stage of psoriatic disease can distinguish between psoriasis patients that will develop PsA from those that will not. Best Abstract on Basic Science Research by a Trainee Award.

### TOUR10

#### Responsiveness of the CDAI When Scored With Patient-Reported vs Clinician-Assessed Joint Counts: Results From the Canadian Early Arthritis Cohort (CATCH) Study

Vivian Bykerk (The Hospital for Special Surgery, New York); Orit Schieir (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Glen Hazlewood (University of Calgary, Calgary); Carol Hitchon (University of Manitoba, Winnipeg); Gilles Boire (Université de Sherbrooke, Sherbrooke); Diane Tin (Southlake Regional Health Centre, Newmarket); Louis Bessette (Laval University, Quebec); Edward Keystone (University of Toronto, Toronto); Carter Thorne (The Arthritis Program Research Group, Newmarket); Janet Pope (University of Western Ontario, London); Susan Bartlett (McGill University, Montreal); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

**Objectives:** While the CDAI is frequently used in routine care settings to guide target-based treatment decisions, traditional in-person clinician-assessed joint counts needed to calculate the CDAI are not available to help guide treatment decisions during remote telehealth visits. The objective of the present study was to compare responsiveness in CDAI scores when derived using patient-reported vs clinician-assessed joint counts that can be collected in the context of virtual care consultations.

**Methods:** Data were from 937 early RA patients enrolled in CATCH between Nov 2011 and July 2020. Patient-reported and clinician-assessed TJC28/SJC28 were simultaneously collected using a homunculus at 2 consecutive visits at 3- and 6-months follow-up, along with MD- and patient global assessments (NRSs 0-10). CDAI and PtCDAI calculated with patient-reported joint counts were scored at each visit (0-76). Descriptive statistics were used to compare sensitivity to change in CDAI when scored with patient-reported vs clinician-assessed joint counts across different levels of disease control over time defined as: (1) Improved from active to controlled (HDA/MDA to LDA/REM); (2) Worsened from controlled to active (REM/LDA to MDA/HDA); (3) Remained active (HDA/MDA), and 4) Remained controlled (REM/LDA).

**Results:** At baseline, the sample of 937 pts had a mean (SD) age of 56 (15), symptoms of 5.5 (2.9) months, 70% were female, 81% were white, all were treated with csDMARDs (73% methotrexate) and CDAI scores were consistent with high disease activity (CDAI 25.0 (14.1), PtCDAI 27.5 (15.9)). CDAI scored with patient-reported and clinician-assessed joint counts both changed in the same direction and by a large magnitude when disease activity levels changed over time (Improved to Controlled and Worsened to Active), though the mean change in traditional CDAI was slightly larger than the PtCDAI when patients improved to controlled disease (Table). There was little change in either CDAI score when disease activity levels were unchanged (remained active or remained controlled) (Table).

**Conclusion:** Results from this large sample observational study suggest

| Disease Activity | Improved to Controlled (HDA/MDA to REM/LDA)<br>(N=164; 20%) |     | Worsened to Active (REM/LDA to MDA/HDA)<br>(N=94; 9%) |     | Remained Active (HDA/MDA)<br>(N=227; 24%) |     | Remained Controlled (REM/LDA)<br>(N=442; 47%) |     |
|------------------|-------------------------------------------------------------|-----|-------------------------------------------------------|-----|-------------------------------------------|-----|-----------------------------------------------|-----|
|                  | 95% CI                                                      | SEM | 95% CI                                                | SEM | 95% CI                                    | SEM | 95% CI                                        | SEM |
| CDAI             | 14.1 (12.7, 15.4)                                           | 0.7 | -12.2 (-14.1, -10.3)                                  | 1.0 | 2.2 (0.8, 3.6)                            | 0.7 | 1.0 (0.7, 1.3)                                | 0.2 |
| PtCDAI           | 11.1 (9.5, 12.7)                                            | 0.8 | -11.0 (-13.9, -8.1)                                   | 1.5 | 1.3 (-0.4, 3.0)                           | 0.9 | 1.2 (0.5, 1.9)                                | 0.4 |
| CDAI-PtCDAI      | 3.0 (1.3, 4.7)                                              | 0.8 | -1.2 (-3.7, 1.4)                                      | 1.4 | 0.9 (-0.7, 2.6)                           | 0.8 | -0.2 (-0.8, 0.4)                              | 0.3 |

that both versions of the CDAI scored with clinician-assessed and patient-reported joint counts were sensitive to change over time and provide further evidence that a PtCDAI may provide useful information about changes in patient disease control that can help inform treatment decision-making in virtual care.

### TOUR11

#### miRNA Biomarkers for Methotrexate Response in Psoriatic Arthritis Patients

Omar Cruz Correa (University Health Network, Toronto); Darshini Ganatra (Krembil Research Institute, University Health Network, Toronto); Ameth Garrido (Krembil Research Institute, University Health Network, Toronto); Rohan Machhar (Toronto Western Hospital, Toronto); Starlee Lively (Krembil Research Institute, Toronto); Mohit Kapoor (Krembil Research Institute, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto)

**Objectives:** Psoriatic arthritis (PsA) is an immune-mediated inflammatory arthritis that develops in up to 30% of psoriasis patients. PsA, greatly increases morbidity and may increase mortality risk. Early diagnosis and prompt management of inflammation are essential for preventing joint damage and disability. Methotrexate (MTX) is often the first-line treatment in PsA patients. However, many patients are unresponsive to therapy. Micro RNAs (miRNAs) regulate gene expression and have been associated with the pathogenesis of immune-mediated disorders. We aimed to identify miRNAs associated with articular and cutaneous response to MTX in PsA patients.

**Methods:** We obtained serum samples from 70 biologic-naïve PsA patients (CASPAR criteria) before initiation and 6 months after MTX treatment. Articular response to MTX was defined as achieving a treatment target of low disease activity ( $4 \leq \text{DAPSA} < 14$ ) or remission ( $\text{DAPSA} < 4$ ) and cutaneous response to MTX was defined as a reduction of 50% in Psoriasis Area Severity Index (PASI). miRNA expression was assessed

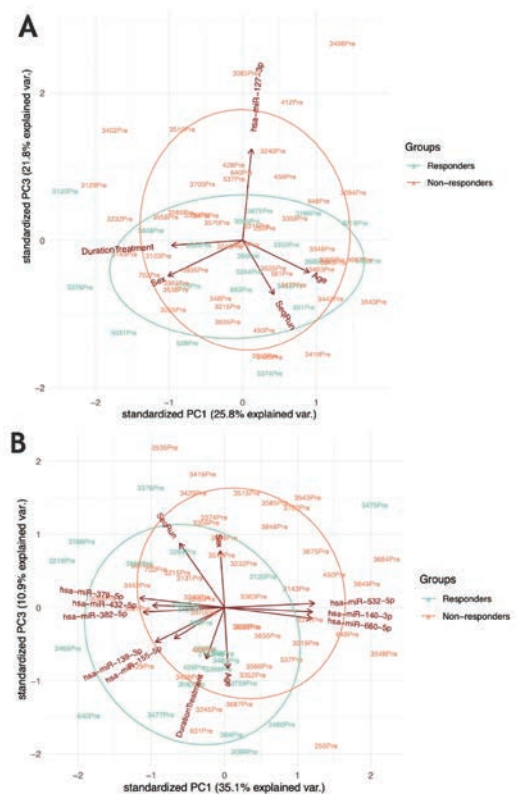


Figure 1. Principal component analysis of samples before initiation of methotrexate (MTX) treatment. A. Patients showing an articular response to MTX (reaching a treatment target of low disease activity and remission: DAPSA score below 14 and below 4, respectively) present lower expression of miR-127-3p. B. Patients showing a cutaneous response to MTX treatment (reaching a reduction of 50% in PASI) present lower expression of miR-140-3p, miR-660-5p and miR-532-5p and higher expression of miR-155-5p, miR-432-5p, miR-382-5p, miR-139-3p and miR-379-5p.



through next-generation sequencing. Total RNA was isolated from serum samples before and after MTX treatment. miRNA sequencing libraries were prepared and sequenced on an Illumina HiSeq2500 following the 75 base-pair single read protocol, at a depth of 12-13 million reads/sample which allows detection of low expressed transcripts. After quality control, reads were aligned to known human miRNA sequences (miRbase version 22). Differential expression was assessed by linear modeling with empirical Bayes moderation as implemented in the Limma R package. Models were corrected for sequencing batch, age, sex, ethnicity, BMI, MTX treatment duration, smoking, and use of NSAIDs.

**Results:** Articular response to MTX treatment was observed in 20 patients and cutaneous response was observed in 24 patients. Pretreatment expression levels of miR-127-3p were significantly lower in patients showing an articular response to MTX ( $P < 0.01$ ). Amongst the genes targeted by miR-127-3p is MAPK4, a member of the mitogen-activated protein kinase family implicated in the pathogenesis of psoriasis and PsA. We also identified a set of 8 miRNAs (miR-155-5p, miR-140-3p, miR-432-5p, miR-382-5p, miR-660-5p, miR-532-5p, miR-139-3p and miR-379-5p) associated with cutaneous response to MTX ( $P < 0.05$ ) (Figure 1).

**Conclusion:** We identified miR-127-3p and a set of 8 miRNAs as potential biomarkers for articular and cutaneous response, respectively, to MTX treatment in PsA patients.

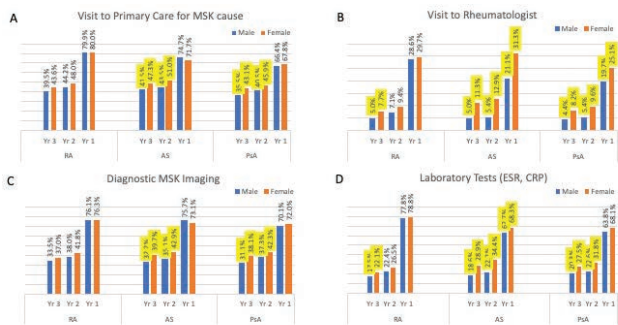
## TOUR12

### Sex-related Disparities in Healthcare Access and Utilization in Adult Patients With Rheumatoid Arthritis, Ankylosing Spondylitis and Psoriatic Arthritis in Ontario

Sanjana Tarannum (Women's College Research Institute, Women's College Hospital; Institute of Medical Science, University of Toronto, Toronto); Jessica Widdifield (Sunnybrook Research Institute, ICES, University of Toronto, Toronto); Fangyun Wu (ICES, Toronto); Sindhu Johnson (Toronto Scleroderma Program, Mount Sinai Hospital; Division of Rheumatology, Toronto Western Hospital; Department of Medicine, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Paula Rochon (Women's Age Lab, Women's College Hospital; Department of Medicine and Dalla Lana School of Public Health, University of Toronto, Toronto); Lihi Eder (Women's College Research Institute, University of Toronto, Toronto)

**Objectives:** Our aim was to describe sex-related disparities in healthcare access and utilization in patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in Ontario.

**Methods:** We assembled 3 inception cohorts of adult RA, AS and PsA patients diagnosed between April 2010 and March 2017 using Ontario health administrative data. Healthcare utilization was assessed per year for 3 years before and 3 years after the date of diagnosis on a rheumatology billing claim (index date) and compared between male and female patients in each cohort. We evaluated healthcare access in terms of visits to physicians (primary care, rheumatologist, other musculoskeletal (MSK) specialist and dermatologist), diagnostic laboratory tests and musculoskeletal imaging. Among individuals  $\geq 66$  years, prescription dispensations for rheumatic



**Figure:** Pattern of healthcare access and utilization in male and female patients with RA, AS and PsA in year 3, year 2 and year 1 before diagnosis. A - Visit to primary care physician for MSK cause, B - Visit to rheumatologist, C - Diagnostic MSK imaging, D - Laboratory test (ESR, CRP). Highlighted values indicate standardized differences  $> 0.10$  (significant).

drugs (NSAIDs, corticosteroids, conventional DMARDs (cDMARDs) and biologic DMARDs (bDMARDs)) and pain control medications (opioids) were ascertained. Standardized difference greater than 0.10 was considered clinically meaningful.

**Results:** A total of 41,277 patients with RA (69% females), 8,150 patients with AS (51% females) and 6,446 patients with PsA (54% female) were analyzed. While male patients were significantly older than female patients with RA (M 60.4 y, F 57.1 y), mean age at the time of diagnosis of PsA and AS was similar in males and females. Multimorbidity (Aggregated Diagnosis Group  $\geq 10$ ), especially depression and osteoporosis, was more common in female patients whereas cardiovascular diseases were significantly more frequent in males across the 3 cohorts. Healthcare utilization before index date was higher in females in all cohorts but most notable 2 to 3 years prior to index date in PsA and AS. A significantly higher percentage of female patients had at least 1 visit to primary care physicians (Figure 1A), to rheumatologists (Figure 1B), at least 1 MSK-imaging (Figure 1C) and at least 1 diagnostic blood test (Figure 1D) before diagnosis. Following diagnosis, healthcare utilization between male and female patients were comparable. Overall DMARD prescriptions in older male and female patients were similar except more female patients with AS being prescribed cDMARDs. Female patients were also more likely to use opioids in the third year after diagnosis.

**Conclusion:** MSK-related healthcare utilization was more common in females compared to males prior to the diagnosis of AS and PsA which may suggest prolonged prodromal phase of the disease in females. Interestingly, sex-disparities in RA were not as prominent. More frequent use of opioid medications in older female patients suggest suboptimal control of pain in these patients.

## TOUR13

### Structural Neural Underpinnings of Low Mood and Anxiety in Childhood Onset Systemic Lupus Erythematosus

Sarah Mossad (Department of Psychology, The Hospital for Sick Children, Toronto); Santiago Arciniegas (Neurosciences and Mental Health, Research Institute, The Hospital for Sick Children; Institute of Biomedical Engineering, University of Toronto, Toronto); Tala El Tal (Division of Rheumatology, The Hospital for Sick Children, Toronto); Lawrence Ng (University of Toronto, The Hospital for Sick Children, Toronto); Paris Moaf (The Hospital for Sick Children, Toronto); Helen Branson (Department of Diagnostic Imaging, The Hospital for Sick Children, University of Toronto, Toronto); Adrienne Davis (Division of Emergency Medicine, Hospital for Sick Children, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto); Deborah Levy (Division of Rheumatology, SickKids Hospital; Faculty of Medicine, University of Toronto, Toronto); Ashley Danguenan (Department of Psychology, The Hospital For Sick Children, Toronto); George Ibrahim (The Hospital for Sick Children, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto)

**Objectives:** Emotional dysfunction in childhood-onset systemic lupus erythematosus (cSLE) impacts clinical outcomes and quality of life, but the relationship to lupus brain inflammation is poorly understood. We aimed to

Table 1. Group Characteristics

|                                                      | cSLE (n=27)     | controls (n=14) | p-value |
|------------------------------------------------------|-----------------|-----------------|---------|
| Female sex, n (%)                                    | 23(85)          | 13(92)          | 0.83    |
| Age in years, Mean $\pm$ SD                          | 15.5 $\pm$ 1.6  | 14.6 $\pm$ 1.9  | 0.18    |
| Race, n (%)                                          |                 |                 | 0.53    |
| American Indian or Alaskan Native                    | 1 (3.7)         | 0 (0)           |         |
| Asian                                                | 9 (33.3)        | 3 (21.4)        |         |
| Black or African American                            | 3 (11.1)        | 2 (14.3)        |         |
| Other                                                | 5 (18.5)        | 1 (7.2)         |         |
| White                                                | 9 (33.3)        | 8 (57.1)        |         |
| Disease duration in months, Mean $\pm$ SD            | 30.3 $\pm$ 25.1 | -               |         |
| Median SLEDAI-2k in year preceding study visit (IQR) | 2(2-2.3)        | -               |         |
| Depression T-score, Mean $\pm$ SD                    | 61.7 $\pm$ 15.1 | 62.1 $\pm$ 12.5 | 0.9     |
| Anxiety total score, Mean $\pm$ SD                   | 24.3 $\pm$ 14.1 | 24.3 $\pm$ 15.3 | 0.9     |

investigate the structural neural metrics and disease activity measures that predict anxiety and depression in cSLE and non-cSLE children.

**Methods:** A cross-sectional sample of patients with cSLE (meeting ACR and/or SLICC classification criteria for SLE) and healthy controls, aged 10-17 years completed self-reported measures of depression (Beck Depression Inventory-II/Children's Depression Inventory-2) and anxiety (Screen for Child Anxiety Related Disorders). Elevated depression/anxiety symptoms were determined by established clinical cut-offs. T1-weighted sequences were acquired on a 3T Siemens MRI. MRI scans were spatially normalized using the MNI-152 template, and gray and white matter were segmented to estimate brain volume, surface area and cortical thickness in Freesurfer. Measures of disease duration, activity (SLE Disease Activity Index (SLEDAI) 2000), glucocorticoid use and inflammation were collected. Partial least squares (PLS) analyses were used to investigate the association between structural brain metrics and disease measures with depression/anxiety symptom severity.

**Results:** Twenty-seven patients with cSLE (mean age = 15.4 ± 1.7 years) and median SLEDAI = 2.0 (IQR 2-4) and 14 healthy controls were recruited. There were no group differences in age, sex or ethnicity (Table 1). Mean cumulative glucocorticoid use in this sample was 5.6 ± 6.2 g prednisone-equivalent. Eleven cSLE patients had a history of lupus nephritis and one had a history of neuropsychiatric lupus. We did not find group differences in prevalence of clinically elevated depression (cSLE = 12/27, controls = 6/14) or anxiety (cSLE = 11/27, controls = 7/14). Within-group analysis showed that for both cSLE patients and controls, worse mood and anxiety were both predicted by reduced right anterior cingulate thickness. Within the cSLE group, worse mood and anxiety were predicted by higher cumulative steroid use, reduced right fusiform gyrus cortical thickness, and increased left amygdala and right parahippocampal volume and thickness.

**Conclusion:** This cross-sectional sample of cSLE patients had mild disease activity at the time of the study, and a high but similar prevalence of emotion problems compared to controls. Worse emotional functioning was associated with altered structural changes in regions known to underlie emotion processing in both groups. Emotion difficulties in the cSLE group were related to cumulative glucocorticoid use, but not disease activity or inflammatory markers. Further research is needed to examine the role of glucocorticoid exposure in the setting of psychological stress related to having a chronic illness during the adolescent neurodevelopmental period.

#### TOUR14

##### **Acceptability and Usability of the JIA Option Map, a Web-based Patient Decision Aid for Pain Management in Juvenile Idiopathic Arthritis**

Karine Toupin-April (University of Ottawa and Children's Hospital of Eastern Ontario Research Institute, Ottawa); Laurie Proulx (Canadian Arthritis Patient Alliance, Ottawa); Adam Huber (IWK Health Centre, Halifax); Ciaran Duffy (Children's Hospital of Eastern Ontario, Ottawa); Deema Couchman (University of Ottawa, Toronto); Esi Morgan (Seattle Children's Hospital, Cincinnati); Janice Cohen (Children's Hospital of Eastern Ontario Research Institute, Ottawa); Isabelle Gaboury (Université de Sherbrooke, Sherbrooke); Linda Li (Rehab Sciences/Physical Therapy, University of British Columbia, Arthritis Research Canada, Richmond); Natasha Trehan (Take a Pain Check, Toronto); Alexandra Sirois (McGill University, Montreal); Emily Siroich (Canadian Arthritis Patient Alliance, Toronto); Naomi Abrahams (University of Ottawa, Ottawa); Anney Houston (University of Ottawa, Ottawa); Iman Kashif (University of Ottawa, Ottawa); Nupur Vij (University of Ottawa, Ottawa); Elizabeth Stringer (IWK Health Centre, Halifax); Sabrina Cavallo (Université de Montréal, Montreal); William Brinkman (Cincinnati Children's Hospital Medical Center, Cincinnati); Mark Connelly (Children's Mercy Kansas City, Kansas City); Jennifer Weiss (Hackensack University Medical Center, Hackensack); Sabrina Gmuca (Children's Hospital of Philadelphia, Philadelphia); Simon Décarry (Université de Sherbrooke, Sherbrooke); Peter Tugwell (University of Ottawa, Ottawa); Jennifer Stinson (The Hospital for Sick Kids, Toronto)

**Objectives:** Young people with juvenile idiopathic arthritis (JIA) often

experience pain that adversely impacts their quality of life. However, pain is often under-recognized by their health care providers (HCPs), and decision-making for pain management is not optimal. Our team, comprised of patient partners, HCPs and researchers, has developed the JIA Option Map, a web-based patient decision aid that provides personalized evidence-based information on pain management. We aimed to evaluate the acceptability and usability of the JIA Option Map from the perspectives of young people with JIA and parents/caregivers.

**Methods:** We conducted iterative acceptability and usability testing using face-to-face or virtual semi-structured interviews with a total of five adolescents 13-18 years old with JIA, six young adults 19-30 years old with JIA, as well as five parents of youths and adolescents with JIA. We recruited participants from rheumatology clinics and through social media. Participants navigated the web application using the think-aloud method while sharing their screen, and answered questions about ease of use, content, format, potential use and perceived helpfulness. We audiotaped or videotaped the interviews and transcribed and analyzed verbatim using simple descriptive content analysis.

**Results:** All participants felt that the app was easy to navigate, and the format was user-friendly. Participants appreciated the following step-by-step layout: (1) assessment of pain and current management; (2) preferences/values clarification exercise; (3) list of pain management options with their evidence to review; (4) plan of the chosen options and readiness to follow the plan; and (5) summary to share with HCPs. All participants felt the content was appropriate and easy to understand, with the suggestion to simplify the information on methodological quality of studies. They mentioned they would use this app frequently, especially shortly after diagnosis or as they transition into adult care. Participants felt the app would help them learn about options, help them engage in decision-making and prepare to have a fruitful discussion with HCPs. Participants liked the wide range of options, the evidence-based summaries presenting their probabilities of benefits, and the links to online resources. They also appreciated the newly added user dashboard which shows pain and disease severity over time and felt it should be the last step of the app.

**Conclusion:** The JIA Option Map has good acceptability and usability, showing its potential to improve decision-making for pain management options among young people with JIA. The next step will test the effectiveness of the app over time.

#### TOUR15

##### **Proton Pump Inhibitors Suppress IL-1 Mediated Carditis in a Murine Model of Kawasaki Disease**

Paul Tsoukas (Hospital for Sick Children, Toronto); Melissa Kleinau (Hospital for Sick Children, Toronto); Lysa Langevin (Hospital for Sick Children, Toronto); Suzanne Tam (Hospital for Sick Children, Toronto); Lily Morikawa (Hospital for Sick Children, Toronto); Trang Duong (Hospital for Sick Children, Toronto); Rae Yeung (The Hospital for Sick Children, Toronto)

**Objectives:** Kawasaki disease (KD), is the leading cause of acquired heart disease in childhood, with a portion of children developing coronary artery lesions (CAL) despite standard of care treatment, intravenous immunoglobulin (IVIg). Murine and patient data indicate Interleukin-1 (IL-1) contributes to CALs. Calcium mobilization plays a role in inflammasome activation and is key to the immunobiology of KD. Proton pump inhibitors (PPI), a class of medications used to limit gastric acid secretion, have also been shown to have anti-inflammatory properties. This study aims to determine if PPIs inhibit IL-1 production and resulting CALs in the *Lactobacillus casei* cell wall extract (LCWE) induced coronary arteritis murine model of KD.

**Methods:** Human monocyte cell line (THP1) derived macrophages and bone marrow derived macrophages (BMDMs) were stimulated with a TLR1/2 agonist Pam3Cys-Ser-(Lys)<sub>4</sub> (Pam3Cys) and LCWE, in the presence or absence of PPIs. To exclude toxic effects, viability was tested via flow cytometry and trypan blue exclusion. Calcium flux was measured via fluorescent imaging plate reader on THP-1 macrophages. In vivo, KD was induced by intraperitoneal LCWE injection. Mice were injected with

LCWE alone, LCWE+PPI, saline or PPI alone. Coronary artery inflammation was blindly scored by a pathologist.

**Results:** Following stimulation with either Pam3Cys or LCWE, PPIs inhibited BMDM IL-1 production in a dose-dependent manner. Inflammasome activation is prevented by PPI inhibition of signal two. Stimulated macrophages treated with a PPI, in vitro, had less calcium flux than untreated stimulated macrophages. In vivo, compared to untreated KD diseased mice, those treated with PPI were shown to have significantly reduced coronary artery inflammation based on overall cardiac severity score ( $P < 0.01$ ), area of inflammation ( $P < 0.05$ ) and elastin breakdown ( $P < 0.01$ )

**Conclusion:** Our data indicate that PPIs have anti-inflammatory properties: decreasing macrophage IL-1 production in vitro and in vivo, preventing IL-1 induced coronary artery inflammation. The data suggest two novel findings. Firstly, PPIs may inhibit inflammasome activation by preventing intracellular calcium accumulation. Secondly, PPIs have the potential to be a novel inexpensive, oral, and safe adjuvant anti-IL-1 medication to treat KD.

## TOUR16

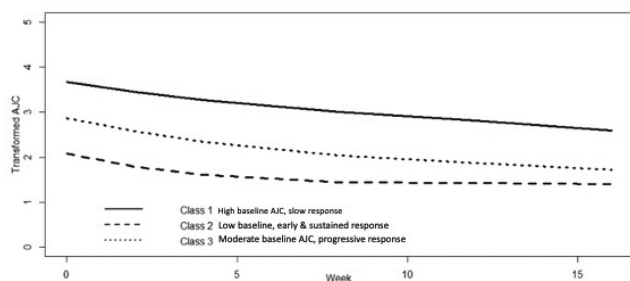
### Latent Classes of Early Responses to Biologics Initiation in Juvenile Idiopathic Arthritis: An Analysis of Four Trials

Lily Lim (University of Manitoba, Winnipeg); Shamsia Shobhan (University of Manitoba, Winnipeg); Armend Lokku (University of Toronto, Toronto); Sarah Ringold (Seattle Children's Hospital, Seattle); Eleanor Pullenayegum (University of Toronto, Toronto)

**Objectives:** Juvenile idiopathic arthritis (JIA) is the commonest childhood-onset chronic rheumatic disease. Patients with polyarticular disease are more likely to require biologic treatment. However, despite biologic treatment, about 20% will require switching because of ineffectiveness. If we can identify JIA patients who are unlikely to respond early after starting biologics, we can switch them to another agent. This will reduce the burden of chronically active disease symptoms and the risk of chronic joint damage. As polyarticular JIA is a heterogeneous disease, we hypothesize that patients may follow different response trajectories after starting biologics. Objectives: 1) To delineate latent classes of early treatment response to biologics in JIA patients in the first 16 weeks after initiation. 2) To identify predictors of early disease response.

**Methods:** The study population was drawn from four JIA biologics trials: Etanercept 2000, Abatacept 2008, TRial of Early Aggressive Therapy (TREAT) 2012 and Tocilizumab 2014. Participants have polyarticular course JIA. The primary outcome was active joint counts (AJC) measured in the first 16 weeks after starting biologics. Semiparametric latent class trajectory analysis with spline modeling was applied to identify latent classes of response to treatment; AJC was transformed for this modeling. We tested baseline disease and treatment characteristics for their abilities to predict class membership of response.

**Results:** There were 480 participants, 74% females. At baseline, 26% were rheumatoid factor positive. 67% were on methotrexate. Baseline AJC was the sole best predictor of class membership. The three classes were: high baseline AJC (median > 30) and slow response (26.5%), low baseline AJC (< 10), early and sustained response (29.7%) and moderate baseline AJC progressive response (43.8%; see Figure). Patients were classified into the three classes with a mean class membership posterior probability of 0.97. Those on methotrexate were less likely to belong to high baseline AJC class. Those in moderate and high baseline AJC classes were more likely to be on prednisone than those in low baseline AJC class.



**Conclusion:** Three latent classes of responses were detectable. Those with the highest baseline AJC demonstrated very slow response in this time window; they should be considered for early switch if they do not respond adequately by 16 weeks. Those in the highest AJC group were less likely to be on concomitant methotrexate. Though methotrexate may not be sufficient to control disease activity, they could be helpful in reducing disease activity, allowing patients to follow more timely and earlier response trajectories.

## TOUR17

### Trajectories of Depressive Symptoms in Systemic Lupus Erythematosus Over Time

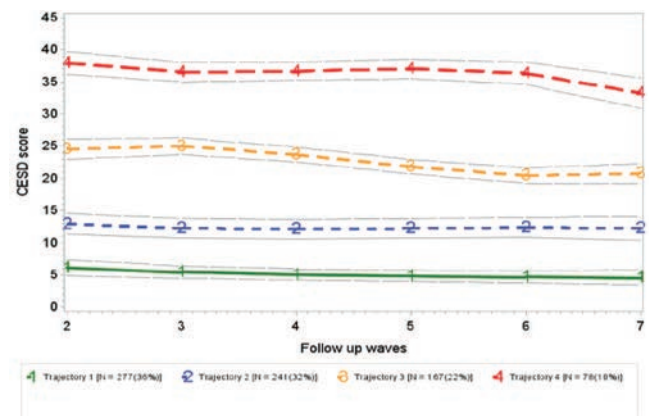
Seerat Chawla (University of California, Los Angeles); Jiandong Su (Toronto Western Hospital, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Patricia Katz (University of California San Francisco, Professor of Medicine and Health Policy, Division of Rheumatology, Department of Medicine, San Francisco)

**Objectives:** Depression is one of the common psychiatric disorders in SLE with an estimated prevalence between 29.9% and 40.3%, which is twice the prevalence among the general population. The longitudinal trajectories of this heterogeneous mood disorder in SLE, however, remain uncharacterized. We aimed to: 1) determine the trajectories of depressive symptoms in patients with SLE and 2) identify baseline characteristics associated with trajectories.

**Methods:** Longitudinal data from the Lupus Outcomes Study at the University of California San Francisco, in which adults with SLE were followed over 7 years, were analyzed. Depressive symptomatology was assessed in years 2-7 using the Center for Epidemiologic Studies Depression Scale (CES-D) and the threshold for depression in SLE was scores  $\geq 24$ . Group-based trajectory modeling was used to determine latent classes for CES-D scores over the six waves of observation. Using members with posterior probability > 0.8, univariable and multivariable ordinal logistic regression analyses were also performed to identify baseline characteristics associated with membership in worse classes of depressive symptoms.

**Results:** 763 patients with two or more waves of CES-D data were included in the analysis. Four trajectories were found to fit the data best (Figure 1). Class 1 (36%) and class 2 (32%) comprised the greatest proportion of the cohort and had average CES-D scores below the threshold for depression over the waves. The mean CES-D score for class 3 (22%) remained near or at the cut-off for depression over time. Class 4 (10%) consisted of the highest scores over the years. There was no significant movement of patients between class trajectories. From the regression models, lower income (odds ratio [OR]: 1.73, 95% confidence interval [CI] 1.03-2.92), SF-36 bodily pain score (OR: 1.58, 95% CI 1.55-1.61), and SF-36 physical functioning score (OR: 1.12, 95% CI 1.12-1.13) were positively associated with higher CES-D scores. Greater age (OR: 0.97, 95% CI 0.96-0.99) and higher education level (OR: 0.79, 95% CI 0.70-0.89) at baseline were negatively associated with higher CES-D scores.

**Conclusion:** Four trajectories of depression were found in adults with SLE





in this novel trajectory analysis. Higher education level and greater age at baseline were determined to be protective factors, while lower income and SF-36 bodily pain and physical functioning scores were risk factors for worse class membership. These mapped trajectories and associated baseline factors provide a tool to improve the screening, treatment, and management of this common psychiatric comorbidity faced by individuals with SLE.

#### TOUR18

##### Association of Subjective Cognitive Report Using PDQ-20 to a Neuropsychological Battery in a Cohort of SLE Patients

Ambika Gupta (University of Toronto, Toronto); Sindhu Johnson (Toronto Scleroderma Program, Mount Sinai Hospital; Division of Rheumatology, Toronto Western Hospital; Department of Medicine, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto); Juan Diaz-Martinez (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto); Kathleen Bingham (University Health Network, Toronto); Mahta Kakvan (Toronto Western Hospital, Toronto); Carmela Tartaglia (University Health Network, Toronto); Lesley Ruttan (University Health Network, Toronto); Joan Wither (Division of Genetics and Development, Krembil Research Institute; Division of Rheumatology, University Health Network; Department of Immunology, University of Toronto, Toronto); May Choi (University of Calgary, Calgary); Marvin Fritzer (University of Calgary, Calgary); Dennisse Bonilla (Toronto Western Research Institute, Toronto); Dorcas Beaton (University of Toronto/Institute for Work and Health, Toronto); Patricia Katz (University of California San Francisco, Professor of Medicine and Health Policy, Division of Rheumatology, Department of Medicine, San Francisco); Robin Green (University Health Network, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** Systemic Lupus Erythematosus (SLE) can lead to a number of neuropsychiatric manifestations including cognitive impairment (CI). Comprehensive neuropsychological battery (NB) of tests is considered the gold standard when diagnosing CI. We aim to compare a subjective questionnaire, the perceived deficits questionnaire (PDQ-20) to the NB and also to other patient-reported outcomes.

**Methods:** This is a cross-sectional study of SLE patients, aged 18-65 years, who attended a single center (Jul 2016 – Mar 2019). Each patient completed a comprehensive NB evaluating six cognitive domains. They also completed the 20 item PDQ-20 questionnaire (subjective cognitive function) along with other patient-reported outcome questionnaires such as the Beck anxiety score, Beck depression score, fatigue severity score (FSS), Short Form Health Survey (SF-36) domains. The variable of main interest was the total score of 19 tests in NB, along with patients' demographics, lupus disease activity, organ damage, treatment and other PROs. Mean  $\pm$  std., median (interquartile range) and count (%) were calculated for these variables. Univariate and multivariable linear regressions were performed to evaluate the associated factors with total PDQ-20 scores. Least Absolute Shrinkage and Selection Operator (LASSO) method was used in the variable selection in multivariable model building process. Linear model assumptions were tested by residual density plots and quantile-quantile plots.

**Results:** Data on 238 patients was analyzed; 89.9% were females with an average age and SLE duration at baseline visit of  $41.1 \pm 12.1$  and  $14.3 \pm 10.0$  years, respectively. In the univariate analysis, PDQ-20 was associated with the NB, SDI, FSS, BECK anxiety and depression score and all SF-36 domains. In the multivariate analysis, PDQ-20 was significantly associated with female gender, SDI, fatigue, BECK depression and anxiety scores, SF-36 Role Emotional domain and glucocorticoid dosage. PDQ-20 was not associated with the NB. There was also no association with age at first visit, SLE disease duration, ethnicity, education level, SLEDAI score, anti-malarial or immunosuppressive treatment with the PDQ-20 score.

**Conclusion:** Subjective cognitive report by PDQ-20 was associated with the NB in univariate analysis but not multivariate analysis. While PDQ-20 was associated with all SF-36 domains in the univariate analysis, this association was significant only with Role Emotional in the multivariate analysis. There was a clear association of PDQ-20 with other subjective patient-reported outcomes.

#### TOUR19

##### Incident and Prevalent Patients With SLE Have Similarly High Symptom Burden, Pain and Fatigue Despite Differences in Disease Activity: Data from the Canadian Network for Improved Outcomes in Systemic Lupus Erythematosus (CaNIOS) National Registry

Kaieen Gu (University of Manitoba, Winnipeg); Paul Fortin (Université Laval, CHU de Québec, Québec); Ann Clarke (University of Calgary, Calgary); Catherine Ivory (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Jennifer Reynolds (University of British Columbia, Department of Medicine, Division of Rheumatology, Vancouver); Antonio Avina-Zubieta (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Richmond); Mark Matsos (McMaster University, Hamilton); Derek Haaland (Department of Medicine, McMaster University, Hamilton); Kimberly Legault (McMaster University, Hamilton); Carol Hitchon (University of Manitoba, Winnipeg); Annaliese Tisseverasinghe (University Of Manitoba, Winnipeg); Janet Pope (University of Western Ontario, London); Lily Lim (University of Manitoba, Winnipeg); CaNIOS Investigators (Winnipeg); Christine Peschke (University of Manitoba, Winnipeg)

**Objectives:** The CaNIOS national registry is a multicenter longitudinal cohort that collects standardized information on SLE patients, including both prevalent and incident patients. We aimed to describe demographics, disease-related measures, and patient-reported outcomes (PROs) in patients on enrolment in the cohort and compare incident and prevalent patients

**Methods:** Baseline visit data was extracted, including demographics, clinical manifestations, treatment, disease activity, damage measures, and PROs including the SLE Activity Questionnaire (SLAQ), the SF-36, global activity, pain and fatigue VAS, categorical questions about flares, disease activity and improvement. Descriptive statistics, including the mean and SD for continuous variables and frequency distributions for categorical variables, were produced. Incident cases were defined as disease onset within 15 months of enrolment. Between-group comparisons were conducted with the independent-samples t-test for continuous variables and the chi-square test for categorical variables. Statistical significance was set at 0.05.

**Results:** There were 681 patients enrolled in the registry from seven Canadian sites as of January 2020; 166 patients (24.4%) were incident cases; with mean age at enrolment  $48.1 \pm 14.9$  years, average disease duration  $12.1 \pm 11.5$  years, 80.6% of patients residing in urban areas, 71.0% white, and 89% female. Mean disease duration for incident patients was 5 months. SLEDAI and Physician Global VAS were higher in incident compared to prevalent patients ( $5.14 \pm 4.85$  versus  $3.41 \pm 3.54$ ;  $P < 0.001$ ) and ( $0.65 \pm 0.71$  versus  $0.30 \pm 0.42$ ;  $P < 0.001$ ) respectively. Patient Global VAS (in the preceding three months) was higher in incident patients ( $4.64 \pm 3.00$  vs  $3.93 \pm 2.81$ ,  $P = 0.026$ ); incident patients were more likely to report any lupus activity (90% vs 84%,  $P = 0.028$ ), and flares (74% vs 64%,  $P < 0.001$ ), but there were no differences in the fatigue and pain VAS scores. Mean SF-36 PCS and MCS scores on initial presentation were  $39.5 \pm 11.8$  and  $45.3 \pm 11.8$ , respectively, and mean SLAQ symptom scores were  $10.1 \pm 5.4$  and global scores were  $12.3 \pm 8.1$ ; these did not differ between incident and prevalent patients. However, incident patients were more likely to report improvement in their lupus over the preceding month (52% vs 22%;  $P < 0.001$ ).

**Conclusion:** Incident patients had higher physician and self-reported disease activity compared to prevalent patients; however, symptoms, pain, fatigue and SF-36 scores did not differ from prevalent patients. This suggests that symptom burden is high, and quality of life is low from disease onset and does not improve with either time or reduced disease activity. Future work will aim to analyze the evolution of PROs in SLE patients over time and the relationship between PROs and other disease measures.

## TOUR20

### SLE Phenotypes Formed From Machine Learning and Their Associations With Cognitive Impairment

Michelle Barraclough (University Health Network, Toronto); Lauren Erdman (The Hospital of Sick Children, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto); Juan Diaz-Martinez (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto); Kathleen Bingham (University Health Network, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Mahta Kakvan (Toronto Western Hospital, Toronto); Carmela Tartaglia (University Health Network, Toronto); Lesley Ruttan (University Health Network, Toronto); Joan Wither (Division of Genetics and Development, Krembil Research Institute; Division of Rheumatology, University Health Network; Department of Immunology, University of Toronto, Toronto); May Choi (University of Calgary, Calgary); Marvin Fritzier (University of Calgary, Calgary); Dennisse Bonilla (Toronto Western Research Institute, Toronto); Dorcas Beaton (University of Toronto/Institute for Work and Health, Toronto); Ben Parker (The University of Manchester, Manchester); Robin Green (University Health Network, Toronto); Patricia Katz (University of California San Francisco, Professor of Medicine and Health Policy, Division of Rheumatology, Department of Medicine, San Francisco); Ian Bruce (University of Manchester, Manchester); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** Cognitive impairment (CI) in SLE is a significant problem with limited treatment options due to uncertainty around the multifaceted cause. Factors associated with CI include depression, pain, fatigue, medications, as well as more specific SLE factors such as disease damage, autoantibodies and inflammation. We aimed to phenotype CI in SLE using machine learning techniques.

**Methods:** SLE patients aged 18-65 years completed the ACR Neuropsychological Battery (ACR-NB) cognitive assessment. Age- and gender-matched normative data were used to obtain z-scores on all 19 tests of ACR-NB. The ACR-NB tests were reduced using principal component analysis (PCA) to generate a factor score (CI Factor Score). Demographic, and clinical data, and patient-reported outcomes including, SF-36, LupusQoL, the PDQ-20 (perceived cognitive deficits), Beck Depression Inventory-II, Beck Anxiety Inventory, and the fatigue severity scale (FSS) were analyzed using similarity network fusion (SNF) to identify patient subtypes. Differences between the SNF-identified subtypes were evaluated using Kruskal-Wallis tests and chi-square tests.

**Results:** Of the 301 patients, 89% were women, mean age  $40.9 \pm 12.1$  and disease duration  $14 \pm 10.1$  years at study visit. The CI Factor Score accounted for 28.8% of the variance. The SNF analysis defined three subtypes with distinct patterns in health-related quality of life (HRQoL), depression, anxiety, fatigue, fibromyalgia, medication usage, and disease

damage (Figure 1). The CI Factor Score was significantly different between the subtypes ( $P = 0.008$ ). Subtype 3 performed worst on the majority of the different cognitive domains. Further exploration revealed statistical differences with depression, anxiety, fatigue, and fibromyalgia between the subtypes (all  $P < 0.00002$ ). Differences were also found relating to organ involvement within the last ten years and damage within specific organs (musculoskeletal  $P = 0.0002$  and cardiovascular  $P = 0.001$ ). No differences were found for SLE disease activity ( $P = 0.24$ ). Subtype 3 had higher levels of all conditions and disease damage, Subtype 2 had lower levels and Subtype 1 mixed levels.

**Conclusion:** The subtype with the greatest psychiatric and disease burden and reduced HRQoL performed worse on cognitive testing and had more musculoskeletal and cardiovascular involvement. Musculoskeletal involvement affects pain levels, which can impact cognition. Cardiovascular damage may be linked to cerebral small vessel disease, which is known to affect cognitive function in SLE patients. Overall, these results aid with phenotyping CI in SLE and provide a baseline for our future longitudinal results. This will then help to determine personalized CI trajectory and treatment options in SLE.

## TOUR21

### Analysis of Referrals by Primary Care Physicians to Rheumatology: A First Step in the Development of a Rheumatologist-led Curriculum for Community Providers

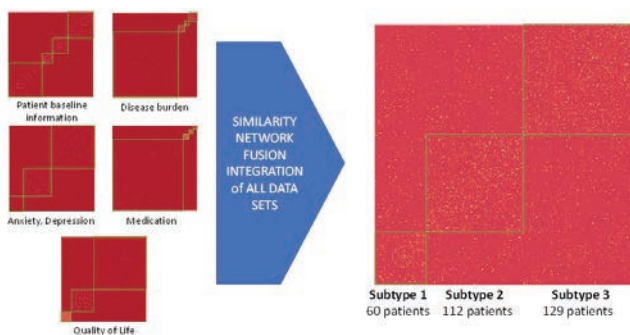
Alan Zhou (University of Ottawa, Department of Medicine, Ottawa); Antonio Cabral (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Julie D'Aoust (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa)

**Objectives:** Unacceptable delays in the recognition and treatment of rheumatic diseases exist in Ontario. Educational interventions aimed at Primary Care Providers (PCPs) may reduce delays by improving PCP confidence in the identification of rheumatic disorders and ensuring appropriate referral of those who would benefit from specialty care. This study sought to characterize local PCP referral patterns and knowledge gaps as a first step in the development of a rheumatologist-led curriculum for community providers in the Ottawa region.

**Methods:** Patients who were first assessed between September 1 and October 31, 2019, at The Ottawa Hospital's Arthritis Centre were identified. Pre-pandemic dates were chosen to avoid confounders related to virtual visits and potential changes in referral patterns. Referrals from non-PCPs and for transfer of care were excluded. First and second visits were reviewed to identify reason for referral, suspected diagnosis by PCP (if any), rheumatologist-established diagnosis, procedures performed, and consults requested by the treating rheumatologist. Two rheumatologists (JD, AC) independently analyzed and compared the reasons for referral and the consulting rheumatologists' final diagnoses, to identify possible PCP knowledge gaps. Full review by the Ottawa Health Science Network Research Ethics Board was waived as this study was deemed a quality improvement initiative.

**Results:** 106 new consults were reviewed. Among the 106 new consults, 85 (80.2%) were given a diagnosis by the second visit. The most common rheumatologist-established diagnoses were rheumatoid arthritis (17/85, 20%), osteoarthritis (15/85, 17.6%), and seronegative spondyloarthritis (13/85, 15.3%). Forty-four (42%) of referring PCPs provided no suspected diagnosis or a diagnosis that differed substantially from the rheumatologist's final diagnosis. Fourteen new consults (13.2%) resulted in procedures (13 aspirations/injections, 1 skin biopsy) and 17 (16%) resulted in referrals to other specialties. The most common identified knowledge gaps included 'differentiating inflammatory arthritis from non-inflammatory pathology' (27/106, 25%), 'management of an established rheumatic disease' (22/106, 21%), and 'approach to peripheral joint pain' (15/106, 14%). Sixty-three patients (59.4%) required ongoing follow-up in rheumatology while 43 (41%) did not.

**Conclusion:** The results of this study provide insight into regional PCP referral patterns to an academic rheumatology clinic, as well as possible PCP



**Figure 1.** Similarity network fusion (SNF) for first visit data. Three subtypes defined by patterns in patient baseline information, health-related quality of life (HRQoL), depression, anxiety, fatigue, and medication usage. Demographic and clinical variables used within the patient baseline and disease burden information included; age, sex, marital and employment status, education and income level, age at diagnosis, disease damage, disease activity and fibromyalgia status.

knowledge gaps in the identification and care of patients with rheumatic diseases that will inform the creation and implementation of a rheumatologist-led, local webinar series.

## TOUR22

### Virtual Assessment in Axial Spondyloarthritis: Validation of Video Observed Spinal Metrology

Laura Passalent (Toronto Western Hospital, Krembil Research Institute, University of Toronto, Toronto); Robert Inman (Toronto Western Hospital, Toronto); Nigil Haroon (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto)

**Objectives:** A shift to virtual clinical encounters was required as a result of the COVID-19 pandemic. A core aspect in the evaluation of axial spondyloarthritis (axSpA) is the spinal physical exam, which includes the assessment of mobility and potential structural damage. To date, there have been very few studies exploring the utility of virtual examination of the spine for patients with axSpA with varying reports of validity and reliability. The purpose of this study was to evaluate the validity of observed spinal mobility measures over live video in the assessment of patients with axSpA.

**Methods:** Adult patients diagnosed with axSpA based on ASAS criteria, attending an urban academic Spondylitis Program and registered in the program's longitudinal research cohort were scheduled for a virtual video follow-up visit. Patients conducted spinal mobility maneuvers based on standardized verbal direction by the attending clinician. Spinal measures were visually estimated by the clinician observer and included tragus-to-wall distance, cervical spinal rotation, lumbar lateral flexion and intermalleolar distance. The modified Schober's maneuver to assess degree of lumbar flexion was estimated based on observed finger-to-floor distance. Spinal measures were compared to patients' last in-person visit within a 24-month period. Concurrent validity of the virtual spinal measures were estimated based on correlation (Pearson's correlation coefficient) to previous in-person Bath Ankylosing Spondylitis Metrology Index (BASMI) scores (10-step analysis) and its individual components. Construct validity was assessed against the previous Bath Ankylosing Spondylitis Functional Index (BASFI), reflecting constructs of mobility and function.

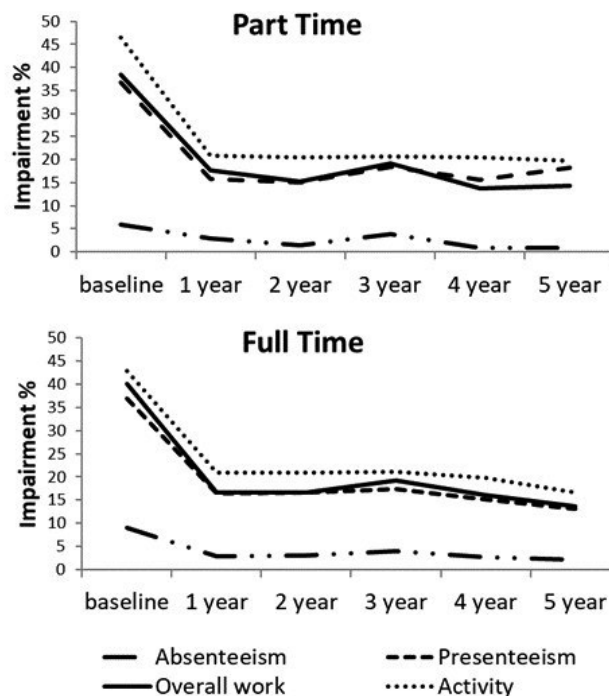
**Results:** A total of 31 patients underwent virtual examination of spinal mobility. Approximately half were male (51.9%) with a mean age of 41.2 years ( $\pm 15.1$ ); mean disease duration 11 years ( $\pm 9.4$ ); mean Bath Ankylosing Spondylitis Disease Activity Index was 2.4 ( $\pm 1.7$ ), indicating low disease activity; 55.2% were receiving biologic treatment and 48.3% were receiving non-steroidal anti-inflammatories. Clinician observers included rheumatology fellows, rheumatology residents and an advance practice physiotherapist. Average time between the last in-person measure and virtual measure was 21.5 months ( $\pm 6.5$ ). Virtual BASMI scores were highly correlated with previous in-person BASMI scores ( $r = 0.75$ ). Virtual component BASMI scores ranged from  $r = 0.62$  (lumbar lateral flexion) to  $r = 0.84$  (cervical rotation) when compared to in-person measures. Virtual BASMI scores were moderately correlated with the BASFI ( $r = 0.61$ ).

**Conclusion:** The results of this study suggest spinal mobility measures conducted over live video by an experienced clinician in rheumatology assessment are a valid substitution for in-person measurement.

## TOUR23

### Persistent Disease Activity Impairs Work Productivity and Non-work Activity Outcomes in Recent Onset Rheumatoid Arthritis.

Carol Hitchon (University of Manitoba, Winnipeg); Marie-France Valois (McGill University, Montreal); Orit Schieir (McGill University, Montreal); Susan Bartlett (McGill University, Montreal); Louis Bessette (Laval University, Quebec City); Gilles Boire (Université de Sherbrooke, Sherbrooke); Glen Hazlewood (University of Calgary, Calgary); Edward Keystone (University of Toronto, Toronto); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Janet Pope (University of Western Ontario, London); Vivian Bykerk (Hospital for Special Surgery, New York); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)



**Objectives:** Reduced work and activity productivity are significant contributors to personal and societal costs associated with rheumatoid arthritis (RA). We sought to describe work productivity in newly diagnosed RA patients and to identify predictors of impaired productivity over time.

**Methods:** Data were from working age, early RA patients (18-64 years; < 1 year of symptoms at baseline) treated with DMARDs according to Treat-2-Target guidelines. Between Nov 2011 and March 2020, participants reported baseline work status (employed, unemployed, retired). Annual work productivity was assessed using the Work Productivity and Activity Index (WPAI). WPAI scores for overall work productivity loss with subscores for absenteeism (time away from work) and presenteeism (reduced productivity at work) and scores for reduced general activity are expressed as impairment percentages (%) with higher numbers indicating greater impairment and less productivity. We used generalized estimating equations (GEE) to estimate associations between change in WPAI scores over the first five years of follow-up with time-varying lagged disease activity (DAS28 at previous visit predicting WPAI at the next visit), while adjusting for baseline age, sex, work commitment (full time; part-time) and comorbidity [Rheumatic Disease Comorbidity Index (RDCI; range 0-9); depression], and time-varying lagged therapy use (Methotrexate (MTX), biologic DMARDs/ JAKi, prednisone) at the previous visit.

**Results:** At baseline, of 673 working age RA patients, 434 (65%) were employed [352 (82%) full time], 159 (24%) were unemployed and 74 (11%) were retired. Employed RA patients were mainly female (75%), Caucasian (81%), had education beyond high school (68%) and had active RA with mean (SD) baseline DAS28 4.7 (1.4). At baseline, employed RA patients reported on average 39.8% (29.8) overall work impairment of 39.8% (29.8) [absenteeism 8.4% (18.6); presenteeism 37.0% (28.0)] and non-work activity impairment of 43.5% (28.5). Work productivity scores improved after 1 year follow-up but remained stable thereafter (Figure). In lagged multivariable GEE models, higher DAS28 was associated with more work impairment over time; mean change (95% confidence interval (CI) in overall work impairment 7.1% (6.2-7.9), absenteeism 1.9% (1.4-2.5), presenteeism 6.6% (5.8-7.4) and activity impairment 7.8% (7.1-8.6). Baseline comorbidity was associated with overall work impairment over time [RDCI mean change 1.9% (0.1-3.6); depression mean change 8.0% (0.4-15.7)].

**Conclusion:** Patients with early RA report 40% reduced work produc-



tivity, mainly from reduced effectiveness while at work. Persistent disease activity contributes to productivity impairment. Interventions to optimize continued engagement in work and addressing RA activity may improve productivity for RA patients and their employers.

#### TOUR24

### Clinical and Economic Burden of Herpes Zoster in Patients With Rheumatoid Arthritis: A Retrospective Cohort Study Using Administrative Claims

David Singer (GSK, Philadelphia); Philippe Thompson-Leduc (Analysis Group, Inc., Montreal); Siyu Ma (GSK & Tufts Medical Center, Philadelphia); Deepshikhar Gupta (Analysis Group, Inc., Menlo Park); Francesca Devine (Analysis Group, Inc., New York); Alexandra Enrique (Analysis Group, Inc., Menlo Park); Wendy Cheng (Analysis Group, Inc., Boston); Mei Sheng Duh (Analysis Group, Inc., Boston); Sara Poston (GSK, Philadelphia); Jeffrey Curtis (University of Alabama at Birmingham, Birmingham)

**Objectives:** The incidence of herpes zoster (HZ) is higher in patients with rheumatoid arthritis (RA) than in the general adult population. With the increased incidence of HZ in patients with RA, it is important to understand the clinical and economic burden associated with HZ in this population.

**Methods:** This was a retrospective cohort study using an administrative claims database with commercial and Medicare Advantage with Part D data from October 2015 - February 2020. Patients with HZ+RA were identified using ICD-10 diagnosis codes in medical claims. The first HZ diagnosis was the index date. A confirmed RA diagnosis was required as defined by  $\geq 2$  RA diagnoses on medical claims  $\geq 6$  weeks apart and  $\geq 3$  months of continuous DMARD treatment. A comparator cohort was identified based on the same criteria for RA but was required not to have HZ. Index date in this cohort was based on the distribution of timing of the HZ+RA cohort index dates. All patients were required to have at least 12 months of continuous medical and pharmacy benefit enrolment before and after index. Outcomes included healthcare resource use (HCRU) and costs after index. Generalized linear models were used to estimate differences in outcomes between cohorts, adjusting for propensity scores and key baseline variables.

**Results:** The study included 1,866 and 38,846 patients in the RA+HZ and RA-only cohorts, respectively. Mean  $\pm$  standard deviation (SD) age in the RA+HZ cohort was  $68 \pm 12$  vs  $66 \pm 13$  in the RA-only cohort. Higher proportions of patients in the RA+HZ cohort used JAK inhibitors or systemic steroids at index compared to the RA-only cohort. Baseline mean  $\pm$  SD total costs were \$52,625  $\pm$  67,774 and \$46,332  $\pm$  65,480 in the RA+HZ and RA-only cohorts, respectively. During the 12-month follow-up, hospitalizations and emergency department (ED) visits occurred more often in the RA+HZ cohort than in the RA-only cohort with an adjusted incidence rate ratio (95% confidence interval [CI]) of 1.16 (1.04-1.30) for hospitalizations and 1.34 (1.21-1.47) for ED visits. Medical costs were higher in the RA+HZ cohort during the 12-month

follow-up compared to the RA-only cohort, with an adjusted cost difference (95% CI) of \$3,428 (446-6,781) (Table 1).

**Conclusion:** Patients with RA+HZ had higher HCRU and medical costs than patients with RA-only in the year following an HZ diagnosis after adjusting for baseline difference between cohorts. These findings provide evidence of the added burden of HZ in patients with RA.

#### TOUR25

### Development of a New 'Resource of Resources' to Support Physical Activity in People Living With Chronic Conditions

Marie Westby (Vancouver Coastal Health Research Institute, Vancouver); Alison Hoens (University of British Columbia/Arthritis Research Canada, Vancouver)

**Objectives:** Although the evidence endorsing physical activity (PA) for people living with chronic conditions including arthritis is substantive, both patients and health care providers (HCPs) struggle with the quantity and quality of resources available to support PA. The objectives of this project were to: (1) identify, evaluate and recommend resources for patients and HCPs that support PA in people living with chronic conditions (including arthritis) and (2) augment the HealthLink BC website to incorporate the recommended resources.

**Methods:** Over 100 patients, clinicians and researchers contributed to a rigorous process including surveys and appraisal of existing resources to recommend the 'best of the best resources' supporting PA in chronic conditions. Surveys included baseline needs assessments of both patients and HCPs as well as preferred websites and formats. After training and practice sessions, evaluators assessed each patient resource using the Patient Education Materials Assessment Tool (PEMAT) and each HCP resource using a 'purpose-built' assessment tool incorporating key features of the PEMAT, AGREE II Instrument and the 2009 National Health and Medical Research Council (NHMRC) Evidence and Grades Tool. Two people independently evaluated each resource and, when discrepancy in scores was greater than 20%, a third person served as the tie breaker. An independent research expert reviewed the top scoring resources for alignment with current evidence.

**Results:** The baseline survey of 487 patients (85% female; 78% 50+ years of age) representing all regions of BC, revealed that most lived with 3 or more chronic diseases (65% with arthritis) and 65% reported they were less physically active than prior to their chronic condition. Seventy-five percent desired access to a 'toolkit' that outlined what and how much PA they should undertake. Less than 45% of the 443 HCP survey respondents (85% female; 46% physiotherapists; 60% community settings) reported using published guidelines to inform the PA support they provide to patients. The majority of the 381 people (48% HCPs; 43% patients) who completed the survey on preferred formats/locations, favored websites linked to professional associations or disease specific organizations (60% and 44% respectively). In partnership with the BC Ministry of Health the resources were loaded onto a custom-built extension of the HealthLink BC website, launched in the fall of 2021, and evaluated at 3 months.

**Conclusion:** An integrated knowledge translation initiative was undertaken to develop an online toolkit of resources to help persons with chronic condition(s) to be more physically active.

#### TOUR26

### Neuro-QOL Upper Extremity Function Scale: Better Ways to Measure Perceived Function and Self Care in RA in the Era of Virtual Medicine

Susan Bartlett (McGill University, Montreal); Orit Schieir (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Janet Pope (University of Western Ontario, London); Gilles Boire (Université de Sherbrooke, Sherbrooke); Edward Keystone (University of Toronto, Toronto); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Carol Hitchon (University of Manitoba, Winnipeg); Louis Bessette (Laval University, Quebec City); Glen Hazlewood (University of Calgary, Calgary); Vivian Bykerk (Hospital for Special Surgery, New

Table 1. Healthcare resource use and costs during 12 months after index date for patients with RA and HZ and patients with RA only

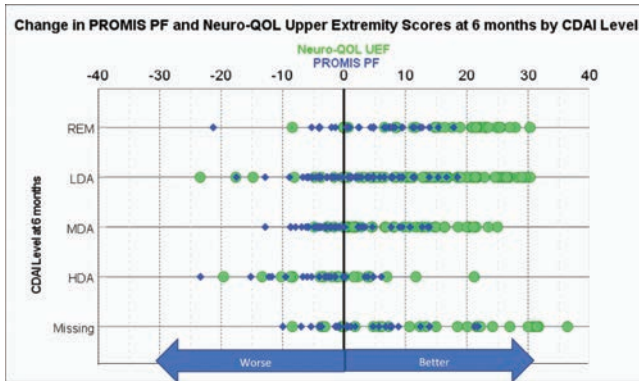
|                                   | RA and HZ<br>(n=1,866) | RA only<br>(n=38,846) | Adjusted incidence rate ratio (95% CI) <sup>2</sup>  |
|-----------------------------------|------------------------|-----------------------|------------------------------------------------------|
| <b>HCRU, Incidence rate PPPY</b>  |                        |                       |                                                      |
| Inpatient admissions              | 0.33                   | 0.24                  | 1.16 (1.04, 1.30)                                    |
| ED visits                         | 1.03                   | 0.77                  | 1.34 (1.21, 1.47)                                    |
| Outpatient visits                 | 26.33                  | 22.22                 | 1.11 (1.08, 1.14)                                    |
| <b>DMC, mean (SD)<sup>3</sup></b> |                        |                       | <b>Adjusted cost difference (95% CI)<sup>3</sup></b> |
| Total costs (medical + pharmacy)  | \$57,291 (75,481)      | \$50,562 (75,213)     | \$3,325 (-58, 7,345)                                 |
| Medical costs                     | \$40,033 (69,732)      | \$33,404 (68,319)     | \$3,428 (446, 6,781)                                 |
| Pharmacy costs                    | \$17,258 (29,997)      | \$17,158 (31,295)     | -\$833 (-1,846, 386)                                 |

<sup>1</sup>All costs are presented in 2020 US Dollars.

<sup>2</sup>Adjusted incidence rate ratios are calculated using a generalized linear model assuming a negative binomial distribution and log link, controlling for propensity score and key baseline measures. Propensity scores included variables selected based on expert review.

<sup>3</sup>Cost differences were estimated using the two-part modelling approach: (1) in the first part, the probability of observing a positive cost was modelled using logistic regression; (2) in the second part, a generalized linear model with a gamma distribution and log link was used to predict costs among patients with positive costs. Both models included the patients' propensity score and relevant baseline characteristics. The 95% CI and approximate p-values were estimated from nonparametric bootstrap procedures with 499 replications.

CI, confidence interval; DMC, direct medical costs; ED, emergency department; HCRU, healthcare resource use; HZ, herpes zoster; n, number; SD, standard deviation; PPPY, per patient per year; RA, rheumatoid arthritis.



York); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

**Objectives:** Brief self-assessment tools that can reliably and precisely quantify hand/wrist function are needed to assess inflammatory activity when a physical exam is not feasible and to capture day-to-day experiences of living with RA. Neuro-QoL, part of the PROMIS family of measures, was created using a patient-centered approach and IRT methodology. The Neuro-QoL Upper Extremity Function (UEF) scale measures ability across fine motor tasks and ADLs that rely on hand function. Our goal was to compare the performance of the 8-item Neuro-QoL UEF in adults with RA with legacy physical function measures. We hypothesized scores would be: 1) strongly ( $r > 0.70$ ) correlated with MHAQ, MDHAQ, and PROMIS PF; 2) moderately ( $r = 0.4$  to  $0.7$ ) correlated with symptoms, disease activity, and QoL; and 3) responsive to change.

**Methods:** Data were from the 0 and 6-month visits of adults enrolled in CATCH. Participants completed the Neuro-QoL UEF, MHAQ, MDHAQ, PROMIS-29, and PT Global at each visit. Rheumatologists recorded joint counts and MD Global. To evaluate content validity, we examined descriptive statistics across CDAI disease activity levels, and Pearson correlations between the Neuro-QoL UEF, legacy measures, CRP & ESR. Responsiveness was assessed by correlating change scores between Neuro-QoL, disease activity and legacy PF scores.

**Results:** The 262 participants were mostly white (83%) women (71%) with a mean (SD) age of 55 (13). Neuro-QoL UEF was moderately-strongly correlated with MHAQ, MDHAQ, PROMIS-PF ( $|r| = 0.63-0.75$ ); moderately correlated with pain and stiffness, ( $|r| = .59, -.64$ ); and CDAI, SDAI, PT & MD Global, TJ & SJ ( $|r| = 0.39-0.58$ ). Neuro-QoL was moderately correlated with PROMIS QoL domains Pain, Fatigue, Anxiety, Depression, Sleep & Participation ( $|r| = 0.39-0.60$ ). Neuro-QoL scores decreased in a dose-response manner across worsening CDAI states. Persons with HDA reported the highest disability, scoring nearly 0.5 SD lower on the Neuro-QoL than PROMIS. Change from 0-6 months in Neuro-QoL UEF was moderately correlated with changes in PROMIS, MHAQ, PT Global, and CDAI ( $|r| = 0.44-0.65$ ). The mean change and range in Neuro-QoL was significantly larger than in PROMIS (8.9 [95% CI 7.5-10.4] vs 5.4 [95% CI 4.4-6.4]) (Figure).

**Conclusion:** During the COVID-19 pandemic when virtual/telemedicine visits are common, clinicians, researchers, and patients can benefit from practical self-report tools that reliably and precisely quantify aspects of physical function most impacted by RA inflammation. Our results offer initial evidence of robust psychometric properties and support use of the 8-item Neuro-QoL UEF scale to self-assess inflammatory activity in the hands and day-to-day experiences of living with RA.

## TOUR27

### Experiences Using Wearable Technology by Persons With Rheumatoid Arthritis Participating in a Physical Activity Counseling Intervention Study: A Relational Ethics Analysis

Jenny Leese (University of Ottawa, Ottawa); Siyi Zhu (1. Arthritis Research Canada, University of British Columbia; 2. Rehabilitation Medicine

Center/Provincial Rehabilitation Key Laboratory, West China Hospital, Sichuan University, Vancouver); Anne Townsend (Lancaster University, Lancaster); Catherine Backman (Rehab Sciences/Occupational Therapy, University of British Columbia, Richmond); Laura Nimmon (University of British Columbia, Vancouver); Linda Li (Rehab Sciences/Physical Therapy, University of British Columbia, Arthritis Research Canada, Richmond)

**Objectives:** Using physical activity wearables is a promising approach to support arthritis self-management. Questions remain, however, about benefits and downsides that may be experienced by persons with arthritis in relationships with themselves (ie, self-perception) and others when using a wearable. Relational ethics is a suitable conceptual lens to explore positives or negatives encountered in these relationships. Our aim was to use this ethics lens to better understand how persons with rheumatoid arthritis (RA) experience their use of a wearable as part of a physical activity counseling intervention study involving a physiotherapist (PT).

**Methods:** Constructivist grounded theory and a relational ethics lens guided data collection and analysis. A sample of persons with RA took part in an initial and follow-up interview following participation in an 8-week randomized controlled trial. Participants used a Fitbit-Flex-2 paired with a new web-based application to self-monitor physical activity and received 4 biweekly calls from a study PT. We took a systematic approach of coding transcripts and forming concepts and key categories underpinned by concepts of relational ethics.

**Results:** Initial interviews took place with 14 participants (12 female; 2 male) aged 29-71 years. Of these, 11 took part in a follow-up interview. Key categories describe positive and negative influences of using a wearable with the PT on how participants constructed a valued moral identity: 1) Participants expressed how being active intertwined with moral values placed on self-control within cultural norms in which they lived. For some, using a wearable helped to “do something right” by reaching step goals or sitting less. Some, however, felt ambivalent (feeling both justified and at fault) when they could not reach a physical activity goal; 2) Participants described how their distrust of wearable data raised moral tensions in their relationship with the PT, which had implications for how mutual trustworthiness was negotiated; 3) Participants conveyed being active as a means of preserving or regaining respect for themselves as an independent and productive person. Some described how interpreting wearable data with the PT helped them to affirm this valued sense of self.

**Conclusion:** The study contributes empirical evidence to sparse literature on how persons with arthritis experience their use of a physical activity wearable positively or negatively. It brings to light salient ethical issues pertaining to autonomy, mutual trust, and respect. It is a key step to informing how to incorporate wearable-enabled programs that support physical activity participation in ways that are ethically aware.

## TOUR28

### Development and Preliminary Acceptability of JIActiv, a Social Media-based Program Promoting Engagement in Physical Activity Among Young People Living with Juvenile Idiopathic Arthritis

Sabrina Cavallo (Université de Montréal, Montreal); Karine Toupin-April (University of Ottawa and Children’s Hospital of Eastern Ontario Research Institute, Ottawa); Ciaran Duffy (Children’s Hospital of Eastern Ontario, Ottawa); Karina Cristea (Université de Montréal, Montreal); Imane Brahmî (Université de Montréal, Montreal); Jihene Tlili (Université de Montréal, Montreal); Sara Ahmed (McGill University, Montreal); Claudine Auger (Université de Montréal, Montreal); Zeinab Ahmadian (Université de Montréal, Montreal); Laurie Proulx (Canadian Arthritis Patient Alliance, Ottawa); Alexandra Sirois (McGill University, Montreal); Natasha Trehan (Take a Pain Check, Toronto); Michele Gibbon (Children’s Hospital of Eastern Ontario, Ottawa); Jennifer Stinson (The Hospital for Sick Kids, Toronto)

**Objectives:** Young people with juvenile idiopathic arthritis (JIA) are at greater risk for adopting chronic sedentary behaviors and not meeting national physical activity (PA) guidelines compared to healthy peers, which can have an important impact on their health, daily function, and

quality of life. To our knowledge few appealing, educational and interactive options exist to promote PA among young people living with JIA. We aimed to develop and evaluate the preliminary acceptability (ie, how well the program is received by users, and how it meets their needs) of the JIAActiv program, a 12-week educational and interactive social media-based program promoting PA from the perspectives of young people with JIA and parents, and to refine program format and content.

**Methods:** The JIAActiv prototype was developed based on our earlier work which included three systematic reviews, as well as a needs assessment with key stakeholders. The JIAActiv program aims to promote PA in young people with JIA through the delivery of evidence-based information and use of behavior-change strategies. A descriptive qualitative study design was used to assess the acceptability of the JIAActiv prototype. Two adolescents 13 to 17 years of age, 13 young adults 18 to 26 years with JIA, and 2 parents were recruited from arthritis patient groups and a Canadian rehabilitation center. The individual virtual interviews were audiotaped, transcribed verbatim, coded, and categorized into emerging themes using simple content analysis. Findings reported on the format, content, and potential usefulness of the program.

**Results:** Most participants preferred Instagram as the platform for the program and appreciated the presented functionalities. All participants felt that the proposed length of the program and the number of activities per week were appropriate. The informational videos, individual educational and interactive group activities were thought to be pertinent and helpful to motivate young people to engage in physical activity. Participants found that the esthetics of the program could be improved by choosing one color scheme for all postings. Most participants thought that having a mentor and access to a HCP would be very helpful to help answer their questions and offer social support. The group format (size and age range of participants) was well accepted by participants.

**Conclusion:** The JIAActiv program has good preliminary acceptability and is potentially useful for promoting engagement in PA among young people with JIA. Participants proposed ideas on how the program could be improved. Additional interview cycles will help to further refine the program. Supported by a CIORA grant.

## TOUR29

### Ocular Manifestations of ANCA-associated Vasculitis

Mats Junek (McMaster University, Hamilton); Lily Zhao (McMaster University, Hamilton); Stephanie Garner (McMaster University, Hamilton); David Cuthbertson (University of South Florida, Tampa); Christian Pagnoux (Vasculitis Clinic, Canadian Network for Research on Vasculitides (CanVasc), Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto); Curry Koenig (University of Utah School of Medicine, Salt Lake City); Carol Langford (Cleveland Clinic, Cleveland); Carol McAlear (University of Pennsylvania, Philadelphia); Paul Monach (Boston University, Boston); Larry Moreland (University of Pittsburgh, Pittsburgh); Philip Seo (Johns Hopkins University, Baltimore); Ulrich Specks (Mayo Clinic, Rochester); Antoine Sreih (Bristol Myers Squibb, Lawrenceville); Kenneth Warrington (Mayo Clinic, Rochester); Peter Merkel (University of Pennsylvania, Philadelphia); Nader Khalidi (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); VCRC Vasculitis Clinical Research Consortium (Philadelphia)

**Objectives:** ANCA-associated vasculitides (AAV) are multisystem diseases that can have multiple ophthalmic manifestations. Although there are some data on ocular disease in granulomatosis with polyangiitis (GPA), even less are available for microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Further, there also few reports differentiating symptoms seen at disease onset versus later in the disease or the ocular complications of AAV.

**Methods:** Patients with GPA, MPA, or EGPA enrolled in a longitudinal study between April 2006 and April 2021 were included in this study. Data concerning diagnosis, demographics, cranial disease manifestations and their time of onset, treatment, and ocular complications were extracted. Prevalence of ophthalmic manifestations at disease onset and incidence of

**Table 1: Number and type of ocular manifestations of vasculitis at disease onset in ANCA-associated vasculitis.**

| Baseline Manifestations                                | GPA         | MPA        | EGPA       |
|--------------------------------------------------------|-------------|------------|------------|
| <b>Total number of patients</b>                        | <b>852</b>  | <b>165</b> | <b>372</b> |
| <b>Any ocular manifestations</b>                       | 258 (30.3%) | 7 (4.2%)   | 13 (3.5%)  |
| <b>Conjunctivitis or episcleritis</b>                  | 111 (13.0%) | 3 (1.8%)   | 3 (0.8%)   |
| <b>Scleritis</b>                                       | 61 (7.2%)   | 3 (1.8%)   | 1 (0.3%)   |
| <b>Uveitis</b>                                         | 22 (2.6%)   | 0 (0.0%)   | 2 (0.5%)   |
| <b>Dacryocystitis and/or lacrimal duct obstruction</b> | 36 (4.2%)   | 0 (0.0%)   | 0 (0.0%)   |
| <b>Orbital Mass or proptosis</b>                       | 26 (3.1%)   | 0 (0.0%)   | 0 (0.0%)   |
| <b>Peripheral ulcerative keratitis</b>                 | 9 (1.1%)    | 1 (0.6%)   | 0 (0.0%)   |
| <b>Retinal Changes</b>                                 | 10 (1.2%)   | 3 (1.8%)   | 5 (1.3%)   |

manifestations over the course of follow-up, median time to onset of new manifestations and complications of disease were calculated.

**Results:** Data from 1389 patients were included for analysis which included 6392.8 patient-years of follow-up. There were 852 cases of GPA, 165 cases of MPA, and 372 cases of EGPA; with 258 (30.3%), 7 (4.2%), and 13 (3.5%) ocular manifestations present at baseline, respectively (Table 1). The most common manifestations seen were conjunctivitis/episcleritis and scleritis; multiple ophthalmic manifestations were seen in 79 (9.3%) of patients with GPA, 3 (1.8%) patients with MPA, and none with EGPA. During follow-up, 56 (6.6%) patients with GPA had incident ocular manifestations (of which 53.6% were new manifestations), while such events were rare in MPA (n = 1) and EGPA (n = 2). Frequent manifestations seen during follow-up were conjunctivitis/episcleritis and dacryocystitis and/or lacrimal duct obstruction. The most common complication seen across all 3 diseases was cataracts, seen in 9.1-15.3% of patients. Non-cataract complications followed a similar pattern to other manifestations: 67 (7.9%) patients with GPA experienced such complications (of whom 31 experienced vision-threatening complications) followed by 10 (2.7%) of those with EGPA, and 7 (4.2%) of those with MPA. Optic Neuritis (n = 8) and orbital wall destruction (n = 12) were only seen in those with GPA; 8 individuals with GPA experienced blindness as well as one with MPA.

**Conclusion:** Among patients with AAV, ophthalmic manifestations and complications are common in GPA, but rare in MPA and EGPA. Inflammatory eye conditions are the most common ophthalmic manifestation seen, and cataracts are the most common complication. New ophthalmic manifestations after disease onset are rare. These data are informative for clinicians caring for patients with AAV and investigators studying this spectrum of vasculitis.

## TOUR30

### Frequency and Patterns of Lipid and Glucose Measurements in Patients With Giant Cell Arteritis

Kaylin Bechard (University of Alberta, Edmonton); Uday Chauhan (University of Alberta Faculty of Medicine & Dentistry, Edmonton); Shabnam Hamidi (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Alison Clifford (University of Alberta, Edmonton)

**Objectives:** Giant cell arteritis (GCA), a large vessel vasculitis treated with high-dose prednisone, is associated with an increased risk of cardiovascular (CV) death. In rheumatoid arthritis (RA), another inflammatory disease with increased CV risk, approximately 70% of patients undergo the recommended lipid and glucose screening as per Canadian guidelines. We aimed to determine whether GCA patients are screened more or less frequently for dyslipidemia and hyperglycemia as compared to RA patients.

**Methods:** A retrospective chart review was performed to identify GCA patients seen at the University of Alberta between 2012-2019. GCA patients were age- and sex-matched to RA patients from the same institution. For inclusion, patients were required to have at least 3 years clinical



Table 1. Demographics and comorbidities of GCA and RA patient groups.

|                                | GCA           | RA              | p-value |
|--------------------------------|---------------|-----------------|---------|
| Female sex                     | 21 (70)       | 21 (70)         | -       |
| Age at screening               | 75.0 +/- 8.4  | 74.5 +/- 8.6    | 0.8     |
| Duration of Diagnosis (months) | 54.5 +/- 30.7 | 108.0 +/- 141.3 | 0       |
| History of MI                  | 1 (3)         | 0 (0)           | 0.3     |
| History of revascularization   | 2 (7)         | 1 (3)           | 0.6     |
| History of PAD                 | 3 (10)        | 1 (3)           | 0.3     |
| Smoking                        | 4 (13)        | 9 (30)          | 0.1     |
| History of Stroke              | 5 (17)        | 1 (3)           | 0.09    |
| Hypertension                   | 6 (20)        | 8 (27)          | 0.5     |

Results listed as mean, standard deviation, number, and percentage of patients. Myocardial infarction (MI), peripheral arterial disease (PAD).

follow-up available, and no prior history of dyslipidemia or hyperglycemia. Fasting glucose, hemoglobin A1C, and lipid levels obtained following the diagnosis of GCA or RA were recorded. Blood tests were analyzed to assess the frequency of insulin resistance and presence of inflammatory lipid profiles. Frequency of adherence to the 2016 Canadian Cardiovascular Society (CCS) lipid and 2018 Canadian Diabetes Association (CDA) glucose recommendations were compared between GCA and RA patients. Data was analyzed using Chi-square and Student t-tests as applicable. P-values < 0.05 were considered statistically significant.

**Results:** Of 50 GCA patients meeting ACR 1990 criteria, 20 were excluded due to pre-existing hyperglycemia or dyslipidemia. 30 GCA patients were compared to 30 age- and sex-matched RA patients. See Table 1 for baseline patient demographics. During follow-up, 8 GCA patients (27%) developed incident diabetes, compared to 1 (3%) RA patient (P = 0.011). Adherence to CDA screening guidelines was 63% in GCA and 70% in RA (P = 0.50). With respect to lipids, GCA patients had significantly lower triglycerides (1.4 vs 1.3, P < 0.0001) and higher total cholesterol (4.9 vs 3.1, P < 0.0001) levels than RA patients. Adherence to CCS lipid screening recommendations was similar between the 2 groups (67% each, P = 1.0). The median 10-year CVD risk of GCA patients was 14.6%.

**Conclusion:** Although 1 in 4 GCA patients developed incident diabetes following their diagnosis, adherence to the CDA screening recommendations was low (63%) and similar to that seen in RA patients. Adherence to CCS lipid screening recommendations was similar (67%) to that previously described in RA patients. Pathways to facilitate awareness, screening, and management of CV risk factors in GCA patients is needed.

### TOUR31

#### Duration of Steroid Therapy and Temporal Artery Biopsy Positivity in Giant Cell Arteritis: A Retrospective Cohort Study

Katherine Majerovich (University College Dublin, Dublin); Mats Junek (McMaster University, Hamilton); Nader Khalidi (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Stephanie Garner (McMaster University, Hamilton)

**Objectives:** Temporal artery biopsy (TAB) is an important investigational tool in the diagnosis of giant cell arteritis (GCA). Glucocorticoid therapy is also often used upon suspicion for GCA to prevent irreversible vision loss. It has been classically recommended to complete a TAB within 14 days of glucocorticoid initiation. However, data has conflicted as to how long biopsies remain abnormal, with one study demonstrating positivity of

44% up to 1 year. The aim of this study was to investigate how duration of glucocorticoid exposure affected TAB positivity in a cohort of patients with suspected GCA.

**Methods:** Data were extracted from two sources: the McMaster GCA Database (n = 52) and those enrolled in a trial evaluating imaging in the diagnosis of GCA (n = 171). Diagnosis of GCA was made clinically using all available material including features on history and exam suggestive of GCA, inflammatory markers, temporal artery magnetic resonance angiography, and temporal artery ultrasound. Individuals who underwent TAB as part of their diagnostic evaluation were included. Data concerning demographics and other investigations were extracted. Individuals were stratified by duration of glucocorticoid pre-treatment by weeks of therapy; those receiving six or more weeks of therapy were pooled due to low numbers. Descriptive statistics were performed and the impact of the duration of glucocorticoid therapy on TAB positivity was assessed using a two-sided Cochran-Armitage Trend test.

**Results:** Data from 223 patients were included. There were 48 TAB-positive and 175 TAB-negative cases. Stratified by TAB positivity, mean ages (standard deviation) of each subgroup were 73.5 (9.5) for positive TABs and 70.7 (10.6) for negative TABs respectively. 35 (72.9%) of the TAB-positive cases, and 123 (70.3%) of TAB-negative cases, were female. Forty-six (95.8%) TAB-positive cases, and 152 (86.9%) of TAB-negative cases, received glucocorticoids pre-TAB. No significant difference in length of glucocorticoid pre-treatment between groups existed. TAB-positive individuals were more likely to have vision loss, jaw claudication, constitutional symptoms, and elevated ESR and CRP (P < 0.01). When stratified by weeks of treatment, there were fewer TABs performed with longer duration of therapy (P < 0.01) (Table 1). The Cochran-Armitage Trend test did not demonstrate a temporal trend between weeks of treatment and TAB positivity (P = 0.11).

**Conclusion:** The results of this analysis suggest that glucocorticoid therapy does not affect TAB positivity to at least 6 weeks, with inconclusive data thereafter. These results suggest the recommendation of obtaining a TAB within 14 days of glucocorticoid initiation is unnecessarily conservative.

### TOUR32

#### Characterization of Patients With Normal Inflammatory Markers in Giant Cell Arteritis

Michael Zeeman (University of Alberta, Edmonton); Uday Chauhan (University of Alberta Faculty of Medicine & Dentistry, Edmonton); Alison Clifford (University of Alberta, Edmonton)

**Objectives:** Giant cell arteritis (GCA) is the most common form of vasculitis in people over the age of 50 years old. Inflammatory markers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), are typically elevated at the time of diagnosis and prompt suspicion for this disease. Given the severe potential consequences of a missed diagnosis, we aimed to study the frequency and clinical correlation of normal inflammatory markers in patients with confirmed GCA.

**Methods:** Electronic medical records of patients diagnosed with GCA by rheumatologists at the University of Alberta between April 2012 and December 2017 were retrospectively reviewed. For inclusion, patients must have 1) met ACR 1990 classification criteria for GCA, 2) had confirmed disease by either temporal artery biopsy or advanced imaging (PET/CT, MRA, CTA) and 3) had ESR and/or CRP measurements prior to gluco-

Table 1: Diagnoses of GCA stratified by duration of glucocorticoid treatment pre-TAB.

| Weeks of treatment | Number of patients | GCA diagnoses | Number of positive TABs |
|--------------------|--------------------|---------------|-------------------------|
|                    | 223                | 118           | 48                      |
| 0                  | 57                 | 23            | 8                       |
| 1                  | 46                 | 28            | 11                      |
| 2                  | 45                 | 25            | 10                      |
| 3                  | 26                 | 8             | 6                       |
| 4                  | 21                 | 10            | 4                       |
| 5                  | 10                 | 8             | 3                       |
| 6                  | 18                 | 16            | 6                       |

Table 1. Case distribution according to inflammatory marker value

| Cut-off Value | Number of Cases | Relative Percent |
|---------------|-----------------|------------------|
| ESR ≤ 25      | 8/38            | 21.1%            |
| ESR 26-49     | 5/38            | 13.2%            |
| ESR ≥ 50      | 25/38           | 65.8%            |
| CRP ≤ 10      | 4/41            | 9.8%             |
| CRP 11-20     | 3/41            | 7.3%             |
| CRP 21-30     | 5/41            | 12.2%            |
| CRP 31-50     | 8/41            | 19.5%            |
| CRP > 50      | 21/41           | 51.2%            |

corticoid administration available. Patients were grouped according to the presence of either normal or elevated ESR or CRP (normal ESR defined as  $\leq 25$  mm/hour, normal CRP as  $\leq 8$  mg/L). Groups with elevated versus normal inflammatory markers were compared with respect to demographics, symptoms, comorbidities, medications, and clinical outcomes.

**Results:** Of 81 total GCA patients, 42 met above study inclusion (38 with available ESR, 41 with available CRP, and 37 with both). Among confirmed cases, 21.6% of patients had either a normal ESR or CRP pre-treatment (21.1% with normal ESR, and 9.8% with normal CRP), while 5.4% of patients had both normal ESR and CRP. See Table 1 for distribution of inflammatory markers observed. Upon limiting the sample to the 34 patients with biopsy-confirmed disease, 20.0% had either normal ESR or CRP and 6.7% had both normal markers. No significant differences in age, sex, comorbidities, or symptoms were observed between patients with elevated versus normal inflammatory markers. Patients with normal ESR were less likely to receive steroid-sparing agents than patients with elevated ESR (0.0% vs 50.0%,  $P = 0.013$ ), however, and were less likely to relapse (12.5% vs 56.7%,  $P = 0.045$ ).

**Conclusion:** Twenty percent of biopsy- or imaging-confirmed GCA patients have either a normal ESR or CRP at diagnosis, and both tests are normal in 5-7% of patients. No clinical features reliably distinguish cases with normal inflammatory markers, but normal ESR may predict a lower risk of future relapse. These findings highlight the importance of routinely checking both ESR and CRP in cases of suspected GCA and maintaining a high index of suspicion in those with typical symptoms or signs. Best Abstract on Quality Care Initiatives in Rheumatology Award

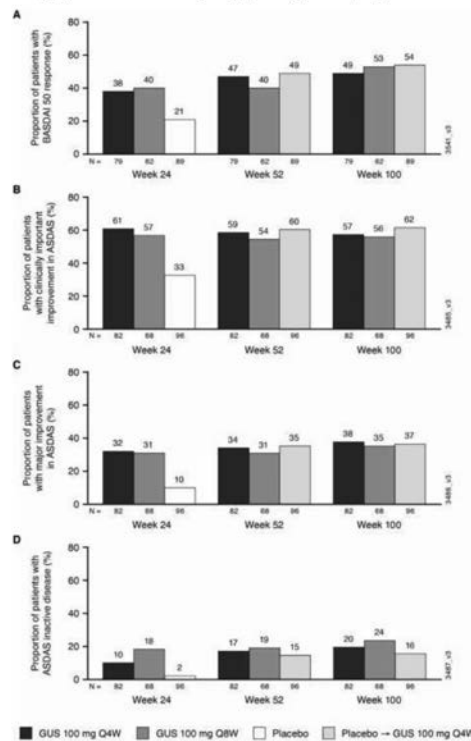
### TOUR33

**Effect of Guselkumab a Selective IL-23p19 Inhibitor, on Axial-Related Endpoints in Patients With Active PsA: Results From a Phase 3, Randomized, Double-blind, Placebo-controlled Study Through 2 Years** Philip Mease (University of Washington, Seattle); Philip Helliwell (University of Leeds, Leeds); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Denis Poddubnyy (Charite Universitätsmedizin Berlin Campus Benjamin Franklin, German Rheumatism Research Centre, Berlin); Xenofon Baraliakos (Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne); Soumya Chakravarty (Janssen Scientific Affairs, Horsham); Alexa Kollmeier (Janssen R&D US, La Jolla); Lillian Xu (Janssen Research & Development, LLC, San Diego); Shihong Sheng (Janssen R&D US, Spring House); Stephen Xu (Janssen Research & Development, LLC, Spring House); May Shawi (Janssen Inc, New Jersey); Désirée van der Heijde (Leiden University Medical Center, Leiden); Atul Deodhar (Oregon Health and Science University, Portland)

**Objectives:** Guselkumab (GUS), resulted in greater mean improvements in BASDAI scores vs placebo (PBO) at W24 among patients (pts) with active PsA and imaging-confirmed sacroiliitis in pooled post-hoc analyses of data from two phase 3 trials, DISCOVER-1&2; improvements were maintained through 1 year. We aimed to further assess maintenance of GUS effect on symptoms of axial involvement among biologic-naïve PsA pts with imaging-confirmed sacroiliitis through 2 years of DISCOVER-2.

**Methods:** In this phase 3, double-blind, PBO-controlled study, 739 bio-naïve pts with active PsA ( $\geq 5$  SJC,  $\geq 5$  TJC, CRP  $\geq 0.6$  mg/dL despite standard therapies) were randomized 1:1:1 and treated with GUS 100 mg every 4 weeks (Q4W;  $n = 245$ ), GUS 100 mg at W0, W4, then Q8W ( $n = 248$ ), or PBO ( $n = 246$ ), with PBO+GUS 100 mg Q4W at W24. Pts identified by imaging as having axial symptoms and sacroiliitis (prior X-ray/MRI, or pelvic X-ray at screening) were evaluated. Efficacy was assessed by change in BASDAI, mBASDAI (excluding Q3 [peripheral joint pain]), and BASDAI Q2 (Spinal Pain) scores and proportions of pts achieving BASDAI 50 response, Spinal Pain score  $\leq 2$ , and AS Disease Activity Score (ASDAS) responses through W100. Through W24, pts who met treatment failure criteria or had missing data were considered nonresponders or to have no change from baseline. After W24, missing data were imputed as nonresponse for binary endpoints or no change from baseline for continuous endpoints. Axial-

**Figure. Proportion of PsA patients with imaging-confirmed sacroiliitis achieving BASDAI 50 response (A), and ASDAS clinically important improvement (decrease  $\geq 1.1$ ) (B), major improvement (decrease  $\geq 2.0$ ) (C), and inactive disease ( $<1.3$ ) (D) through W100 (NRI)**



related outcomes were also summarized by HLA-B27 status (+/-) among 149 pts.

**Results:** 246 pts had imaging-confirmed sacroiliitis. Baseline characteristics were similar across treatment groups (62% male; mean age 44.4 years); mean BASDAI scores ranged from 6.5-6.6. At W24, LSmean/mean changes in BASDAI (-2.4/-2.6) and ASDAS (-1.3/-1.5) scores were greater in GUS than PBO-treated pts. Mean changes from baseline were maintained through W100 in GUS-treated pts for BASDAI (-3.1), Spinal Pain (-3.1), mBASDAI (3.1), and ASDAS (1.7) scores. Similar response patterns were observed for BASDAI 50 response rates among GUS-treated pts (W24 38-40%; W100 49-54%) (Figure). At W24, GUS-treated pts had higher response rates for achievement of ASDAS inactive disease, major improvement, and clinically important improvement vs PBO; response rates were maintained, in some cases further increased, at 2 years. GUS-related improvements in axial symptoms through W100 were consistent across pts who were HLA-B27+/-.

**Conclusion:** In bio-naïve pts with active PsA and imaging-confirmed sacroiliitis, GUS provided durable improvements in axial symptoms through W100, with substantial proportions of pts achieving and maintaining clinically meaningful improvements.

### TOUR34

**Long-term Safety of Guselkumab in Patients With Active Psoriatic Arthritis: Pooled Results From 3 Randomized Clinical Trials Through Up to 2 Years**

Proton Rahman (Memorial University of Newfoundland, St. John's); Christopher Ritchlin (University of Rochester, Rochester); Philip Mease (University of Washington, Seattle); Philip Helliwell (University of Leeds, Leeds); Wolf-Henning Boehncke (Geneva University Hospital and Department of Pathology and Immunology, Genève); Iain McInnes (University of Glasgow, Glasgow); May Shawi (Janssen Inc, New Jersey); Marilise Marrache (Janssen Inc., Toronto); Alexa Kollmeier (Janssen R&D US, La Jolla); Lillian Xu (Janssen Research & Development, LLC, San Diego); Jenny Yu (Janssen R&D US, Pennsylvania); Yanli Wang (Janssen inc, Spring House); Alice Gottlieb (New York Medical College at Metropolitan Hospital, New York)

**Objectives:** Guselkumab (GUS) demonstrated significant efficacy in PsA and a favorable safety profile through W24 in one Ph2 and two Ph3 (DISCOVER [D]-1&2) RCTs. In this study, we assess GUS safety by pooling data across the 1-year (Y) Ph2/D-1, and 2-Y D-2.

**Methods:** Patients (Pts) with active PsA ( $\geq 3\%$  BSA affected by psoriasis in Ph2;  $\geq 3$  SJC/TJC and CRP  $\geq 0.3$  mg/dL in Ph2/D-1;  $\geq 5$  SJC/TJC and CRP  $\geq 0.6$  mg/dL in D-2), biologic-naïve except 13/149 Ph2 and 118/381 D-1 pts who received prior 1-2 TNFi were randomized to GUS 100 mg at W0, W4, and Q8W or PBO in Ph2 or to GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO in D-1/D-2. At W24, PBO pts switched to GUS 100 mg Q8W (Ph2) or Q4W (D-1 & D-2). In these pooled post-hoc analyses, adverse events (AEs; number standardized for 100 patient-years of follow-up [PY]), laboratory investigations (National Cancer Institute Common Terminology Criteria for AEs [NCI-CTCAE] grade), and injection site reactions (ISRs) were reported through W56 for the Ph2 trial, W60 for D-1, and W112 for D-2.

**Results:** 1,229 pts received GUS 100 mg (725 Q4W, 504 Q8W) and were followed for an average of 1.5 Y, representing 1871 PY. Incidences of AEs, serious AEs, infections, serious infections, discontinuations due to an AE, malignancies, and major adverse cardiovascular events were similar between PBO and GUS through W24. No increased rates were seen with up to 2 Y of GUS, except for a somewhat higher rate of SAEs and serious infections in the GUS 100 mg Q8W group during long-term follow-up [CIs overlapped with the PBO-controlled period]. Most of GUS-treated pts with elevated aminotransferases and blood bilirubin had NCI-CTCAE Grade 1/2, with very few Grade 3 and no Grade 4, elevations. The proportions of pts with elevated aminotransferases at W24 were somewhat higher in the GUS Q4W vs Q8W/PBO groups; no unexpected increase with longer treatment. Elevations were more common in pts with vs without methotrexate use at baseline. ISRs occurred in GUS (1%) and PBO (0.5%) pts at W24, with no disproportional increase with up to 2 Y of GUS.

**Conclusion:** In these pooled pts with active PsA, GUS demonstrated a favorable safety profile through up to 2 Y of treatment; the GUS safety profile in PsA was comparable to that observed through up to 5 Y of GUS in pts with moderate-to-severe psoriasis.

### TOUR35

#### Pharmacovigilance Pregnancy Data in a Large Population of Patients With Chronic Inflammatory Disease Exposed to Certolizumab Pegol

Megan Clowse (Duke University Medical Center, Durham); Neda Amiri (Division of Rheumatology, University of British Columbia, Vancouver); Rebecca Fischer-Betz (Heinrich-Heine University, Duesseldorf); Thomas Kumke (UCB Pharma, Monheim am Rhein); Bernard Lauwerys (UCB Pharma, Brussels); Rachna Kasliwal (UCB Pharma, Slough); Frauke Förger (Inselspital, University of Bern, Bern)

**Objectives:** Tumor necrosis factor inhibitors (TNFi) are increasingly being used to treat chronic inflammatory diseases (CID) in women of reproductive age, in line with recent guidelines.[1] Still, limited data on TNFi-exposed pregnancy outcomes are available. Certolizumab pegol (CZP), a PEGylated, Fc-free TNFi, has no/minimal placental transfer from mother to infant during the third trimester.[2] We report outcomes from over 1,000 prospectively reported pregnancies in women with CZP exposure from the UCB Pharmacovigilance safety database.

**Methods:** Details of CZP-exposed pregnancies from the UCB Pharmacovigilance safety database were reviewed from the start of CZP clinical development (July 2001) to November 1, 2020. To avoid potential reporting bias, analysis was limited to prospectively reported cases with known pregnancy outcomes. Pregnancy outcomes reported: live birth, ectopic pregnancy, abortion (spontaneous, medically indicated and elective) and stillbirth. We also report congenital malformations, preterm delivery and, where information was recorded, low birth weight.

**Results:** 1,392 prospective pregnancies (1,425 fetuses) with maternal CZP exposure and known outcomes were reported (rheumatic diseases [rheumatoid arthritis, axial spondyloarthritis and psoriatic arthritis]: n = 951/1,392). Of these, 1,021 (73.3%) had at least first trimester CZP

exposure and 547 (39.3%) were exposed during all trimesters. Mean (SD) maternal age was 31.9 (5.1) years. These pregnancies resulted in 1,259 (88.4%) live births. There were 150 (10.5%) abortions, 11 (0.8%) stillbirths, and 5 (0.4%) ectopic pregnancies. Congenital malformations were present in 35 infants (2.5% of all pregnancies); there was no pattern of specific congenital malformations. 124/1,259 (9.8%) of live births were preterm, and 101/1,259 (8.0%) of infants had low birth weight.

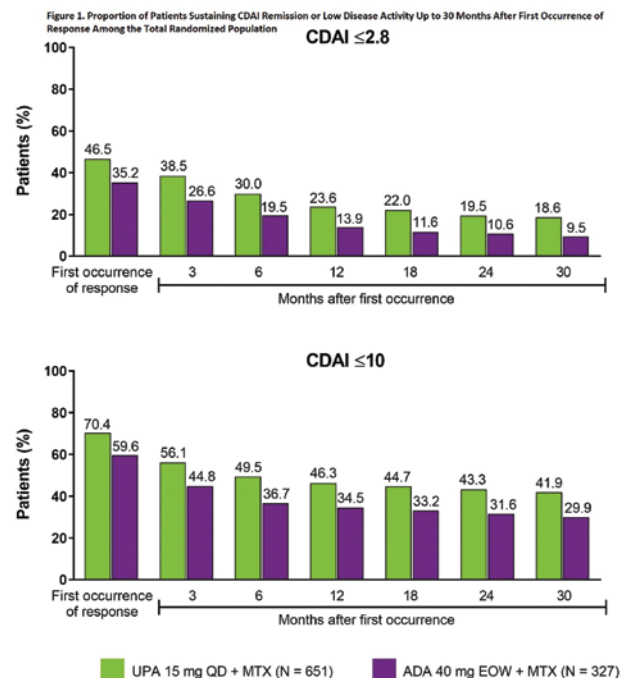
**Conclusion:** This analysis represents one of the largest cohorts of prospective pregnancies with known outcomes, including over 1,000 with at least first trimester CZP exposure. Recognizing limitations of the methodology, including lack of a control group and potential underreporting of outcomes, no increase in specific congenital malformations or adverse pregnancy outcomes after CZP exposure, compared to the general population, was observed.[3,4] These findings offer further reassurance for women of childbearing age who are considering CZP treatment. References: [1.] Sammaritano LR. *Arthritis Rheumatol* 2020;72:529-556. [2.] Mariette X. *Ann Rheum Dis* 2018;77:228-233. [3.] Ventura SJ. *Natl Vital Stat Rep* 2012;60: 1-21. [4.] Lee H. *BMC Pregnancy Childbirth* 2020;20:33.

### TOUR36

#### Sustainability of Response Between Upadacitinib and Adalimumab in Patients With Rheumatoid Arthritis: Results Through 3 Years from the SELECT-COMPARE Trial

Peter Nash (University of Queensland, Brisbane); Arthur Kavanaugh (University of California, San Diego, La Jolla); Maya Buch (Centre for Musculoskeletal Research, Faculty of Biology, Medicine & Health, University of Manchester, Manchester); Bernard Combe (Hopital Lapeyronie, Montpellier); Louis Bessette (Laval University, Quebec); In-Ho Song (AbbVie Inc., North Chicago); Tim Shaw (AbbVie, Maidenhead); Yanna Song (AbbVie, North Chicago); Jessica Suboticki (AbbVie, Mettawa); Roy Fleischmann (University of Texas Southwestern Medical Center, Dallas)

**Objectives:** The primary treatment target for patients with active rheumatoid arthritis (RA) is sustained clinical remission (REM) or low disease activity (LDA). A greater proportion of patients with RA and inadequate response to methotrexate (MTX) receiving the JAK inhibitor, upadacitinib (UPA), achieved REM/LDA compared with adalimumab (ADA), both with background MTX, through 26 weeks in the phase 3, SELECT-





COMPARE trial. We assessed sustainability of response over 3 years from the SELECT-COMPARE long-term extension.

**Methods:** Patients on background MTX received UPA 15 mg once daily, PBO, or ADA 40 mg every other week. Patients who did not achieve at least 20% improvements in tender and swollen joint counts (Weeks 14-22) or LDA (CDAI  $\leq 10$  at Week 26) were rescued from UPA to ADA or PBO/ADA to UPA. This post hoc analysis evaluated clinical REM (CDAI  $\leq 2.8$ ; SDAI  $\leq 3.3$ ), LDA (CDAI  $\leq 10$ ; SDAI  $\leq 11$ ), and DAS28 (CRP)  $< 2.6/\leq 3.2$  at first occurrence, as well as over 3 years following initial response, in patients randomized to UPA or ADA. Kaplan-Meier was used to define time from when response was first achieved to earliest date at which response was lost, discontinuation of study drug, or losing response at time of rescue.

**Results:** Through 3 years, a significantly higher proportion of patients receiving UPA + MTX vs ADA + MTX achieved CDAI REM (47% vs 35%,  $P = 0.001$ ) as well as CDAI LDA (70% vs 60%,  $P = 0.001$ ). At 30 months after first occurrence of response, CDAI REM/LDA was sustained in 19%/42% of patients randomized to UPA and 10%/30% of patients randomized to ADA (Figure 1). Time to initial clinical response did not appear to be predictive of sustained disease control. Through the last follow-up visit, 37%/58% of patients receiving UPA, and 27%/48% on ADA remained in CDAI REM/LDA, respectively. Of patients who lost CDAI REM, 68% on UPA and 55% on ADA remained in LDA. Similar proportions on UPA and ADA recaptured CDAI REM/LDA (UPA, 40%/17%; ADA, 48%/19%). Similar results were observed for REM/LDA based on SDAI and for DAS28 (CRP).

**Conclusion:** Among patients with inadequate response to MTX, a higher proportion receiving UPA + MTX achieved remission or LDA across disease activity measures vs ADA + MTX. UPA-treated patients demonstrated a consistently higher sustained response rate over 3 years compared to those receiving ADA. Furthermore, significant proportions of patients who lost response on either UPA or ADA were able to recapture remission or LDA.

#### TOUR37

##### Whole Exome Sequencing to Identify Diagnostic Variants in a Cohort of Patients With Systemic Inflammatory Disease

Jason An (Division of Rheumatology, St. Michael's Hospital, University of Toronto, Toronto); Madeline Couse (The Hospital for Sick Children, Toronto); Daniela Dominguez (The Hospital For Sick Children, Toronto); Michelle Bathish (McMaster University, Hamilton); Roberta Berard (Children's Hospital, LHSC, London); Tania Cellucci (McMaster University, Hamilton); Dilan Dissanayake (Division of Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto); Liane Heale (McMaster University and McMaster Children's Hospital, Hamilton); Ronald Laxer (Division of Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto); Christian Marshall (Dept. Paediatric Laboratory Medicine, The Hospital for Sick Children, Toronto); Johannes Roth (Children's Hospital of Eastern Ontario, Ottawa); Robert Rottapel (University of Toronto, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto)

**Objectives:** Systemic Inflammatory Diseases (SID) are rare conditions that can arise from deleterious variants in immunologic genes that disrupt immune regulation. Gene panels containing few genes are often non-diagnostic in SID patients, whereas subsequent whole exome sequencing (WES) may identify genetic variants potentially responsible for disease. We report results from WES of a clinically heterogeneous cohort of patients with suspected monogenic SID.

**Methods:** We conducted a multicenter cohort study of patients with suspected monogenic SID and non-diagnostic recurrent fever and/or hemophagocytic lymphohistiocytosis (HLH) gene panels. Demographic and clinical data was retrospectively extracted from chart review and entered in a dedicated database. We performed paired end WES with Illumina sequencers. We examined genes from clinical gene panels with established

inflammatory, immune deficiency, or cytopenic diseases in two stages. First, we used a limited 'Panel 1' (29 genes) and then an expanded 'Panel 2' (613 genes). We restricted to rare (minor allele frequency  $< 1\%$ ) and predicted damaging variants (CADD score  $> 15$ ). Variants were considered in light of individual patient's disease manifestations. A variant was deemed diagnostic if it was rare, damaging, and associated with a disease consistent with the patient's phenotype and inheritance pattern. Summary statistics were used for the prevalence of demographic and clinical features in the cohort, as well as the number variants reported from panel 1 and panel 2.

**Results:** The study included 59 participants, 46% male, 53% European and 34% adults ( $> 18y$ ) at the time of sequencing. The median age of disease onset was 9 years ( $Q1 = 2, Q3 = 15$ ). The most common organ systems involved were immunologic (96%), mucocutaneous (95%), and musculoskeletal (81%). Most patients (81%) had raised inflammatory markers (ESR/CRP/Serum Amyloid A). Examination of Panel 1 identified 25 variants (15 genes) in 21 individuals yet not were diagnostic. Panel 2 identified 409 variants (244 genes) in 58 individuals, with 3 diagnostic variants. These were homozygous TREX1 variants leading to a diagnosis of Aicardi-Goutières Syndrome, POMP heterozygous frameshift variant accounting for a case of POMP-Related Autoinflammation and Immune Dysregulation Syndrome, and RELA heterozygous frameshift variant contributing to Behcet's-like disease.

**Conclusion:** In a cohort of suspected monogenic SID patients with diverse clinical features, using expanded clinical gene panels for inflammatory diseases led to additional molecular diagnoses in 5% of the cohort. Our work highlights the diagnostic utility of WES in this population. Next steps include investigation of extended immune genes identified by bioinformatic approaches to further enhance diagnostic yield.

#### TOUR38

##### Systemic Lupus Erythematosus Genetic Risk and Neuropsychiatric Lupus Manifestations

Hui-Ki Tran (The Hospital for Sick Children, Toronto); Fangming Liao (The Hospital for Sick Children, Toronto); Jingjing Cao (The Hospital for Sick Children, Toronto); Daniela Dominguez (The Hospital For Sick Children, Toronto); John Hanly (Dalhousie University and Nova Scotia Health Authority, Halifax); SLICC Systemic Lupus International Collaborating Clinics (SLICC, Pittsburgh); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto)

**Objectives:** Neuropsychiatric systemic lupus erythematosus (NPSLE) is clinically heterogeneous and significantly affects the survival and quality of life of SLE patients. Genetics plays a role in SLE pathogenesis, but its role in NPSLE has not been determined. We investigated the association between SLE genetic susceptibility loci and NPSLE in a large, multi-ethnic cohort of adult SLE patients.

**Methods:** Patients recently diagnosed with SLE using American College of Rheumatology (ACR) classification criteria were recruited from 1999-2011 to the Systemic Lupus International Collaborating Clinics (SLICC) Registry at 31 international centers in Asia, Europe, and North America. Patients were genotyped on the Illumina Infinium Global Screening Array (GSA). Ancestry was genetically inferred using principal components and ADMIXTURE with the 1000 Genomes Project as a referent. Cases were those who ever experienced an NP event, included in the ACR case definitions for NPSLE and attributed to SLE using the SLICC attribution rules (Hanly et al. 2007). Cases were then categorized into mutually exclusive NPSLE groups based on strict (Model A) and less stringent (Model B) attribution criteria. Patients who never developed an NP event or an NP event not attributed to SLE were controls. HLA and non-HLA SLE polygenic risk scores (PRSs) were calculated. Binary and multinomial logistic regressions were conducted, adjusting for genetically inferred ancestry, sex and for covariates significantly associated with NPSLE in the cohort (oral/nasal ulcers, serositis, duration of follow-up, lupus anticoagulant positivity). In binary logistic regression, only Model A patients were cases, and Model

B patients were included as controls. Multinomial logistic regressions compared patients in Model A and Model B, to controls.

**Results:** 896 SLE patients were included in the study; 89% were female and 50% of European ancestry. The median age of SLE diagnosis was 33.4 years (IQR, 23.5-43.3). Median duration of follow-up was 10.5 years (IQR, 6.19-14.9). There were 119 Model A NPSLE cases. We were unable to detect associations between NPSLE and non-HLA SLE PRS (Model A) in marginal nor in multivariate-adjusted binary logistic models (odds ratio, OR 0.86, 95% CI 0.70-1.06). Similarly, we were unable to detect associations in multivariate-adjusted multinomial logistic regressions (Model A vs controls: OR = 0.86, 95% CI 0.70-1.07; Model B vs controls: OR = 1.05, 95% CI 0.82-1.34).

**Conclusion:** We were unable to detect association between polygenic risk scores for SLE and risk of NPSLE in a multi-ethnic cohort of SLE patients. Future analyses include testing additional genetic loci and gene pathways in association with NPSLE sub phenotypes.

### TOUR39

#### Anti-MPP1 Autoantibodies Are Associated With Peripheral Neuropathy in Systemic Lupus Erythematosus

Eugene Krustev (University of Calgary, Calgary); Katherine Buhler (University of Calgary, Calgary); Francesca Cardwell (University of Waterloo, Waterloo); Marvin Fritzler (University of Calgary, Calgary); Ann Clarke (University of Calgary, Calgary); May Choi (University of Calgary, Calgary)

**Objectives:** Neuropsychiatric systemic lupus erythematosus (NPSLE) affects 17 - 75% of lupus patients and can involve the central (CNS) and peripheral nervous system (PNS). Several autoantibodies have been associated with CNS NPSLE, but there are no known autoantibodies specific for PNS involvement. M-Phase Phosphoprotein 1 (MPP1; also known as kinesin family member 20B, KIF20B) is a protein involved in cell division. Anti-MPP1 autoantibodies were identified in patients with idiopathic ataxia and are possibly associated with autoimmune peripheral neuropathy. The aim of this study was to explore the association between anti-MPP1 and NPSLE in our local SLE cohort.

**Methods:** Patients fulfilled the ACR or SLICC classification criteria (CC) for SLE. Age, sex, race, SLEDAI-2K, SLICC CC, and sera were collected at the time of enrolment and up to two follow-up visits. NPSLE events fulfilling the ACR case definitions were identified from date of SLE diagnosis by medical record review. Anti-MPP1 titers were determined by an addressable laser bead immunoassay (ALBIA) utilizing a purified recombinant protein and results expressed as median fluorescence units (MFU). A titer of  $\geq 1:500$  MFU was considered positive. Chi-squared and t-tests were performed to compare demographic and clinical characteristics, including NPSLE manifestations, between patients who were ever anti-MPP1 positive (MPP1+) versus those who were never positive (MPP1-). Multivariable logistic regression analysis was used to determine associations between MPP1+ and variables that were statistically significant in the univariable analysis ( $P < 0.05$ ).

Table 1. Neuropsychiatric manifestations categorized according to the American College of Rheumatology case definitions in the SLE cohort who were ever anti-MPP1 positive (MPP1+) versus those who were not (MPP1-)

| Neuropsychiatric SLE Manifestations             | MPP1- (n=234) | MPP1+ (n=59) | Odds Ratio (95%CI)     |
|-------------------------------------------------|---------------|--------------|------------------------|
| Any Neurological Manifestation                  | 72.3%         | 72.9%        | 1.0 (0.5, 2.0)         |
| Any Central Neurologic Manifestation            | 70.2%         | 64.4%        | 0.8 (0.4, 1.4)         |
| <b>Any Peripheral Neurologic Manifestation</b>  | <b>13.7%</b>  | <b>33.9%</b> | <b>3.2 (1.7, 6.2)</b>  |
| Polyneuropathy                                  | 8.5%          | 8.5%         | 1.0 (0.4, 2.8)         |
| <b>Mononeuropathy</b>                           | <b>1.3%</b>   | <b>10.2%</b> | <b>8.7 (2.1, 36.0)</b> |
| <b>Cranial Neuropathy</b>                       | <b>3.4%</b>   | <b>18.6%</b> | <b>6.5 (2.5, 17.0)</b> |
| Acute Inflammatory Demyelinating Polyneuropathy | 0.0%          | 1.7%         | 12.0 (0.5, 299.0)      |
| Autonomic Disorder                              | 1.3%          | 1.7%         | 1.3 (0.1, 13.0)        |
| Myasthenia Gravis                               | 0.9%          | 0.0%         | 0.7 (0.0, 16.5)        |

Bold indicates statistically significant result ( $p < 0.05$ ). Abbreviations: MPP1, M-phase phosphoprotein 1. Plexopathy omitted as no events recorded for either group.

**Results:** We assessed 301 SLE patients for anti-MPP1 expression. Mean disease duration was  $11.4 \pm 11.5$  years, 92.4% were female and 19.9% participants were MPP1+. 293 patients had available medical records for assessment of NPSLE manifestations. 72.4% of patients met criteria for at least one NPSLE manifestation. When PNS NPSLE manifestations were examined, patients with any peripheral neuropathy (OR 3.2, 95% CI 1.7-6.2), mononeuropathy (OR 8.7, 95% CI 2.1-36.0), or cranial neuropathy (OR 6.5, 95% CI 2.5-17.0) were more likely to be MPP1+ (Table 1). There was no difference between MPP1+ and MPP1- when total and central NPSLE manifestations were compared (Table 1). Multivariable analysis demonstrated that any peripheral neuropathy (OR 4.8, 95% CI 2.2-10.8) and cranial neuropathies remained significantly associated with MPP1+ (OR 9.7, 95% CI 2.9-32.2).

**Conclusion:** Anti-MPP1 may be an important biomarker for peripheral neuropathies, in particular, cranial neuropathies in SLE. These findings are being validated in an international cohort and further histologic assessment is needed to uncover the pathophysiological mechanism.

### TOUR40

#### Rethinking the Role of the Synovium in Late-Stage Knee Osteoarthritis: Ultrasound Imaging and Histopathological Features of Synovial Inflammation and Damage

Holly Philpott (Western University, London); Trevor Birmingham (Western University, London); McKenzie Carter (Western University, London); Robert Giffin (Western University, London); Edward Vasarhelyi (Western University, London); Steven MacDonald (Western University, London); Brent Lanting (Western University, London); Tom Appleton (St. Joseph's London Rheumatology Centre and Western University, London)

**Objectives:** Common chronic diseases associated with chronic inflammation (eg, liver disease and atherosclerosis) result in tissue remodeling, fibrosis, and damage, marking the transition from early to later stages of disease. The interpretation of clinical imaging findings in any given patient with OA may be markedly different depending on the relative presence of synovial inflammation versus synovial damage. Since synovium is critical for joint health, it is important to understand how the contribution of synovial inflammation and tissue damage, measured by histopathology, contributes to the appearance of synovial inflammation on routine clinical imaging tools such as ultrasound (US). The objective of this study was to investigate the ability of a non-invasive imaging method (US) to assess each histopathological feature of synovial inflammation and damage.

**Methods:** Patients ( $n = 118$ ) with late-stage knee OA undergoing surgery were included. Musculoskeletal ultrasound (US) was performed pre-operatively. Synovial biopsies were acquired at surgery. Four features of inflammation (synovial lining thickness, sub-synovial infiltrate, vascularization, and fibrin) and four features of damage (synovial lining erosion, fibrosis, vasculopathy, and perivascular edema) were assessed on 5 high powered fields per patient. Mean feature scores were binned into categories for None ( $< 0.5$ ), Mild (0.5-1.5), and Moderate/Severe ( $> 1.5$ ). Relationships between histopathological features were assessed by Spearman or Pearson correlation as appropriate. Associations between histopathological features of inflammation or tissue damage (predictors) and US measures of inflammation (outcomes) were assessed using linear or logistic regression, while adjusting for age, sex, and body mass index (BMI).

**Results:** Patients presented with a range of severity of synovial inflammation and damage. The histopathological features of synovial inflammation were inversely correlated to features of damage. Multivariate linear and logistic regression showed that histopathological features of inflammation such as synovial lining thickness, sub-synovial infiltrate, and vascularization were associated with higher odds of having moderate/severe synovitis and larger effusion-synovitis depth measures on US. Conversely, features of synovial damage such as synovial lining erosion, vasculopathy, and fibrosis were associated with lower odds of having moderate/severe synovitis and smaller effusion-synovitis depth measures on US.

**Conclusion:** US can reliably assess the presence of histopathological features of synovial inflammation. The inverse relationship between inflam-

mation and synovial damage suggests that OA-related inflammation may give rise to synovial damage. Taken together, the absence of inflammation on US imaging in patients with symptomatic, late-stage knee OA is not reassuring but instead may be a sign of synovial damage and more severe joint failure. Best Abstract by a Post-Graduate Research Trainee Award

#### TOUR41

##### Scleroderma Presentation in the Canadian Scleroderma Research Group Indigenous Population

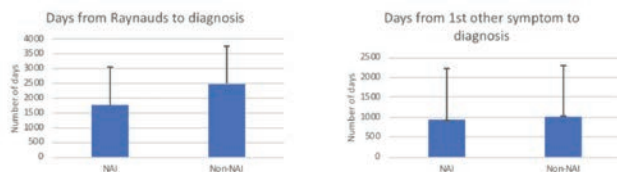
Curtis Sobchak (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Maggie Larche (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Canadian Scleroderma Research Group (CSRG) (Montreal)

**Objectives:** Given the burden of rheumatic disease in the North American Indigenous (NAI) population, the Canadian Rheumatology Association has highlighted Aboriginal Rheumatology as an area needing greater understanding. Indigenous patients with rheumatoid arthritis (RA) often have worse disease than the general population yet are less likely to see specialized care. While Indigenous populations appear to have earlier onset systemic sclerosis (SSc) than the general population, it is unclear if they experience delayed diagnosis (symptom onset to disease diagnosis), or more/less healthcare utilization during this time. We analyzed data from the Canadian Scleroderma Research Group (CSRG) registry to compare the length of time from symptom onset to disease diagnosis and healthcare utilization between NAI and non-NAI populations. We also determined if these data appeared to be impacted by a person's rural or urban location.

**Methods:** Data were obtained from the CSRG, a national longitudinal registry of patients > 18 years old with SSc. Patients who self-identified as Métis, Inuit and First Nations were included as NAI. All other registry participants were categorized as non-NAI. We characterized the 2 groups at entry into the registry (sex, tobacco use, income, education, location, comorbidities). Location was deemed urban or rural by Canada Post guidelines. Time from first symptom (Raynaud's or 1st other) to SSc diagnosis was compared between those who were and were not NAI. Healthcare utilization by group as it related to SSc presentation (visits specialists, allied health, tests done, hospital admissions) were summarized.

**Results:** Of 1561 patients, 79 (5.1%) self-identified as NAI. Age, gender and comorbidities appeared similar between the two groups, with NAI having a higher proportion of tobacco use, RA, diabetes and lower level of education and income. Proportionately, more NAI patients lived in a rural area than non-NAI patients. There was no significant difference in time from Raynaud's to diagnosis or 1st other symptom to SSc diagnosis between NAI and non-NAI populations, regardless of location (Figure 1). There were also no group differences in healthcare utilization, including visits to healthcare professionals, tests performed and hospitalizations.

**Conclusion:** This study suggests that, unlike other rheumatological conditions, SSc appears to be appropriately diagnosed without a time delay in those who are NAI compared to non-NAI patients. NAI SSc patients also access care at the same rate as non-NAI populations prior to SSc diagnosis. It's important to consider that this small NAI population may represent a biased sample given their participation in a registry.



#### TOUR42

##### Prediction Tool for Damage Accrual Trajectory in Incident Systemic Sclerosis

Ariane Barbacki (McGill University Health Centre, Montreal); Ada Man (University of Manitoba, Winnipeg); Mianbo Wang (Lady Davis

Institute for Medical Research, Montreal); Mandana Nikpour (Australian Scleroderma Interest Group (ASIG), Melbourne); Yuqing Zhang (Harvard Medical School, Boston); Dylan Johnson (University of Alberta, Edmonton); Murray Baron (McGill University, Jewish General Hospital, Montreal)

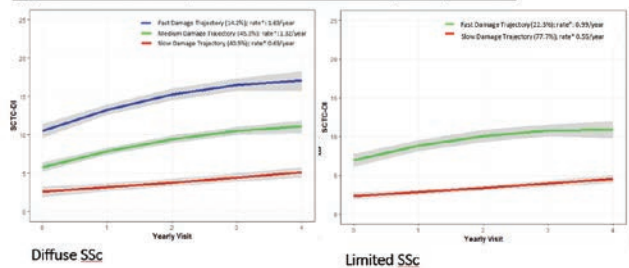
**Objectives:** Systemic sclerosis (SSc) is an autoimmune disease associated with the accrual of organ damage over time, which can be measured using the Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI). The natural history of SSc is heterogenous and can be associated with a high mortality. The aim of this study was to build a prediction model that could identify newly diagnosed SSc patients at higher risk of accruing damage quickly.

**Methods:** Incident adult SSc cases were identified in the Australian Scleroderma Interest Group (ASIG) and Canadian Scleroderma Research Group (CSRG) registries. Patients meeting 2013 ACR-EULAR Scleroderma classification criteria were included. Using a combination of group-based trajectory modeling and substantive knowledge, we identified two trajectories of damage accrual (fast, slow) for each of diffuse and limited patients. Baseline variables associated with trajectory membership were entered into logistic regression models. Using backward selection, prediction models for the two cutaneous SSc subset groups were built independently since their actual DI trajectories were very different. ROC curves were analyzed to determine the optimal cut-offs for the predictive variables. The Hosmer-Lemeshow Goodness-of-Fit test was used to determine prediction accuracy.

**Results:** 402 patients were included. The mean age was 53 years, 20% were men, 85% were Caucasian, and 47% had diffuse disease. For the diffuse subset, the mean length of follow-up was 3.0 years (SD ± 1.2) and 60% were in the fast trajectory, whereas the mean length of follow-up was 3.1 years (SD ± 1.1) and 23% were in the fast trajectory in the limited subset (Figure 1). The final prediction model included male sex and baseline SCTC-DI for the diffuse subset, and only baseline SCTC-DI for limited. The ROC curves for the limited and diffuse prediction models showed good discriminative abilities (AUC 0.91 and 0.89, respectively). In limited patients, a baseline DI ≥ 5 predicts a fast damage trajectory with a sensitivity of 0.70 and specificity of 0.96. In diffuse patients, a baseline DI ≥ 4 in men and ≥ 6 in women, predicts a fast damage trajectory with a sensitivity of 0.83 and specificity of 0.86. The Hosmer-Lemeshow Goodness-of-Fit test confirmed the prediction accuracy of both models (P = 0.77 for diffuse and P = 0.33 for limited).

**Conclusion:** Baseline disease damage as measured by the SCTC-DI, and sex can be used as predictors of future damage trajectories. These prediction models may be useful in the clinical or trial design setting.

Figure 1 - Incident Systemic Sclerosis Damage Trajectories



#### TOUR43

##### Identification of Urinary Biomarkers that Predict Treatment Outcomes in Lupus Nephritis

Laura Whittall-Garcia (University Health Network, Toronto); Kirubel Goliad (University of Toronto, Toronto); Michael Kim (Krembil Research Institute, Toronto); Dennis Bonilla (Toronto Western Research Institute, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto);



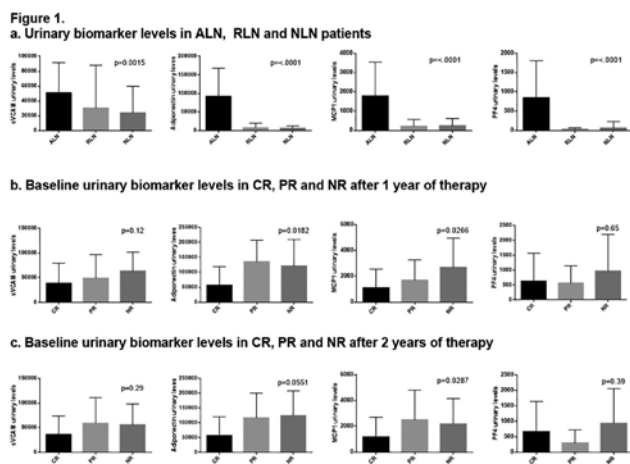
Paul Fortin (Université Laval, CHU de Québec, Québec); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Joan Wither (Division of Genetics and Development, Krembil Research Institute; Division of Rheumatology, University Health Network; Department of Immunology, University of Toronto, Toronto)

**Objectives:** We have previously shown that 15 urine biomarkers (of 129 tested by Luminex), including Clusterin, Cystatin C, NGAL, PF4, vWF, sVCAM-1, GM-CSF, GRO, IL-15, IL-6, MCP-1, Adiponectin, PAI-1, MMP-7 and TIMP-1, discriminate between active Lupus Nephritis (ALN) and non-LN patients. Herein, we aimed to determine the ability of these urinary biomarkers to predict renal response to conventional therapy.

**Methods:** Our study had a 2-stage approach. In an exploratory cohort, we used Luminex to examine whether our previously identified urinary biomarkers at the time of the renal flare ( $\pm 3$  months) or  $12 \pm 3$  months after treatment of biopsy-proven ALN could predict treatment responses. A larger validation cohort was then used to further investigate the utility of the most predictive urinary biomarkers by ELISA, including patients with biopsy-proven ALN ( $\pm 3$  months of renal flare), using as controls patients with LN in remission (RLN) or without LN (NLN). Longitudinal outcomes in response to therapy were determined using previously published criteria.

**Results:** Twenty-one patients were included in the exploratory cohort, 19 (90.5%) of whom had proliferative LN. Twelve (57.14%), 4 (19.06%), and 5 (23.8%) patients had a complete (CR), partial (PR) and no (NR) remission at  $24 \pm 3$  months, respectively. At baseline there was no difference in urinary biomarkers levels between CR, PR and NR; however, the drop in levels following  $12 \pm 3$  months of treatment was significantly higher in patients with CR than NR for sVCAM, Adiponectin, MCP-1, PF4, IL-15 and vWF. To validate the clinical utility of these biomarkers, 55 biopsy-proven ALN, 65 RLN and 142 NLN patients were studied, of which 233 (88.08%) were women, 139 (52.7%) were Caucasian, with a mean age of 39.5 years and mean disease duration was 10.83 years. sVCAM, Adiponectin, MCP-1 and PF4 discriminated between ALN and non-ALN (RLN and NLN) (Figure 1a). In addition, adiponectin ( $P = 0.03$ ) and MCP-1 ( $P = 0.005$ ) were able to differentiate between proliferative and non-proliferative LN, and correlated with markers of disease severity, including baseline serum creatinine, proteinuria, and the activity index on the kidney biopsy. The levels of adiponectin and MCP1 at baseline were also significantly lower in patients who achieved CR at 1 and 2 years in comparison to those that did not (Figure 1b and c).

**Conclusion:** Baseline and/or decreases in urinary biomarker levels can discriminate between CR, PR and NR following conventional therapy, allowing institution of more aggressive therapy in patients with a high likelihood of a poor prognosis.



#### TOUR44

##### Serologic Phenotypes Distinguish SLE Patients With Myositis and/or Interstitial Lung Disease (ILD)

Thaisa Cotton (McGill University, Montreal); Marvin Fritzler (University of Calgary, Calgary); May Choi (University of Calgary, Calgary); Boyang Zheng (McGill University Health Center, Montreal); Omid Niaki (McGill University, Montreal); Christian Pineau (McGill University Health Centre, Montreal); Luck Lukusa (Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal)

**Objectives:** To determine if a serologic phenotype can be identified in SLE patients with myositis and/or ILD.

**Methods:** Adult SLE patients (without myositis or ILD at baseline) had annual assessments and provided bio-samples between 2000-2017. Potential new-onset myositis was identified using the SLICC Damage Index (SDI) muscle atrophy/weakness item, the SLEDAI-2K item for myositis, and annual serum creatinine kinase testing. Potential new-onset ILD was identified using the SDI pulmonary fibrosis item. Chart review confirmed cases. Randomly sampled patients from baseline visit (from 2000 onward) became a sub-cohort ( $N = 72$ ). Cases and sub-cohort were compared regarding baseline characteristics. Patients' myositis-related biomarkers were assessed at baseline and one randomly selected follow-up between baseline and end of observation (date of myositis/ILD diagnosis or Dec. 31, 2017). Line immunoassay (Euroimmun AG, Luebeck, Germany) detected autoantibodies to Mi2- $\alpha$ , Mi2- $\beta$ , MDA5, NXP2, TIF1 $\gamma$ , PM/Sc175, PM/Sc1100, Ku, SRP, Jo-1, EJ, OJ, PL7, PL12, Ro52, HMGCR, NT5c1A/Mup44, CENP-A, -B, Sc170, NOR90, RNAP, and Th/To (hPOP1). An addressable laser bead immunoassay was used to detect antibodies to TERF-1. KL-6 levels were determined by ELISA (R&D Systems). Descriptive analyses and hazards ratios (HRs) were generated for myositis and/or ILD incidence, focusing on baseline serology and adjusting for demographic variables (sex, ethnicity, and age at SLE diagnosis) and positive biomarkers.

**Results:** The median (IQR) SLE duration at baseline was 1.8 (0.41-5.6) years. Between 2000-2017, 14 SLE patients (12, 85.7% female) developed myositis and/or ILD over an average follow-up of 9.2 years (incidence 17.6 cases per 1000 patient-years). Thirteen of these (92.9%) had at least one medium/high positive biomarker at baseline, versus 47 (65.3%) SLE patients who never developed myositis and/or ILD. The most common baseline biomarkers in patients with myositis and/or ILD were KL-6, anti-Ku, anti-Ro52. In multivariate Cox regression analyses, SLE patients were more likely to develop myositis and/or ILD if they had elevated baseline KL-6, anti-Ku positivity, or anti-CENP-B positivity. Potential limitations include the relatively low number of events.

**Conclusion:** In this SLE sample, KL-6, anti-Ku, and anti-CENP-B at baseline were highly associated with myositis and/or ILD risk. Ours is the first study of this serologic phenotype, identifying SLE patients most at risk of myositis/ILD.

#### TOUR45

##### Serious Infections in Offspring Exposed In Utero to Tumor Necrosis Factor Inhibitors With High Versus Low Placental Transfer

Leah Flatman (McGill University, Montreal); Michal Abrahamowicz (McGill, Montreal); Yvan St. Pierre (McGill University, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal)

**Objectives:** Tumor necrosis factor inhibitor (TNFi) subtypes have differential trans-placental passage; infliximab and adalimumab (both monoclonal immunoglobulins) have the highest transfer, reaching higher fetal than maternal blood levels, while certolizumab (a pegylated Fab fragment) and etanercept (a fusion protein) display the lowest passage (less than 0.25% and 4-7% respectively). Thus, depending on the TNFi subtype, the risk of immunosuppression may differ, and some offspring may be exposed to supra-therapeutic doses of TNFi. However, data on serious infections in

offspring stratified by TNFi subtype do not exist to the best of our knowledge. We evaluated the risk of serious infections in offspring born to mothers with chronic inflammatory diseases who used TNFi during pregnancy. We compared offspring exposed in utero to TNFi with high placental transfer to offspring exposed in utero to TNFi with low placental transfer.

**Methods:** We identified offspring born to mothers with rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, and/or inflammatory bowel diseases between 2011 and 2019 in the IBM MarketScan commercial database. Drug exposure was defined as  $\geq 1$  filled prescription during pregnancy and separated into high (ie, infliximab, adalimumab, golimumab) and low (ie, certolizumab, etanercept) placental transfer. Serious infections were based on  $\geq 1$  hospitalization with infection in the offspring's first year of life. We performed multivariable time-to-event analysis using a Cox proportional hazards model, adjusting for maternal demographics, disease type, co-morbidities, pregnancy complications, and drug usage.

**Results:** We identified 26,088 offspring, among whom 2,902 (11.1%) were exposed to TNFi during pregnancy. The incidence rate (IR) of serious infections in offspring exposed to TNFi with high vs low placental transfer was, respectively, 2.27 (95% confidence interval [CI] 1.61-3.12) cases per 100 person-years at risk vs IR 1.59 cases per 100 person-years at risk (95% CI 0.76-2.92). In multivariable analysis, we were unable to clearly demonstrate an increased risk of serious infections with the usage of TNFi with high versus low placental transfer (adjusted hazard ratio 1.20; 95% CI 0.54-2.64), but the confidence interval was wide.

**Conclusion:** In one of the largest cohorts of TNFi-exposed offspring ever assembled, we were unable to establish a clear excess risk of serious infections in children exposed in utero to TNFi with high versus low placental transfer.

#### TOUR46

##### The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO): A Nationwide Multi-center Prospective Cohort

Lourdes Arreola (University of British Columbia, Vancouver); Julia Tan (University of British Columbia, Vancouver); Carrie Ye (University of Alberta, Edmonton); Janet Roberts (Division of Rheumatology, Dalhousie University, Dartmouth); Aurore Fifi-Mah (University of Calgary, Calgary); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal); Sabrina Hoa (Rheumatology Division, Department of Medicine, Centre hospitalier de l'Université de Montréal (CHUM), Montreal); Janet Pope (University of Western Ontario, London); Nancy Maltez (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Tom Appleton (St. Joseph's London Rheumatology Centre and Western University, London); May Choi (University of Calgary, Calgary); Ines Colmegna (The Research Institute of the MUHC, Montreal); Jan Dutz (University of British Columbia, Department of Dermatology and Skin Science, Vancouver); Daniel Ennis (University of British Columbia, Vancouver); Megan Himmel (University of Toronto, Toronto); Robert Rottapel (University of Toronto, Toronto); Alexandra Saltman (University of Toronto, Toronto); Annaliese Tisseverasinghe (University Of Manitoba, Winnipeg); Shahin Jamal (Division of Rheumatology, University of British Columbia, Vancouver)

**Objectives:** To describe the clinical presentation, management and early outcomes of patients exposed to ICI with Rh-irAE or PAD recruited and followed prospectively from multiple sites across Canada. Background: Immune Checkpoint Inhibitors (ICI) have altered the landscape of cancer therapy. However, toxicities are common and up to 80% of patients will develop immune-related adverse events (irAE), including rheumatic irAEs (Rh-irAE), which can often limit their cancer treatment. Our knowledge of clinical manifestations and optimal management of patients with Rh-irAE continues to evolve as these agents are being used to treat a wider variety of cancers. Currently available data is limited to retrospective case series and case reports. There is also scarce data on the use of ICI in patients with pre-existing autoimmune disease (PAD) as these patients are often excluded from clinical trials.

**Methods:** Adult patients with Rh-irAE from cancer immunotherapy

(CTLA-4, PD-1 or PDL-1 inhibitors) or those with PAD exposed to cancer immunotherapy are prospectively recruited across 9 academic sites in Canada. Standardized clinical and biologic data are also collected. We describe clinical characteristics and management of patients recruited between January 2020 and October 2021.

**Results:** 103 patients were recruited from 9 sites. From those, 92 had Rh-irAE, 47 had pre-existing musculoskeletal and rheumatic diseases, and 20 had other PAD. The most frequent Rh-irAE were joint manifestations ( $n = 73$ ). Other Rh-irAE included muscle symptoms ( $n = 7$ ), connective tissue disease ( $n = 6$ ), vasculitis ( $n = 2$ ) and sarcoid ( $n = 3$ ). Prednisone was the most common treatment ( $n = 92$ ). Intraarticular corticosteroids were used in 14 patients. Fifty-eight patients required conventional synthetic disease-modifying anti-rheumatic drugs (DMARD) and only one required biologic DMARD to control the Rh-irAE. The ICI was discontinued due to the Rh-irAE in 22 patients. There were no deaths related to Rh-irAE.

**Conclusion:** The CanRIO prospective national cohort provides valuable insight into real-world spectrum and management of Rh-irAE secondary to immunotherapy for cancer.

#### TOUR47

##### Use, Procurement Cost, and Adverse Events from IVIg Use in Rheumatic Disease

Francisca Lambert-Fliszar (McGill University Health Centre, Montreal); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Arielle Mendel (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal)

**Objectives:** Intravenous immunoglobulin (IVIg) is used in several rheumatic diseases due to postulated immunomodulatory properties. However, IVIg is a scarce and costly resource and poses a risk of adverse events (AEs). We evaluated the safety, effectiveness, and procurement cost of IVIg in an ambulatory rheumatic disease sample.

**Methods:** We identified tertiary clinic patients receiving IVIg for rheumatic disease between January 2015 and September 2020. We performed retrospective chart reviews from IVIg initiation until 3 months following the last infusion. We evaluated demographic and disease characteristics and clinical effectiveness of IVIg, based on the treating clinicians' assessments. Potential AEs were adjudicated by two independent physicians using pre-established rating scales. Finally, we determined if appropriate (ideal body weight-based) dosing was used and estimated the yearly procurement costs (CAN\$).

**Results:** Of 25 patients receiving IVIg for rheumatic disease over the study period, 22 had sufficient clinical records to be included. Mean age was 53 years and 16 (72%) were women (Table). The treatment indication in 18 patients (82%) was inflammatory myositis (dermatomyositis, antisynthetase syndrome, overlap and necrotizing myositis); the remaining indications were SLE ( $n = 2$ ), Sjogren's syndrome ( $n = 1$ ), and cutaneous vasculitis ( $n = 1$ ). Patients had a mean of 15 infusions (SD 14) spanning 1271 total hours. Of 21 patients with  $\geq 3$  months follow-up after IVIg initiation, 18 (86%) showed clinical improvement. Of these, 14 had clinical follow-up at 3 months following cessation of therapy and of these, 10 (71%) had stable or quiescent disease while 4 (29%) relapsed. We identified 11 potential AEs in 7 patients, representing 3.2 events per 100 IVIg infusions (95% CI 1.8-5.8). AEs included headache (6), urticaria (3), chills with back pain (1), and hypertension (1); none required an emergency room visit or hospitalization. One patient was switched to subcutaneous Ig. The appropriate IVIg dose could be calculated for 15 patients (height not recorded in the remainder); 7 (47%) received  $> 100$  g excess IVIg over their treatment period and the total cumulative excess was 1242 g. The cost of IVIg ranged from 61-\$90/g, giving a total estimated procurement cost of \$1.48 million during the study period.

**Conclusion:** The majority of our patients received IVIg for inflammatory

|                                           | <b>Patients (n = 22)</b> |
|-------------------------------------------|--------------------------|
| <b>Age mean (range)</b>                   | <b>53 (19-74)</b>        |
| <b>Sex female n (%)</b>                   | <b>16 (72%)</b>          |
| <b>Diagnosis n (%)</b>                    |                          |
| Inflammatory myositis                     | 18 (86)                  |
| SLE                                       | 3 (14)                   |
| Sjogren's                                 | 1 (5)                    |
| <b>Indications n (%)</b>                  |                          |
| Myositis                                  | 18 (82)                  |
| Chillblains                               | 1 (5)                    |
| Lupus nephritis                           | 1 (5)                    |
| Interstitial nephritis and pancytopenia   | 1 (5)                    |
| Cutaneous vasculitis                      | 1 (5)                    |
| <b>IVIg mean number of infusions (SD)</b> | <b>14.7 (14.5)</b>       |
| <b>IVIg mean gram (SD)</b>                | <b>911 (883)</b>         |
| <b>Concurrent prednisone</b>              | <b>17 (77)</b>           |
| <b>Concurrent immunosuppressant</b>       | <b>15 (68)</b>           |
| <b>Adverse events n (%)</b>               |                          |
| Headache                                  | 6                        |
| Urticaria                                 | 3                        |
| Chills                                    | 1                        |
| Hypertension                              | 1                        |
| <b>Recommended dose n* (%)</b>            | <b>6/15 (40)</b>         |
| * <=5 g above target dose                 |                          |

myositis. Most patients (86%) improved 3 months into therapy and a significant proportion of those (29%) relapsed after stopping therapy. Nearly 1 in 3 patients had a potential IVIg-related AE. A treatment course cost up to \$254,964, and one potential area of improvement is using recommended ideal body weight-based dosing.

#### TOUR48

##### Most Patients With Immune Mediated Inflammatory Diseases Do Not Report Increased Disease Activity Following COVID-19 Vaccination

Carol Hitchon (University of Manitoba, Winnipeg); Charles Bernstein (University of Manitoba, Winnipeg); Ruth Marrie (University of Manitoba, Winnipeg)

**Objectives:** COVID-19 vaccines are well-tolerated and reduce COVID-19 infection severity in the general population. Highly immunogenic vaccines may increase risk of disease flare for immune-mediated inflammatory diseases (IMIDs) such as lupus, inflammatory arthritis (IA) and inflammatory bowel disease (IBD). We sought to determine early COVID-19 vaccine reactogenicity (common vaccine-related adverse events) and IMID disease flares post-COVID-19 vaccination in patients with IMIDs.

**Methods:** Between March 2021 and Sept 2021, patients with CTD (n = 70; 70% lupus) or IA (n = 67; 77% rheumatoid arthritis), and IBD (n = 82; 40% Crohn's) self-reported disease activity prior to and 1 month post both COVID-19 vaccinations (V1 and V2). CTD and IA also reported flare status. Disease activity was assessed by the Systemic Lupus Activity Questionnaire (SLAQ) for CTD, the RAPID-3 for IA and the IBD Symptoms Inventory-short form (IBDSI) for IBD. Patient-reported flare was assessed using the SLAQ ("Have you had a flare?") for CTD and the RA Flare index (calculated index and self-report flare: "Are you in a flare?") for IA. Patients reported solicited (those commonly reported in the general population) adverse events for 7 days after each vaccination. Descriptive statistics are presented.

**Results:** Patients were predominantly female (80%), White (73%), with a mean (SD) age of 55.5 (15) years, body mass index 28 (6); 9 had suspected or diagnosed COVID-19 illness. The majority received a mRNA vaccine (V1 76%; V2 96%) and had the same vaccine each dose (73%). Disease activity scores were similar pre and post each vaccine dose for CTD, IA, and IBD [SLAQ median (interquartile range-IQR) pre-V1 = 8.0 (6.5), post-V1 = 7 (7), pre-V2 = 6 (7), post-V2 = 5 (6); RAPID-3 median (IQR) pre-V1 = 4 (9.7), post-V1 = 7.7 (10.1), pre-V2 = 7.5 (11), post-V2 = 6.5 (10.2); IBDSI pre-V1 20 (24), post-V1 18.5 (22.9), pre-V2 16.5 (22) post-V2 13.5 (19)]. The proportion of patients reporting disease flare was similar pre and post each vaccine (any CTD flare: pre-V1 = 61%, post-V1 = 65%, pre-V2 = 58%, post-V2 = 48%; moderate or severe CTD flare pre-V1 19%, post-V1 25%, pre-V2 19%, post-V2 18%; any IA flare state pre-V1 = 20%, post-V1 = 25%, pre-V2 = 21 %, post-V2 = 17%; RA flare index median (IQR) pre-V1 9 (21), post-V1 19 (22), pre-V2 18 (22) post-V2 16 (18). Of those with complete solicited reactogenicity data (n = 81) 97% had symptoms with a median (range) of 4 (1-12) new symptoms (not present at baseline) but did not seek medical assessment.

**Conclusion:** COVID-19 vaccination did not increase disease activity in most patients with IMIDs. New vaccine-related side effects were common but were mostly self-managed.



# POSTER PRESENTATIONS

## 1 Physical Activity in Axial Spondyloarthritis: A Cross-Sectional Study of Awareness and Adherence to Canadian Guidelines.

Sandra Vijayan (Royal College of Surgeons in Ireland, Dublin); Robert Inman (Toronto Western Hospital, Toronto); Nigil Haroon (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto); Laura Passalent (Toronto Western Hospital, Krembil Research Institute, University of Toronto, Toronto)

**Objectives:** Despite the known benefits of physical activity (PA), literature suggests patients with axial spondyloarthritis (axSpA) fail to meet recommended guidelines. This is significant since exercise, a critical component of physical activity, is considered the cornerstone of axSpA management. This study aims to determine: (i) awareness of established PA guidelines, (ii) the degree to which patients with axSpA are meeting these guidelines and (iii) to understand factors that influence adherence to regular PA.

**Methods:** A prospective cross-sectional study was conducted of English-speaking adults attending an urban academic clinic in Toronto, Canada; aged 18 years and older; diagnosed with axSpA (based on ASAS criteria) and registered in a longitudinal cohort. Patients completed an electronic survey that included the 'Short Questionnaire to Assess Health-enhancing Physical Activity' (SQUASH) to assess PA engagement. Patients were also asked about awareness of national PA guidelines. Clinical and sociodemographic variables of the participants were obtained from the clinic's database according to their most recent protocol visit within a year of completing the electronic survey. Descriptive statistics were used for the univariate analysis. Bivariate analyses, including Chi-squared tests and t-tests, were performed to examine factors associated with PA adherence.

**Results:** In total, 155 respondents participated in the study. The majority of respondents were male (89%), with a mean age of 43.9 ( $\pm$  12.8) years; the majority were classified with AS (72%); the average disease duration was 20.6 ( $\pm$  11.6) years. Most respondents were receiving either NSAID therapy (88%) and/or biologics (65%). Less than half of the cohort (46.5%) were aware of national PA guidelines: 31 % were aware of frequency recommendations; 43.7% were aware of duration recommendations and only 13.6 % were aware of strength recommendations. Nonetheless, the majority of axSpA patients (72.9%) met or exceeded recommended PA targets. Most patients (72%) reported participating in leisure-walking as a main form of PA; this met or exceeded guidelines. Adherence to PA guidelines was associated with lower disease activity, measured by BASDAI ( $P = 0.007$ ); higher function as measured by BASFI (0.014) and lower body mass index (BMI) ( $P = 0.0045$ ). **Conclusion:** This study suggests the majority of axSpA patients are meeting national PA recommendations despite not being fully aware of established guidelines. Furthermore, axSpA patients may be gaining the subsequent health benefits. Targeting low disease activity, high function, & optimal lifestyle indicators, like BMI, provides a framework for focused interventions to improve adherence to PA guidelines in axSpA patients.

## 2 The Association between Vedolizumab and the Development of New-onset Features of Spondyloarthritis in Patients With Inflammatory Bowel Disease: A Pilot Study.

Maria Tauqir (Western University, London); Sherry Rohekar (Western University, London); Tristan Boyd (Western University, London); Trimadhu Sharma (Lawson Research Institute, London); Vipul Jairath (Western University & London Health Sciences Centre, London); Reena Khanna (London Health Sciences Centre, London); Nilesh Chande (London Health Sciences Centre, London); Terry Ponich (London Health Sciences Centre, London); Jamie Gregor (London Health Sciences Centre, London); Michael Sey (London Health Sciences Centre, London); Melanie Beaton (London Health Sciences Centre, London); Keith McIntosh (London Health Sciences Centre, London); Adam Rahman (London Health Sciences Centre, London)

**Objectives:** Vedolizumab is a humanized IgG1 monoclonal antibody to  $\alpha 4\beta 7$  integrin that has been approved for treatment of inflammatory bowel disease (IBD). Previous case series have suggested that vedolizumab may induce new-onset features of spondyloarthritis (SpA), such as sacroiliitis and peripheral arthritis. However, it is unclear whether these features developed after initiation of vedolizumab, were already present and under-investigated, or were masked by prior treatment with immunosuppressive therapy including tumour necrosis factor inhibitors (TNFi). Our objective was to evaluate the association between vedolizumab and development of de novo features of SpA in TNFi-experienced and TNFi-naive IBD patients.

**Methods:** We performed a prospective observational study of 13 TNFi-naive and 11 TNFi-experienced IBD patients. Patients were evaluated by a rheumatologist prior to the initiation of vedolizumab and at follow-up visits, 8 and 24 weeks after administration. A thorough clinical history as well as physical examination was conducted by a rheumatologist to assess for any features of SpA. Clinical outcome measures for SpA and IBD, such as the Bath Ankylosing Spondylitis Disease Activity Index and Bath Ankylosing Spondylitis Metrology Index, were collected at each visit. MRI of the sacroiliac joints was also performed at each visit using the Spondyloarthritis Research Consortium of Canada protocol. These were centrally read by a radiologist, blinded to all clinical information.

**Results:** Twenty-four patients were recruited. One patient had evidence of burn-out sacroiliitis on MRI at baseline while another could not tolerate MRI; both were withdrawn. Five patients were lost to follow-up for several reasons including the COVID-19 pandemic. One of these patients developed polyarthralgia after vedolizumab initiation. Sixteen of the 17 remaining patients (9 TNFi-naive, 8 TNFi-experienced) did not demonstrate new clinical or radiological signs of SpA. One TNFi-experienced patient developed a worsening hip effusion at 24-week follow-up, although this patient had pre-existing osteoarthritis identified on baseline MRI.

**Conclusion:** The majority of patients treated with vedolizumab did not develop new manifestations of SpA, which does not support the hypothesis that vedolizumab induces de novo features of SpA. Larger studies are needed.

## 3 Real-world 12-month Retention on Secukinumab Among Axial Spondyloarthritis Patients Within the Canadian Spondyloarthritis (CanSpA) Research Network

Robert Inman (Toronto Western Hospital, Toronto); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal); Majeed Khraishi (Department of Medicine, Memorial University of Newfoundland, St. John's); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Shamiza Hussein (Novartis, Montreal); Drew Neish (IQVIA, Montreal); Patrick Leclerc (Novartis Canada, Montreal)

**Objectives:** Axial spondyloarthritis (axSpA) is a chronic, immune-mediated, inflammatory condition consisting of two clinically defined subsets, non-radiographic axial spondyloarthritis (nr-axSpA), and ankylosing spondylitis (AS), the latter characterized by structural damage of the spine and/or sacroiliac joints. It is estimated that up to 1% of the Canadian population lives with AS. Secukinumab was approved in Canada in April 2016 for the treatment of AS and has demonstrated efficacy and safety through extensive clinical trials, some accumulating five years of continuous treatment. Real-world evidence from the European Spondyloarthritis (EuroSpA)

Table 1: Baseline characteristics of ax-SpA patients

|                                                      | All patients (n=146) | b/tsDMARD naive (n=34) | b/tsDMARD experienced (n=112) |
|------------------------------------------------------|----------------------|------------------------|-------------------------------|
| Age (years), mean (SD)                               | 43.3 (11.0)          | 43.0 (11.3)            | 43.4 (11.0)                   |
| Male, n (%)                                          | 79 (54.1%)           | 24 (70.6%)             | 55 (49.1%)                    |
| BMI (kg/m <sup>2</sup> ), median (IQR), [N missing]  | 26.7 (7.4) [31]      | 24.9 (5.7) [5]         | 27.4 (8.0) [26]               |
| Smoker at index, n (%), [N missing]                  | 33 (25.8%) [18]      | 9 (29.0%) [3]          | 24 (24.7%) [15]               |
| Years since diagnosis, mean (SD)                     | 5.0 (4.8)            | 5.1 (5.1)              | 5.0 (4.7)                     |
| HLA-B27 positive status, n (%), [N missing]          | 89 (71.2%) [21]      | 26 (83.9%) [3]         | 63 (67.0%) [18]               |
| C-reactive protein (mg/L), median (IQR), [N missing] | 3.0 (5.2) [43]       | 4.0 (14.2) [11]        | 3.0 (4.3) [32]                |
| BASDAI, median (IQR), [N missing]                    | 6.9 (2.3) [12]       | 6.8 (3.1) [4]          | 6.9 (2.2) [8]                 |
| ASDAS-CRP, median (IQR) [N missing]                  | 3.5 (1.2) [80]       | 3.5 (1.1) [16]         | 3.5 (1.3) [64]                |

collaboration was recently published describing use of secukinumab in 13 national European SpA registries. Nevertheless, there is limited evidence on its real-world use in Canada. The objective of this study was to use the Canadian Spondyloarthritis (CanSpA) Research Network to describe the Canadian axSpA population treated with secukinumab and assess its real-world retention.

**Methods:** This is an observational, registry-based cohort study of Canadian ax-SpA patients 18-65 years who attend a clinic participating in CanSpA research network and have been treated with secukinumab. The CanSpA research network is a centralized database that collects information on patient and disease characteristics, medical history, treatment, effectiveness and safety outcomes pooled from multiple Canadian databases: University Health Network (UHN), Rhumadata®, and Newfoundland SpA Co-morbidities. Patients were indexed on the date of first secukinumab prescription, and retention was assessed at 12 months for the overall population, by prior use of a biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD), and by sex. Baseline demographics and clinical characteristics are also reported.

**Results:** Based on preliminary analysis, 146 patients with documentation of an axSpA diagnosis were included. The mean (SD) age was 43.3 (11.0) years and 79 (54.1%) were male. Previous experience with a b/tsDMARD at index was documented for 76.7% of the patients. At 12 months post-initiation, secukinumab retention rates were 62.9% for the overall population, 55.7% and 65.0% for b/tsDMARD-naïve and -experienced patients, and 65.8% and 59.4% for male and female patients, respectively (Table 1).

**Conclusion:** From the preliminary results of this real-world nationwide study of 146 Canadian axSpA patients, secukinumab shows good 12-months' retention rates and represents a valuable therapeutic option for the treatment of axSpA. In contrast to previous studies, retention rates were lower and differences in retention among b/tsDMARD-naïve and -experienced patients were not notable. These differences could be due to the small number of b/tsDMARD-naïve patients in the study.

#### 4

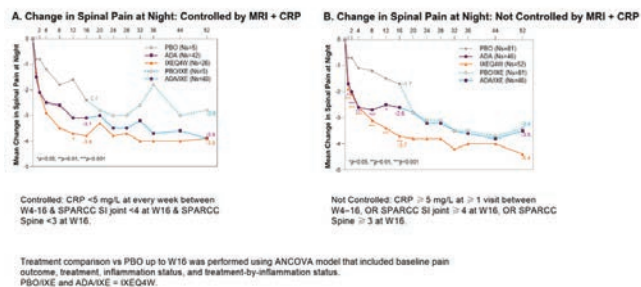
### Ixekizumab Shows a Distinct Pattern of Pain Improvement Beyond Measurable Inflammation as Assessed by MRI or CRP or BASDAI Questions 5 & 6 in Patients With Ankylosing Spondylitis

Kurt de Vlam (UZ Leuven, Leuven); Philip Conaghan (University of Leeds, Leeds); Philip Mease (University of Washington, Seattle); Proton Rahman (Memorial University of Newfoundland, St. John's); Venkatesh Krishnan (Eli Lilly and Company, Indianapolis); Rebecca Bolce (Eli Lilly and Company, Indianapolis); David Sandoval (Eli Lilly and Company, Indianapolis); So Young Park (Eli Lilly and Company, Indianapolis); Gaia Gallo (Eli Lilly & Company, Indianapolis); Walter Maksymowych (Department of Medicine, University of Alberta, Edmonton)

**Objectives:** To evaluate pain improvement over 16 weeks (W) with ixekizumab (IXE) in patients with ankylosing spondylitis (AS), based on longitudinal status of inflammation (assessed by serum CRP values or spinal MRI Spondyloarthritis Research Consortium of Canada (SPARCC) score). Pain improvement was measured by MRI, CRP level, and BASDAI 5/6.

**Methods:** The Phase III COAST-V (NCT02696785) 52W, multi-center, randomized, double-blind, placebo (PBO)-controlled study examined the efficacy of IXE in patients with active AS. Adalimumab (ADA) was used as an active reference arm for the first 16W. Patients originally assigned to PBO or ADA were re-randomized to IXE at W16. Change in spinal pain at night (SP-N) and Short Form 36 Health Survey (SF-36) Bodily Pain were measured during study visits and analyzed while controlling for inflammation status using MRI, CRP levels and mean BASDAI 5/6 (Q5: Duration, Q6: Intensity of morning stiffness). Observed data analyses are presented for each group stratified by treatment arm. Initial analysis: 'controlled inflammation' is defined as MRI SPARCC SI joint < 4 and MRI SPARCC Spine < 3 at W16, CRP < 5mg/L at every visit W4-16, or BASDAI 5/6 improvement ≥ 2 points at W12 and W16. Second analysis: control is defined as CRP < 5 mg/L at every week between W4-16 and MRI SPARCC SI joint < 4 at W16 and MRI SPARCC Spine < 3 at W16.

**Figure. Change in Spinal Pain at Night over 52 weeks by MRI + CRP**



**Results:** When inflammation was controlled per MRI, patients treated with IXEQ4W (-3.9, P < 0.001) and ADA (-2.8, P = 0.02) experienced significant reduction in SP-N vs PBO (-1.6) at W16; further improvements were experienced in patients re-randomized to IXE by W52 (Figure). When inflammation was not controlled per MRI, IXEQ4W (-3.5, P < 0.01) and ADA (-3.1, P = 0.02) experienced significant reduction in SP-N at W16; all IXE-treated patients had further reductions at W52. When inflammation was controlled per MRI+CRP, IXEQ4W (-3.8, P = 0.2) and ADA (-3.1, P = 0.4) had reduction in SP-N at W16 vs PBO (-2.4); all IXE groups had further improvements at W52. When inflammation was not controlled as measured by MRI+CRP, IXEQ4W (-3.7, P < 0.001) had significant reduction in SP-N vs PBO (-1.7), whereas improvement with ADA (-2.6, P = 0.06) was not significant; all IXE-treated patients had further reduction by W52. For SF-36 bodily pain, improvements were observed at W16 and W52 whether inflammation was controlled or not controlled per MRI, CRP, MRI+CRP, or BASDAI 5/6.

**Conclusion:** This analysis adds support to the hypothesis that IXE improves pain in patients with and without measurable inflammation.

#### 5

### Sustained Functional Remission in Axial Spondyloarthritis (axSpA): Which Are the Primary Outcomes That Should be Targeted to Achieve This?

Walter Maksymowych (Department of Medicine, University of Alberta, Edmonton); Robert Inman (Toronto Western Hospital, Toronto); Louis Bessette (Laval University, Quebec); Proton Rahman (Memorial University of Newfoundland, St. John's); Emmanouil Rampakakis (JSS Medical Research Inc, Montreal); Odalis Asin-Milan (Janssen Inc, Toronto); Meagan Rachich (Janssen Inc, Toronto); Marilise Marrache (Janssen Inc, Toronto); Allen Lehman (Janssen Inc, Toronto)

**Objectives:** A treat-to-target (T2T) strategy is advocated for the management of axSpA although no consensus exists as to the appropriate target/outcome; there is agreement that the key domain is disease activity. The ASDAS is recommended however the BASDAI is more feasible. Functional impairment is associated with inflammation/structural damage and is assessed in axSpA using BASFI. Sustained (≥ 6 months duration) low BASFI (< 3) may therefore be an appropriate target. Objectives were to determine 1) to what degree duration of low disease activity impacts function and 2) which patient and disease characteristics predict sustained low BASFI focusing on a comparison of sustained (≥ 6 months) low ASDAS versus BASDAI.

**Methods:** Multi-centre, prospective BioTRAC registry collected real-world patient reported outcomes, clinical, and laboratory data on axSpA patients

| Table . Predictors of low BASFI (<3) Between 12 and 18 Months |      |           |         |
|---------------------------------------------------------------|------|-----------|---------|
| Parameter                                                     | OR   | 95% CI    | P-Value |
| BASFI-Baseline                                                | 0.7  | 0.6, 0.8  | <0.001  |
| Low BASDAI (<3): M6 and M12 vs persistent BASDAI >3           | 10.5 | 4.0, 27.2 | <0.001  |
| Low BASDAI (<3): M6 or M12 vs. persistent BASDAI >3           | 5.2  | 2.4, 11.1 | <0.001  |
| ASDAS-ID: M6 and M12 vs. persistent ASDAS >1.3                | 3.7  | 1.1, 13.1 | 0.040   |
| ASDAS-ID: M6 or M12 vs. persistent ASDAS >1.3                 | 2.2  | 0.8, 6.0  | 0.144   |



treated with infliximab or golimumab (2002-2018). The impact of achieving low BASDAI (< 3) and/or ASDAS-inactive disease (ID) (< 1.3) at 6 and 12 months, at only 6 or 12 mos, or at neither time point, and the interaction of CRP at 6 and 12 months with BASDAI, on the BASFI score at 18 mos was analyzed by generalized linear models (GLM) adjusted for age, gender, baseline disease duration, and baseline BASFI. Generalized estimating equations (GEE) were used in univariate and multivariate analyses to test baseline patient demographic and disease characteristics, treatment, sustained low BASDAI and/or ASDAS-ID at 6 and 12 months, in predicting low BASFI (< 3) between 12 and 18 months.

**Results:** 1620 pts enrolled had sustained low BASDAI (33.7%) and ASDAS-ID (15%). In univariate GEE of baseline variables, age and baseline BASDAI, BASFI, and ASDAS were significant predictors of sustained low BASFI. In univariate GEE of follow-up variables, sustained low BASDAI and ASDAS-ID were also predictors. In multivariate GEE, sustained low BASDAI and baseline BASFI were predictors of low BASFI (Table), and sustained ASDAS-ID was a weak predictor. In GLM models, sustained low BASDAI and baseline BASFI plus age were strong predictors of BASFI score at 18 months, while sustained ASDAS-ID was a weak predictor. A significant interaction was observed between duration of low BASDAI and normal CRP (< 5 mg/L at 6 and 12 months) with CRP remission as an independent predictor of function among patients on sustained low BASDAI.

**Conclusion:** Aiming for sustained low BASDAI (< 3) may be a valid and more feasible T2T treatment strategy than ASDAS-ID for routine care in axSpA. Further validation is required to achieve consensus for a T2T strategy.

## 6

### Impact of Inflammatory Arthritis on COVID-19 Outcomes: The Impact Study

Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Edna Hutchings (Canadian Research Education (CaRE) Arthritis Ltd., Edmonton); Stephanie Wichuk (University of Alberta, Edmonton); Mohammed Osman (University of Alberta, Edmonton); Ameeta Singh (University of Alberta, Edmonton); Ashlesha Sonpar (University of Alberta Hospital, Edmonton); Ilan Swartz (University of Alberta, Edmonton); Bo Pan (University of Alberta, Edmonton); Walter Maksymowych (Department of Medicine, University of Alberta, Edmonton)

**Objectives:** The Impact of Inflammatory Arthritis on COVID-19 Outcomes study was created to understand the impact of inflammatory arthritis (IA) and associated immunomodulatory treatments on COVID-19 outcomes. We hypothesized that IA patients would have increased risk of more severe disease and benefit from vaccination.

**Methods:** We prospectively used a monthly administered Redcap survey to consented rheumatoid arthritis (RA) (RAPPORT registry) and spondyloarthritis (SpA) (FORCAST registry) electronically from November 2020 to November 2021. Survey questions included COVID-19 test positivity, symptom severity associated with COVID-19, vaccination rates and vaccine-related side effects. Descriptive statistics were used for patient characteristics, COVID-19 symptoms and vaccination rates.

**Results:** Of 2154 candidate patients, 767 (36%) patients from our cohort answered at least the baseline survey with 178 (23%) patients answering up to 10 surveys. Participating patients were mostly females (n = 274 (37% males), 570 diagnosed with RA, and 197 with SpA. Only 39 (5%) patients were taking prednisone, while 286 (37%) took methotrexate, 626 (82%) took biologics or small molecule inhibitors (58% being TNF inhibitors). Mean HAQ at baseline was 0.56 (SD 0.55, n = 217). Overall, only 19/767 (3%) patients tested positive for COVID-19, 3 (16%) testing positive twice. Mean age of COVID-19 positive patients was 54 (SD 11.2) years (all RA patients): one patient was on a biologic, 6 (32%) were on disease modifying anti-rheumatic drugs, 7 (37%) on non-steroidal anti-inflammatory drugs and 17 (90%) reported taking steroids. Seven (9%) patients were admitted to hospital due to COVID-19 symptoms with only one patient requiring ICU admission, and another patient with VTEs. 101/767 (13%) of patients

reported visiting a doctor for symptoms suggestive of COVID-19. Of 648 patients who were vaccinated, 63 (10%) were single- and 583 (90%) were double-vaccinated, the majority receiving Pfizer (80%), followed by Moderna (23%), and AstraZeneca (6%). 421 (65%) patients reported side effects from the vaccine, most common being injection site pain, fatigue, and muscle aches. 136 (21%) patients reported arthritis flare but only 16 (3%) patients saw a doctor for vaccine side effects. No worsening in arthritis pain, stiffness, or HAQ scores were reported in a subset of these patients (n = 21) 1-month pre- and post-COVID-19 vaccination.

**Conclusion:** Despite emergence of the Delta variant during the study, our study highlights the relatively lower proportion rate of COVID-19 infection and complications in patients with IA. It also underscores the increased vaccination rates in IA patients with infrequent vaccine-related adverse effects requiring medical intervention.

## 7

### Early Switching and Smoking Associated With BDMARD Refractory Disease: A 15-year Follow-up of the Alberta Biologics Pharmacovigilance Cohort

Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Britney Jones (University of Alberta, Edmonton); Jill Hall (University of Alberta, Edmonton); Joanne Homik (University of Alberta, Edmonton); Anthony Russell (University of Alberta, Edmonton); Luck Lukusa (Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Walter Maksymowych (Department of Medicine, University of Alberta, Edmonton)

**Objectives:** We evaluated rheumatoid arthritis (RA) patients with at least one year of follow-up after their first advanced therapy (biologic/JAK inhibitor), to identify characteristics associated with later multiple failure of advanced therapies (refractory disease).

**Methods:** The Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT) registry is a prospective inception cohort of northern Alberta RA patients starting their first advanced therapy. For the current analyses, we assessed patients with at least one year of follow-up after biologic/JAK inhibitor initiation. Using the one-year post enrolment date as time-zero, multivariable Cox regression was performed to evaluate factors potentially associated with ultimate occurrence of multiple failures of advanced therapies (> 3 biologic classes or JAK inhibitors). Patients stopping their biologic/JAK inhibitor and not initiating another advanced therapy were censored.

**Results:** Of 2338 RAPPORT patients, there were 6 deaths in the first year, and an additional 225 without one year of follow-up. Of the 2107 subjects with at least one year of follow-up after their first biologic/JAK inhibitor, at our time-zero, 7.5% were on prednisone, 57.5% on concomitant methotrexate and 81% were on TNF inhibitors, with mean DAS-28-CRP 2.8 (SD 1.2) and mean HAQ 1.5 (SD 0.7) at our time-zero. Over an average 6 (SD 4.5) years of follow-up from time-zero, 271 (12.9% of the 2107) received > 3 advanced therapies. In the unadjusted and adjusted models

**Table 1. Unadjusted and Fully Adjusted Cox Multivariable Analyses Evaluating Characteristics Associated With Later Developing Refractory Disease<sup>a</sup>**

| Characteristics at time-zero                                         | Refractory RA cohort (N=2107) |                                   |
|----------------------------------------------------------------------|-------------------------------|-----------------------------------|
|                                                                      | Unadjusted HR (95% CI)        | Adjusted HR (95% CI) <sup>b</sup> |
| Secondary education                                                  | 1.31 (1.03, 1.68)             | 0.94 (0.66, 1.33)                 |
| Unemployed                                                           | 1.35 (1.04, 1.76)             | 1.17 (0.80, 1.70)                 |
| Current smoker                                                       | 1.34 (1.02, 1.76)             | 1.30 (1.01, 1.68)                 |
| Year of cohort entry, 2011 onward                                    | 2.27 (1.74, 2.96)             | 2.13 (1.44, 3.17)                 |
| On anti-TNF biologic <sup>c</sup>                                    | 0.36 (0.28, 0.46)             | 0.49 (0.34, 0.72)                 |
| Current prednisone                                                   | 3.37 (2.65, 4.28)             | 2.61 (1.86, 3.67)                 |
| DAS28-CRP (Reference: Remission or LDA) <sup>d</sup>                 |                               |                                   |
| High disease activity                                                | 6.49 (4.55, 9.27)             | 4.80 (2.77, 8.30)                 |
| Moderate disease activity                                            | 3.16 (2.41, 4.13)             | 2.65 (1.77, 3.96)                 |
| DAS28 remission/LDA since 1st advanced therapy <sup>e</sup>          |                               |                                   |
| At 3-4 months                                                        | 0.52 (0.40, 0.68)             | 1.09 (0.73, 1.62)                 |
| At 1 year                                                            | 0.47 (0.32, 0.69)             | 1.16 (0.66, 2.03)                 |
| Early switch from 1st biologic or JAK inhibitor (prior to time zero) | 4.86 (3.79, 6.22)             | 3.26 (2.26, 4.69)                 |

<sup>a</sup>Receiving ≥3 biologic classes/JAK inhibitors <sup>b</sup>Adjusted for all variables shown as well as sex, Caucasian maternal race, age, disease duration, rheumatoid factor, comorbid conditions, concomitant methotrexate/hydroxychloroquine/other DMARDs (infliximab, golimumab, adalimumab, certolizumab pegol, <sup>c</sup>LDAs=low disease activity<sup>d</sup> 3-4 months or 1 year reflects timing from initiation of first advanced therapy (i.e. recorded before our time-zero).



(Table 1), risk of our outcome of interest was associated with current (time-zero) smoking, current (time-zero) prednisone, moderate or high DAS28-CRP at time-zero, and entry into the cohort from 2011 onwards. As expected, risk of our outcome was higher in subjects who switched from their first bDMARD/JAK inhibitor in the first year before our time-zero, while risk was lower in subjects on anti-TNF biologic use at time-zero.

**Conclusion:** In patients receiving any biologic/JAK inhibitor for at least one year, factors associated with ultimately receiving > 3 biologic classes/JAK inhibitors included smoking, prednisone, high disease activity, and having already switched advanced therapies within one year of the first initiated advanced therapy. Subjects entering RAPPORT since 2011 were more likely to ultimately receive ≥ 3 advanced therapies, possibly representing increasing therapy options and/or more aggressive approaches. Continued effort towards smoking cessation is an important adjunctive goal in RA care.

## 8

### Radiological Validation of a Novel MRI Reporting System for Axial Spondyloarthritis

Sandeep Dhillon (McMaster University, Hamilton); Christina Ma (McMaster University, Hamilton); Raj Carmona (McMaster University, Hamilton); Euan Stubbs (McMaster University, Hamilton); Nader Khalidi (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); George Ioannidis (McMaster University, Hamilton); Rana Kamhawy (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); John O'Neill (McMaster University, Hamilton)

**Objectives:** Challenges in the diagnosis of axial spondyloarthritis (SpA) have resulted in increasing use of magnetic resonance imaging (MRI). Often, bone marrow edema (BME) on MRI alone without a global radiologic assessment is mistakenly used to arrive at an imaging diagnosis. Given this, our group proposed a novel categorization system for MRI reporting of the sacroiliac joints (SIJs) in a recent publication (O'Neill, 2019). This abstract aims to update previously presented data validating this novel reporting system.

**Methods:** In this retrospective review we identified 92 patients who had spondylitis MRI protocol ordered by one of two rheumatologists for suspected SpA from 2012 to 2018. Two rheumatologists retrospectively applied the novel classification system to the original MRI reports. The original reading radiologist also retrospectively applied the novel classification system to the original MRI reports. Two MSK radiologists, blinded to the initial imaging diagnoses, completed a separate reading of the MRI images to generate a new report based on the novel classification system. A comparative assessment of the old and new reports was performed to assess the quality of the new framework.

**Results:** Rheumatologists disagreed on the re-interpretation of the original MRI reports in 11/92 (12.0%) patients. Consensus rheumatologist opinion and the original radiologist disagreed on the re-interpretation of 13/64 (20.3%) patients. There was 100% rheumatologist agreement on the interpretation of the new novel categorization system report as per MSK radiologist consensus report. Of all patients, 58 (63.0%) were recategorized into new categories compared to the rheumatologist's interpretation of the original report. Six patients changed from a category of sacroiliitis to an alternate or indeterminate diagnosis and one patient changed from a category of indeterminate diagnosis to sacroiliitis.

**Conclusion:** We present an update on a novel categorization system for reporting in axial SpA. There was significant heterogeneity in the re-interpretation of the original reports between the rheumatologists and the original reading radiologist with complete agreement utilizing the new reporting system. This indicates that current practices of reporting MRIs for SIJs lack precision and can lead to miscommunication between physicians. There were many changes in the categorization of patients between the original and new MRI reports, suggesting this novel system may have implications on clinical practice.

## 9

### Prevalence, Incidence and Predictors of Uveitis in Spondyloarthritis in a Canadian Cohort

Vanessa Ocampo (University of Toronto, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Mitchell Sutton (Toronto Western Hospital, Toronto); Nigil Haroon (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto); Vinod Chandran (Krembil Research Institute, Toronto Western Hospital, Toronto); Steve Ramkissoon (Toronto Western Hospital, Toronto)

**Objectives:** Spondyloarthritis (SpA) encompasses Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Inflammatory bowel disease-associated spondyloarthritis, Reactive Arthritis, and undifferentiated spondyloarthritis. These conditions share a number of extramusculoskeletal manifestations, the most common being acute anterior uveitis. **PURPOSE** To determine the frequency of SpA associated uveitis, to elucidate associated clinical features of SpA in patients with uveitis, and to identify SpA features that can predict flares of uveitis.

**Methods:** Cohort: Patients followed in the axSpA and PsA clinics at a single centre from January 2001 to December 2020 at 6–12-month intervals, according to a standard protocol including demographic and clinical variables, treatment, and acute phase reactants. Statistical Analysis: T and chi-squared tests were performed at baseline visits on demographic and clinical factors on both the SpA and PsA populations, to compare patients with and without UV. Cox proportional-hazard models with time-dependent covariates were performed on patients with UV, with their first instance of a UV flare as the outcome event. Univariate analysis was done for each clinical and demographic factor, controlling for age, sex, and disease duration. Factors significant (< 0.1) in the univariate analysis were included in a multivariate analysis, controlling for age, sex and disease duration.

**Results:** A total of 3306 patients were included, 1724 patients with axSpA and 1582 patients with PsA (Table 1). 30.2% of the axSpA cohort having uveitis (UV), vs 7.6% in the PsA. The rate of flares per person years at risk was 12.12% in the axSpA cohort, vs 1.71% in the PsA. There were more men in the total cohort (axSpA 65% and PsA 56%). Most patients were Caucasian (axSpA 67%, 94% PsA). Among axSpA patients 1169 (68%) were HLA\*B27+, and 435 had UV. Among PsA patients 201 (16%) patients were HLA\*B27+, and 32 had UV. The multivariate analysis of the axSpA cohort showed that higher CRP (HR 1.009 P = 0.004) increased the risk of a flare, while biologic agents decrease risk of flare (HR 0.702 P = 0.040) in patients with UV. In the PsA cohort, being HLA\*B27+ (HR 3.084 P = 0.007) increased the risk of a UV flare, while being on a DMARD decreased the risk of a flare (HR 0.262 P = 0.0088)

**Conclusion:** Uveitis is more common in the axSpA than in the PsA population. New onset of UV was also more commonly seen in the axSpA cohort. Factors that increase the risk of new uveitis flare were elevated CRP in

Table 1

| Variable             | axSpA       | PsA         | p-value |
|----------------------|-------------|-------------|---------|
| n                    | 1724        | 1582        |         |
| UV                   | 521 (30)    | 121 (8)     | <0.001  |
| age                  | 38.3 (13.2) | 44.9 (13.2) | <0.001  |
| sex                  | 1117 (65)   | 882 (56)    | <0.001  |
| Caucasian            | 1135 (66)   | 1350 (85)   | <0.001  |
| Alcohol              | 808 (47)    | 703 (44)    | 0.16    |
| HLA-B27+             | 1169 (68)   | 201 (16)    | <0.001  |
| Tender               | 2.6 (6.1)   | 6.9 (8.7)   | <0.001  |
| Swollen              | 1.3 (3.3)   | 3.3 (4.8)   | <0.001  |
| Active               | 3.8 (7.9)   | 9.0 (9.8)   | <0.001  |
| Damaged              | 3.6 (8.2)   | 2.6 (6.7)   | 0.004   |
| Peripheral Arthritis | 48 (3)      | 87 (5)      | <0.001  |
| NSAIDs               | 917 (53)    | 1035 (65)   | <0.001  |
| DMARDs               | 217 (13)    | 574 (36)    | <0.001  |
| Biologics            | 435 (25)    | 140 (9)     | <0.001  |

NSAID: non-steroidal anti-inflammatory drugs, DMARD: Disease modifying rheumatic drug

the axSpA cohort and being a male or HLA-B27+ in the PsA population. Best Abstract on Spondyloarthritis Research Award.

## 10 Help-seeking Behaviors and Treatment Preferences For Sleep Problems Among Persons With Arthritis

Emilie McGuire (University of British Columbia, Vancouver); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver); Josée Savard (Université de Laval, Québec); Paul Fortin (Department of Rheumatology, CHU de Québec-Université Laval, Québec); Elham Rahme (Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal); Deborah Da Costa (McGill University Health Center, Montreal)

**Objectives:** Sleep disturbances, including difficulty initiating sleep, maintaining sleep, and/or early morning awakenings are prevalent among persons with inflammatory arthritis (IA) and have been shown to contribute to worsening of symptoms including fatigue, pain, and health related quality of life. Cognitive behavioral therapy for insomnia (CBTi) is considered first-line treatment for insomnia, but accessibility is limited. Internet delivered CBTi has the potential to overcome accessibility barriers. To guide the tailoring of an internet delivered CBTi for persons with arthritis experiencing insomnia, a needs assessment was conducted to identify help-seeking behaviors, insomnia management strategies and treatment preferences.

**Methods:** We conducted an online survey with 251 individuals with arthritis (mean age ± standard deviation: 61.5 years ± 13.1) recruited through social media ads on Instagram, Twitter and Facebook and through the arthritis patient organizations Arthritis Consumer Experts, Arthritis Research Canada's Patient Advisory Board and Patients Intéressés par la Recherche en Arthrite. Participants completed self-report questions assessing insomnia symptoms (Insomnia Severity Index – ISI), help-seeking behaviors and barriers, and treatment preferences for sleep problems.

**Results:** Of the total sample in the past year, 65.7% had at least once used prescription medications and 36.7% had used over the counter medication to facilitate sleep. Among participants with probable insomnia (ISI score ≥ 8, n = 210), 59.3% had ever discussed their sleep problem with a health care provider and 42.1% perceived a need to talk to a health care provider about their sleep problems in the past year but decided not to seek care. Most commonly endorsed reasons for not seeking treatment were having developed ways of coping (51.8%), perceptions of insomnia as an expected response to a stressful life situation (48.8%) and having previously spoken to their doctor about difficulty with sleep, but he/she was unable to help (45.2%). Among patients with probable insomnia, 25.1% rated medication treatment as very acceptable, while 43.5% rated nonmedication treatment as very acceptable, and 90.7% reported that they would be likely or very likely to try a nonmedication approach delivered over the internet and tailored to arthritis to improve sleep.

**Conclusion:** Given the prevalence, chronicity and adverse consequences associated with insomnia in individuals with arthritis, this study suggests that efforts designed to increase awareness of the effectiveness of behavioral treatments are needed. Behavioral interventions such as CBTi are acceptable to individuals with arthritis and these findings will guide the evaluation of an internet delivered CBTi program tailored to persons with arthritis experiencing insomnia. Supported by a CIORA grant.

## 11 Baring It All: A Survey and Recommendations on Sexual and Reproductive Health Needs of Women+ With Rheumatic, Inflammatory, and Psoriatic Diseases

Wendy Gerhart (Canadian Spondylitis Association, Phelpsston); Laurie Proulx (Canadian Arthritis Patient Alliance, Ottawa); Rachael Manion (Canadian Association of Psoriasis Patients, Ottawa); Antonella Scali (Canadian Psoriasis Network, Toronto)

**Objectives:** To gain a better understanding of how living with inflammatory, rheumatic and psoriatic diseases affects reproductive and sexual health-related concerns for women+ throughout the life cycle.

**Methods:** Four national patient organizations collaborated to release the Women's Sexual and Reproductive Health Survey on International Women's Day, 2021. People who identified as female (women+) were asked about their experiences with family planning, menopause, sexual health, parenting, pain, mental health, and paying for medications.

**Results:** Over 400 individuals from across Canada participated in the survey. Results were analyzed based on geography, age, and self-identification as a member of a racialized community and/or as LGBTQ2S+. Information was collected about counselling and medication safety related to pregnancy and breastfeeding, postpartum disease flares, pain, and perimenopause/menopause. As well, participants shared their experiences with accessing health benefits (including prescription drug, device and professional services), challenges with paying for medication and their out-of-pocket costs for health products and services.

**Conclusion:** Based on the findings of this survey, to improve outcomes for women+, the following recommendations are made: 1) Destigmatize discussions of reproductive and sexual health in women+ living with these conditions and ensure these discussions are part of routine patient care. We recommend that healthcare providers raise these topics with patients early and often. 2) Healthcare professionals should share patient education resources with women+ with these conditions with a focus on: a) How to communicate effectively with healthcare providers, romantic partners, and loved ones about reproductive and sexual health needs and concerns. b) How to navigate reproductive and sexual health at different life stages (ie, contraception, family planning, parenting, menopause, etc.). c) The impacts of medications on sexual and reproductive health of women+ and on the health of their children. d) The role of mental health as an aspect of sexual health and living with inflammatory arthritis, rheumatic, and psoriatic conditions. 3) Rheumatologists and dermatologists should counsel patients about the impact of medications and other treatments on reproductive and sexual health early and regularly to ensure patients can make informed decisions. 4) Researchers should consider the sex and gender impacts of access to care and treatment, medication safety, mental health, parenting and aging including within racialized communities and LGBTQ2S+ communities to ensure that women+ have the best evidence to inform decision-making.

## 12 Real-world 12-month Retention on Secukinumab Among Psoriatic Arthritis Patients Within the Canadian Spondyloarthritis (CanSpA) Research Network

Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal); Majed Khraishi (Department of Medicine, Memorial University of Newfoundland, St. John's); Robert Inman (Toronto Western Hospital, Toronto); Shamiza Hussein (Novartis, Montreal); Drew Neish (IQVIA, Montreal); Patrick Leclerc (Novartis Canada, Montreal)

**Objectives:** Psoriatic arthritis (PsA) is an immune-mediated disease causing joint pain, stiffness, and swelling that develops in up to 30% of patients with psoriasis, with an estimated prevalence in Canada of up to 0.45%. Treatment aims to minimize disease activity, optimize functional status, improve quality of life and prevent structural damage. Secukinumab has demonstrated efficacy and safety for PsA, with some of the trials accumulating five years of continuous treatment. Real-world (RW) evidence from the EuroSpA collaboration

Table 1: Baseline characteristics of PsA patients

|                                                      | All patients (n= 210) | b/tsDMARD naïve (n= 64) | b/tsDMARD experienced (n= 146) |
|------------------------------------------------------|-----------------------|-------------------------|--------------------------------|
| Age (years), mean (SD)                               | 49.6 (10.8)           | 49.1 (11.4)             | 49.8 (10.6)                    |
| Male, n (%)                                          | 106 (50.5%)           | 36 (56.3%)              | 70 (47.9%)                     |
| BMI (kg/m <sup>2</sup> ), median (IQR), [N missing]  | 29.8 (8.5) [17]       | 30.0 (8.2) [2]          | 29.7 (8.7) [15]                |
| Smoker at index, n (%), [N missing]                  | 52 (27.8%) [23]       | 13 (23.6%) [9]          | 39 (29.5%) [14]                |
| Years since diagnosis, mean (SD)                     | 9.1 (8.8)             | 8.6 (9.8)               | 9.3 (8.4)                      |
| C-reactive protein (mg/L), median (IQR), [N missing] | 5.0 (8.6) [44]        | 4.9 (9.8) [9]           | 5.0 (8.3) [35]                 |
| DAPSA28, median (IQR), [N missing]                   | 21.4 (27.6) [90]      | 19.6 (25.6) [18]        | 24.6 (28.2) [72]               |
| DAS28-CRP, median (IQR), [N missing]                 | 3.0 (1.8) [74]        | 2.8 (1.6) [18]          | 3.0 (1.8) [56]                 |
| PASDAS, median (IQR), [N missing]                    | 4.4 (1.9) [155]       | 4.9 (2.2) [45]          | 4.3 (1.8) [110]                |

was recently published describing secukinumab use in 13 European SpA registries. Nevertheless, there is limited evidence on its RW use in Canada. The objective of this analysis was to use the Canadian Spondyloarthritis (CanSpA) Research Network to describe the Canadian PsA population treated with secukinumab and assess retention at 12 months.

**Methods:** This is an observational, registry-based cohort study of Canadian PsA patients 18-65 years old who attend a clinic participating in the CanSpA research network and have received treatment with secukinumab. The CanSpA research network is a centralized database that collects patient-level information on patient and disease characteristics, medical history, treatment and safety, and outcome pooled from multiple Canadian databases: University Health Network (UHN) in Ontario, Rhumadara\* in Quebec, and Newfoundland SpA Co-morbidities. Patients were indexed on the date they first initiated secukinumab. Retention was assessed at 12 months for the overall population, as well as according to prior use of biologic and targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARD) and sex. Baseline demographics and clinical characteristics are also reported.

**Results:** This preliminary analysis included 210 patients with a mean (SD) age of 49.6 (10.8) years, 50.5% of whom were male (Table 1). Previous experience with a b/tsDMARD was documented at index for 69.5% of the patients. The 12 months' retention rate was 73.2% for the overall population, 81.3% and 69.7% for the b/tsDMARD-naïve and -experienced, and 79.1% and 67.3% for the male and female patients, respectively.

**Conclusion:** This study is the first nationwide study to describe RW retention of secukinumab in 210 Canadian PsA patients. Similar to other registry studies in the U.S. and Europe, the preliminary results of this study showed 12 months' retention rates of secukinumab are high particularly for b/tsDMARD-naïve patients and male patients. These findings further support secukinumab as a first-line option for the treatment of PsA.

### 13

#### Psoriatic Arthritis and COVID-19 — Patient Perspectives in a Large Psoriatic Arthritis Cohort

Neda Pirouzmand (Toronto); Ashish Mathew (Copenhagen Center for Arthritis Research (COPECARE), Toronto); Mitchell Sutton (Toronto Western Hospital, Toronto); Daniel Pereira (University Health Network, Toronto); Vinod Chandran (Krembil Research Institute, Toronto Western Hospital, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto)

**Objectives:** We aimed to estimate the frequency of COVID-19 infection among patients with psoriatic arthritis (PsA), to understand patients' perspectives regarding the pandemic and to evaluate the standard of virtual care offered during the pandemic.

**Methods:** An online survey was conducted between June and September 2021 using the DADOS electronic data capture platform. Eligible participants had a diagnosis of PsA (CASPAR criteria) and had consented to be contacted via email. Convenience sampling was used to draw patients from a database. 591 patients were individually emailed, of whom 193 patients consented and were provided with their unique survey login credentials. The survey was completed by 151/193 patients (78.2%). Participants were asked to answer questions by reflecting on the time period between the second week of March 2020 and their date of survey completion.

**Results:** Of the 151 patients who completed the survey, there were 85 (56%) men, and 66 (44%) women, with a mean age of 58 years and disease duration of 19 years. At their most recent pre-pandemic visit, 40% had active arthritis (n = 148). Comorbidities included lung disease in 38%, diabetes in 18% and cardiac disease in 51% (n = 148). During the pandemic, the mean patient-reported joint symptom severity was 4.12 (on a 0-10 scale, SD = 2.33), skin symptoms was 3.23 (2.14), and overall symptoms was 3.73 (2.07). 111 (74%) respondents found that they would accept the impact of the PsA over the past month for the next few months. Of 78 patients who were tested for SARS-CoV2-19, 4 tested positive. All 4 were admitted to hospital, 2 to Intensive Care Unit. 150/151 patients (99.3%) received at least

one vaccine dose. 59/150 (39.3%) participants believed their PsA medications increased their COVID-19 risk. Virtual consults were conducted for 129 (85%) participants (telephone = 102, Ontario Telemedicine Network = 25, unspecified = 2). A group of 113/129 (88%) participants were happy with their virtual consultations. Most patients (83%) would happily continue with virtual consultations until the pandemic is overcome. The average satisfaction level regarding pandemic care was 7.85 (SD = 2.64) on a 0-10 scale.

**Conclusion:** COVID-19 prevalence was low among our patients. On average, our patients were satisfied with their care during the pandemic. Most of our patients would happily continue with virtual care for the duration of the pandemic.

### 14

#### ASIA: Autoantibodies, Apoptosis and Autophagy

Charmaine van Eeden (University of Alberta, Edmonton); Naima Mohazab (University of Alberta, Edmonton); Desiree Redmond (University of Alberta, Edmonton); Arthur Jones (University of Alberta, Edmonton); Mohammed Osman (University of Alberta, Edmonton); Jan Willem Cohen Tervaert (University of Alberta, Edmonton)

**Objectives:** Silicone Breast implant related illness, a form of autoimmune syndrome induced by adjuvants (ASIA), results in severe patient morbidity – particularly stemming from myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and fibromyalgia (FM). Comparison of cell free mitochondrial DNA (mtDNA) integrity, mitochondrial mass, autoantibodies and cellular death in ASIA and idiopathic FM patients. Understanding these factors may improve our understanding of FM and ME/CFS and can help improve differentiating them.

**Methods:** Markers associated with dysregulated mitochondrial functions and/or autophagy were measured via qPCR and ELISA. Cell free mitochondrial DNA integrity was defined as the ratio of small to large fragments of 16S-RNA. Flow Cytometry with Annexin V and Propidium Iodide was used to evaluate cell death.

**Results:** ASIA and FM patients were indistinguishable via clinically validated surveys. The severity of fatigue, as measured by the multi-dimensional fatigue inventory (MFI) was equivalent in ASIA (16 (2.46)) and Fibromyalgia (16 (2.82)) patients. FM severity, as measured by widespread pain (WPI) and symptom severity scale (SSS) medians were 11 (3.95) and 9 (2.08), or and 10 (4.02) and 8 (2.02) in ASIA or FM patients, respectively. Leukocytes from ASIA patients are more susceptible to death than those of healthy controls (P = 0.004) and Fibromyalgia patients (P = 0.03). Intriguingly, increased mitochondrial fragmentation and mitochondrial mass was observed in ASIA patients when compared to both healthy controls and Fibromyalgia patients. ASIA patients were also twice as likely to test positive for autoantibodies against beta 1 adrenergic and G-protein coupled receptors, than healthy controls.

**Conclusion:** Increased mitochondrial DNA fragmentation (with increased apoptotic cells) and increased Beta 1 adrenergic autoantibodies have both been linked to decreased efferocytosis and autophagy, respectively. Collectively, our data suggests that in contrast to FM patients, ASIA patients may have dysregulation of both of these pathways. Further analysis is required to understand the functional implications of our findings, which may lead to integrating novel therapeutic approaches for these patients. Funding: Dutch Kidney Foundation (17PhD01) Arthritis Society (19-0558).

### 15

#### Rituximab Off-label Maintenance Dosing in Systemic Autoimmune Rheumatic Disease: A Retrospective Review

Carolyn Kasprzak (Alberta Health Services, Calgary); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary); Deonne Dersch-Mills (Alberta Health Services, Calgary); Alexandra Charlton (Alberta Health Services, Calgary)

**Objectives:** Rituximab is used off-label for systemic autoimmune rheumatic diseases (SARDs) including myositis, systemic lupus erythematosus (SLE), scleroderma (SSc), and Sjogren's syndrome (SjS). However, the optimal maintenance dosing regimen has not yet been defined. Our study compared the effi-



cacy and safety of rituximab maintenance “low dose” (500 mg every 6 months) to “high dose” (1g q2weeks x2 every 6 months) in patients with SARDs.

**Methods:** A retrospective cohort design was used to review SARD patients approved for rituximab from October 2008 - March 2021. Data sources included the Alberta Health Services’ Short Term Exceptional Drug Therapy (STEDT) database, Alberta Precision Labs database, Alberta Pharmaceutical Information Network database, and patient charts. Descriptive statistics were used to describe patient outcomes. Between the high dose and low dose groups, Cox Regression analysis was used to compare the number of patients discontinuing rituximab and 2-sided Fisher’s Exact Tests were used to compare the number of flares and hypogammaglobulinemia.

**Results:** 62 patients (44% Myositis, 27% SLE, 16% SSc, 13% SjS) were included. Eleven received high dose, 22 low dose, 17 were switched from high to low, and 12 were atypically dosed. Over a median follow-up of 2.2 years, low dose patients had a higher incidence of flares (36% vs. 27%,  $P = 0.71$ ), and high dose patients appeared 76% less likely to discontinue treatment with rituximab (HR 0.24, 95% CI, 0.03-1.94), though a statistically significant difference was not shown between the high and low dose groups. In patients who continued on rituximab, patient outcome parameters (including patient scales, prednisone dose, number of other concomitant steroid-sparing agents, C-reactive protein and creatinine kinase) appeared similar in both high dose and low dose groups. For patients switched to a lower dose, 29% had an indicator of possible decreased effect, however this did not result in more discontinuations. Reported adverse reactions were low (16%) and similar between all dosing groups. However, more patients in the high dose group experienced hypogammaglobulinemia than in the low dose group ( $P = 0.08$ ).

**Conclusion:** There were fewer individuals on higher dosing rituximab that discontinued and/or had a flare, than on lower dosing, and safety appeared similar; however, our study was not large enough to determine a statistically significant difference between the regimens. Larger clinical trials are needed to assess efficacy and cost-effectiveness using the low dose maintenance rituximab for patients with SARDs.

## 16

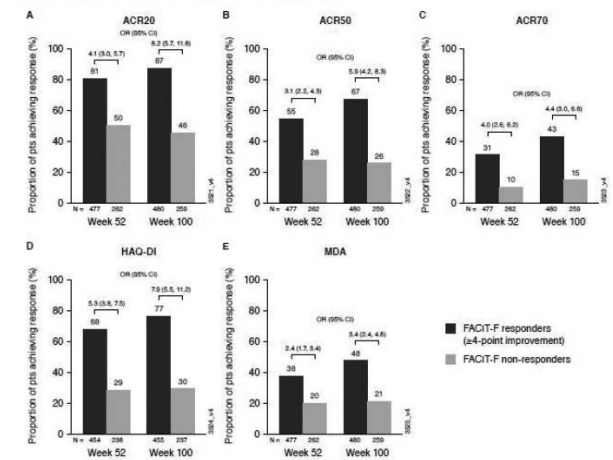
### Relationships Between Fatigue and Hemoglobin/C-Reactive Protein Levels and Associations Between Fatigue and Clinical Response in Patients With Active Psoriatic Arthritis: Results From Two Randomized Controlled Trials of Guselkumab.

Proton Rahman (Memorial University of Newfoundland, St. John’s); Philip Mease (University of Washington, Seattle); Atul Deodhar (Oregon Health and Science University, Portland); Laure Gossec (Sorbonne Université and Rheumatology Department, Hôpital Pitié Salpêtrière, Paris); Arthur Kavanaugh (University of California, San Diego, La Jolla); Soumya Chakravarty (Janssen Scientific Affairs, Horsham); Alexa Kollmeier (Janssen R&D US, La Jolla); Yang Liu (Janssen R&D US, San Diego); Xiwu Lin (Janssen R&D US, Spring House); May Shawi (Janssen Inc, New Jersey); Chenglong Han (Janssen R&D US, Spring House)

**Objectives:** Fatigue is a key patient (pt)-reported symptom of PsA. Post-hoc analyses from the Phase 3 DISCOVER-1 (D1) and -2 (D2) studies explored 1) correlation of fatigue with systemic inflammation (CRP) and hemoglobin (Hgb); 2) relationship between improvements in fatigue and clinical outcomes with guselkumab (GUS).

**Methods:** Pts with active PsA despite standard therapies in D1 (swollen joint count [SJC]  $\geq 3$ , tender joint count [TJC]  $\geq 3$ , CRP  $\geq 0.3$  mg/dL) and D2 (SJC  $\geq 5$ , TJC  $\geq 5$ , CRP  $\geq 0.6$  mg/dL) were randomized 1:1 to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24. Fatigue was evaluated using the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) scale. FACIT-F scores, as well as their correlation with CRP and Hgb were determined in pts with anemia (Hgb  $< 13.5$  [males] or  $< 12$  [females] g/dL) and without anemia through W24. Relationships between FACIT-F score and CRP/Hgb were assessed via a mixed model for repeated measures (MMRM). Associations between FACIT-F response in GUS-treated pts (Q4W+Q8W+PBOàQ4W) and achievement of ACR 20/50/70, Health

**Figure. Achievement of ACR20/50/70, HAQ-DI, and MDA Responses by FACIT-F Response Status Among GUS-treated Patients at W52 and W100 of DISCOVER-2**



Assessment Questionnaire Disability Index (HAQ-DI), and Minimal Disease Activity (MDA) responses were evaluated at W52 for D1/D2 and at W100 for D2.

**Results:** All pts pooled across treatment groups ( $N = 1120$ ), significant correlations between FACIT-F scores and mean CRP/Hgb levels were seen at each visit. Through W24, anemic pts had numerically lower FACIT-F scores (28.7-33.3) vs non-anemic pts (30.3-36.3). Among 112 pts with anemia at BL but not at W24, mean FACIT-F scores improved from 31 (W0) to 37 (W24). MMRM results showed that CRP and Hgb levels were significant predictors of FACIT-F (each  $P < 0.0001$ ). GUS-treated pts achieving  $\geq 4$ -point improvement in FACIT-F score at W52 (52-62% of 381 pts in D1 and 64-66% of 739 bio-naïve pts in D2) were more likely to also achieve ACR20/50/70, HAQ-DI, and MDA responses than FACIT-F non-responders (Figure). With continued GUS through W100, 65% of D2 pts with FACIT-F response showed an even stronger propensity than FACIT-F non-responders for achieving ACR20 (odds ratio [OR] = 8.2 [5.7-11.8]), ACR50 (OR = 5.9 [4.2-8.3]), ACR70 (OR = 4.4 [3.0-6.6]), HAQ-DI (OR = 7.9 [5.5-11.2]), and MDA (OR = 3.4 [2.4-4.8]) responses vs FACIT-F non-responders.

**Conclusion:** In pts with active PsA, CRP and Hgb levels were key predictors of FACIT-F scores. FACIT-F responders were more likely to achieve favorable clinical outcomes through up to 2 years of GUS.

## 17

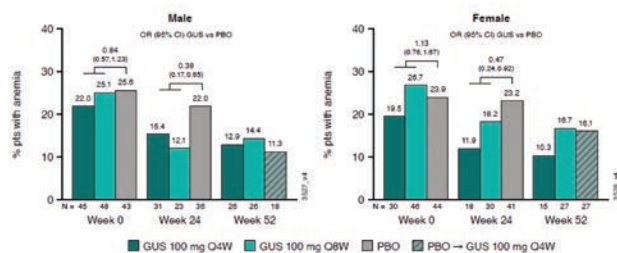
### Guselkumab Improves Anemia in Patients with Active Psoriatic Arthritis: Results From Two Phase 3 Randomized Controlled Clinical Trials

Arthur Kavanaugh (University of California, San Diego, La Jolla); Yang Liu (Janssen R&D US, San Diego); Proton Rahman (Memorial University of Newfoundland, St. John’s); Philip Mease (University of Washington, Seattle); Laure Gossec (Sorbonne Université and Rheumatology Department, Hôpital Pitié Salpêtrière, Paris); Lillian Xu (Janssen Research & Development, LLC, San Diego); Elizabeth Hsia (Janssen Research & Development, LLC/University of Penn, Philadelphia); May Shawi (Janssen Inc, New Jersey); Chenglong Han (Janssen R&D US, Spring House); Marlies Neuhold (Janssen Scientific Affairs, Zug); Atul Deodhar (Oregon Health and Science University, Portland)

**Objectives:** Anemia related to systemic inflammation can be an important feature of PsA. Hemoglobin (Hgb) levels have been shown to be inversely related to disease activity in other rheumatic diseases. This post-hoc analysis assessed the effect of guselkumab (GUS), on anemia in the pooled Phase 3 DISCOVER 1 & 2 trials.

**Methods:** 1120 patients with active PsA, biologic naïve (~30% of DISCOVER-1 patients received 1-2 TNFi), were treated with GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO with crossover

**Figure. Proportion of Pts with Anemia by Sex and Treatment Group Through W52**



to GUS 100 mg Q4W at W24. Treatment was given for 1 (DISCOVER 1) or 2 years (DISCOVER 2). Mean Hgb levels and number of patients with anemia (Hgb < 13.5 g/dL males; < 12.0 g/dL females) were assessed by treatment group through 1 year. A logistic regression model estimated ORs and 95% CI for achieving anemia resolution (anemia at baseline [BL] but not W24). The binary endpoint was anemia responder status at W24 (Y/N); predictors examined included age, sex, SJC/TJC and CRP.

**Results:** Approximately 24% of Males (N = 136) and Females (N = 120) patients were anemic at BL. Patients with anemia at BL had more SJC and TJC, CRP, and fatigue than patients without anemia. For both GUS groups, mean Hgb levels increased from BL through W52 for males and females, particularly among patients who were anemic at BL. For PBO patients, following PBO/GUS at W24, they increased to levels similar to GUS-randomized patients at W52. The proportions of males and females meeting criteria for anemia decreased over time (Figure). Patients with anemia resolution comprised more males, had shorter duration of PsA and lower CRP levels at BL than pts with unresolved anemia at W24. Females and patients with higher BL CRP levels were significantly less likely to achieve anemia resolution at W24 than males and pts with lower BL CRP, respectively. Patients with anemia resolution (N = 112) appeared to exhibit better outcomes at W24 than patients with unresolved anemia (N = 136), with numerically fewer mean SJC ([6.76] vs 6.2 [8.01]) and TJC (10.7 [11.07] vs 12.5 [11.89]), less CRP (0.8 [0.92] vs 2.3 [2.73]), and less fatigue (FACIT-F 37.4 [10.60] vs 33.0 [10.45]).

**Conclusion:** GUS treatment through 1-year increased Hgb levels and lessened the prevalence of anemia. Anemia resolution was more likely in males and patients with lower CRP levels at BL and was associated with improved clinical status relative to patients with persistent anemia.

## 18

### Prevalence of Pre-existing Autoimmune Conditions in Metastatic Melanoma Patients Starting Immune Checkpoint Inhibitors

Alexandra Ladouceur (McGill University, Montréal); Marina Amara De Avila Machado (Research Institute of the McGill University Health Centre, Montréal); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montréal); Cristiano Soares de Moura (The Research Institute of the McGill University Health Centre, Montréal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montréal)

**Objectives:** Since patients with pre-existing autoimmune conditions are commonly excluded from clinical trials with immune checkpoint inhibitors (ICI), we aimed to describe the characteristics of “real-world” metastatic melanoma patients diagnosed with autoimmune conditions and starting ICI.

**Methods:** Using US administrative health claims data from MarketScan, we identified a cohort of adults with metastatic melanoma (based on International Classification of Diseases, ICD physician billing or hospitalization diagnostic codes) who started ipilimumab (IPI), pembrolizumab (PEM), nivolumab (NIVO), or IPI/NIVO over Jan. 2012-July 2019. Cohort entry was defined as the date of first prescription for one of these drugs. Inclusion criteria required health/drug plan coverage for 12 months before cohort entry. Pre-existing autoimmune conditions were identified within the 12 months before cohort entry, based on > 1 ICD physi-

cian billing or hospitalization diagnostic code for the condition of interest. **Results:** We studied 3409 adults with metastatic melanoma (2071 male). Over a quarter (N = 908, 26.6%) had pre-existing autoimmune conditions at baseline. Of these, the most frequent was hypothyroidism (N = 380), myopathy and myositis (N = 76), type I diabetes mellitus (N = 44), rheumatoid arthritis (N = 36) and vitiligo (N = 24). Pre-existing autoimmune conditions were more frequent in women versus men (31.9% vs 23.2%). There was no clear difference in the proportion of patients with pre-existing autoimmune disease among the newly diagnosed metastatic melanoma patients when we compared from one year to the other (from 2012 until 2019). There was a non-significant trend towards fewer patients with pre-existing autoimmune conditions in patients treated with combination IPI/NIVO (22%) versus ICI monotherapy (IPI 26%, NIVO 29% and PEM 28%).

**Conclusion:** Pre-existing autoimmune conditions are present in a considerable number of metastatic melanoma patients receiving ICI. Combination therapy with IPI/NIVO improves outcomes in metastatic melanoma, though with more frequent adverse events. Pre-existing autoimmune conditions might be seen by clinicians as a relative contraindication for combination ICI, but this should be evaluated in future studies.

## 19

### Investigation of the Immune Endophenotypes of Early Rheumatoid Arthritis With Single-cell RNAseq Analysis of Patients' PBMC

Jean Vencic (Université de Sherbrooke, Sherbrooke); Sophie Roux (Université de Sherbrooke, Sherbrooke); Michelle Scott (Université de Sherbrooke, Sherbrooke); Hugues Allard-Chamard (Université de Sherbrooke, Sherbrooke)

**Objectives:** Rheumatoid Arthritis (RA) is an auto-immune disease well-known for the uncertainty of treatment response hence the hypothesis of a plurality of immune endophenotypes all leading to a common RA diagnosis. The project firstly aims to compare the RNA expression profile of immune cells from several RA patients to determine and characterize their distinct immune endophenotypes. Then, the most relevant biomarkers for each endophenotype will be used to create a tool capable of relating a new expression profile to a characterized endophenotype. For now, although various studies have looked at immune cell RNA expression in RA, too few combine the resolution level of using single-cell RNA sequencing (scRNAseq) and the unbiased expression of untreated patients.

**Methods:** To conduct this project, scRNAseq data have been generated from peripheral blood mononuclear cell samples of patients presenting with RA, before initiation of treatments. The point of using resolution at the cellular level is that different cell types are activated and act differently during symptomatic flares. For the bioinformatics analysis pipeline, after a step of quality-filtering, cells are clustered using the Leiden algorithm and the differentially expressed genes for each cluster are computed to find a cell type annotation.

**Results:** For now, two scRNAseq samples (a control and an untreated RA at diagnosis) of around 200 million reads each were used to build the bioinformatics analysis pipeline. As a preliminary study, several clustering methods were tested concluding that the unsupervised Leiden algorithm presented the best results. Moreover, the quality of the cluster annotation was evaluated while artificially reducing the input number of reads showing robust quality until around 50%. Finally, the genes differentially expressed between the whole two samples were computed as if it was regular bulk-RNAseq and the cellular pathways related to those genes were fetched showing as expected enrichment in immune pathways.

**Conclusion:** This unique project aiming at comparing RNA expression between untreated RA at diagnosis patients is yet in its early steps. However, the construction of the bioinformatics pipeline and the preliminary analysis show interesting results and have laid the groundwork for the analysis of new samples. The enriched cellular pathways recently found in a first intention approach tend to show the need for a more profound analysis comparing RNA expression of specific cell subtypes which will be explored in the near future thanks to the single-cell method used in this project.

### Novel Variants in RELA Driving Familial Chronic Mucocutaneous Ulceration Resembling Behcet's Disease: A Case Series

Jason An (Division of Rheumatology, St. Michael's Hospital, University of Toronto, Toronto); Pallavi Pimpale (NIH, Bethesda); Madeline Couse (The Hospital for Sick Children, Toronto); Dilan Dissanayake (Division of Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto); Daniela Dominguez (The Hospital for Sick Children, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto); Amina Lodhi (McMaster University, Burlington); Christina Pelajo (Hospital Pequeno Principe e Hospital de Clínicas - UFPR, Curitiba); Ivona Aksentijevich (NIH, Bethesda); Ronald Laxer (Division of Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto)

**Background:** Recently, monogenic forms of Behcet disease (BD) have been described. Here we report two families with novel variants in the RELA gene driving monogenic Behcet's-like disease.

**Cases:** Family I: A 29-year-old female was seen at St Michael's Hospital, Toronto, for childhood-onset orogenital ulcers and flares of body pains. Tests revealed elevated inflammatory markers during flares, but negative/normal ferritin, ANA, ENA, C3/4, RF, and serum amyloid A. Her mother, two maternal aunts, maternal grandmother, and her 9-year-old son had similar symptoms. The patient was started on colchicine and etanercept for presumed BD, leading to a significant improvement in orogenital ulcers. Exome sequencing revealed a novel variant in RELA (c.1144C > T, p. Gln382\*), shared between the proband and her son. Pathogenicity was bioinformatically suggested by its absence in control databases, CADD score of 31, and a low observed:expected score (0.038) indicating haploinsufficiency. The variant introduces a premature termination codon within the Transcriptional Activation Region, predicted to lead to a truncated protein that disrupts NF- $\kappa$ B signaling. ClinVar lists several other loss-of-function variants in RELA as pathogenic. The variant thus met criteria for "Likely Pathogenic" according to the American College of Medical Geneticists (ACMG) classification.

Family II: A family was referred to the National Institutes of Health for an undifferentiated inflammatory disease in a father and six (of his nine) children. Clinical features included orogenital ulcers, arthralgias, fatigue, rash, and folliculitis in most affected members. Lab findings (in some) included elevated inflammatory markers and positive ANA. All six affected children were diagnosed with BD and received various immunomodulatory medications. A gene panel performed in five affected individuals (two were unavailable for testing) revealed a shared heterozygous frameshift mutation (c.1311\_1312insA, p. E438Rfs\*9) in RELA. The frameshift is predicted to result in a truncated protein, impacting function. Pathogenicity of this variant was suggested by its absence in control databases, a low observed:expected score (0.04; pLI of 1), and "Likely Pathogenic" classification by ACMG.

**Discussion:** RELA belongs to the NF- $\kappa$ B family and is a key homeostatic regulator of mucosal immunity and integrity. Pathogenic variants of RELA may either reduce protein expression or generate truncated RELA proteins with impaired function. This dominantly inherited immune dysregulatory disorder resembles BD where the range and severity of manifestations depend on the specific variant. These cases illustrate the utility of genetic studies in patients with undifferentiated systemic inflammatory disease, for which the molecular diagnosis can inform treatment choices as well as family planning.

### 21

#### COVID-19 Vaccine Uptake Among Individuals With Immune-mediated Inflammatory Diseases

Jessica Widdifield (Sunnybrook Research Institute, ICES, University of Toronto, Toronto); Lihi Eder (Women's College Research Institute, University of Toronto, Toronto); Simon Chen (ICES, Toronto); Jeffrey Kwong (ICES, Toronto); Carol Hitchon (University of Manitoba, Winnipeg); Diane Lacaille (Arthritis Research Canada, University of

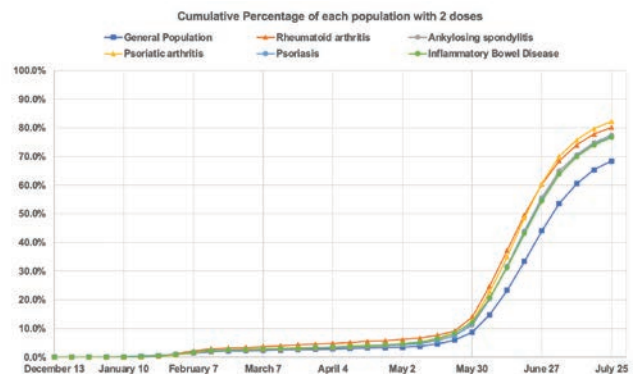
British Columbia, Vancouver); Antonio Avina-Zubieta (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Richmond); Lawrence Svenson (University of Calgary, Calgary); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal)

**Objectives:** Ontario's COVID-19 vaccination program commenced in December 2020, initially prioritizing seniors 80 years and older. On April 27, high density 'hot spot' regions began vaccinating adults 45 years and older, and the provincial eligibility for immunocompromising health conditions commenced May 3-6 along with adults 50 years and older, before expanding to all ages on May 18. It is unknown whether individuals with Immune-Mediated Inflammatory Disease (IMID) have been adequately vaccinated or whether delays in uptake have occurred, which may be a result of vaccine hesitancy (owing to unknown safety and efficacy concerns in this population who were excluded from trials, negative experiences from prior vaccines, and the changing guidance on immunosuppressive treatment adjustments). We compared the COVID-19 vaccine uptake among IMID patients and the general population.

**Methods:** We studied all residents 16 and older who were alive and actively enrolled in the Ontario Health Insurance Plan (OHIP) on December 14, 2020, when the vaccination program began. Individuals with selected IMIDs - Rheumatoid arthritis (RA), Ankylosing spondylitis (AS), Psoriatic Arthritis (PsA), Psoriasis (PsO), Inflammatory Bowel Disease (IBD) - were identified using disease-specific case definitions applied to health administrative data. Vaccination status was extracted from the Ontario Ministry of Health's COVaxON data source between December 2020 and July 31, 2021. The weekly cumulative proportion of individuals with 1 dose and 2 doses (separately determined) up until the end of study period is expressed as the vaccinated proportion of each population.

**Results:** Our study population comprised 12,417,126 general population comparators, and 138,301 individuals with RA, 28,506 with AS, 17,645 with PsA, 182,299 with PsO, and 108,782 with IBD. By end of July 2021, the cumulative proportion with at least 1 dose was 77.7% for the general population, 86.6% for RA, 84.5% for AS, 88.4% for PsA, 84.1% for PsO, and 83.8% for IBD. The cumulative proportion with 2 doses by July 31, 2021, was 68.4% among the general population, and ranged 76-82% for IMIDs (Figure). Among those vaccinated, the majority of individuals (72%) in both the general population and IMID groups received BNT162b2 (Pfizer-BioNTech) vaccines. The median interval between 1st and 2nd doses ranged between 60-70 days for BNT162b2, 53-61 days for mRNA-1273 (Moderna), and 70-74 days for ChAdOx1 nCoV-19 (AstraZeneca/COVISHIELD).

**Conclusion:** While implementation of COVID-19 vaccination programs has differed provincially, these Ontario estimates are the first to reassuringly show higher uptake and coverage of COVID-19 vaccines among IMID patients.



### 22

#### Evaluating the Effects of Continuity of Rheumatology Care on Patient Outcomes for Individuals With Rheumatoid Arthritis

Abel Davtyan (University of Toronto, Toronto); Jin Luo (Institute for



Clinical Evaluative Sciences, Toronto); Lih Eder (Women's College Research Institute, University of Toronto, Toronto); Gillian Hawker (University of Toronto, Toronto); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary); Carter Thorne (The Arthritis Program Research Group, Newmarket); Jessica Widdifield (Sunnybrook Research Institute, ICES, University of Toronto, Toronto)

**Objectives:** We examined whether continuity of rheumatology care influences survival, hospitalization, and emergency department (ED) visits for RA patients.

**Methods:** We studied a closed inception cohort of RA patients diagnosed between 2000-2009 (and a minimum of 2 rheumatology visits). Following cohort entry, rheumatology continuity was categorized into 3 mutually exclusive groups: 1) High Continuity (at least 2 rheumatology visits within first year, followed by annual rheumatology visits); 2) Intermediate (rheumatologist visit occurred during > 50% of the measurement periods/years); and 3) Low (those not retained in rheumatology care). A landmark analysis (with the landmark set at 5 years from diagnosis-following exposure measurement period) was performed to separately determine all-cause mortality, unscheduled hospitalization, and ED visit rates determined from landmark date to end of follow-up (2019) for each group. To estimate rate ratios across exposure groups, modified Poisson regression models (with robust error variances) were used, adjusting for demographics, comorbidities, primary care continuity, and rheumatology access/supply measures. Excess mortality was obtained by subtracting the mortality in the general population from the observed age/sex mortality rate in each RA group.

**Results:** Among 38,528 (95.5%) incident RA patients who survived until the landmark date, 22,221 (57.7%) were categorized as having high continuity, 6,636 (17.2%) as intermediate, and 9,671 (25.1%) as low. The high continuity group had a higher proportion of females, residents from urban areas, and higher socioeconomic status. Across all outcomes, the intermediate group had the highest rates. Age/sex adjusted mortality rates were 22.8 (95% CI 21.8-23.7), 26.2 (95% CI 25.0-27.7), and 23.5 (95% CI 23.3-23.8) deaths per 1000 PY for the low, intermediate, and high groups, respectively (Table). High and low continuity age/sex adjusted mortality rates were not statistically different. However, relative to the high group, mortality rate ratios were 0.95 (95% CI 0.9-1.00) for low, and 1.05 (95% CI 1.00-1.11) for intermediate. The observed general population mortality rate was 19.4 deaths (95% CI 19.2-19.7) per 1000 PY and all groups had significantly excess mortality rates. For ED visits, the high continuity group had the lowest rates. For hospitalizations, the low continuity group had significantly lower rates and rate ratios.

**Conclusion:** RA patients with high continuity of rheumatology care have fewer ED visits, and improved survival. The lower rates for individuals who were not retained in rheumatology care likely reflect those with milder or time-limiting disease. However, all 3 groups portrayed higher excess mortality compared to the general population, underscoring the importance of rheumatology care.

|                                                   | LOW CONTINUITY                | INTERMEDIATE CONTINUITY       | HIGH CONTINUITY               |
|---------------------------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Crude Mortality Rate per 1000 PY                  | 23.5<br>(95% CI 22.5-24.5)    | 24.6<br>(95% CI 23.4-25.9)    | 23.2<br>(95% CI 22.5-23.8)    |
| Age-sex Adjusted Mortality Rate per 1000 PY       | 22.8<br>(95% CI 21.8-23.7)    | 26.2<br>(95% CI 25.0-27.7)    | 23.5<br>(95% CI 23.3-23.8)    |
| Adjusted Mortality Rate Ratio                     | 0.95<br>(95% CI 0.90-1.00)    | 1.05<br>(95% CI 1.00-1.11)    | REF                           |
| Excess Mortality Rate per 1000 PY                 | 3.4<br>(95% CI 2.6-4.1)       | 6.8<br>(95% CI 5.8-8.1)       | 4.1<br>(95% CI 4.1-4.2)       |
| Age-sex Adjusted ED visit Rate per 1000 PY        | 699.7<br>(95% CI 690.6-708.8) | 773.8<br>(95% CI 759.8-787.7) | 635.7<br>(95% CI 630.7-640.7) |
| Adjusted ED visit Rate Ratio                      | 1.12<br>(95% CI 1.08-1.16)    | 1.14<br>(95% CI 1.08-1.20)    | REF                           |
| Age-sex Adjusted Hospitalization Rate per 1000 PY | 180.8<br>(95% CI 177.5-184.1) | 207.4<br>(95% CI 203.0-211.8) | 193.5<br>(95% CI 191.4-195.6) |
| Adjusted Hospitalization Rate Ratio               | 0.94<br>(95% CI 0.91-0.98)    | 1.02<br>(95% CI 0.98-1.06)    | REF                           |

23

**Disease Modifying Anti-rheumatic Drugs (DMARDs) and Biologic Therapy Use During Pregnancy: A Single-center Mixed Methods Study**  
 Lauren Glick (University of Toronto, Toronto); Dharini Mahendira (St. Michael's Hospital, University of Toronto, Toronto); Justin Shamis

(University of Toronto, Toronto); Taneisha McGhie (University of Toronto, Toronto)

**Objectives:** Rheumatic diseases including inflammatory arthritis and connective tissue diseases can be associated with significant morbidity in women of child-bearing age. These diseases and their treatments can impact fetal and maternal outcomes. Although there is growing evidence to support the safety of many anti-rheumatic drugs (ARDs) in pregnancy, patients often discontinue treatments in the peripartum period due to concern of fetal harm. This study sought to identify perinatal medication use patterns at a single tertiary care center and to understand patient perspectives surrounding their use.

**Methods:** Electronic medical records were reviewed for women attending the rheumatic diseases in pregnancy clinic, a rheumatology clinic with subspecialty input, at St. Michael's Hospital in Toronto, Canada, from January 2013 until March 2020. A 12-item questionnaire was administered to women attending this clinic from January 2018 until September 2021. Data was analyzed using descriptive statistics.

**Results:** Thirty-eight women and forty-five pregnancies were identified, with rheumatoid arthritis (N = 12, 32%), systemic lupus erythematosus (N = 18, 27%) and seronegative arthritis (n = 8, 16%) representing the majority. Twenty-nine patients (60%) were exposed to disease modifying anti-rheumatic drugs (DMARDs) and eight patients (16%) were exposed to biologics during pregnancy. Of those who experienced peri-partum medication changes, the highest proportion (57%) occurred pre-partum. Patients who received pre-pregnancy counselling were more likely to undergo medication adjustments prior to conception and were more likely to utilize a DMARD or biologic during pregnancy. Our survey was completed by 22 respondents. Nineteen women (86%) reported that they would consider ARD use in pregnancy with the highest degree of comfort reported for DMARDs (N = 19, 86%), compared to steroids (N = 3, 14%), non-steroidal anti-inflammatory drugs (N = 6, 27%) and biologics (N = 3, 14%). Seventeen participants felt that their questions were answered by health care providers, with the majority (82%) describing their rheumatologist as their primary information source. 41% did not feel that the provided resources were adequate to assist with their decisions about medication use in pregnancy.

**Conclusion:** While the majority of women in our cohort continued on ARDs during pregnancy, most survey respondents reported discomfort with use of many ARDs, particularly, anti-TNF biologics. This discrepancy between patient perspectives and available evidence is important to consider when counseling patients on ARD use in pregnancy. Respondents relied on their rheumatologist as their primary information source, highlighting the important role specialists can play in informing patient decisions. Resources provided to patients in this area were perceived as inadequate by many individuals, demonstrating an area for future improvement.

24

**IgG4-Related Prostatitis Manifesting as Urinary Obstruction in a 28-Year-Old Male**

Drew Bowie (University of British Columbia, Division of Rheumatology, Vancouver); Aria Jazdarehe (University of British Columbia, Vancouver); Azin Ahrari (University of British Columbia, Vancouver); Silvia Chang (Radiology, University of British Columbia, Vancouver); Henry Tran (University of British Columbia, Vancouver); Shahin Jamal (Division of Rheumatology, University of British Columbia, Vancouver); Luke Chen (Hematology, University of British Columbia, Vancouver); Karen Tran (University of British Columbia, Vancouver)

**Background:** Immunoglobulin G4-related disease (IgG4-RD) is a systemic lymphoproliferative disorder characterized by elevated serum IgG4 levels and tumefactive lesions which can involve nearly every organ system. Involvement of the prostate is rare but has been reported in limited cases.

**Case Description:** A 28-year-old man of Asian descent with a history of sinusitis and priapism presented to hospital with rigors and obstructive urinary symptoms. He was diagnosed with IgG4-RD one month prior to presentation, following pathological analysis of a submandibular mass

which demonstrated chronic sclerosing sialadenitis. On presentation, white blood cell count, C-reactive protein, and prostate serum antigen levels were all within normal limits. Examination was notable for a large, firm prostate, and a foley catheter was inserted. Contrast CT of the abdomen was unremarkable. Further workup revealed elevated serum IgG4 levels (9.22 g/L), and he was subsequently started on prednisone 35 mg daily. Imaging to screen for systemic IgG4-RD involvement demonstrated paravertebral soft tissue involvement and he was given a dose of rituximab 1000 mg IV. MRI revealed diffuse prostatitis. Five days after starting prednisone and one day after receiving rituximab, he successfully passed trial of void and was discharged home.

**Conclusion:** IgG4-related prostatitis is a rare and underrecognized manifestation of IgG4-RD. Our case highlights the need to consider IgG4-related prostatitis as an etiology of urinary obstruction in young individuals. Resolution of symptoms following treatment with steroids may be diagnostic of IgG4-related prostatitis, and may potentially avoid the need for invasive diagnostic procedures such as prostate biopsy.

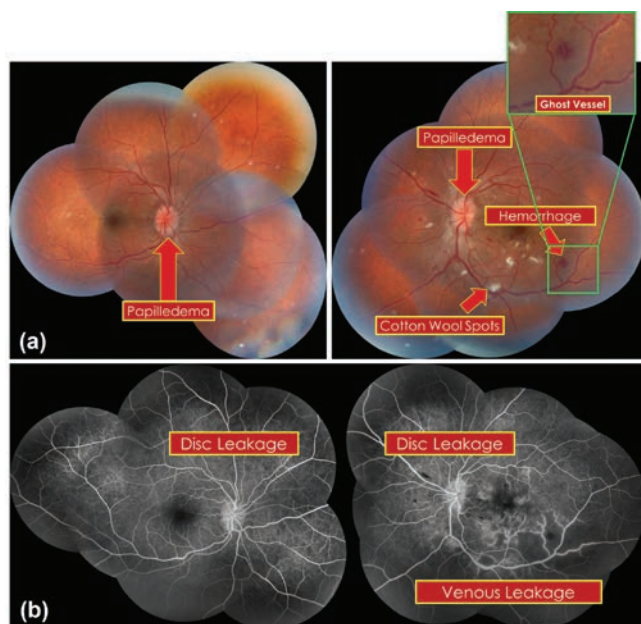
## 25

### More than Meets the Eye: A Case of Retinal Vasculitis in SLE

Hengameh Kheirkhah (University of Calgary, Calgary); Etienne Benard-Seguín (University of Calgary, Calgary); Elzbieta Kaminska (University of Calgary, Calgary); Fiona Costello (University of Calgary, Calgary); Kevin Warrian (University of Calgary, Calgary); May Choi (University of Calgary, Calgary)

**Background:** While retinal vasculitis as a primary manifestation of SLE is uncommon, SLE also accounts for only 4% of cases of retinal vasculitis. Here, we present a case of a young female with SLE, who primarily presented with retinal vasculitis and raised intracranial pressure.

**Case Description:** A 26-year-old female presented with a one-month history of bilateral decreased visual acuity and 3-month history of headache. Ophthalmology assessment showed bilateral enlarged blind spots, and dilated fundus exam (Figure 1a) revealed bilateral disc edema and peripapillary hemorrhages with cotton wool spots in the left eye. A fluorescein angiogram (Figure 1b) revealed significant retinal vasculitis involved both the arteries and veins in the left eye. A CT venogram was unremarkable. Cranial and orbital MR imaging showed hyperintensity of the intracranial optic nerve segments, and punctate hyperintense signal changes in the subcortical white areas of the brain. The cerebrospinal fluid (CSF) analysis revealed an elevated opening pressure, leukocyte count of  $17 \times 10^6/L$ , red blood cell count of  $1 \times 10^6/L$ , protein of 0.24 g/L, with negative gram stain and



cytopathology. Her infectious and malignancy workup were unremarkable. She was also investigated for underlying autoimmune etiology. As she had thrombocytopenia (platelet  $92 \times 10^9/L$ ), leukopenia (white blood cell  $2.7 \times 10^9/L$ ), positive antinuclear antibody ( $\geq 1:640$ , speckled pattern), +anti-dsDNA, +anti-Smith, and hypocomplementemia, she was diagnosed with SLE and had also met the 2012 Systemic Lupus International Collaborating Clinics (SLICC) classification criteria for SLE. She also had antibodies to chromatin, Smith (Sm), Sm/ribonucleoprotein (RNP), and RNP-68.

She was initially treated with pulse methylprednisolone for three days and then prednisone, hydroxychloroquine, and mycophenolate mofetil. However, her follow-up retinal assessments over the next month showed only a partial reduction in her retinal vasculitis with persistent paracentral scotoma so she was promptly switched to cyclophosphamide. Although both mycophenolate mofetil and cyclophosphamide have been shown to reduce vasculopathy and resolve cotton wool spots, there is limited evidence to support their role in preventing the progression of retinal vaso-occlusion. A repeat retinal assessment is currently pending.

**Conclusion:** This case highlights the need to consider a broad differential diagnosis for retinal vasculitis, including SLE. Retinal vasculitis in SLE, although uncommon, can be the first manifestation of SLE and needs to be recognized early so that timely, aggressive treatment can be initiated.

## 26

### A Rare Case of Interstitial Lung Disease in Type I Cryoglobulinemic Vasculitis

Katherine Majerovich (University College Dublin, Dublin); Gerard Cox (McMaster University, Hamilton); Stephanie Garner (McMaster University, Hamilton)

**Background:** Type I cryoglobulinemic vasculitis is a subtype of cryoglobulinemic vasculitis characterized by precipitated immunoglobulin complexes that circulate in plasma and may occlude medium- and small-sized vessels. Commonly affected organ systems include the skin, kidneys, and peripheral nervous system. Pulmonary system involvement is rare.

**Case Description:** A 42-year-old man was admitted to hospital in the Spring of 2020 when he presented with purpuric lesions, fingertip ulcerations, arthritis and dry cough. He was found to have type I cryoglobulinemia secondary to paraproteinemia via monoclonal gammopathy of undetermined significance (MGUS), kappa light chain IgG subtype. A CT chest at that time was normal. He initially responded to steroids, and he was prescribed cyclophosphamide. This was stopped due to profound neutropenia requiring dose reduction and Filagistrim. Steroids were tapered. At review by Hematology, it was felt that intervention was not indicated for his MGUS. During this period of time his cough progressed, and he developed dyspnea on exertion. He was then referred for management to a combined Rheumatology & Respiriology clinic. Upon review at the combined clinic he was found to be hypoxic and CXR demonstrated mixed interstitial and airspace disease. His presenting symptoms of fatigue, night sweats, digital ischemia and purpuric lesions had returned. He was reinitiated on prednisone. A follow-up CT revealed continued bibasilar opacities, ground-glass changes, and septal thickening. COVID-19 screen was negative. Bronchoscopy and bronchoalveolar lavage were negative for alveolar hemorrhage and infection. Surgical lung biopsy revealed organizing pneumonia with fibrosis. At this point an application for Rituximab was made and prednisone was increased to 50 mg with clinical response. A follow-up pulmonary function test revealed improved but persisting moderately severe restrictive impairment, with significant diffusion impairment (44%). Currently, he is much improved clinically and has been able to return to work. Over four months, his cutaneous manifestations improved and are now managed with calcium channel blockers.

**Conclusion:** This case illustrates a unique scenario of interstitial lung changes in the context of type I cryoglobulinemic vasculitis; although pulmonary vasculitis may be associated with diffuse alveolar hemorrhage, interstitial lung changes are not commonly encountered. This case shows an example of interstitial lung changes in context of cryoglobulinemic vasculitis that responded to treatment with high-dose steroids and Rituximab.



### miR-190a-5p and miR-26b-5p Are Potential miRNA Biomarkers for Psoriatic Arthritis

Omar Cruz Correa (University Health Network, Toronto); Darshini Ganatra (Krembil Research Institute, University Health Network, Toronto); Ameth Garrido (Krembil Research Institute, University Health Network, Toronto); Rohan Machhar (Toronto Western Hospital, Toronto); Starlee Lively (Krembil Research Institute, Toronto); Mohit Kapoor (Krembil Research Institute, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto)

**Objectives:** Psoriatic arthritis (PsA) is an immune-mediated inflammatory arthritis, that develops in up to 30% of psoriasis patients. PsA significantly increases morbidity and may increase mortality risk. Early diagnosis and prompt management of inflammation are essential for preventing joint damage and disability. However, we currently lack the means of predicting which psoriasis patients will develop PsA, and a large number of patients remain undiagnosed. Micro RNAs (miRNAs) regulate gene expression and have been associated with the pathogenesis of immune-mediated disorders. With this research, we identified miRNAs associated with the development of PsA.

**Methods:** We obtained serum samples from 28 PsA patients satisfying CASPAR criteria, 35 cutaneous psoriasis patients (PsC, confirmed not to have PsA by a rheumatologist), and 28 healthy controls. miRNA expression was assessed through next-generation sequencing. Total RNA was isolated from serum samples, miRNA sequencing libraries were prepared and sequenced on an Illumina HiSeq2500 following the 75 base-pair single read protocol, at a depth of 12-13 million reads/sample which allows detection of low expressed transcripts. After quality control, reads were aligned to known human miRNA sequences (miRbase version 22). miRNAs with low expression (10 counts in at least 20 samples) were excluded from further analysis. Differential expression was assessed by linear modelling with empirical Bayes moderation as implemented in the Limma R package. Models were corrected for sequencing batch, age, sex and duration of psoriasis. Identification of miRNA gene targets was carried out using the microRNA Data Integration Portal (mirDIP) and enrichment of specific biologic pathways was examined using the pathway Data Integration Portal (pathDIP). Analysis was restricted to literature curated pathways and experimentally detected protein-protein interactions with a prediction confidence of 0.99.

**Results:** Two miRNAs (miR-190a-5p and miR-26b-5p) were significantly down-regulated in PsA patients when compared to healthy

controls (FDR-adjusted p-value < 0.05, Figure 1). Expression levels of miR-190a-5p were also significantly lower in PsA patients compared to PsC patients. Significantly enriched pathways targeted by both of these miRNAs included canonical and non-canonical Wnt, TGF beta, and Hedgehog signaling pathways.

**Conclusion:** We identified serum expression levels of miR-190a-5p and miR-26b-5p as potential biomarkers for the development of PsA.

28

### Reduced IgG Sialic Acid Content: A Distinctive Characteristic of Symptomatic Anti-Nuclear Antibodies Positive Individuals

Carolina Munoz-Grajales (University of Toronto, Toronto); Sindhu Johnson (Toronto Scleroderma Program, Mount Sinai Hospital; Division of Rheumatology, Toronto Western Hospital; Department of Medicine, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Zareen Ahmad (Toronto Scleroderma Program, Division of Rheumatology, Mount Sinai Hospital; Department of Medicine, University of Toronto, Toronto); Dennisse Bonilla (Toronto Western Research Institute, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto); Arthur Bookman (University of Toronto, Toronto); Joan Wither (Division of Genetics and Development, Krembil Research Institute; Division of Rheumatology, University Health Network; Department of Immunology, University of Toronto, Toronto)

**Objectives:** Currently the immune changes that lead to the transition from asymptomatic Anti-Nuclear Antibody (ANA) positivity to symptomatic disease are unknown. Studies in our laboratory revealed that increased levels of proinflammatory factors, particularly TNF- $\alpha$ , are restricted to symptomatic ANA+ individuals. Based upon this observation and the similarities between the ANA-associated SARDs (Systemic Lupus Erythematosus (SLE), Sjogren's Syndrome, and Systemic Sclerosis) and Rheumatoid Arthritis, where progression from asymptomatic to symptomatic autoimmunity is associated with reduced sialylation of the IgG Fc region and accumulation of pro-inflammatory cytokines, herein we proposed to investigate whether or not a similar shift in sialylation occurs as asymptomatic ANA+ individuals progress to SARD.

**Methods:** An enzyme-linked lectin assay was developed that uses Sambucus Nigra Agglutinin, a lectin that binds sialic acid, to detect sialylated IgG. This assay was then used to determine the extent of sialylation on IgG purified from the plasma of 10 ANA- healthy controls (ANA-HC), 15 ANA+ asymptomatic (ANA+NS) individuals, and 15 SLE patients. Differences in the ability of the IgG to elicit inflammation between the ANA+ groups were investigated by stimulating monocyte derived dendric cells (moDC) from ANA-HC with aggregated IgG. IL-6 and TNF- $\alpha$  in the culture supernatants and serum were measured by ELISA. Cellular profiling of peripheral blood immune populations was performed using flow cytometry.

**Results:** The sialic acid content of IgG was significantly reduced in SLE patients compared to ANA+NS individuals ( $P = 0.0229$ ) and ANA-HC ( $P = 0.0012$ ) (Figure 1A). There was a negative correlation between sialylation of IgG and serum levels of TNF- $\alpha$  ( $\rho = -0.54$ ,  $P = 0.0039$ ) and proportion of T follicular helper cells ( $\rho = -0.37$ ,  $P = 0.032$ ) (Figure 1B) in the patients from which the IgG was purified. When moDC were stimulated with heat-aggregated IgG from ANA+NS and SLE patients, there was a trend to increased production of these cytokines, as compared to heat-aggregated IgG from ANA-HC, which was statically significant for TNF- $\alpha$  ( $P = 0.008$ ) (Figure 1C) in SLE. The levels of TNF- $\alpha$  produced in response to heat-aggregated IgG demonstrated a negative correlation with the extent of IgG sialylation ( $\rho = -0.5$ ,  $P = 0.02$ ) (Figure 1D).

**Conclusion:** The reduced levels of sialylated IgG and their association with increased levels of TNF- $\alpha$  production in SLE patients, as compared to ANA+NS individuals and ANA-HC, are compatible with the concept that

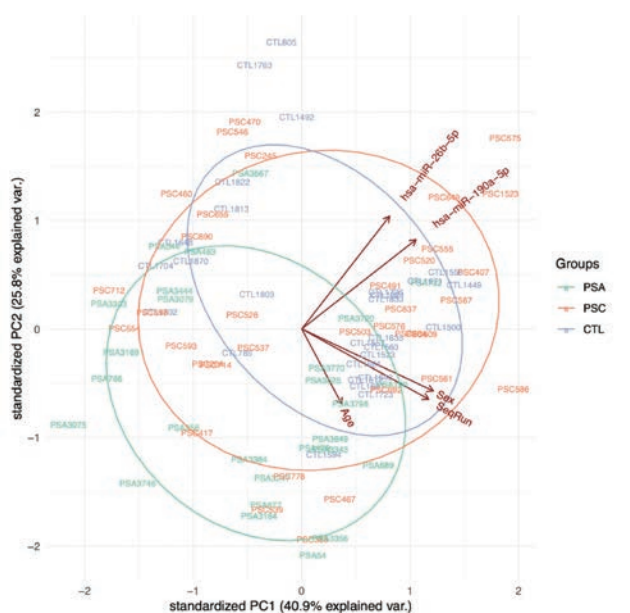
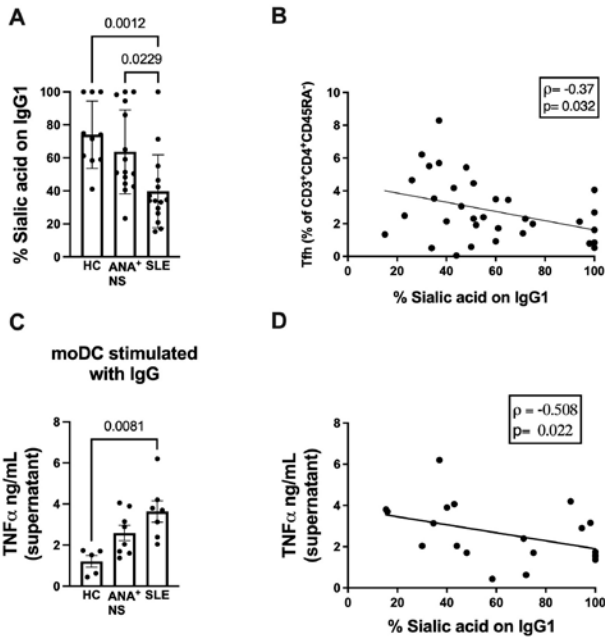


Figure 1. Principal component analysis of samples included in the study. The first two components shows the tendency of lower expression of miR-190a-5p and miR-26b-5p in psoriatic arthritis patients (PsA) when compared to cutaneous psoriasis patients (PsC) and healthy controls (CTL).



**Figure 1**



de-sialylation of IgG promotes the transition from asymptomatic to symptomatic autoimmunity in SARD.

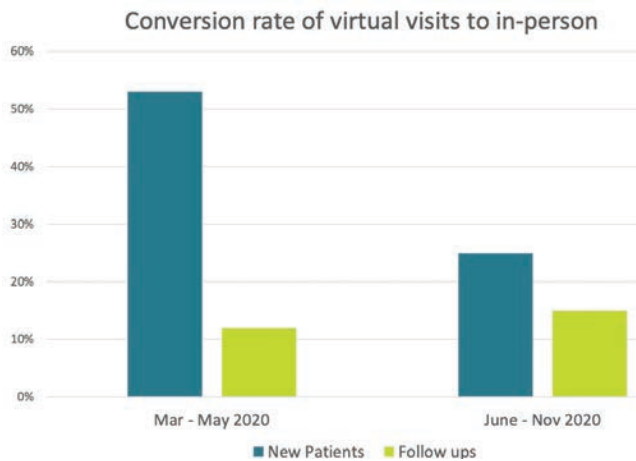
29

**Rheumatology Virtual Triage: Factors Determining Patients' Appropriateness for In-person or Virtual First Triage Visit**

Aos Aboabat (University of Toronto, Toronto); Chandra Farrer (Women's College Hospital, Toronto); Natasha Gakhal (Women's College Hospital, Toronto)

**Objectives:** 1. To measure the conversion rate of virtual rheumatology visits to in-person (IP) visits between: March – May 2020: All new consultations were assessed virtually during wave 1 of the pandemic. June – November 2020: Post intervention. 2. To identify reasons for conversion of virtual visits to IP, recognize common features of a successful virtual visit as well as design future interventions to decrease conversion rate to incorporate telemedicine more effectively in rheumatology practice.

**Methods:** Primary outcome: Conversion rate of virtual visits to IP at baseline and post intervention. Intervention: A change to the triaging algorithm was made where the first 2 urgent categories were booked preemptively as IP initial visits (ie, vasculitis, inflammatory arthritis, SLE & acute gout) in June 2020. We reviewed and collected data from 20 patients' charts who were assessed virtually pre intervention (Mar – May 2020) and 20 patients' charts who were assessed post intervention (June – Nov 2020).



**Results:** Conversion rates from virtual visits to an IP visit were: Mar – May 2020: 53% for new visits & 12% for follow-up visits. June – Nov 2020: 25% for new visits & 15% for follow-up visits (Figure). Physical examination and bedside procedures were the only causes for conversion: Physical exam was the major cause for conversion of new consults (80%) & majority of these new referrals were phone consults. Bedside procedures were the major cause of conversion of follow-up visits (66.6%).

**Conclusion:** Virtual care can be very effective in rheumatology practice in providing follow-up and new consultations. Studies are needed to validate the virtual rheumatologic examination. Future interventions are needed to decrease conversion rates. We will continue to collect data on utilization of investigation. The rate of conversion rate was largely affected by the pandemic case counts and the hospital capacity to accommodate in-person visits.

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**Implementing the EIA Detection Tool to Improve Triage Accuracy and Reduce Wait Times: A Quality Improvement Project**

Preet Gujral (London Rheumatology, University of Ottawa, Ottawa); Stephanie Gottheil (London Rheumatology, Western University, London); Chiara Gottheil (London Rheumatology, London); Joseph Carson (London Rheumatology, Western University, London)

**Objectives:** Rheumatology has one of the longest wait times for subspecialists in Ontario, exacerbated by the shift to virtual care during the COVID-19 pandemic. Long wait times lead to delays in treatment and may increase joint damage. The objective of this quality improvement study was for all urgent rheumatology patients in our new community clinic to be seen within 4 weeks of referral by July 31st, 2022. The first phase of our project, funded by a CRA Summer Studentship, aimed to develop and test one change idea by August 20, 2021.

**Methods:** Our study design was based on the Model For Improvement with Plan-Do-Study-Act (PDSA) cycles. Outcome measures were consultation wait times and referral triage accuracy. After establishing baseline performance, we conducted a root cause analysis through fishbone diagramming and process mapping with stakeholders. Change ideas were developed using a driver diagram and PICK chart. We focused on improving the triage accuracy of unclear referrals by asking patients to complete the validated Early Inflammatory Arthritis (EIA) Detection Tool through an online process before scheduling their appointment. In PDSA 1, we tested the process with one mock patient. In PDSA 2, we modified instructions and tested it with four patients who had unclear referrals. In PDSA 3, we refined the administrative process and continued testing over four weeks.

**Results:** We conducted a baseline analysis using run charts and descriptive statistics for 1237 referrals between April 2020 -June 2021. Referrals were assigned a pre-consult score based on urgency: P1 (emergent), P2 (urgent), P3 (non-urgent), P4 (elective). A post-consult score (P1-P4) was assigned based on rheumatologist diagnosis after initial consultation. Baseline triage accuracy was 73%, and more non-urgent cases were expedited (24%) than urgent cases delayed (14%). Average wait times for urgent cases increased from 11 days in August 2020 to 44 days in August 2021. Root cause analysis suggested that inaccurate triage may be contributing to lengthening wait times. We implemented the new triage process in August 2021. Over four weeks, 13/72 referrals (18.1%) had unclear urgency. All 13 patients completed the EIA Tool within two days. Most patients (12/13, 92.3%) scored above the EIA cut-off; however, we have not yet evaluated post-consultation triage accuracy.

**Conclusion:** We implemented the validated EIA Detection Tool into our triage process. Next, we will evaluate whether the process improves triage accuracy and reduces wait times for urgent referrals.

31

**Pain Experiences and Decision-making Needs for Pain Management Among Young Women with Hypermobile Ehlers-Danlos Syndrome and Generalized Joint Hypermobility Spectrum Disorder**

Anneey Houston (University of Ottawa, Ottawa); Gail Paterson (The

Arthritis Society, Ottawa); Julie Richer (Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa); Karine Toupin-April (University of Ottawa and Children's Hospital of Eastern Ontario Research Institute, Ottawa)

**Objectives:** Pain is one of the most common symptoms experienced by individuals with hypermobile Ehlers-Danlos syndrome (hEDS) and generalized hypermobility spectrum disorder (G-HSD). Understanding decision-making needs is crucial to develop interventions to help patients better manage their condition. Yet, little is known about the experiences and needs of these young women. We wished to describe experiences of pain, as well as decision-making needs related to pain management among young women with hEDS and G-HSD.

**Methods:** Using a qualitative descriptive study design, we conducted semi-structured virtual interviews of young women diagnosed with hEDS or G-HSD aged 18 to 30 years of age. Participants were recruited through social media. Interview guide questions were based on the Ottawa Decision Support Framework. Interviews were audio-recorded, transcribed verbatim and analyzed using simple content analysis.

**Results:** 10 women with hEDS and four women with G-HSD participated in the interviews. Of those, nine had postural orthostatic tachycardia syndrome, three had mast cell activation syndrome and two had rheumatic conditions (ie, juvenile idiopathic arthritis and ankylosing spondylitis). Participants regularly experienced various types of pain: musculoskeletal (n = 14, mean = 6 on a scale of 0 [no pain] to 10 [worst pain]), gastrointestinal (n = 13, mean = 4.69), headaches/migraines (n = 12, mean = 5.71) and neuropathic (n = 5). The following themes emerged: (1) Complexity of hEDS and G-HSD pain; (2) Multidimensional impact of pain; (3) Desperation for pain relief; (4) Satisfaction of their pain management strategies; (5) Lack of patients' and healthcare providers' knowledge on diverse pain management options; (6) Lack of communication and decision support about pain management from healthcare providers; (7) Desire for shared decision making.

**Conclusion:** This study revealed the important impact of hEDS and G-HSD pain on the daily lives of individuals and the unmet decisional needs for evidence-based information and communication about pain management strategies. These findings can inform the development of a decision support intervention to support decision-making on pain management options.

### 32

#### Beyond the VAS in Rheumatoid Arthritis: Results From a Multi-modal Pain Assessment Pilot Study

Dana Wiens (University of Manitoba, Winnipeg); Cairistin McDougall (University of Saskatchewan, Saskatoon); Irene Smolik (University of Manitoba, Winnipeg); Yvonne Lee (Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston); Hani El-Gabalawy (University of Manitoba, Winnipeg); Liam O'Neil (University of Manitoba Faculty of Health Sciences, Winnipeg)

**Objectives:** Pain is a common experience amongst Rheumatoid Arthritis (RA) patients and their first-degree relatives (FDR), but objectively measuring pain remains a challenge. To better understand how to capture and quantify pain, we sought to undertake a multi-modal pain assessment pilot study.

**Methods:** In this pilot study, we enrolled 15 RA patients and 14 FDR (n total = 29), and recorded baseline demographics. QST, which included pressure pain threshold (PPT) and temporal summation (TS) was performed. Participants completed a digital pain map using custom software on an Android Tablet to capture pain location and intensity on an electronic homunculus. Pain map scores were calculated using a weighted formula. We analyzed the data using Wilcoxon signed rank test, chi-square, spearman rank correlation and linear regression where appropriate.

**Results:** The median age for FDR and RA were 43 and 44 years respectively. There were no differences in trapezius PPT (4.62 kgf IQR 2.8 vs 4.09 kgf IQR 4.9, P = 0.631) or forearm TS (1.67 IQR 2.3 vs 2.34 IQR 2.3, P = 0.497) between RA and FDR. Peripheral sensitization was also similar

between RA and FDR, with no differences in joint and non-joint PPT (all p-values > 0.05). VAS pain was higher in RA (64 IQR 44.5) compared to FDR (29 IQR 57), but this did not reach statistical significance (P = 0.335). Digital pain map scores were significantly higher in RA patients (29.7 IQR 24.0) compared to FDR (8.7 IQR 16.2, P = 0.009). Pain map score correlated strongly with mHAQ score, a standardized measure of functional disability (R = 0.78, P < 0.001). No significant association between PPT or TS and mHAQ was observed (R = -0.16, R = 0.28 respectively). Using linear regression, we found that pain map score was independently associated with mHAQ after controlling for age, sex, opioid use, and RA diagnosis ( $\beta$  = 1.30, 0.61 to 1.99, P < 0.001).

**Conclusion:** Digital pain maps are a novel and feasible method to capture pain that distinguishes RA patients from FDR and is closely associated with functional disability. Central and peripheral sensitization were similar between RA and FDR, suggesting that changes to pain processing may occur in individuals at risk of developing RA in the absence of joint inflammation.

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#### Diagnostic Testing in IgG4-related Disease

Daniel Onwuka (Artus Health Centre, Vancouver); Andre Mattman (Medical Biochemistry, University of British Columbia, Vancouver); Shing Zhan (Medical Biochemistry, University of British Columbia, Vancouver); Grace van der Gugten (Department of Pathology and Laboratory Medicine, St Paul's Hospital, Vancouver); Luke Chen (Hematology, University of British Columbia, Vancouver); Mollie Carruthers (Rheumatology, University of British Columbia, Vancouver)

**Objectives:** We compared the performance characteristics of Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS) and Binding Site Immunonephelometry (BSIN) to aid in the diagnosis of IgG4-related disease (IgG4-RD) in an extension analysis.

**Methods:** We analyzed a total of 881 IgG4 measurements taken between December 2011 and December 2020, which were collected from provincial laboratory providers. The ACR/EULAR criteria were used to determine whether patients were positive for IgG4-RD. Using this data, we compared LC-MS/MS and BSIN according to sensitivity, specificity, positive and negative predictive values, and Area Under the Curve (AUC) of their respective Receiver Operating Characteristic (ROC) curves. Sensitivity and specificity calculations were derived from the optimal thresholds defined by the Youden index.

**Results:** IgG4 measurements were taken using BSIN for 43 IgG4-RD positive cases and 174 disease negative cases. IgG4 measurements were taken using LC-MS/MS for 102 IgG4-RD positive cases and 562 disease negative cases. The specificity of BSIN and LC-MS/MS was 92.53% and 86.30%, respectively. The sensitivity of BSIN and LC-MS/MS was 79.07% and 86.27%, respectively. The AUC of BSIN and LC-MS/MS was 90.36% and 92.16%, respectively.

**Conclusion:** In this larger study, we found that BSIN performed slightly better than LC-MS/MS in terms of specificity, whereas LC-MS/MS performed slightly better than BSIN in terms of sensitivity. LC-MS/MS remains an important, alternate test method for the diagnosis of IgG4-RD. Best Abstract on Research by an Undergraduate Student Award.

### 34

#### Developing a Novel 3D Printed Knee Model for Teaching and Learning Ultrasound-guided Knee Joint Arthrocentesis and Injection

Leigha Rowbottom (Alberta Health Services, Calgary); Eugene Krustev (University of Calgary, Calgary); Maria Powell (University of Calgary, Calgary); Kristina Roche (Memorial University of Newfoundland, St. John's); Craig Martin (St. John's); Evan Walters (Memorial University of Newfoundland, St. John's); Irene Ma (University of Calgary, Calgary)

**Objectives:** Knee joint arthrocentesis and injections are essential procedures amongst medical trainees. However, previous studies have found medical providers lack competency and confidence in performing these procedures. Knee joint simulators can improve learner experience, confidence, and

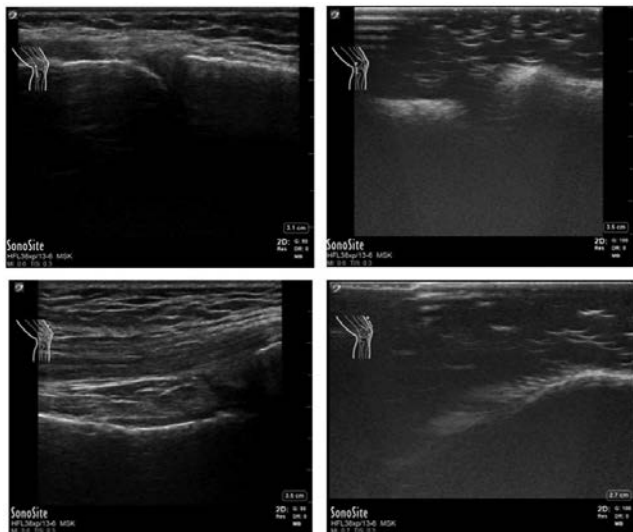


Figure 1: Clockwise from left hand corner, Image A – Longitudinal view of medial human knee with joint line visualized; Image B – Longitudinal view of medial simulator knee with joint line visualized; Image C – Longitudinal view of suprapatellar region on a human knee; Image D – Longitudinal view of suprapatellar region of simulator knee.

learning outcomes with joint injections and aspirations. However, commercially available simulators are expensive, thus limiting their access and use in medical training. We have developed a novel cost-effective 3D-printed knee model as an alternative simulation tool for use in medical education. The aim of this study was to utilize an expert feedback driven approach to develop and refine our 3D-printed knee model as a tool for teaching ultrasound (US) guided knee joint injections and arthrocentesis.

**Methods:** An US session was conducted by a point of care US expert (n = 1) using the 3D printed knee simulator and a human knee joint as a comparator. Still images and cineloops were obtained of the simulator and human knee using a high frequency (6-13 MHz) linear transducer (X-PORTE, FUJIFILM Sonosite, Inc., Bothell, WA). Qualitative feedback was collected to assess anatomical fidelity (sonographic resemblance) and overall user experience.

**Results:** Comparative images were obtained from several standard anatomical sites on both the simulation and real knee joints (Figure 1). Based on expert feedback, the overall length of the suprapatellar region was felt to be too short but did not limit sonographic evaluation. Presence of a hyper-echoic structure limited far field visualization in both the suprapatellar and the infrapatellar region. The patella and joint lines were readily visualized with confidence. US imaging on the simulator required the use of maximum gain, which limited user experience.

**Conclusion:** Further development and refinement of the 3D printed model is required to improve visualization of the femur, as well as differentiation of musculature from synovial fluid and periarticular structures. Our plan is to improve the existing model utilizing this expert feedback and then obtain further qualitative data from a panel of US experts and rheumatologists on our improved prototype. Ultimately, our goal is to develop a cost-effective and realistic knee simulator that can be used to teach medical trainees US-guided knee joint injections and aspirations.

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### Greater Preeclampsia Knowledge in SLE With a Specific Educational Tool: Interim Analyses

Joo Young (Esther) Lee (McGill University, Division of Experimental Medicine, Montreal); Arielle Mendel (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Isabelle Malhamé (McGill University Health Centre, Department of Medicine, Division of General Internal Medicine, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Évelyne Vinet (Department of Medicine,

Division of Rheumatology, McGill University Health Centre, McGill University, Montreal)

**Objectives:** Pregnant women with systemic lupus erythematosus (SLE) are at high risk of preeclampsia, leading to substantial maternal and fetal morbidity. Aspirin reduces preeclampsia risk, but recent studies suggest aspirin is used only in a minority of SLE pregnancies. It is necessary to improve preeclampsia counselling and management in this population. Therefore, we are conducting the PREPARE (PREeclamPsia knowledge & Aspirin adheRence in lupus prEgnancies) trial, a randomized controlled trial (RCT), evaluating an educational tool on preeclampsia knowledge and aspirin adherence in SLE pregnancies. We present interim analyses of this tool's effect on preeclampsia knowledge.

**Methods:** We are recruiting consecutive pregnant SLE women up to the 16th gestational week at 5 Canadian SLICC centres (ie, Montreal, Halifax, Quebec, Winnipeg, and Calgary) since May 2018. Participants are randomly assigned to receive either the specifically designed educational tool (intervention) or standard of care (control). At baseline (ie, first trimester) and second trimester visits, the participants completed self-administered preeclampsia knowledge questionnaires (scored out of 30 by the research team blinded to the intervention). The current analyses include participants enrolled at the coordinating center, accounting for nearly half of the total planned sample size. We performed a univariate linear regression analysis to assess the effect of the educational tool on preeclampsia knowledge (ie, mean score difference between the two groups from baseline to second trimester visit).

**Results:** Thirty-eight pregnant SLE women were included in the study, with 20 exposed to the intervention. Baseline characteristics were well-balanced between the two groups with similar mean maternal age between the intervention (32.9 years, standard deviation, SD, 4.6) and control group (34.2 years, SD 4.1) and proportion of participants with post-secondary education (Table 1). The difference in mean preeclampsia knowledge scores between second trimester and baseline visits in the intervention group was 5.3 points (95% CI 1.6, 8.9) and in the control group was 0.9 points (95% CI -2.9, 4.7). The mean difference in knowledge scores for those receiving the educational tool was 4.4 points higher (95% CI 0.6, 8.2) than those receiving standard of care.

**Conclusion:** Approximately midway into the trial, we observed an improvement in preeclampsia knowledge from baseline to second trimester visit in pregnant women with SLE who received the educational tool compared to those who did not. Our RCT is well-poised to provide a new evidence-based approach to improve preeclampsia knowledge in pregnant women with SLE, which could help to optimize aspirin use and outcomes in SLE pregnancies. Supported by a CIORA grant.

Table 1. Baseline characteristics in the study population.

|                                          | Intervention (n=20) | Control (n=18) |
|------------------------------------------|---------------------|----------------|
| Age, mean years (SD)                     | 33 (± 4.6)          | 34 (± 4.1)     |
| Gestational age, mean days (SD)          | 62 (± 17.9)         | 62 (± 21.0)    |
| Received post-secondary education, n (%) | 15 (83%)            | 13 (76%)       |
| Ethnicity, n (%)                         |                     |                |
| Caucasian                                | 6 (30%)             | 12 (67%)       |
| Native North American                    | 1 (5%)              | 0              |
| Hispanic                                 | 4 (20%)             | 0              |
| Black                                    | 4 (20%)             | 3 (17%)        |
| Asian                                    | 4 (20%)             | 2 (11%)        |

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### Higher Prevalence of Aspirin Use With a Specific Educational Tool in SLE Pregnancies: Interim Results

Joo Young (Esther) Lee (McGill University, Division of Experimental Medicine, Montreal); Arielle Mendel (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Isabelle Malhamé (McGill University Health Centre, Department of Medicine, Division of General Internal Medicine, Montreal); Sasha Bernatsky



(McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal)

**Objectives:** Pregnant women with SLE are at substantial risk of preeclampsia. International practice guidelines recommend aspirin (ASA) in this population as it has shown to halve preeclampsia risk in high-risk women. However, recent evidence shows that only a quarter of pregnant SLE women use ASA. It is therefore imperative to understand ASA use patterns to promote ASA adherence. To do so, we are conducting the PREPARE (PREeclamPsia knowledge & Aspirin adheRence in lupus prEgnancies) trial, a randomized controlled trial, evaluating a specifically designed educational tool. We present the tool's effect on ASA use and adherence as well as ASA dosages used at the 2nd trimester visit according to the intervention status.

**Methods:** We are recruiting consecutive pregnant SLE women up to the 16th gestational week at 5 Canadian SLICC centres. Participants were randomly assigned to receive the educational tool (intervention) or standard of care (control). At baseline (ie, 1st trimester) and 2nd visits (ie, 2nd trimester for ongoing pregnancies or 4-8 weeks after miscarriage), the participants completed self-reported ASA questionnaires and the modified Adherence to Refills and Medications Scale (ARMS). We measured the proportion of ASA users, mean ARMS scores, and dosage at both visits. We estimated a 95% CI for difference in proportion of ASA users between the groups using the Wilson procedure and mean ARMS score difference between the groups using the Student's test.

**Results:** Thirty-eight participants were included with 20 exposed to the intervention. Baseline characteristics, including maternal age and proportion of participants who had post-secondary education, were well-balanced (Table 1). Baseline ASA use prevalence was 65% and 44% in the intervention and control group, respectively. Proportion of ASA users at the 2nd visit were 100% in the intervention and 83% in the control group, with a difference of 17% (95% CI -2.7, 39.2). At the 2nd visit, mean ARMS score was not different between the two groups [difference of 0.3 points (95% CI -0.8, 1.4)]. Among ASA users who did not have miscarriage, 7% and 18% used 80-81mg, and 93% and 82% used 160-162mg in the intervention and control group, respectively.

**Conclusion:** Halfway into the trial, we observed a trend for higher ASA use in pregnant SLE women who received a specifically designed educational tool compared to those receiving standard of care. The PREPARE trial is on track to provide a new evidence-based approach to optimize aspirin use and potentially improve outcomes in this population. Supported by a CIORA grant.

Table 1. Baseline characteristics in the study population.

|                                          | Intervention (n=20) | Control (n=18) |
|------------------------------------------|---------------------|----------------|
| Age, mean years (SD)                     | 33 (± 4.6)          | 34 (± 4.1)     |
| Gestational age, mean days (SD)          | 62 (± 17.9)         | 62 (± 21.0)    |
| Received post-secondary education, n (%) | 15 (83%)            | 13 (76%)       |
| Ethnicity, n (%)                         |                     |                |
| Caucasian                                | 6 (30%)             | 12 (67%)       |
| Native North American                    | 1 (5%)              | 0              |
| Hispanic                                 | 4 (20%)             | 0              |
| Black                                    | 4 (20%)             | 3 (17%)        |
| Asian                                    | 4 (20%)             | 2 (11%)        |

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### Immunization Rates Among Rheumatoid Arthritis Patients in a Canadian Outpatient Clinic

Kristie Chau (Royal College of Surgeons in Ireland, Toronto); Jocelyn Chow (Newcastle University - School of Medical Education, Newcastle Upon Tyne); Gabrielle Sraka (McMaster University, Hamilton); Elaine Soucy (Credit Valley Rheumatology, University of Toronto, Mississauga); Andrew Chow (Credit Valley Rheumatology, University of Toronto, Mississauga)

**Objectives:** To assess immunization rates among patients with rheumatoid arthritis taking JAK inhibitors and biologic agents in an outpatient clinical setting

**Methods:** We conducted a retrospective chart review of the electronic health records of patients at an urban rheumatology clinic between July 2010 to July 2021. Our study sample consisted of active and inactive patients diagnosed with rheumatoid arthritis who were previously or are currently being treated with the following classes of medications: JAK inhibitors (tofacitinib, upadacitinib, baricitinib), Anti-CD20 (rituximab), Anti-IL6 (tocilizumab, sarilumab), Anti-TNF (infliximab, etanercept, adalimumab, golimumab, certolizumab) and CTLA4-Ig (abatacept). We collected data regarding vaccination status for herpes zoster and pneumococcus and influenza vaccination within 12 months of their last clinic visit, in line with Canadian guidelines for immunization in patients who have immune mediated disorders or immunosuppression.

**Results:** 143 Active and Inactive Rheumatoid Patients were identified. The proportions of patients currently on or previously trialed JAK inhibitors, Anti-CD20, Anti-IL6, Anti-TNF and CTLA4-Ig were 73.4%, 5.6%, 3.5%, 14.7% and 2.8%, respectively. In total, 84.6% of patients had received at least one dose of the herpes zoster vaccine while 62.9% and 7.7% of patients were immunized against pneumococcus and the influenza virus respectively. The rates of immunization varied vastly amongst different drug classes as follows: JAK inhibitors: herpes zoster 81.9%, pneumococcal 62.8% and influenza 6.7%; Anti-CD20: herpes zoster 87.5%, pneumococcal 87.5% and influenza 12.5%; Anti-IL6: herpes zoster 100%, pneumococcal 40% and influenza 40%; Anti-TNF: herpes zoster 95.2%, pneumococcal 61.9% and influenza 4.8%; CTLA4-Ig: herpes zoster 75%, pneumococcal 50% and influenza 0%

**Conclusion:** Immunization coverage has significantly improved across herpes zoster and pneumococcal vaccine types and medication subgroups. There has been an increase, compared to data collected in 2020, in herpes zoster immunizations among patients on anti-CD20, anti-IL6, anti-TNF and CTLA4-Ig drug classes. The immunization rate of herpes zoster vaccine in patients on JAK inhibitors has remained stable compared to the previous audit in 2020. The increase in herpes zoster vaccination uptake may have resulted from continued and further improved identification and surveillance of patients who do not have any documented vaccination. However, there has been a significant decrease in influenza vaccine uptake in all medication subgroups compared to the previous audit. Increasing the scale and scope of these efforts along with identifying other limiting factors to vaccine uptake is required to further improve vaccination rates and documentation for the pneumococcal and influenza vaccines.

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### Drug Survival of JAK Inhibitors and Biologic DMARDs in Rheumatoid Arthritis Patients

Jocelyn Chow (Newcastle University - School of Medical Education, Newcastle Upon Tyne); Gabrielle Sraka (McMaster University, Hamilton); Kristie Chau (Royal College of Surgeons in Ireland, Toronto); Elaine Soucy (Credit Valley Rheumatology, University of Toronto, Mississauga); Andrew Chow (Credit Valley Rheumatology, University of Toronto, Mississauga)

**Objectives:** To perform a local practice audit to assess the duration of drug survival amongst Rheumatoid Arthritis (RA) patients taking JAK-inhibitors and biologic DMARDs in a Canadian outpatient clinic.

**Methods:** Using the electronic medical records, patients prescribed a JAK inhibitor with a diagnosis of RA were included. Start and stop date, line of treatment and reasons for stopping were collected. The review included dates between July 2010 to August 2021. Median, mean, and range were calculated using a 95% confidence interval. The primary outcome is drug survival defined by days between start and stop date. If the drug was not discontinued, the stop date was noted as August 15, 2021. The drugs examined include: JAK-inhibitors (Tofacitinib, Baricitinib, Upadacitinib), anti-CD20 monoclonal antibodies (Rituximab), Interleukin-6 inhibitors (Tocilizumab, Sarilumab), TNF-alpha inhibitors (Infliximab, Etanercept, Adalimumab, Golimumab, Certolizumab), and T-cell (Abatacept).

**Table 1: the drug survival durations of n = 115 patients with RA on 12 different drugs listed from shortest to longest**

| Drug name    | n  | Median (days) | Range     | Mean (days) | CI interval    |
|--------------|----|---------------|-----------|-------------|----------------|
| Upadacitinib | 31 | 150.0         | 25, 485   | 195.9       | 143.6, 248.2   |
| Sarilumab    | 3  | 223.0         | 85, 2956  | 1088.0      | -408.0, 2584.0 |
| Certolizumab | 6  | 292.0         | 120, 681  | 346.3       | 170.6, 522.0   |
| Adalimumab   | 28 | 334.0         | 68, 4652  | 692.0       | 293.0, 1031.0  |
| Abatacept    | 28 | 375.5         | 77, 4569  | 1007.4      | 563.0, 1451.8  |
| Rituximab    | 14 | 443.0         | 1, 4327   | 757.1       | 207.4, 1306.8  |
| Baricitinib  | 12 | 473.0         | 90, 797   | 471.0       | 322.9, 619.1   |
| Tofacitinib  | 86 | 486.5         | 36, 2526  | 617.7       | 512.3, 722.4   |
| Golimumab    | 28 | 487.0         | 147, 3586 | 689.4       | 437.5, 941.3   |
| Infliximab   | 33 | 531.0         | 55, 3045  | 611.8       | 420.0, 803.6   |
| Tocilizumab  | 29 | 546.0         | 77, 41248 | 2444.9      | -302.7, 5192.5 |
| Etanercept   | 38 | 663.0         | 29, 37589 | 2520.0      | 588.0, 4452.0  |

**Results:** A total of 115 patients with RA were recruited on 12 different drugs. The drug survival durations are listed from shortest to longest.

**Conclusion:** Drug survival for all drugs examined did not demonstrate any correlation between class of drug and duration contrary to the current literature. This study's population may be biased as most patients were failing multiple agents, for example JAK-inhibitors were mostly third- or fourth-line treatments, albeit drug survival did not decrease in duration. Comparing first-line JAK inhibitors and first-line biologics may demonstrate different lengths of drug survival as opposed to these results. To further this investigation, predictors of drug survival could be examined using disease activity and drug class switching using a larger sample size.

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#### Intra-individual Change in Cognitive Function Among Adults With Systemic Lupus Erythematosus: A Longitudinal Markov Analysis

Stefan Perera (University of Toronto, Department of General Internal Medicine, Toronto); Richard Cook (University of Waterloo, Department of Statistics and Actuarial Science, Waterloo); Ker-Ai Lee (University of Waterloo, Department of Statistics and Actuarial Science, Waterloo); Patricia Katz (University of California San Francisco, Professor of Medicine and Health Policy, Division of Rheumatology, Department of Medicine, San Francisco); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** Cognitive impairment is prevalent among patients living with Systemic Lupus Erythematosus (SLE). Studies have focused on the prevalence of cognitive impairment in SLE cross-sectionally; however, there is little data examining SLE and cognition both longitudinally and at the intra-individual level. Our study aims to investigate how cognitive function changes in participants with SLE over time, and to understand what variables are associated with cognitive improvement or decline.

**Methods:** A total of 1281 participants with SLE from a single center were followed annually for seven years using telephone interviews. Cognition was measured annually using the Hopkins Verbal Learning Test-Revised (HVLTR-verbal learning and memory) and the Controlled Oral Word

Association Test (COWAT-verbal fluency). The Systemic Lupus Activity Questionnaire (SLAQ) and Center of Epidemiologic Studies Depression Scale (CESD) were used to assess disease severity and depression. A two-state Markov Analysis was used to model probabilities of transition between cognitive states: lower cognitive function [Z score < -1.5] and higher cognitive function [Z score ≥ -1.5] (Figure 1). Logistic regression analyses were used to examine the association between selected clinical variables and cognitive change.

**Results:** Most SLE patients demonstrated stability in cognition longitudinally. However, among those with change as assessed by the COWAT, individuals with SLE were 19 times more likely to improve in cognition than to experience cognitive decline. Using the COWAT, higher levels of depressive symptoms by CESD were associated with less likelihood of experiencing improvement in cognition (RR 0.98; 95% CI 0.96-0.99); and greater disease severity by SLAQ was associated with an increased risk of cognitive decline (RR 1.05; 95% CI 1.02-1.09). Using the HVLTR, participants were 2.8 times as likely to improve in cognition than to experience cognitive decline. Increasing age (RR 1.02; 95% CI 1.01-1.03) and higher education level (RR 1.82; 95% CI 1.28-2.58) were associated with a greater likelihood of improving cognition assessed by HVLTR. Higher disease severity by SLAQ (RR 1.02; 95% CI 1.01-1.03) and depressive symptoms by CESD (RR 1.05; 95% CI 1.03-1.07) were associated with cognitive decline.

**Conclusion:** Most individuals with SLE experience stability in cognitive function over time. However, among those with SLE that do experience change in cognition, improvement in cognition was more common than decline. Increasing age and higher education levels were associated with a greater chance of cognitive improvement. Self-reported higher levels of SLE disease severity and depressive symptoms were barriers to experiencing cognitive improvement and were risk factors for experiencing cognitive decline in both assessments.

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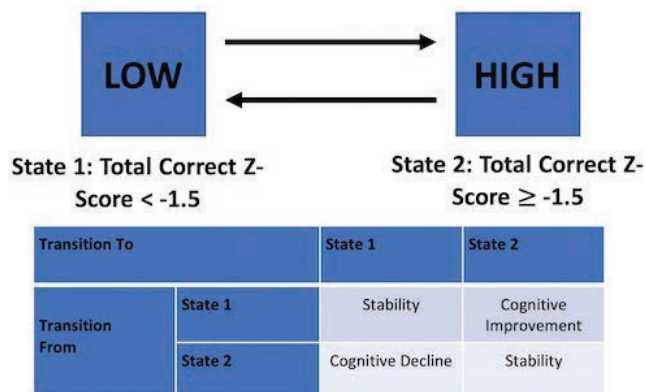
#### "We Don't All Speak With One Voice": A Qualitative Study Exploring Perceptions of Including Patient Preferences in Clinical Trial Design

Megan Thomas (University of Calgary, Calgary); Deborah Marshall (University of Calgary, Calgary); Adalberto Loyola-Sanchez (University of Alberta, Calgary); Susan Bartlett (McGill University, Montreal); Annelies Boonen (Department of Rheumatology, Maastricht University Medical Center, Maastricht); Liana Fraenkel (Yale University, New Haven); Laurie Proulx (Canadian Arthritis Patient Alliance, Ottawa); Marieke Voshaar (Radboud University, Amsterdam); Nick Bansback (University of British Columbia/Arthritis Research Canada, Vancouver); Rachelle Buchbinder (Monash University, Melbourne); Francis Guillemin (Université de Lorraine, Nancy); Mickael Hilgsmann (Maastricht University, Maastricht); Dawn Richards (Canadian Arthritis Patient Alliance, Toronto); Pamela Richards (Bristol NHS Trust, Bristol); Beverly Shea (University of Ottawa, Ottawa); Peter Tugwell (University of Ottawa, Ottawa); Marie Falahee (University of Birmingham, Birmingham); Glen Hazlewood (University of Calgary, Calgary)

**Objectives:** Researchers must make many decisions when designing clinical trials, and these decisions influence the evidence on treatments that is generated. Patients with rheumatic diseases can express preferences on various elements of their care, including available treatments, and this information can be used to help design clinical trials. Our aim was to explore stakeholder perceptions of using preference elicitation methods to design clinical trials within rheumatology.

**Methods:** We conducted 60-minute semi-structured interviews with patients, and clinicians/researchers within rheumatology using the Zoom platform. We used a purposive + snowball sampling approach to recruit participants. Interviews were audio-recorded and transcribed using Zoom's auto-transcript feature. We used Braun and Clarke thematic analysis to analyze our data.

**Results:** We interviewed 17 patients, and 9 clinicians/researchers, until reaching data and inductive thematic saturation in both groups. From our analyses, we developed three themes related to including patient prefer-



ences in clinical trial design: Overall perceptions, Barriers, and Facilitators. Patients and clinicians/researchers generally shared the perception that patient preferences are important to consider. A key barrier identified was the additional work required to measure or incorporate preferences into trial design. A key facilitator was the movement towards patient engagement in research to encourage including patient preferences when designing trials. **Conclusion:** Our findings allowed us to consider the potential applications of patient preferences to trial design according to stakeholders involved in the trial process. There may be a need to increase awareness and understanding on preference elicitation methods as an appropriate research strategy. Future research should be conducted to develop comprehensive guidance on how to include patient preferences when designing clinical trials in rheumatology.

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#### **Retention and Tolerability of Mandated Biosimilar Switching for Etanercept and Infliximab at One Year: A Large Single-center Experience in British Columbia**

Jason Kur (University of British Columbia, Vancouver); James Connell (Calgary)

**Objectives:** In 2019, British Columbia Pharmacare mandated switching of all patients on Enbrel and Remicade for rheumatology indications to an approved biosimilar version. We aim to review the retention rates after one year in patients with rheumatic diseases who switched between biosimilar medications (etanercept or infliximab) due to mandated changes in BC Pharmacare coverage for patients with rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis.

**Methods:** We conducted a retrospective chart review of patients who switched from one biosimilar (Enbrel, Remicade) to another (Inflectra, Erelzi, Brenzys). Retention rates and associated adverse events (inefficacy or side effects) were reported. The team reviewed 76 patient charts from one outpatient rheumatology clinic. Patients with rheumatic disease (rheumatoid or inflammatory arthritis, ankylosing spondylitis, or psoriatic arthritis) who switched from etanercept or infliximab to a biosimilar due to changes in BC Pharmacare coverage in 2019 were included. Patients with no follow-up after the switch, patients who originally switched due to inefficacy or side effects of the original medication, patients who discontinued the original medication, and patients who declined switching due to private coverage were excluded.

**Results:** 78% of patients remained on a biosimilar after one year. The mean follow-up time was 10.1 months from when the switch was initiated. 22% of patients who switched to biosimilars did not remain on the new medication over the study duration. Of those, 11% switched back to the originator and 11% switched to a biologic with a different mechanism of action because of inefficacy or side effects. There were no significant differences in the odds of retention based on medication (Inflectra, Erelzi, Brenzys) [JC1] or disease type (rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis).

**Conclusion:** Overall, switching from Enbrel and Remicade to an approved biosimilar as mandated by BC Pharmacare for rheumatology indications was well tolerated in this review, with 78% of patients remaining on their biosimilar one year after the policy was implemented. There were no significant differences in the odds of retention based on medication or disease type between rheumatoid arthritis, psoriatic arthritis or ankylosing spondylitis.

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#### **Adult-onset Still's Disease: Points to Consider**

Leonardo Martin Calderon (Western University, London); Janet Pope (University of Western Ontario, London)

**Objectives:** Adult-onset Still's disease (AOSD) is a rare and complex auto-inflammatory disease of unknown etiology. AOSD has varied presenting clinical features which can result in diagnostic uncertainty and prolonged time prior to treatment. NSAIDs, glucocorticoids, conventional DMARDs, and biologics are used in the management of AOSD with varying results. Furthermore, factors associated with de-escalation of therapies remain unclear. The purpose of this project is to review the literature and create a

consensus on points to consider in the diagnosis, prognosis, and treatment of AOSD.

**Methods:** A scoping review of the AOSD literature over the last 15 years was performed. MEDLINE and EMBASE were searched, and studies included if they provided information regarding the epidemiology, differential diagnosis, diagnostic criteria, complications, prognosis, and initial, chronic, and refractory treatment approaches in AOSD. Following narrative information synthesis, a meeting was held with 5 experienced clinicians across Canada for the creation of a consensus on points to consider in AOSD.

**Results:** The annual incidence and prevalence of AOSD is observed to be between 0.16 to 0.62 per 100,000 and 3.9 to 6.9 per 100,000, respectively. AOSD most commonly affects young adults and women. Women are more likely to have severe complications from AOSD including macrophage activation syndrome, disseminated intravascular coagulation, or thrombotic thrombocytopenic purpura. The Yamaguchi criteria remains the most widely used diagnostic tool with a sensitivity of 96.2% and specificity of 92.1%. Common presentation manifestations include intermittent high fevers (> 39.0 degrees Celsius), arthralgias/arthritis, pharyngitis, lymphadenopathy, and a maculopapular rash. Other manifestations can variably involve the cardiovascular, respiratory, and GI systems. Common laboratory abnormalities include leukocytosis with neutrophilia, elevated ESR and CRP, elevated ferritin, and transaminitis. AOSD patients are most commonly ANA and RF negative. Initial treatment includes NSAIDs, glucocorticoids, and conventional DMARDs. Disease refractory to initial therapy is managed through IL-1 and IL-6 inhibitors such as Anakinra or Tocilizumab. Elevated ESR, pericarditis, and non-response to corticosteroids are some of the factors associated with refractory and chronic disease requiring advanced therapies and long-term follow-up

**Conclusion:** AOSD is a rare and multi-faceted autoinflammatory disease with a diverse presentation profile. Clinicians are recommended to consider AOSD, following exclusion of infections, malignancies, and autoimmune diseases, as a cause for fever of unknown etiology. Herein we provide points to consider in the diagnosis and management of AOSD following expert consensus.

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#### **Transition Readiness Among Patients Transferring From Pediatric to Adult Rheumatology: Expectations and Goal-setting**

Teresa Semalulu (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Alessana Carmona (McMaster University, Hamilton); Tania Cellucci (McMaster University, Hamilton); Liane Heale (McMaster University and McMaster Children's Hospital, Hamilton); Stephanie Garner (McMaster University, Hamilton); Jan Gorter (McMaster University, Hamilton); Mark Matsos (McMaster University, Hamilton); Michelle Bathish (McMaster University, Hamilton)

**Objectives:** Transition programs for adolescents with JIA and jSLE are designed to increase patients' healthcare self-management skills to enable a successful transition to adult care. Quantifying improvements in self-management skills is essential to understanding the effectiveness of transition programs. Identifying patient characteristics associated with lower/higher levels of transition readiness is necessary to address individual needs. At the McMaster Children's Hospital Rheumatology Transition Clinic, JIA and jSLE patients work alongside a multidisciplinary team to enhance self-management skills through goal setting. The objectives of this study were to (1) measure changes in transition readiness over time in adolescents with JIA and jSLE and (2) determine the potential impact of sex and age on these changes.

**Methods:** The TRANSITION-Q is a 14-item validated self-administered questionnaire used to determine healthcare self-management skills. Adolescents (age 14-18) with JIA and jSLE are seen by an adult and pediatric rheumatologist in our multidisciplinary transition clinic. Participants complete the TRANSITION-Q at the time of consent (baseline) and at each follow-up visit scheduled at the discretion of the treating physician. The adolescent then reviews their responses and, with the support of a Child Life Specialist, establishes goals to improve self-management skills. TRANSITION-Q scores were determined for the entire study population



Figure 1a: Transition Q Score at Baseline

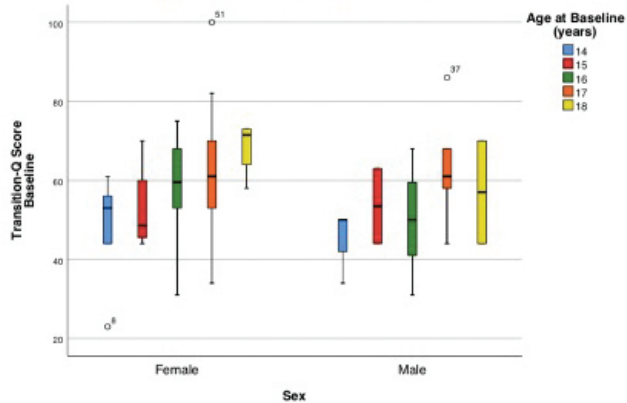
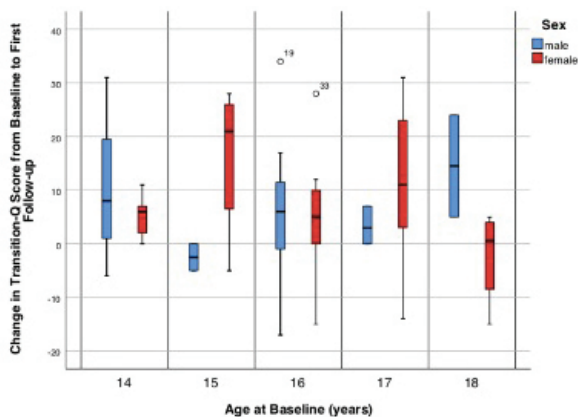


Figure 1b: Transition-Q Score from Baseline to First Follow-up



and then separately by sex and age group. Regression analyses determined if baseline or changes in TRANSITION-Q scores were different by sex and age group.

**Results:** A total of 61 adolescents participated in the study; female ( $n = 41$ ), JIA ( $n = 52$ ), mean (SD) age 16.2 (1.2) years and mean (SD) age at diagnosis of 12.2 (4.2) years. The group mean (SD) TRANSITION-Q score at baseline was 57.2 (14.5). Mean baseline TRANSITION-Q scores were not significantly different in females compared to age-matched males. There was considerable variability in baseline scores within each age group (Figure 1a). The majority of TRANSITION-Q scores increased from baseline ( $n = 42$ , 69%), although 9 participants had decreased scores (16%). There were no sex-differences in the amount of improvement over time. Age was not related to the amount of change in TRANSITION-Q scores over time (Figure 1b).

**Conclusion:** Baseline TRANSITION-Q scores did not differ significantly between sexes and there was high variability among age-matched males and females; thus, providers should not have predetermined expectations of transition readiness based on age or gender. Despite variability in transition preparedness at baseline, scores generally improved with goal setting. Therefore, goal setting may be used to successfully increase transition readiness over time, regardless of differences in age, sex or transition preparedness at baseline.

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#### Impact of the COVID-19 Pandemic on Juvenile Idiopathic Arthritis Presentation and Research Recruitment: Results From the CAPRI Registry

Molly Dushnicky (McMaster University, Burlington); Catherine Campbell (Michael De Groot School of Medicine, Hamilton); Karen Beattie (McMaster University, Hamilton); Roberta Berard (Children's Hospital, LHSC, London); Tania Cellucci (McMaster University, Hamilton);

Mercedes Chan (University of British Columbia, Vancouver); Tommy Gerschman (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital, Calgary); Nicole Johnson (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Lillian Lim (Division of Rheumatology, University of Alberta, Edmonton); Nadia Luca (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Paivi Miettunen (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Kimberly Morishita (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Jean-Philippe Proulx-Gauthier (CHU de Quebec, Quebec); Dax Rumsey (University of Alberta, Edmonton); Heinrike Schmeling (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Rosie Scuccimari (McGill University Health Centre, Montreal); Herman Tam (BC Children's Hospital, Vancouver); Jaime Guzman (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Michelle Barthish (McMaster University, Hamilton)

**Objectives:** The COVID-19 pandemic has disrupted healthcare and clinical research worldwide. Timely diagnosis and initiation of therapy is critical to improving long-term outcomes and preventing irreversible joint damage in patients with JIA. The diagnosis hinges on timely referral and joint examination, both difficult to accommodate when the pandemic forced many medical encounters to occur virtually. Several reports have shown an impact on rheumatology care. Higher rates of JIA disease flares presenting to hospitals during the pandemic have been reported, perhaps due to delayed follow-up intervals. The aim of this study was to characterize COVID-related disruptions in initial presentation of JIA to pediatric rheumatology care and research recruitment in Canada. We hypothesize that disruption of care would result in prolongation of time from symptom onset to first assessment and a greater severity at presentation, while research disruption would be reflected by a drop in Registry recruitment.

**Methods:** Data was obtained from the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) National Registry, which started in 2017 and enrolls children with JIA within 3-months of diagnosis, following them at every clinic visit. The Registry prospectively collects and shares data on disease course, outcomes, and adverse events. Data from the year pre-pandemic (March 11, 2019-March 10, 2020) was compared to data collected during the first year of the pandemic (March 11, 2020-March 10, 2021). Outcomes included time from symptom onset to first assessment, disease severity at presentation and registry recruitment. Proportions and medians were used to describe categorical and continuous variables, respectively.

**Results:** The median time from symptom onset to first assessment was 138 days pre-pandemic versus 146 days during the pandemic. JIA category frequencies remained stable, predominantly oligoarticular JIA (44% pre-pandemic, 46.8% pandemic), except for systemic JIA (12 cases pre-pandemic, 1 pandemic). Clinical features, disease activity (cJADAS10), disability (CHAQ) and quality of life (JAQQ) scores were similar between the two cohorts. Pre-pandemic, 225 patients were enrolled, compared to 111 in the pandemic year, with the greatest decrease from March to June 2020.

**Conclusion:** We did not observe the hypothesized delay in presentation or increased severity at presentation. This suggests that within Canada, pediatric rheumatology care adapted well to provide ongoing support and care to new patient consults. Research disruption was associated with a 50% enrollment decrease in the pandemic year, most significantly from March to June 2020. It has since improved, consistent with a limit in non-essential research staff presence in hospitals early on. Best Abstract on Clinical or Epidemiology Research by a Trainee - Phil Rosen Award.

#### 45

#### Evaluation of Methotrexate Intolerance in Children With Morphea

Jeanine McColl (Hospital for Sick Children/University of Toronto, Toronto); Ronald Laxer (Division of Rheumatology, The Hospital for

Sick Children and University of Toronto, Toronto); Elena Pope (Dept. Dermatology, The Hospital for Sick Children, Toronto); Cathryn Sibbald (University of Toronto, Toronto)

**Objectives:** Methotrexate is an immunosuppressant used to treat a variety of diseases. The prevalence of intolerance using the Methotrexate Intolerance Severity Score (MISS) in children with Juvenile Idiopathic arthritis (JIA) ranges from 25-75%, and intolerance in this population is associated with higher doses and younger ages.[1-4] We observed a high frequency in the rates of intolerance to MTX among patients treated for morphea and other inflammatory skin disorders (eczema, psoriasis, alopecia areata). Objectives were to determine the prevalence and predictors of methotrexate intolerance in children with morphea compared to children with inflammatory skin diseases and JIA/uveitis.

**Methods:** Patients aged 2-18 years taking methotrexate for a minimum of 3 months to treat morphea, inflammatory skin disease, or uveitis/JIA were recruited. Methotrexate intolerance was calculated using MISS, a questionnaire validated in children with JIA. 2 Participants completed 16 questions across 4 domains (abdominal pain, nausea, vomiting, and behavioral symptoms). Each item was ranked 0 to 3, with a total possible score of 36. Intolerance was defined by a score of 6 or higher. A one-way ANOVA compared absolute intolerance scores.

**Results:** Of 48 participants (mean (SD) age 11.3 ( $\pm$ 4.1) years, 70.8% female) 15 had morphea, 16 had JIA/uveitis, and 17 had inflammatory skin disease (Table 1). The overall mean MISS score was 4.1 (SD  $\pm$ 5.2). Age, sex, duration, and dose did not correlate with overall MISS. MISS mean total for oral dosing was 2.5 (SD  $\pm$ 3.4) with a range of 0-13, compared to a mean total MISS of 6.78 (SD =  $\pm$ 6.8) for subcutaneous dosing. JIA/ uveitis patients had the highest mean total MISS 6.3 (SD  $\pm$  7.1) followed by morphea patients 3.7 (SD  $\pm$ 4.0), and inflammatory skin disease patients 2.2 (SD  $\pm$ 2.8). The route of administration significantly correlated with MISS gastrointestinal and behavioral scores (P = 0.01). The odds ratio of intolerance according to route of administration was 11.2 (95% CI 2.03-61.89).

**Conclusion:** Methotrexate intolerance was highest among JIA/uveitis patients. The only predictor for risk of intolerance was subcutaneous route of administration. Future work could examine methotrexate intolerance and disease activity over time, and interventions designed to minimize intolerance. References: [1.] Bulatovic M. Arthritis Rheum 2011;63:2007-13. [2.] Franova J. Pediatr Rheumatol Online J 2016;14:36. [3.] Kyvsgaard N. PLoS One 2019;14:e0219539. [4.] Patil P. Clin Rheumatol 2014;33:403-7.

Table 1: Demographics (Total + each group separately)

|                                               | All patients (n=48) | Morphea (n=15)  | Atopic Dermatitis/ Alopecia/PsO (n=17) | JIA/uveitis (n=16) |           |
|-----------------------------------------------|---------------------|-----------------|----------------------------------------|--------------------|-----------|
| Current Age (yrs)                             | 11.3 $\pm$ 4.1      | 11.7 $\pm$ 3.9  | 12.1 $\pm$ 4.91                        | 0.1 $\pm$ 3.0      | NS        |
| Age at diagnosis (yrs)                        | 6.8 $\pm$ 4.4       | 8.6 $\pm$ 4.6   | 6.4 $\pm$ 4.6                          | 5.7 $\pm$ 3.4      | NS        |
| Sex                                           |                     |                 |                                        |                    |           |
| Female (N, %)                                 | 34 (70.8%)          | 13 (27.1%)      | 9 (18.8%)                              | 12 (25%)           | NS        |
| Male (N, %)                                   | 14 (29.2%)          | 2 (4.1%)        | 8 (16.7%)                              | 4 (8.3%)           |           |
| Current MTX dose (Mg/kg/dose (mean $\pm$ SD)) | 0.41 $\pm$ 0.13     | 0.46 $\pm$ 0.12 | 0.33 $\pm$ 0.08                        | 0.43 $\pm$ 0.14    | P = 0.004 |
| Initial MTX dose (Mg/kg/dose (mean $\pm$ SD)) | 0.45 $\pm$ 0.14     | 0.50 $\pm$ 0.11 | 0.41 $\pm$ 0.13                        | 0.31 $\pm$ 0.09    | P < 0.001 |
| MTX dose route                                |                     |                 |                                        |                    |           |
| SC (N, %)                                     | 18 (37.5)           | SC 7 (14.6)     | SC 1 (2.1)                             | SC 9 (18.8)        | P = 0.004 |
| PO (N, %)                                     | 30 (62.5)           | PO 8 (16.7)     | PO 16 (33.3)                           | PO 7 (14.6)        |           |
| Duration of MTX (months)                      | 22.3 $\pm$ 19.1     | 21.0 $\pm$ 15.8 | 10.6 $\pm$ 8.1                         | 35.2 $\pm$ 22.2    | P = 0.001 |
| Systemic manifestations (n, %)                |                     | 3 (20%)         |                                        |                    |           |

NS = not significant (p > 0.05)

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### Prevalence and Titer Distribution of Antinuclear Antibodies in Juvenile Idiopathic Arthritis – A Systematic Review

John Storwick (University of Calgary, Calgary); Amanda Brett (University of Calgary, Calgary); Katherine Buhler (University of Calgary, Calgary); Alex Chin (Calgary Laboratory Services/University of Calgary, Calgary); Heinrike Schmelting (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Nicole

Johnson (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); May Choi (University of Calgary, Calgary); Marvin Fritzler (University of Calgary, Calgary)

**Objectives:** Antinuclear Antibodies (ANA) are detected in almost all subtypes of Juvenile Idiopathic Arthritis (JIA), however, traditionally are a marker of uveitis risk. Although common in JIA, ANA, detected by the HEp-2 immunofluorescence assays (IFA), lack specificity and can be present in healthy children at low titers. There is no international consensus as to what serum dilution should be used for JIA ANA IFA testing. This systematic review determined the distribution of ANA titers in JIA with the primary aim of finding the serum screening dilution that should be used when considering a diagnosis of JIA.

**Methods:** On February 17th, 2021, five databases (EMBASE, Medline, PubMed, SCOPUS and Cochrane Reviews) were searched, identifying 1506 abstracts of which 192 were duplicates and 1197 did not meet inclusion criteria, leaving 108 full texts to be reviewed. Studies were excluded if ANA titers were not reported, data was collected prior to 2000, populations included adult patients, were not in English, or did not use an indirect immunofluorescence assay (IFA). Eight full texts were unobtainable, and 82 were excluded, with 46 being excluded because ANA titers were not reported. Data extraction was done on the remaining 26 full texts.

**Results:** 6022 patients were identified; 5569 had JIA, 273 were controls. Of all seven JIA subtypes, Persistent Oligoarthritis was the most common (33.3%) and had the highest frequency of ANA positivity (46.9%). The most reported ANA screening titer was 1:80, [732/1935 (37.8%)] (Table 1). An ANA titer of 1:80 also had the highest proportion of JIA patients who ANA's exceeded the reference range for each individual study [35.1% (95% CI = 33.7-36.4%)]. Seventeen studies (58%) included patients with uveitis. Of those reported, 120/168 (71%) JIA-uveitis patients were ANA positive. The sensitivity and specificity of ANA in JIA-uveitis were 71.4% (95% CI = 64.3%-78.6%) and 70.1% (95% CI = 67.9%-72.3%). Specific ANA titers were not reported in relation to the uveitis subset.

**Conclusion:** Our results revealed a large variation of ANA IFA serum dilutions used in the context of JIA, with the common being 1:80. Unfortunately, the current literature is disappointing and lacks comparison of ANA titers between JIA and healthy controls. Additional studies are needed to address the paucity of data to inform the ANA IFA screening dilutions of importance in JIA and how ANA titers can be used to determine the risk of developing uveitis.

Table 1: Proportional analysis of different ANA titres for JIA (N=5791) and sensitivity/sensitivity of those with uveitis.

| ANA screening dilution* | Cumulative Proportion% |
|-------------------------|------------------------|
| 1:40                    | 34.2 (32.9 - 35.4)     |
| 1:80                    | 35.1 (33.7 - 36.4)     |
| 1:100                   | 33.8 (32.1 - 35.6)     |
| 1:160                   | 34.1 (32.1 - 36.0)     |
| 1:320                   | 30.6 (26.4 - 34.7)     |
| 1:640                   | 3.7 (1.4 - 5.9)        |
|                         | <b>Sensitivity %</b>   |
|                         | 71.4 (64.3 - 78.6)     |
|                         | <b>Specificity %</b>   |
|                         | 70.1 (67.9 - 72.3)     |

\*For studies with multiple ANA titres, serum screening dilution values were designated at the higher titre value.

\*\*The cumulative proportion was calculated such that patients who were above the reference range at 1:640 were also included at 1:320, 1:160, and so on. Those patients within the reference range from a cohort were not included in the calculation until the highest reported dilution for a member of their cohort. † Specific ANA titers were not reported for patients with uveitis. ANA = antinuclear antibody; ANA+Uveitis = Patient designated as ANA elevated and diagnosed with uveitis.

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### Comparative Evaluation of Juvenile-onset Systemic Sclerosis and Adult-onset Systemic Sclerosis

Jennifer Lee (University of Toronto, Toronto); Brian Feldman (The Hospital for Sick Children, Toronto); Ronald Laxer (Division of Rheumatology, The Hospital for Sick Children and University of Toronto, Toronto); Zareen Ahmad (Toronto Scleroderma Program, Division of Rheumatology, Mount Sinai Hospital; Department of Medicine, University of Toronto, Toronto); Elvira Bangert (Queen's University, Kingston); Shafina Hasmani (Mount Sinai Hospital, Toronto); Mohammad Movahedi (University Health Network, Toronto); Sindhu Johnson (Toronto Scleroderma Program, Mount Sinai Hospital; Division of Rheumatology, Toronto

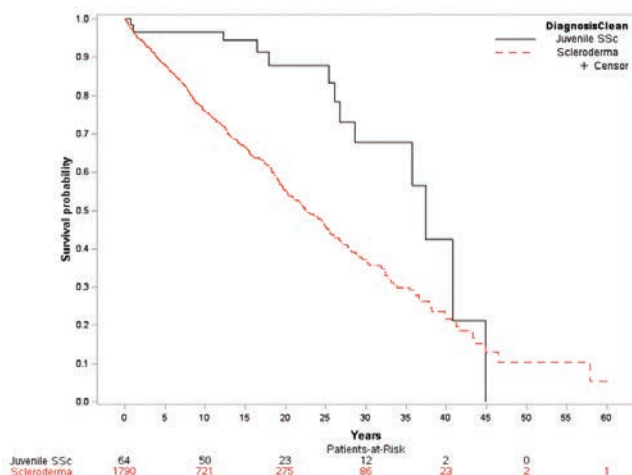
Western Hospital; Department of Medicine, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** To comparatively evaluate the clinical manifestations, autoantibodies, comorbidities and survival in patients with juvenile-onset systemic sclerosis (jSSc) and adult-onset systemic sclerosis (SSc).

**Methods:** We conducted a retrospective cohort study of adults and children ( $\leq 16$  years old) from the Toronto Scleroderma Program who fulfilled the American College of Rheumatology/European League Against Rheumatism classification criteria for SSc. Clinical manifestations, autoantibodies, co-morbidities and survival were compared between jSSc and SSc patients. The primary outcome was the time from diagnosis to death from all causes. Survival probabilities were determined through Kaplan-Meier survival curves. A multivariable Cox proportional hazards regression model was performed to evaluate the hazard ratio (HR) in all-cause mortality.

**Results:** We included 1,955 patients [jSSc n = 64 (3.3%) and SSc n = 1891 (96.7%)]. Throughout the disease course, when compared to SSc, jSSc patients more frequently had calcinosis [46.9% versus 22.6%, relative risk (RR) 2.01 (95% CI 1.53-2.65)], digital ulcers [45.3% versus 33.1%, RR 1.34 (95% CI 1.02-1.77)], and scl-70 antibodies [28.1% versus 18.7%, RR 1.28 (95% CI: 0.87-1.88)]. jSSc patients less frequently had telangiectasia [51.6% versus 66.8%, RR 0.75 (95% CI 0.59-0.95)], pulmonary hypertension [9.4% versus 25.6%, RR 0.33 (95% CI 0.15-0.70)], and anti-centromere antibodies [9.4% versus 22.5%, RR 0.38 (95% CI 0.18-0.81)]. There were no differences in the frequency of interstitial lung disease (35.9% versus 35.1%) or renal crisis (3.1% versus 6.8%). jSSc patients had fewer comorbidities including coronary artery disease [RR 0.18 (95% CI 0.03-1.28)] and hypertension [RR 0.20 (95% CI 0.07-0.61)]. None of the jSSc patients developed cancer, peripheral vascular diseases, atrial fibrillation or stroke. Thirteen (26.3%) jSSc patients and 586 (31.0%) SSc patients died. jSSc patient had better survival than SSc patients (log-rank  $P = 0.0002$ ; Figure 1). SSc patients had an adjusted HR of 2.1 (95% CI 1.2-3.7,  $P = 0.01$ ) for all-cause mortality compared to jSSc patients.

**Conclusion:** jSSc patients have more frequent cutaneous manifestations but not more frequent internal organ manifestations compared to adult SSc. Long-term survival appears to be more favorable in jSSc patients.



#### 48 Predictors of Health-related Quality of Life in Rheumatoid Arthritis Patients

Nejat Hassen (University of British Columbia, Arthritis Research Canada, Richmond); Yufei Zheng (Arthritis Research Canada, Richmond); Hui Xie (Arthritis Research Canada/Faculty of Health Sciences at Simon Fraser University, Richmond); Karim Khan (University of British Columbia, Vancouver); Jacek Kopec (Arthritis Research Canada, Richmond); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver)

**Objectives:** Health-related quality of life (HRQoL) is lower in rheumatoid arthritis (RA) patients compared to the general population, yet a comprehensive study evaluating predictors and the relative contribution of sociodemographic, RA-related, comorbidities, and lifestyle factors is lacking. Our study's objectives were to identify factors that predict 1) HRQoL one year after baseline assessment; and 2) change in HRQoL over 12 months.

**Methods:** Survey data from a longitudinal quality of care study of RA patients recruited from a population-based cohort identified using administrative data were analyzed. Participants who completed questionnaires in 2015 and 2016 assessing sociodemographic, health status (RA-related and comorbidities), and lifestyle factors were included. HRQoL was measured using EQ5D-VAS. Three model selection procedures for multivariable linear regression models – stepwise selection ( $p$ -entry  $< 0.05$ ;  $p$ -exit  $\geq 0.15$ ), all-possible selection, and LASSO method – were used to select important HRQoL predictors. Models were compared using cross-validation (CV) and the model with smallest CV error was selected. Model selections without and with 2015 EQ5D-VAS were conducted to determine best models for absolute value, and change in HRQoL, respectively. We used sum of  $R^2$  values to assess the variance explained by each model and to determine the relative contributions of sociodemographic, RA-related, comorbidities, and lifestyle factors. Data analyses were conducted using RStudio 1.3.1093.

**Results:** Our sample included 168 individuals with RA (72% women, mean age  $70.7 \pm 10.6$  years, mean disease duration  $24.3 \pm 11.9$  years). EQ5D-VAS in 2016 was  $67.5/100 \pm 19.4$ . The model controlling for baseline 2015 HRQoL had lower AIC and better predictive ability ( $R^2$ ) for 2016 HRQoL. HRQoL in the previous year contributed most to predicting HRQoL. Of the RA-related factors, only disease activity and physical function were significant predictors. Both variables were highly correlated ( $r = 0.69$ ) and likely capture similar disease effects. Of the comorbidities, only depression predicted HRQoL, and it contributed greater to HRQoL than RA-related factors. Lifestyle and sociodemographic factors evaluated contributed little to HRQoL. Significant predictors and variance explained by model with 2015 HRQoL is presented in Table 1. Our study limitations include potential respondent bias and a predominantly White and older sample with longstanding disease. Our findings may not be generalizable to samples with different characteristics.

**Conclusion:** HRQoL in our RA sample was multifactorial. Predictors from different domains contributed to HRQoL. HRQoL in the previous year contributed most to predicting future HRQoL. Depression was the second most important predictor. Early identification and management of depression may improve overall HRQoL in RA patients.

| Variable                                                                                                                                                                                                                                                                                                                                                                                                                                             | Coefficient (95%CI)  | p-value | $R^2$ |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|---------|-------|
| Age >65yo (yes vs. no)                                                                                                                                                                                                                                                                                                                                                                                                                               | 5.61 (0.42, 10.81)   | 0.034   | 0.019 |
| Alcohol consumption (yes vs. no)                                                                                                                                                                                                                                                                                                                                                                                                                     | 7.14 (1.88, 12.39)   | <0.01   | 0.052 |
| Depression score (0-27)                                                                                                                                                                                                                                                                                                                                                                                                                              | -0.71 (-1.35, -0.07) | 0.030   | 0.086 |
| RADAI (0-10)                                                                                                                                                                                                                                                                                                                                                                                                                                         | -0.06 (-0.12, 0.00)  | 0.058   | 0.073 |
| Sex (male)                                                                                                                                                                                                                                                                                                                                                                                                                                           | 4.74 (-0.64, 10.12)  | 0.084   | 0.010 |
| 2015 HRQoL (0-100)                                                                                                                                                                                                                                                                                                                                                                                                                                   | 0.39 (0.23, 0.55)    | <0.01   | 0.162 |
| <b>Total model <math>R^2=0.40</math></b>                                                                                                                                                                                                                                                                                                                                                                                                             |                      |         |       |
| *Variables evaluated for inclusion in the multivariable model included sociodemographic factors (age, sex, ethnicity, marital status, rural vs. urban residence, education, employment, income), health status factors (RA-related measures [physical function (HAQII), disease activity (RADAI), pain, fatigue], and comorbidities, including depression (PHQ9), obesity), and lifestyle factors (physical activity, smoking, alcohol consumption). |                      |         |       |

#### 49 Co-management of Rheumatoid Arthritis Patients With Cardiology Correlates With Fewer Cardiac Events

Jorge Guerra (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital, Temple); Andres Belmont De Santiago (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital, Temple); Shirley Reed (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital, Temple); Kendall Hammonds (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital, Temple); Courtney Shaver (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital,



Temple); Robert Widmer (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital, Temple); Beth Scholz (Texas A&M University College of Medicine - Baylor Scott & White Memorial Hospital, Temple)

**Objectives:** Rheumatoid Arthritis (RA) is a systemic autoimmune disease with important cardiovascular implications. Cardiovascular disease represents over half of RA deaths and is a causative factor of significant morbidity. Although traditional cardiovascular risk factors play a role in the development of cardiovascular disease, the rheumatoid patient faces additional components of atherosclerotic plaque formation attributed to agents of chronic inflammation. It is therefore imperative to identify ways to optimize detection and management of RA patients with coronary artery disease (CAD). In this retrospective study we evaluated whether RA patients followed by a cardiologist have fewer cardiac events and hospitalizations compared to patients followed by rheumatology without cardiology co-management.

**Methods:** This is a retrospective study of patients diagnosed with RA and CAD. Patients were identified and filtered via EPIC Database search engine. Parameters were set from January 1, 2014, to June 1, 2020. Inclusive criteria consisted of patients with ICD 10 criteria for both RA and CAD, and those with at least one Cardiology and Rheumatology office visit. A total of 139 patients met criteria. Characteristics were described using descriptive statistics. Chi-square test, Wilcoxon signed rank sum test, and Cochran-Armitage test tested for associations and trends.

**Results:** Of the 139 identified patients, there were 100 females (72%) and 39 males (28%) with a mean age of 72 (range: 26 – 98). Data was divided into three groups based on duration of RA: 40 patients with RA duration < 5 years (29%), 51 patients with RA duration > 5 but < 10 years (37%), and 48 patients with RA duration > 10 years (35%). Most patients (70%) had at least one cardiac-related hospitalization prior to establishing care with cardiology (average: 1.3 range: 0 - 8). Once established, 73% of patients did not have any further cardiac-related hospitalizations. However, only 22% of them did not have any non-cardiovascular hospitalizations. This association was significantly different ( $P < 0.0001$ ). Despite this, patients with regular cardiology follow-up did not demonstrate statistically significant increases in adverse events (Table 1). Data was stratified by length of RA. The difference in cardiovascular hospitalizations was not significantly different among the three groups ( $P > 0.05$ ).

**Conclusion:** Our study revealed that patients followed by both Rheumatology and Cardiology have fewer cardiac-related hospitalizations, fewer adverse cardiac events, and improved survival. It is important to optimize management of RA patients to help decrease the rates of cardiac morbidity and mortality – with co-management representing a cornerstone of care.

**Table 1. Adverse Events by Hospitalization Type**

| Adverse Events in Cardiac-Related Hospitalizations vs Non-Cardiac-Related Hospitalizations |             |                 |         |
|--------------------------------------------------------------------------------------------|-------------|-----------------|---------|
| Adverse Event                                                                              | Cardiac (%) | Non-Cardiac (%) | p-value |
| STEMI                                                                                      | 0.7         | 0.7             | >0.05   |
| NSTEMI                                                                                     | 1.4         | 0.7             | >0.05   |
| Stroke                                                                                     | 0.7         | 4.3             | >0.05   |
| Cardiovascular Death                                                                       | 0           | 0               | >0.05   |
| All-Cause Mortality                                                                        | 0.7         | 3.6             | >0.05   |

### 50 Multimorbidity Patterns and Associations With Disability Differ in Men and Women in the First Year Following RA Diagnosis: Results From the Canadian Early Arthritis Cohort (CATCH)

Orit Schieir (McGill University, Montreal); Susan Bartlett (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Glen Hazlewood (University of Calgary, Calgary); Louis Bessette (Laval University, Quebec); Gilles Boire (Université de Sherbrooke, Sherbrooke); Carol Hitchon (University of Manitoba, Winnipeg); Edward Keystone

(University of Toronto, Toronto); Janet Pope (University of Western Ontario, London); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Vivian Bykerk (The Hospital for Special Surgery, New York); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

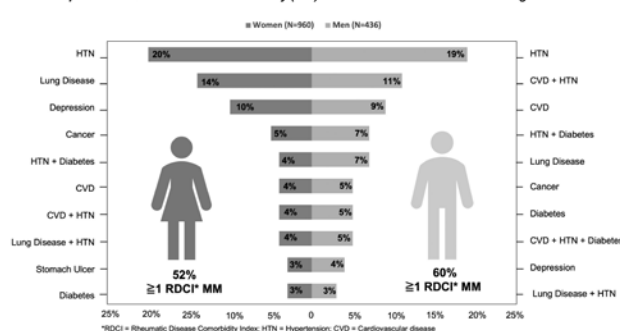
**Objectives:** Chronic disease multimorbidity (MM) is prevalent in RA. MM can vary in complexity and different combinations of chronic conditions may have different physical and psychological impacts on patients. The objective of the present study was to identify the most prevalent MM patterns in women and men around RA diagnosis and estimate their associations with disability over the first year of follow-up, in a large real-world incident RA cohort.

**Methods:** Data were from early RA patients (< 1 year of symptoms) diagnosed and treated in rheumatology clinics across Canada that enrolled in CATCH from Jan 2007 through March 2020. Participants completed the Rheumatic Disease Comorbidity Index (RDCI) at baseline and repeat assessments of disease activity (DAS28) and disability (MHAQ) every 3 months over 1-year follow-up. We identified the top 10 most prevalent MM patterns by sex by first coding the presence/absence of each condition and then ranking the prevalence of all possible reported combinations. We estimated sex-stratified longitudinal associations between prevalent MM patterns and repeated measures of disability in the first year follow-up with generalized estimating equations (GEE), adjusted for age, education, symptom duration, smoking, obesity and time-varying measures of DAS28 disease activity.

**Results:** The sample included 2,576 ERA patients, 1843 (72%) were female, with a mean(sd) age of 56 (15) years and 6 (3) months of symptoms. At baseline, 95% were treated with csDMARDs (mostly methotrexate (74%)) and 2% with a biologic. More than half of patients (54%) reported  $\geq 1$  MM. Prevalence, patterns and complexity of MM differed by sex. HTN, lung disease and depression were the most prevalent MM patterns reported in women, and HTN, CVD, and CVD+HTN were the most prevalent patterns in men (Figure). More complex MM patterns involving multiple conditions were more prevalent in men (26%) than in women (12%) (Figure). In fully adjusted multivariable GEE models, depression (beta: 0.14, 95% CI: 0.04-0.24) in women, and lung disease + HTN (beta: 0.22, 95% CI: 0.03-0.42) in men, were significantly associated with higher disability over time.

**Conclusion:** Results from this large real-world incident cohort study suggest that multimorbidity is common around the time of RA diagnosis and differs between men and women. Results suggest potential shared risk factors and pathways between identified MM patterns and highlight the need to screen for and treat MM conditions, particularly those which increase disability.

**Top 10 Salient Patterns of Multimorbidity (MM) in Women and Men Around RA Diagnosis**



### 51 The Impact of Comorbidities on the Simple Disease Activity Index (SDAI) and its Components Over the First Year of Follow-up – An Analysis From the Canadian Early Arthritis Cohort (CATCH)

Lillian-Ruiheng Chen (Centre de recherche du CHU de Québec-Université Laval, Québec); Orit Schieir (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Janet Pope (University of Western Ontario, London); Susan Bartlett (McGill University, Montreal); Gilles Boire (Université de Sherbrooke, Sherbrooke); Glen Hazlewood (University of Calgary, Calgary); Carol Hitchon (University of Manitoba, Winnipeg); Edward Keystone (University of Toronto, Toronto); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Narcisse Singbo (Centre de recherche du CHU de Québec-Université Laval, Québec); Vivian Bykerk (The Hospital for Special Surgery, New York); Louis Bessette (Laval University, Québec); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

**Objectives:** Comorbid conditions have been shown to negatively influence the achievement of treatment targets in rheumatoid arthritis (RA) patients. The objective is to look at the relationships between comorbidities and components of common clinical disease activity scores, such as tender (TJC) and swollen (SJC) joint count, patient global assessment (PtGA), physician global assessment (MDGA), C-reactive protein (CRP) and pain in early RA.

**Methods:** Using the Rheumatic Disease Comorbidity Index (RDCI), the influence of comorbidities on each component's trajectory in time has been assessed in early RA (ERA) patients over the first year of treatment with conventional synthetic DMARDs using data from the Canadian Early Arthritis Cohort (CATCH). The adjusted effects of RDCI scores (0, 1, 2, and  $\geq 3$ ) on the trajectory of the SDAI, on each component of the SDAI, and on pain was evaluated over the first year of follow-up with generalized estimating equations (GEE). Data were adjusted for confounders.

**Results:** This sample size included 2248 ERA patients with a mean symptom duration (SD) of 5.71 (2.96) months; mean age (SD) was 55 (15) years old and 72% were female. At baseline, 1664 (74%) were treated with methotrexate with a mean weekly dose (SD) of 20.0 mg (4.2) and 1340 (60%) also received other conventional synthetic DMARDs. The mean (SD) SDAI at enrolment was 29 (15) and 90% were classified as having moderate-high SDAI. RDCI scores of 0, 1, 2 or  $\geq 3$  were obtained in 888 (40%), 547 (24%), 451 (20%), and 362 (16%) participants, respectively. Although disease activity did not differ by comorbidity status at baseline, patients with RDCI of 0 had better improvement (rate of change) in SDAI, PtGA, MDGA and pain over time relative to patients with multiple RDCI conditions ( $P < 0.05$ ). A significant higher rate of change in SJC was observed in patients with RDCI of 1 and 2 compared with participants having RDCI score of 3 or higher ( $P = 0.01$ ). The RDCI scores were not significantly associated with the change of TJC and CRP over one year.

**Conclusion:** In this ERA cohort, having multiple comorbidities was associated with worse improvement and disease activity assessed by SDAI, SJC, PtGA, and MDGA were the components of SDAI that were most influenced by the presence of comorbidities. The results demonstrate a negative effect of having comorbidities at disease onset of RA on the evolution of both patients and physicians reported outcomes.

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### Formulation of an Interdisciplinary Care Pathway for Early Rheumatoid Arthritis

Ksenia Gukova (University of Calgary, Calgary); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary); Glen Hazlewood (University of Calgary, Calgary); Hector Arbillaga (Calgary); Paul MacMullan (University of Calgary, Calgary); Gabrielle Zimmerman (Alberta SPOR SUPPORT Unit Knowledge Translation and Implementation Science, Edmonton); Cheryl Barnabe (University of Calgary, Calgary); May Choi (University of Calgary, Calgary); Megan Barber (University of Calgary, Calgary); Alexandra Charlton (Alberta Health Services, Calgary); Becky Job (Alberta Health Services, Calgary); Kelly Osinski (Alberta Health Services, Calgary); Nicole Spencer (University of Calgary, Calgary); Marlene Knott (Alberta Health Services, Calgary); Paris Pirani (Alberta Health Services, Calgary)

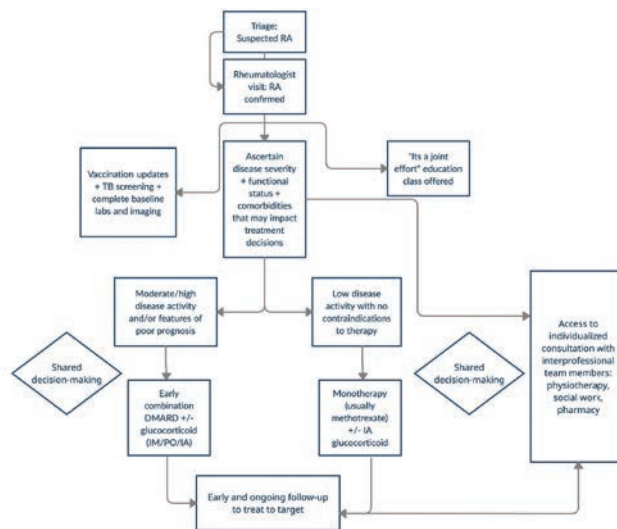


Figure 1: Calgary Early Rheumatoid Arthritis Care Pathway Overview

**Objectives:** A care pathway is a guide for the mutual decision-making and organization of care processes for a well-defined group of patients. It facilitates communication and care coordination among multidisciplinary team members, patients, and families. Our goal is to develop an interdisciplinary care pathway for patients with early rheumatoid arthritis (RA), including protocols for referral triage, diagnosis, and management, using input from members of our division.

**Methods:** The care pathway was developed in four main phases. In Phase 1, an anonymous survey consisting of 57 questions was electronically distributed to division rheumatologists. This provided data to a small interprofessional working group of rheumatology team members who drafted an initial care pathway informed by evidence-based practice in Phase 2. In Phase 3, an education day was held with approximately 40 physicians (including practicing rheumatologists and rheumatology residents), members of our interprofessional team (nursing, social work, physiotherapists, and pharmacists), and two clinic managers, to review the proposed care elements through presentations and small group discussions. The care pathway was revised for content and implementation considerations based on feedback received. The care pathway was summarized in a 20-page document outlining our team approach to early RA care. An accompanying 14-page document was also developed to support nurses in answering telephone calls from patients on common issues. Phase 4 consists of ongoing implementation efforts and evaluation of the care pathway across multiple practice sites.

**Results:** Our care pathway promotes an approach to patient-centered early RA care using an interdisciplinary approach. Care pathway elements include early workup, pre-treatment screening and vaccinations, choice of initial DMARDs, and use of steroids using shared decision-making strategies (Figure 1). Our triage system for stratifying the urgency of referrals for early inflammatory arthritis, as well as protocols for our nursing case manager roles, are also highlighted in this document, along with our interdisciplinary team roles to support optimal patient care. Pathway implementation has been facilitated by nursing protocols and evaluation, including continuous monitoring of key indicators.

**Conclusion:** The 'Calgary Early RA Care Pathway' emphasizes a patient-centered and interdisciplinary approach to early RA identification and treatment. Implementation and evaluation of this care pathway is ongoing to support optimal care for patients. Supported by a CIORA grant.

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### Do Risk-taking Behaviors Predict COVID-19 Vaccine Acceptance in People With Rheumatic Disease?

Valeria Valerio (The Research Institute of the McGill University Health Centre, Montreal); Emmanouil Rampakakis (JSS Medical Research Inc, Montreal); Marie Hudson (McGill University, Jewish General

Hospital, Lady Davis Institute for Medical Research, Montreal); Emily McDonald (McGill University Health Centre, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Elizabeth Hazel (McGill University, Montreal); Ines Colmegna (The Research Institute of the MUHC, Montreal)

**Objectives:** Several factors associate with vaccine acceptance. It is unknown if risk-taking behaviors among rheumatic disease (RD) patients are linked to COVID-19 vaccine acceptance.

**Methods:** Between November-December 2020 (before COVID-19 vaccine roll-out in Canada), a cross-sectional survey was completed by RD patients presenting for influenza immunization to a university-affiliated hospital network. Demographics, RD diagnosis, treatment, and the likelihood to receive a future COVID-19 vaccine were assessed. We used the DOSPERT health and safety subscale and the medical risk domain add-on to evaluate the likelihood of engaging in risk behaviors (eg, heavy alcohol use) and medical risk attitudes. A risk-taking score was calculated based on the sum of the scores of each question, transformed to a 0-100 scale (%) and converted to a three-level categorical variable (low, moderate, high) by tertiles. According to the likelihood to receive a future COVID-19 vaccine, patients were classified as significantly hesitant (scores 0-7.4), mildly hesitant (scores 7.5-9.9), or non-hesitant (score 10).

**Results:** One hundred and eighty-seven RD patients completed the survey. Participants had a mean age of  $55.1 \pm 17.9$ , and most were females ( $n = 134$ , 71.7%) and living with rheumatoid arthritis ( $n = 90$ , 48.1%) or systemic lupus erythematosus/vasculitis ( $n = 51$ , 27.3%). Most patients were non-hesitant to receive a future COVID-19 vaccine ( $n = 103$ , 55.1%), while a quarter were significantly hesitant ( $n = 52$ , 27.8%). Significantly hesitant individuals were less likely to engage in 'drinking heavily at a social function' (significantly hesitant: 7.7% vs. non-hesitant: 21.4%; OR = 0.3, 95% CI: 0.1-0.9), while those mildly hesitant towards vaccination tended to be more likely to 'sunbathe without sunscreen' (mildly hesitant 25% vs. non-hesitant: 12.6%; OR = 2.3, 95% CI: 0.9-6.2). Upon adjusting for age, sex, language, low-risk-taking RD patients were more likely to be hesitant to receive a future COVID-19 vaccine as compared to moderate/high-risk patients (OR: 1.9; 95% CI: 1.01-3.55).

**Conclusion:** COVID-19 vaccine hesitant RD patients are less likely to engage in risk-taking. Future research could focus on whether promotion of vaccine safety might increase vaccine uptake in this group.

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### Is Chronic Fatigue Syndrome (CFS) Related to Disease Activity in ANCA-associated Vasculitis?

Naima Mohazab (University of Alberta, Edmonton); Charmaine van Eeden (University of Alberta, Edmonton); Desiree Redmond (University of Alberta, Edmonton); Lamia Khan (University of Alberta, Edmonton); Elaine Yacyszyn (Division of Rheumatology, University of Alberta, Edmonton); Alison Clifford (University of Alberta, Edmonton); Mohammed Osman (University of Alberta, Edmonton)

**Objectives:** Fatigue is a major burden of disease in patients with ANCA-Associated Vasculitis (AAV) and results in a decreased quality of life. The incidence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in AAV patients is, however, unknown. The aim of our study is to evaluate the presence of chronic fatigue in patients with a diagnosis of AAV, ie, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis or microscopic polyangiitis, and to identify potential clinical and biopsychosocial determinants and compare them to healthy volunteers (HC).

**Methods:** 64 AAV and 20 HC participants included in our study completed the validated DePaul Symptom Questionnaire (DSQ). Patients were labelled with CFS/ME when they fulfilled the Canadian Consensus Criteria. For assessing health-related quality of life in patients, we used The Short Form (36) Health Survey. Disease activity was scored using the Birmingham Vasculitis Activity (BVAS), whereas the Vasculitis damage index (VDI) was used to evaluate damage. Mental comorbidities were analyzed to understand potential biopsychosocial factors related to chronic fatigue. To assess

anxiety and depression we used the Hospital Anxiety and Depression scale (HADS). We also used the Cognitive Failure Questionnaire (CFQ) to estimate the frequency of cognitive failure. Sleep quality was assessed using The Pittsburgh Sleep Quality Index (PSQI). In addition, Fibromyalgia questionnaire was used to assess widespread pain. Statistical analysis was carried out using Fischer's exact test.

**Results:** We found that 32/64 (50%) of AAV patients fulfilled the case definition for CFS/ME. There was no relationship between the presence of AAV patients with CFS/ME compared to AAV patients without CFS/ME with BVAS ( $P = 0.65$ ), VDI ( $P = 1$ ), or C-reactive protein ( $P = 0.07$ ) in our study population. However, a considerable and statistically significant correlation was present in patients with AAV suffering from CFS/ME with anxiety ( $P = 0.0095$ ), depression ( $P = 0.0001$ ), cognitive failure ( $P = 0.0002$ ), fibromyalgia ( $P = 0.0031$ ), sleep disorder ( $P = 0.0007$ ). Also, we found a substantial reduction in a role physical functioning ( $P = 0.0001$ ), vitality ( $P = 0.0001$ ), and social functioning ( $P = 0.0001$ ) were extremely apparent in AAV patients with ME/CFS (compared to AAV patients without ME/CFS or HC).

**Conclusion:** Chronic fatigue affects AAV patient's mental wellbeing. From our analysis we conclude that chronic fatigue, cognitive failure, anxiety/depression, sleep and pain, co-occur independently of vasculitis disease activity. We postulate that adjunct therapies aimed at improving these symptoms should be utilized for patients with AAV suffering from fatigue. Funding: Dutch Kidney Foundation (17PhD01) Arthritis Society (19-0558)

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### A PRAGmatic Study of Vitamin D Status in ANCA-associated Vasculitis (PRAVDA): Protocol From the Toronto Vasculitis Clinic

Irena Doubelt (Vasculitis Clinic, Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto); Christian Pagnoux (Vasculitis Clinic, Canadian Network for Research on Vasculitides (CanVasc), Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto)

**Background:** Vitamin D may participate in the pathogeny of several immune-mediated diseases. It may have a significant role in initiation, progression and/or severity of antineutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV), though data are limited.

**Objective:** To conduct a pragmatic study to assess associations of vitamin D status, followed by vitamin D supplementation as indicated, to disease manifestations, activity and/or relapse in a local cohort of patients with AAV.

**Methods:** PRAVDA is a 12-month exploratory, prospective, pragmatic trial assessing 25-hydroxy-vitamin D<sub>3</sub> (25[OH]D<sub>3</sub>) status at baseline in patients with AAV, followed by an adjustment in vitamin D<sub>3</sub> dose supplementation as indicated based on baseline level. One hundred consecutive patients with AAV followed in the Toronto Vasculitis Clinic at Mount Sinai Hospital, Ontario, Canada will be enrolled. Vitamin D status will be measured at baseline ( $\pm$  3-4 weeks of enrollment), followed by repeat measurement at 12-months ( $\pm$  2 months). Patients with insufficient ( $< 75$  nmol/L) and/or deficient vitamin D status ( $< 50$  nmol/L) at entry visit will be informed and counselled to increase their vitamin D<sub>3</sub> supplementation by 1,000 IU/day (to a maximum of 2,000 IU/day; patients reportedly taking 2,000 IU/day of vitamin D will only be encouraged to take it regularly, without being asked to increase their dosage). The primary outcome is disease outcome (activity and relapse) at 12 months. Should disease relapse occur during the study period, it will be encouraged for the physician to measure 25(OH)D<sub>3</sub> at the time of relapse. The secondary outcomes will assess for associations of vitamin D status (baseline and/or 12-months) with specific disease manifestations (eg. lung fibrosis and renal function).

**Conclusion:** This is the first prospective study to assess correlations between vitamin D status and AAV manifestations/outcomes following a pragmatic vitamin D<sub>3</sub> dose adjustment in AAV. This study will inform providers about the utility of implementing routine vitamin D status measurements in patients with AAV, and whether stringent vitamin D supplementation should be further assessed with a larger randomized controlled trial.



### Observational Cohort Study of an Online Musculoskeletal Ultrasound Course

Shirley Lake (University of Toronto, Toronto); Lynfa Stroud (University of Toronto, Toronto); Christopher Penney (University of Calgary, Calgary); Diane Wilson (Lunenburg); Maria Bagovich (University of Toronto, Toronto); David Bong (Instituto Poal de Reumatologia, Barcelona); Susan Barr (University of Calgary, Calgary); Ryan Brydges (University of Toronto, Toronto)

**Objectives:** The Canadian Rheumatology Ultrasound Society (CRUS) has delivered a point-of-care musculoskeletal ultrasound (MSK US) course annually since 2010, normally held in-person over two weekends. The COVID-19 pandemic has required that the course be delivered completely online. We aimed to determine the impact of this change by comparing the homework adherence, and acquisition of MSK US knowledge and skills in the new online cohort versus a historical in-person cohort. We hypothesized that learning online is as efficacious as in-person learning.

**Methods:** Participants attended two weekends (October and March), in-person (2018-2019 cohort) or online (2020-2021 cohort). All were asked to submit US images every 2 weeks for 3 to 5 months after each weekend, for which they received written feedback from expert faculty. As a part of the on-line instructional approach, participants also had the opportunity to meet one-on-one on Zoom with assigned mentors. We compared the percentage of participants who submitted any US homework images, and the overall homework completion rate. Two independent, blinded reviewers scored a sample of submitted US images using published criteria.

**Results:** For the 2018-2019 cohort, 63% (17/27 students) submitted US homework, and had an average homework completion rate of 39%. Few (5, 19%) completed all their homework batches, and 56% (15) completed one or none. For the 2020-2021 online cohort, 71% (17/24 students) submitted US homework, and had an average homework completion rate of 48%. Few (4, 17%) completed all their homework batches, and 29% (7) completed one or none. Post-course evaluation forms revealed high satisfaction scores that were similar in both groups. Scores reflecting US skills have been collected and final results comparing the two groups will be presented.

**Conclusion:** Students were overall satisfied with the online course. The two cohorts had similar rates of participation, though the online cohort did complete a greater percentage of their US homework. We expect few differences in their acquired MSK US skills, which may influence course planners as they consider a return to in-person teaching beyond the pandemic.

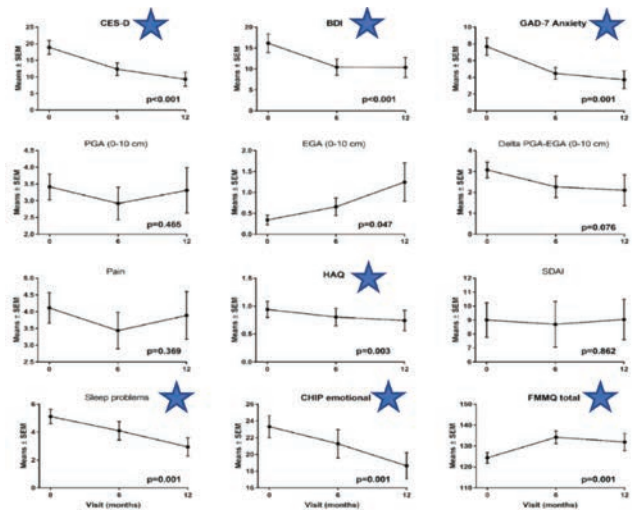
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### Mindfulness-based Stress Reduction (MBSR) in Rheumatoid Arthritis (RA) Patients: A Patient-related Outcomes (PRO)-oriented Pilot Trial

Isabelle Gaboury (Université de Sherbrooke, Sherbrooke); Patricia Dobkin (McGill University, Montréal); Marie-Claude Beaulieu (Université de Sherbrooke, Sherbrooke); France Gervais (Rimouski); Françoise Gendron (Sherbrooke); Pasquale Roberge (Université de Sherbrooke, Sherbrooke); Pierre Dagenais (Department of Medicine, Division of Rheumatology, Centre Hospitalier Universitaire de Sherbrooke, Université de Sherbrooke, Sherbrooke); Sophie Roux (Université de Sherbrooke, Sherbrooke); Gilles Boire (Université de Sherbrooke, Sherbrooke)

**Objectives:** In a pragmatic pilot study, group sessions of Mindfulness-Based Stress Reduction (MBSR), an eight-week non-pharmacological approach, were offered to patients with clinically controlled RA but elevated negative Patient-Related Outcomes (PROs) and/or elevated Patient Global Disease Activity (PGA) scores.

**Methods:** During each 4-week period preceding the start of 4 successive MBSR groups held between November 2017 and June 2019, patients reported in clinical remission on stable treatment at last visit were reassessed at their regular follow-up, and referred to research assistants if still clinically controlled and interested. Inclusion criteria were either elevated



**Figure. Evolution over time following MBSR group sessions.** CES-D: Center for Epidemiologic Studies Depression scale; BDI: Beck Depression Index; GAD7: General Anxiety Disorder-7; PGA: Patient Global Disease Activity scale; EGA: Physician Global Disease Activity scale; Pain: 0-10 cm Visual Analog Scale (VAS); HAQ: Modified Health Assessment Questionnaire; SDAI: Simple Disease Activity Index; Sleep problems: 0-10 cm VAS (10 being the worst possible); CHIP: Coping with Health Injuries and Perturbations; FMMQ: Five Facets of Mindfulness Questionnaire. Global p-values were calculated with linear mixed regression models for continuous outcomes. p-values were adjusted ( $p_{adj}$ ) using False discovery rate correction. ★ indicates  $p_{adj} \leq 0.01$

( $\geq 16$ ) Center for Epidemiologic Studies Depression (CES-D) score or a difference  $\geq 2/10$  (Delta) between PGA and Physician General Assessment (EGA). Questionnaires on depression (CES-D and BDI), anxiety (GAD-7), sleep quality, function (M-HAQ), coping strategies (CHIP), mindfulness (FMMQ), and Simple Disease Activity index (SDAI) were evaluated at baseline and 6 and 12 months after the intervention. Scores were compared between baseline and 6 and 12 months. Differences were assessed with linear mixed regression models. P values were adjusted for multiple comparisons. Eleven participants were interviewed about their experience after the 6-month assessment using a semi-structured interview guide.

**Results:** Out of 306 tagged patients, 241 were not offered MBSR: 168 (69.7%) not eligible, 55 (22.8%) declined, 18 (7.5%) other reason. Of the 65 proposed MBSR, 39 (60%) consented, 31 took part to at least 1 meeting, and 28 (43%) completed both the baseline and the 6- and/or 12-month evaluation. Timing, site and frequency of the meetings, extremes of age and comorbidities were reported as barriers to participation. Results showed significant and progressive improvements from baseline to 12 months post-MBSR for depression, anxiety, emotional coping, sleep quality, mindfulness and function (Figure). PGA, Pain and SDAI did not change significantly. Emotional coping was the only strategy significantly modified by MBSR. Qualitative interviews at 6 months in 10 patients indicated persistent subjective patient benefits including integration of MBSR techniques and effective coping strategies into daily life.

**Conclusion:** Hurdles to offering MBSR to controlled RA patients with high negative PROs are numerous. Nonetheless, MBSR had lasting benefits on outcomes that are important to patients, particularly anxiety, depression, sleep, and function. MBSR enabled patients to use fewer emotional coping strategies, a maladaptive approach to illness critical to quality of life. MBSR did not appear to improve PGA or pain and did not increase SDAI remission. The reasons for the apparent PGA/other PROs require further studies. Supported by a CIORA grant.

### Assessment of Adult Rheumatologists' Knowledge, Comfort Level, and Perceived Barriers in Supporting Youth With Chronic Rheumatic Diseases in Canada

Madhavi Prasad (London Health Sciences Centre, London); Michelle Bathish (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Roberta Berard (Children's Hospital, LHSC, London)

**Objectives:** Transitioning from pediatric to adult rheumatology care around age 18 is an important and often stressful period in patients' lives. Factors influencing transition include increasing autonomy over one's care, increased morbidity, hospital and administrative policy changes, and psychosocial concerns. These medical and life changes, occurring at a vulnerable time, can last into adulthood and can lead to gaps in care and loss to follow-up after transfer to adult care. In contrast to pediatricians and pediatric trainees who are familiar with adolescent psychosocial concerns and behaviors, adult rheumatologists report having inadequate training in transition issues, specifically psychosocial concerns, and are less familiar with transition guidelines. The purpose of this study was to develop a survey to assess the comfort level, current practices, and barriers to provision of optimal care faced by adult rheumatologists in supporting young adults with rheumatic conditions in Canada.

**Methods:** Development of the survey began with a literature review in PubMed using the search terms "transition", "rheumatology" and "young adult". The majority of published surveys were targeted towards patients' experiences or pediatric rheumatologists and asked generalized questions pertaining to psychosocial concerns. Questions about confidence, transition education, current practices and barriers were developed using the milestones listed by the Royal College of Physicians and Surgeons of Canada for the entrustable professional activities (EPAs) applicable to care for patients transitioning to adult practice. Feedback was obtained from adult rheumatologists and the Canadian Rheumatology Association (CRA) Transition Working Group prior to finalizing survey questions.

**Results:** A 39-question survey was developed targeting Canadian adult rheumatologists and adult rheumatology trainees. The survey contained questions pertaining to demographics and transition practices. EPAs addressed included Core EPA 12P- "Supporting adolescents/young adults with rheumatologic disease in the transition from the pediatric to adult care setting". Topics covered in the survey included mental health, contraception, body image, sexuality, and drug use.

**Conclusion:** Transition to adult care can be a challenging process for patients, parents, and healthcare providers. By developing a survey that collects specific information about psychosocial concerns, we aim to understand current practices and identify barriers that adult rheumatologists face to inform future educational interventions and identify potential areas for quality improvement initiatives. The survey will be distributed electronically through the Canadian Rheumatology Association in both English and French in October 2021.

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#### Decline in Clinical Severity of Paget's Disease of Bone: Comparison Between a Contemporary Cohort and a Historical Cohort

Evelyne Gendron (CHU de Québec-Université Laval, Québec); Frédéric Bouchard (Université Laval, Québec); Narcisse Singbo (Centre de recherche du CHU de Québec-Université Laval, Québec); Jacques Brown (Department of Rheumatology, CHU de Québec-Université Laval, Québec); Laetitia Michou (Department of Rheumatology, CHU de Québec-Université Laval, Québec)

**Objectives:** European and Australian studies have reported a decrease in the prevalence, incidence and clinical severity of Paget's disease of bone (PDB). There are no studies on the clinical characteristics of PDB in the Québec area. The purpose of this study was to describe the characteristics of patients with PDB diagnosed after the year 2000 in our region and to compare them to a historical cohort diagnosed before 2000.

**Methods:** In this retrospective descriptive cohort study, sociodemographic

data and clinical characteristics for the contemporary cohort were collected from electronic medical records of patients with PDB followed at our university hospital. For the historical cohort, the same data were collected from the research files of PDB participants in our research program. Inclusion criteria were: age > 18 years, having PDB diagnosed by a rheumatologist, and being followed in our hospital. Quantitative variables were reported as median and interquartile range and qualitative variables reported as percentage. Chi-square tests were used to compare categorical variables. Continuous values were compared with Wilcoxon-Mann-Whitney tests. Statistical analyses were performed by the use of SAS 9.4. A p value < 0.05 was considered statistically significant.

**Results:** 90 patients with PDB were identified in the contemporary cohort: 52.2% were men and 60% have monostotic involvement. 20.7% were symptomatic at diagnosis. In comparison to the historical cohort of 295 patients, patients in the contemporary cohort were older at diagnosis ( $68.3 \pm 12.6$  vs  $62.5 \pm 10.9$ ;  $P < 0.0001$ ). Statistically significant decreases were identified in total alkaline phosphatase levels at diagnosis ( $119.0$  ( $85.0$ - $181.0$ ) vs  $153.0$  ( $96.0$ - $254.0$ );  $P = 0.0178$ ), pagetic bone number ( $1.0$  ( $1.0$ - $3.0$ ) vs  $2.0$  ( $1.0$ - $4.0$ );  $P = 0.0085$ ), pagetic bone fractures ( $5.6\%$  vs  $28.3\%$ ;  $P = 0.0004$ ), bone deformities ( $10.0\%$  vs  $44.0\%$ ;  $P < 0.0001$ ), and the percentage of patients who had orthopedic surgery related to PDB complications ( $7.8\%$  vs  $30.4\%$ ;  $P = 0.0079$ ). There was no significant difference for pagetic bone pain ( $58.9\%$  vs.  $43.8\%$ ;  $P = 0.0605$ ), secondary osteoarthritis ( $42.2\%$  vs.  $51.0\%$ ;  $P = 0.3739$ ), and hearing impairment ( $57.9\%$  vs.  $52.9\%$ ;  $P = 0.7911$ ).

**Conclusion:** The contemporary cohort is characterized by older age at diagnosis, a majority of monostotic disease and fewer complications of PDB. This decline in clinical severity of PDB in Québec is consistent with studies reported in other countries.

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#### Increased Risk of Severe Infections and Mortality in Patients With Newly Diagnosed Antineutrophil Cytoplasmic Antibody-associated Vasculitis: A Population-based Study

Kai Zhao (Arthritis Research Canada, Coquitlam); Hui Xie (Arthritis Research Canada/Faculty of Health Sciences at Simon Fraser University, Richmond); Antonio Avina-Zubieta (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Richmond)

**Objectives:** To evaluate the risk of severe infection and infection-related mortality among patients with newly diagnosed anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV).

**Methods:** We conducted an age- and gender-matched cohort study of all patients with incident AAV between January 1, 1997, and March 31, 2015, using administrative health data from British Columbia, Canada. Primary outcome was the first severe infection after AAV onset necessitating hospitalization or occurring during hospitalization. Secondary outcomes were total number of severe infections and infection-related mortality.

**Results:** We identified 559 AAV patients and matched them with 5,590 non-AAV individuals from the general population, yielding 187 and 510 first severe infections during 2,603 and 36,111 person-years follow-up, respectively. The crude incidence rate ratios for first severe infection and infection-related mortality were 5.08 (95% CI, 4.30-6.01) and 3.72 (95% CI, 2.44-5.67), respectively. The corresponding adjusted hazard ratios were 3.77 (95% CI 2.94-4.85) and 3.84 (95% CI, 2.13-6.91). AAV patients had an increased risk of a greater total number of severe infections with crude rate ratio of 5.07 (95% CI, 4.50-5.70) and adjusted rate ratio of 3.23 (95% CI, 2.77-3.78).

**Conclusion:** AAV is independently associated with increased risks of first severe infection (3.8-fold), a greater total number of severe infections (3.2-fold) and infection-related mortality (3.8-fold).

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#### Discontinuation/Switching After Etanercept Biosimilar (ETA-B) and Originator (ETA-O) Initiation in Rheumatoid Arthritis

Cristiano Soares de Moura (The Research Institute of the McGill University Health Centre, Montreal); Luck Lukusa (Montreal); Stephanie



Keeling (University of Alberta, Division of Rheumatology, Edmonton); Walter Maksymowych (Department of Medicine, University of Alberta, Edmonton); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal)

**Objectives:** The first biosimilar etanercept (ETA-B) was approved in Canada in 2016, but real-world data comparing therapy persistence of ETA-B with its equivalent originator product (ETA-O) remain scarce. We compared therapy changes (discontinuation/switching) after ETA-B and ETA-O initiation in rheumatoid arthritis (RA).

**Methods:** We selected a cohort of etanercept-naïve RA patients starting ETA-B or ETA-O between January 2016 and May 2020 from a prospective inception cohort in Canada. We restricted the analyses to patients with at least one follow-up visit within six months after treatment initiation. We assessed the first change of therapy, either discontinuation or switching (to any biologic, including ETA-O to ETA-B or vice-versa). We used Cox regression to compare time to first change in therapy (discontinuation/switching), between ETA-O and ETA-B. The model adjusted for sex, maternal race/ethnicity, and baseline age, RA duration, and use of any other prior biologic or prednisone.

**Results:** We studied 141 RA patients initiating etanercept (24% biosimilar) between 2016-2020. Biosimilar initiation increased over time, representing 27% of all etanercept new users in 2016-17 and 74% in 2018-19. During follow-up, there were 53 (38%) events (first discontinuation/switching) among 141 etanercept users, 43% in the ETA-O and 27% in the ETA-B group. In the multivariate analysis, we were unable to detect a clear difference in risk of discontinuation/switching, comparing ETA-B to ETA-O (hazard ratio 1.01, 95% confidence interval 0.52-1.95; Table 1). Prednisone use at the time of ETA initiation was associated with a greater risk of discontinuation/switching.

**Conclusion:** Initiators of biosimilar etanercept in this RA sample increased over 2016-2019. We were unable to detect clear differences in discontinuation/switching, between ETA-B and ETA-O initiators.

**Table 1 – Cox proportional hazard model results for therapy change among etanercept-naïve users.**

| Baseline characteristics                      | Unadjusted HR (95% CI)   | Adjusted HR (95% CI) <sup>a</sup> |
|-----------------------------------------------|--------------------------|-----------------------------------|
| Biosimilar etanercept                         | 1.00 (0.53, 1.91)        | 1.01 (0.52, 1.95)                 |
| Female sex                                    | 0.99 (0.55, 1.81)        | 0.99 (0.54, 1.84)                 |
| Caucasian mother race/ethnicity               | 1.20 (0.60, 2.40)        | 1.49 (0.69, 3.22)                 |
| Age at etanercept initiation, years           | 1.00 (0.98, 1.02)        | 1.00 (0.98, 1.02)                 |
| RA duration at etanercept initiation, years   | 1.00 (0.97, 1.03)        | 0.99 (0.96, 1.03)                 |
| Prior biologic (before etanercept initiation) | 1.66 (0.89, 3.12)        | 1.59 (0.80, 3.16)                 |
| Prednisone at time of ETA                     | <b>6.05 (1.41, 25.9)</b> | <b>5.63 (1.10, 28.7)</b>          |

<sup>a</sup> Adjusted for all variables shown.

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### Mycophenolate and Azathioprine Are Associated With Risk of Hospitalized Viral Respiratory Infection in Rheumatoid Arthritis and Systemic Lupus Erythematosus

Cristiano Soares de Moura (The Research Institute of the McGill University Health Centre, Montreal); Marina Machado (McGill University/Federal University of Minas Gerais, Montreal); Celline Almeida-Brasil (McGill University Health Centre, Montreal); Jeffrey Curtis (University of Alabama at Birmingham, Birmingham); Kevin Winthrop (Oregon Health Sciences University, Portland); Michal Abrahamowicz (McGill, Montreal); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal)

**Objectives:** Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients may be at a higher risk of severe infections because of their underlying condition and/or use of immunosuppressive medications. The objective of this study was to evaluate the risk factors for hospitalization for viral respiratory infections among RA and SLE patients.

**Methods:** We studied adult RA and SLE individuals identified in the MarketScan database (2011-2018) with an outpatient diagnosis (including emergency room, ER) of viral pneumonia or other viral respiratory infec-

**Table 1 – Baseline characteristics of RA and SLE patients with outpatient viral infection, MarketScan 2011-2018.**

| Characteristic                     | RA/SLE cohort (n= 54,561) |
|------------------------------------|---------------------------|
| SLE as underlying condition, N (%) | 9286 (17.0)               |
| Female sex, N (%)                  | 43668 (80.0)              |
| Mean age (Standard Deviation, SD)  | 57.4 (13.9)               |
| Diabetes                           | 10416 (19.1)              |
| Hypertension                       | 29941 (54.9)              |
| COPD/asthma                        | 14611 (26.8)              |
| Hydroxychloroquine/chloroquine     | 12473 (22.9)              |
| Methotrexate                       | 14446 (26.5)              |
| Mycophenolate                      | 791 (1.45)                |
| Azathioprine                       | 921 (1.69)                |

tions. We required patients to be covered in the medical/pharmacy plan one year before time zero (date of outpatient infection). The outcome was hospitalization for viral infection within the 30 days after time zero. We used multivariate Poisson regression models to assess risk factors associated with the outcome, including recent use (in the 90 days prior to time zero) of relevant medications: hydroxychloroquine (HQN) or chloroquine (CQ), methotrexate, mycophenolate (MMF), azathioprine (AZA), other immunosuppressants (cyclophosphamide, sulfasalazine, and leflunomide), corticosteroids, biologics, and NSAIDs, age, sex, setting in which viral infection was initially identified (ER or other), underlying condition (RA or SLE), and comorbidities.

**Results:** We identified 63,971 episodes of outpatient viral respiratory infections among 54,561 RA/SLE patients (80% female, average age 57.4 years, standard deviation 13.9 – Table 1). During the 30-day period following outpatient infection, we found 480 occurrences of hospitalization for viral respiratory infections. In adjusted multivariate analyses, use of MMF (adjusted RR, aRR 2.54, 95% CI: 1.51-4.28), AZA (aRR 1.90, 95% CI: 1.12-3.22) and corticosteroids (aRR 1.57, 95% CI: 1.29-1.91) were significantly associated with the risk of hospitalized viral respiratory infections. HQN/CQ was not associated with the outcome studied (aRR 0.89, 95% CI: 0.702-1.12). In the same model, comorbidities, ER presentation, and older age were also significantly associated with hospitalized viral infection.

**Conclusion:** Among RA/SLE patients with an outpatient viral infection, MMF and AZA, as well as corticosteroids, comorbidities, ER presentation and older age, were all significantly associated with subsequent need for hospitalization. Our results for HCQ/CQ are consistent with recent clinical trials showing no protective effect of these drugs to reduce the risk of severe COVID-19.

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### Placental Changes in Pregnancies With Anti-Ro/La Antibodies

Nikola Wilk (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal); Mayssa Moukarzel (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Jessica Simoneau (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Wadi Mawad (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Gabriel Altit (Department of Pediatrics, Division of Neonatology, Montreal Children's Hospital, McGill University, Montreal); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal)

**Objectives:** Some maternal rheumatological conditions are known to be associated with placenta-mediated pregnancy complications, such as preeclampsia. Yet, placental changes in this population remain understudied. Our objectives were to review placental pathological changes in anti-Ro/La-positive pregnancies and compare them to those observed in anti-Ro/La-negative pregnancies from mothers with and without rheumatic diseases.



**Table 1 – Placenta pathology according to maternal anti-Ro/La and autoimmune disease status**

|                                                | Group 1<br>Anti-Ro/La-positive<br>(n=38) | Group 2<br>Anti-Ro/La-negative<br>rheumatic disease<br>(n=9) | Group 3<br>Control (n=8) |
|------------------------------------------------|------------------------------------------|--------------------------------------------------------------|--------------------------|
| Ischemic-hypoxic change                        | 2 (5.3%)                                 | 0                                                            | 0                        |
| Decidual thrombi                               | 2 (5.3%)                                 | 1 (11.1%)                                                    | 0                        |
| Fetal thrombi                                  | 2 (5.3%)                                 | 0                                                            | 0                        |
| Chronic villitis                               | 3 (7.9%)                                 | 0                                                            | 0                        |
| Decreased placental weight                     | 9 (23.7%)                                | 2 (22.2%)                                                    | 0                        |
| Perivillous fibrinoid change                   | 4 (10.5%)                                | 2 (22.2%)                                                    | 0                        |
| Villous maturation<br>inappropriate (advanced) | 7 (18.4%)                                | 0                                                            | 0                        |
| Villous infarction                             | 3 (7.9%)                                 | 2 (22.2%)                                                    | 0                        |
| Fetal vascular malperfusion                    | 4 (10.5%)                                | 0                                                            | 0                        |

All *p* values were above 0.05.

**Methods:** Using an electronic database, we identified all pregnancies referred for fetal echocardiogram between 2013 and 2021 at the McGill University Health Centre, with the following key words within the clinical indication field: “congenital heart block”, “anti-Ro”, “anti-La”, “lupus”, “SLE”, “Sjogren”, or “mixed connective tissue disease”. Pregnancies with a fetus exhibiting cardiac anatomical and/or genetic anomalies were excluded. Pregnancies were classified as follows: 1) those with positive anti-Ro/La antibodies, 2) those with a rheumatic disease with negative anti-Ro/La, and 3) control pregnancies identified from the fetal echocardiography database without maternal rheumatic disease nor anti-Ro/La.

**Results:** Out of 117 pregnancies screened, 62 were included, with a total of 75 fetuses studied. In total, 55 placenta pathology results were available, for a total of 38 placenta in the first group, 9 in the second group and 8 in controls. Placenta was described as normal in only 34.2% of anti-Ro/La-exposed pregnancies and 44.4% of anti-Ro/La-negative autoimmune disease pregnancies compared to 75.0% of controls ( $P = 0.27$ ). Different pathological changes were observed (Table 1), including ischemic-hypoxic changes, chronic villitis, decreased placental weight, inappropriately advanced villous maturation and fetal vascular malperfusion, all more frequent in the anti-Ro/La-positive pregnancies, although not statistically significant. Interestingly, these changes occurred in the setting of having similar incidence of gestational hypertension (4 [8.5%] vs 2 [18.2%] vs 2 [11.8%],  $P = 0.67$ ), and preeclampsia/eclampsia (no cases).

**Conclusion:** Though limited by a small sample size, we observed a potential trend for more placental pathological anomalies in anti-Ro/La-exposed pregnancies compared to those from mothers with and without rheumatic disease. It is possible that confounding by maternal disease severity contributed to our findings. However, prior evidence demonstrates that anti-Ro/La antibodies are transported across the placenta via Fc $\gamma$  receptors on the trophoblast and bind apoptotic fetal cells. Further studies are needed to investigate placental changes in anti-Ro/La-exposed pregnancies.

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### Glucagon-like Peptide 1 (GLP-1) Receptor Agonists in Patients With Obesity and Rheumatoid or Psoriatic Arthritis: A Scoping Review

Derin Karacabeyli (University of British Columbia, Vancouver); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver)

**Objectives:** Outline and appraise the literature evaluating the role of glucagon-like peptide 1 (GLP-1) receptor agonists for weight loss in patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA), as well as the effect of GLP-1 receptor agonists on disease activity in patients with RA or PsA with or without obesity.

**Methods:** MEDLINE, PubMed, and Embase were searched using permutations of the search terms: “GLP1”, “rheumatoid arthritis”, “psoriatic arthritis”, and “psoriasis”. English publications (including conference abstracts) evaluating the role of GLP-1 receptor agonists in RA, PsA, and psoriasis were eligible. Review articles, editorials, and studies assessing GLP-1 receptor agonists’ impact on patients without RA, PsA, or psoriasis were excluded. Articles were reviewed and data were extracted by one author. Articles were individually appraised, then grouped by design to identify prevailing findings.

**Results:** Fourteen studies were included, 4 pertaining to RA (2 basic science and 2 conference abstracts ie, 1 case report and 1 uncontrolled prospective cohort) and 10 pertaining to psoriasis (1 basic science, 1 mouse model, 2 case reports, 1 combined case report/basic science, 3 uncontrolled prospective cohorts, and 2 randomized controlled trials). No studies primarily evaluating PsA were identified. Basic science experiments demonstrated potential immunomodulatory effects of GLP-1 receptor agonists. Reductions in oxidative stress and key proinflammatory cytokines and pathways were seen in two experiments using stimulated fibroblast-like synoviocytes as a model of RA. Similar anti-inflammatory effects were observed in psoriasis experiments through effects on invariant natural killer T cells and AMPK phosphorylation. Publications of GLP-1 receptor agonists in patients with RA were limited to two conference abstracts. One noted mean DAS-28 improvement (4.2 to 2.7) and weight loss (-3.4kg) in 9/15 participants (60%); the other described a change in DAS-28 from 5.5 to 3 after a patient started liraglutide. In psoriasis, 4 of 5 clinical studies (80%) demonstrated significant improvements in Psoriasis Area Severity Index and weight/BMI. No major adverse events were reported. Transient nausea was noted in 4/6 studies (67%). Common limitations included small sample sizes, short follow-up periods, and lack of control groups.

**Conclusion:** With established weight loss properties and possible immunomodulatory and anti-inflammatory effects, GLP-1 receptor agonists warrant further study as a potential adjunctive therapy in the management of rheumatoid and psoriatic arthritis in patients with obesity.

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### Developing and Characterizing an Osteochondral Model for Evaluating Psoriatic Arthritis Therapies

Atoosa Ziyayyan (Krembil Research Institute, University of Toronto, Toronto); Katerina Oikonomopoulou (Krembil Research Institute, Toronto); Vinod Chandran (Krembil Research Institute, Toronto Western Hospital, Toronto); Sowmya Viswanathan (Krembil Research Institute, Toronto)

**Objectives:** The absence of a cure for psoriatic arthritis (PsA) and limited studies surrounding its models increases the need to develop a reliable PsA model. We are developing a high-throughput ex vivo PsA model that can capture the multi-tissue interactions often omitted in in vitro culture studies and challenging to conduct in in vivo models and evaluate novel therapeutic agents. Osteoarthritis (OA) and PsA share common features. OA is a less inflammatory disease than PsA. Therefore, samples from OA patients are commonly used as controls for studies in PsA. Our lab has developed and validated an explant co-culture model of cartilage and synovium tissues from end-stage OA patients to evaluate injectable therapies. This co-culture system is modified to include PsA synovial fluid (SF) and bone. The presence of bone is essential in the PsA model since both bone formation and bone destruction are seen in PsA joint. In addition, including PsA SF is critical since it is enriched with essential immune cells activated in PsA, such as T cells and macrophages. The overall objective is to develop and characterize a human osteochondral model for evaluating PsA therapies. Aim 1: Modify/optimize a human OA joint ex vivo model to be more representative of PsA. Aim 2: Validate the proposed model using an anti-IL-17A drug, a standard treatment for PsA.

**Methods:** To develop the ex vivo model, SF is obtained from PsA patients, and tissues are obtained from OA patients following total knee replacement surgery. The groups in this study contain cartilage-bone and synovium (COCUL)+ medium; baseline, COCUL+ proinflammatory cytokines;

positive control, COCUL +OA SF; OA group, and COCUL + PsA SF; PsA group. An anti-IL-17A drug is used to validate this model. Following readouts are investigated; qPCR on cartilage-bone and synovium explant tissues, histology of cartilage-bone and synovium, ELISA on the secreted factors into the medium of all conditions.

**Results:** Histology confirms the maintenance of synovium architecture and increased cell infiltration in the positive control, PsA and OA co-culture groups compared to the baseline. There has been an upregulation of genes associated with inflammation in the PsA group relative to the OA group. We are looking to add additional controls and do more optimizations to confirm these findings and validate them with an anti-IL-17 treatment.

**Conclusion:** Our model enables monitoring changes in the bone, cartilage, and synovium in response to various factors such as proinflammatory cytokines and SF in an ex vivo environment.

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### **“It’s a Dance Between Managing Both”: A Qualitative Study Exploring Perspectives of Persons With Knee Osteoarthritis and Type 2 Diabetes Mellitus on the Impact of Osteoarthritis on Diabetes Management and Daily Life**

Lauren King (University of Toronto, Toronto); Esther Waugh (University of Toronto, Toronto); Crystal Mackay (University of Toronto, Toronto); Jane Stretton (Patient Research Partner, Toronto); Ian Stanaitis (Women’s College Research Institute, Women’s College Hospital, Toronto); Lorraine Lipscombe (University of Toronto, Toronto); Gillian Hawker (University of Toronto, Toronto); Janet Parsons (University of Toronto, Toronto)

**Objectives:** The links between osteoarthritis (OA) and other common chronic conditions are increasingly being appreciated in epidemiological studies. Type 2 diabetes mellitus (T2DM) and knee OA commonly co-occur. Although concomitant symptomatic knee OA may increase risk of T2DM complications, no studies have examined patients’ perspectives on the intersection and interrelationship of these conditions. We sought to explore individuals’ experiences living with both knee OA and T2DM, with a focus on the impact of OA on T2DM management and daily life.

**Methods:** Semi-structured telephone interviews were conducted with 18 persons with a physician diagnosis of T2DM and symptomatic knee OA recruited from an urban family medicine clinic and a community arthritis rehabilitation program (Arthritis Society) in Ontario, Canada. Interview transcripts were inductively coded and analysed using thematic analysis, informed by interpretive description. Interviewing stopped after no new themes or subthemes were identified.

**Results:** The 18 participants were in the following age groups: two 40-49 years, two 50-59 years, five 60-69 years, and nine  $\geq$  70 years, included nine woman, and represented a range of both OA and T2DM disease severity. Three overarching themes were constructed: OA impacts diabetes control, OA is a health priority, and Minimization of OA by health care providers. Participants with T2DM described how concomitant painful, disabling knee OA made it difficult to engage in physical activity, negatively impacting blood sugar control. Joint pain itself, and the effect of pain on sleep and emotional health, were also seen to affect blood sugar control. Beyond diabetes management, the impact of OA-related pain and functional limitations on nearly all aspects of daily life led participants to view their OA as a health priority. Despite this, many participants relayed that their health care providers paid little attention to their OA, such that they were left to self-manage and advocate for their own OA care. Balancing both conditions required navigating a medical system that provided piecemeal disease-specific care.

**Conclusion:** These findings shed light on patients’ experiences of living with symptomatic knee OA in the context of T2DM. Individuals with T2DM see symptomatic knee OA as a barrier to T2DM self-management and quality of life yet are frequently met with insufficient support from health professionals. Greater recognition of and management of knee OA in persons with T2DM could help improve patient-centered care and disease outcomes.

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### **Cost Impact of Switching to Biosimilar Infliximab and Etanercept in British Columbia**

Alison McClean (School of Population and Public Health, University of British Columbia, Vancouver); Michael Law (Centre for Health Services and Policy Research, Vancouver); Mark Harrison (University of British Columbia/Arthritis Research Canada, Vancouver); Lucy Cheng (School of Population and Public Health, University of British Columbia, Vancouver); Fiona Clement (School of Public Health, University of Alberta, Calgary); Mina Tadrous (Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto); Nick Bansback (University of British Columbia/Arthritis Research Canada, Vancouver)

**Objectives:** Biosimilar medicines offer the potential for significant cost savings, but their uptake in North America has been relatively low. In 2019, the province of British Columbia (BC) became the first jurisdiction in North America to mandate switching from originator to biosimilar infliximab and etanercept in order to maintain coverage offered by the provincial government. We examined the impact of this policy on utilization and spending of the relevant biosimilars in patients with inflammatory arthritis and inflammatory bowel disease.

**Methods:** We used administrative data for the entire population of BC. Individuals were eligible for inclusion if they (1) were  $\geq$  18 years (2) had rheumatic or inflammatory bowel disease, and (3) were eligible for public drug coverage during the study period (Jan 2013 - Dec 2020). Individuals who ever received infliximab or etanercept and the number of switches were quantified. Using interrupted time series analysis, we examined the impact of the biosimilars policy on public and private payer spending on biosimilar infliximab and etanercept among individuals with diagnosis codes related rheumatic and inflammatory bowel disease.

**Results:** Over the entire study period, \$607 million and \$256 million was spent on infliximab and etanercept, respectively. Biosimilar spending was responsible for 9.9% and 12.9% of this expenditure on infliximab and etanercept, respectively. There was a sustained increase in the proportion of total spending on biosimilar etanercept and infliximab of 76.2% (95% CI 75.2, 77.2) and 80.9% (95% CI 77.7, 84.2), respectively, after the biosimilar policy was introduced, greater in the arthritis cohort than bowel disease. The overwhelming majority of switches to biosimilar infliximab (98.2%) and etanercept (94.4%) occurred post-policy.

**Conclusion:** There was a marked increase in biosimilar uptake, relative to the originator, after the introduction of a mandatory switching policy. The analysis is being updated with more recent data to understand the longer-term impact of the policy. It will also seek to understand patterns of those that switched compared to those that did not and potential impact on patients in terms of persistence on treatments and hospitalizations/physician visits. The results will help inform other provinces and jurisdictions in North America who are implementing or considering similar switching policies. Supported by a CIORA grant.

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### **Productivity Loss for Parents of Children With Arthritis: The Impact of Disease Activity Status**

Luiza Grazziotin (University of Calgary, Calgary); Gillian Currie (University of Calgary, Calgary); Maarten Ijzerman (University of Melbourne, Melbourne); Michelle Kip (University of Twente, Enschede); Erik Koffijberg (University of Twente, Twente); Marinka Twilt (University of Calgary, Calgary); Susanne Benseler (Section of Rheumatology, Department of Paediatrics, Alberta Children’s Hospital/University of Calgary, Calgary); Joost Swart (University of Utrecht, Utrecht); Sebastiaan Vastert (University of Utrecht, Utrecht); Nico Wulfraat (University of Utrecht, Utrecht); Rae Yeung (The Hospital for Sick Children, Toronto); Deborah Marshall (University of Calgary, Calgary); UCAN CAN-DU Investigators Understanding Childhood Arthritis Network (Toronto)

**Objectives:** This study estimates the loss of productivity of parents who care for children with juvenile idiopathic arthritis (JIA) and explore the impact of the disease activity status.

**Table 1.** Description of WPAI results for all participants (n=209) at baseline stratified by disease activity status.

|                                                                                                                                                                                           | Active disease<br>(n=165) | Inactive disease<br>(n=40) | Total<br>(n=209)* |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|----------------------------|-------------------|
| <b>Employment<sup>2</sup></b>                                                                                                                                                             |                           |                            |                   |
| Yes                                                                                                                                                                                       | 135 (81.8%)               | 27 (67.5%)                 | 165 (78.9%)       |
| <b>Percent work time missed due to children arthritis (absenteeism) (%)</b>                                                                                                               |                           |                            |                   |
| Mean (SD)                                                                                                                                                                                 | 12.1% (15.5)              | 6.4% (12.6)                | 11.0% (15.0)      |
| Median (IQR)                                                                                                                                                                              | 5.9% (0-20)               | 0.0% (0-9.1)               | 3.5% (0-19)       |
| <b>Percent impairment while working due to children arthritis (presenteeism) (%)</b>                                                                                                      |                           |                            |                   |
| Mean (SD)                                                                                                                                                                                 | 21.3% (21.2)              | 9.2% (18.4)                | 19.3% (21.1)      |
| Median (IQR)                                                                                                                                                                              | 10.0% (0-30)              | 0.0% (0-10)                | 10.0% (0-30)      |
| SD: standard deviation; IQR: interquartile range                                                                                                                                          |                           |                            |                   |
| <sup>1</sup> Question presented to all participants (n=209); <sup>2</sup> Questions presented to participants that are employed only (n=165); * Four patients had missing disease status. |                           |                            |                   |

**Methods:** The ongoing prospective, multicenter study “Canada-Netherlands Personalized Medicine Network in Childhood Arthritis and Rheumatic Diseases (UCAN CAN-DU)” enrolls children younger than 18, diagnosed with JIA and their parents from centers across Canada and the Netherlands. The family-reported socioeconomic disease burden was captured in standardized e-health instruments including the validated Work Productivity and Activity Impairment Questionnaire (WPAI): Specific Health Problems. WPAI measures the number of hours missed due to child’s health and due to other reasons, hours worked, degree their child’s health affected productivity while working (0-10, where 0 represents no effect and 10 complete impairment), and in regular unpaid activities (0-10) for a period of seven days. Absenteeism was calculated as the average percent of hours of work time missed, and presenteeism as the average percent impairment while working due to child’s JIA. Demographics for both patients and caregivers, and disease status (ie, active, and inactive using Wallace criteria) of the patient were also collected on the e-health platform. Results were described using mean, standard deviation (SD), and proportion, and compared by disease status using two-way t-tests.

**Results:** A total of 209 caregivers answered the questionnaires at baseline. Parent’s mean age was 43 years (SD 7.1), and 74% (n = 154) were female. Most children with JIA (79%, n = 165) experienced active disease at baseline. Most parent participants (79%, n = 165) were employed, and this percentage was lower for children with inactive disease status (81.8% vs 67.5%, for active and inactive disease, respectively). Among employed parents, for a period of seven days, a mean of 3.5 hours (SD 5.0) was missed due to child’s JIA (absenteeism percentage: 11% (SD 15.0)), and 1.8 hours (SD 5.9) due to other reasons. The absenteeism percentage was statistically different between active and inactive disease status (12.1% vs 6.4%,  $P < 0.05$ , respectively). The degree to which their child’s health affected work productivity and productivity in regular unpaid activities was 1.9 (SD 2.1) and 2.1 (SD 2.4), respectively. The mean presenteeism percentage was 19.3% (SD 21.1), also statistically higher for active than for inactive disease, (21.3% vs 9.2%,  $P < 0.05$ , respectively). Results are summarized in Table 1.

**Conclusion:** JIA results in socioeconomic burden to parents, including impact on absenteeism and presenteeism measures. However, those effects were significantly lower in parents of children experienced inactive disease status at the time.

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### Transition Us Together: Development of a Parent-Centered Toolkit to Support Adolescents With Rheumatic Disease Transition to Adult Care

Molly Dushnicky (McMaster University, Burlington); Karen Beattie (McMaster University, Hamilton); Jan Gorter (McMaster University, Hamilton); Michelle Batthish (McMaster University, Hamilton)

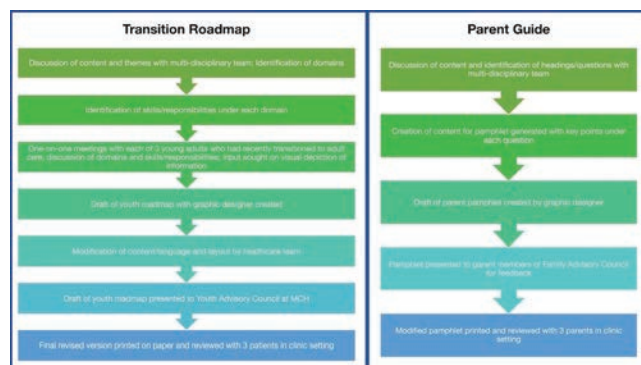
**Objectives:** The management of pediatric rheumatic disease in adolescents is complex, due to intricacies of treatment, attention required for disease monitoring, the interplay between physical health, psychosocial wellbeing and challenges associated with their transition from pediatric to adult

healthcare systems. This transition is marked by higher symptom burden and higher morbidity and mortality. Within pediatric rheumatology, up to 50% of transfers to adult care are unsuccessful, with loss-to-follow-up and low treatment adherence being the most common issues. Parents also face challenges in understanding their changing role and how to support their children during this time. To date, few resources have focused on supporting both parents and patients through this period. Our team sought to develop a patient- and parent-oriented toolkit to support families as they prepare for the transfer to adult rheumatology care.

**Methods:** Our multidisciplinary team developed a toolkit for patients and their parents to help prepare them for the transition to adult care. The toolkit was created using an iterative process (Figure 1) of reviewing existing resources with guidance and feedback from rheumatology patients and their parents. Input from other patient populations was sought from the Family and Youth Advisory Councils at McMaster Children’s Hospital.

**Results:** The two components of the toolkit include a Transition Road Map and a Parent Guide to Transition. Five domains of transition readiness were established as pillars of the Road Map: Self-Advocacy, Medication Management, Overall, Health and Safety, Lifestyle and Behaviors, and Future Planning. Within each domain, a checklist to achieve self-management was created, with each intended to be generalizable to adolescents with any rheumatic condition but could also be adapted to other chronic conditions. Feedback from the Youth Advisory Council included comments such as “I wish this existed in Pediatric Cardiology clinic”. Further, items on each checklist can be completed at an adolescent’s own pace, in any order, and can continue to be worked on as they transfer to adult care. The Parent Guide describes the transition process, highlights important information including the differences between pediatric and adult care, and provides tips to parents on supporting and empowering their child towards being a leader and advocate for their own care.

**Conclusion:** A Parent Toolkit directed at the Transition from Pediatric to Adult Rheumatology Care was co-created, with multiple stakeholders, and was well received by youth with various conditions. Ongoing research on its impact on transition readiness of youth and transition experiences of parents is underway.

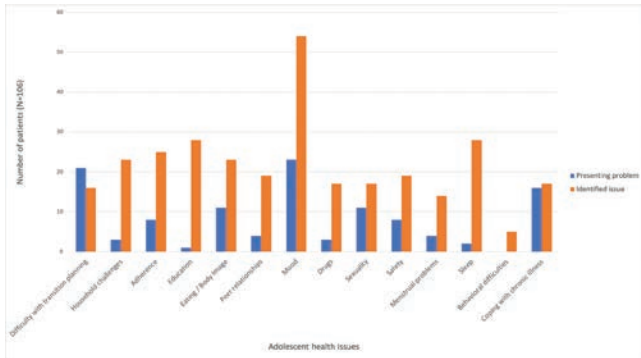


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### High Adolescent Health Needs and Relationship to Disease in Patients With Childhood-onset Systemic Lupus Erythematosus

Chelsea DeCoste (IWK Health Centre, Halifax); Paris Moaf (The Hospital for Sick Children, Toronto); Lawrence Ng (University of Toronto, The Hospital for Sick Children, Toronto); Dragana Ostojic-Aitkens (The Hospital for Sick Children, Toronto); Fatima Faruq (The Hospital for Sick Children, Toronto); Bryan Maguire (The Hospital for Sick Children, Toronto); Deborah Levy (Division of Rheumatology, SickKids Hospital; Faculty of Medicine, University of Toronto, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto); Alene Toulany (The Hospital for Sick Children, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto)





**Objectives:** To characterize the burden of adolescent health issues faced by patients with childhood-onset systemic lupus erythematosus (cSLE), as well as describe demographic and disease characteristics associated with adverse adolescent health.

**Methods:** We conducted a retrospective cohort study of adolescents aged 12-18 years with cSLE who were seen by Adolescent Medicine (AM) specialists in the Lupus Clinic at SickKids Hospital between July 2018-July 2020. As part of our cSLE care model, patients presenting with adolescent health issues were routinely seen by AM. Adolescent health issues were characterized using the HEADDSS framework (Home, Education/employment, peer group Activities, Drugs, Sexuality, and Suicide/depression), which was standardly recorded for all AM visits. Issues were classified as presenting and/or identified problems at each visit. Adolescent health burden was tabulated as the number of individual adolescent issues identified per patient. Multiple Poisson regression was used to examine associated patient factors, including age, gender, material deprivation score (measure of social marginalization that accounts for income, housing quality, educational attainment, and family structure), SLE disease activity and damage indices, and high-dose glucocorticoid exposure (> 3 months and any-time dose of > 30 mg prednisone equivalent).

**Results:** 226 adolescents with cSLE were seen in the Lupus Clinic during the observation period, of which 106 (47%) were seen by AM. Of these, 88 (83%) were female. Median age at first visit was 14 years (IQR 13-16). Patients had a median of 2 (1-3) visits with AM over the study period. Figure 1 shows the range of adolescent health issues described across all visits, of which mood was identified as the top adolescent issue (presenting problem in 22% and identified issue in 51% of patients). Patients had an average of 2.8 ± 2.31 separate adolescent health issues identified. In multiple regression analyses, higher adolescent issue burden was associated with higher glucocorticoid exposure (RR = 1.72, 95% CI 1.32-2.24), disease damage (RR = 1.30, 95% CI 1.30, 95% CI 0.99-1.70), higher material deprivation (RR = 1.16, CI 1.03-1.29), and lower disease activity (RR = 0.96, 95% CI 0.92-0.99). The most common service provided by AM was psychoeducation at 54%.

**Conclusion:** Adolescents with cSLE experience a wide range of physical and psychosocial issues in addition to their underlying disease. We found that increased cSLE disease severity and social marginalization put teens at higher risk of worse adolescent health issues, highlighting the need to discuss adolescent health during rheumatology clinic visits, and the importance of integrating AM specialists into routine cSLE care. Best Abstract on Pediatric Research by Young Faculty Award.

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### Assessing a Nursing Inter-professional Model of Care in Rheumatology

Alison Kelsall (Arthritis Research Canada, University of British Columbia, Vancouver); Michelle Teo (University of British Columbia, Penticton); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver)

**Objectives:** Canada faces rheumatology workforce shortages, with wide regional disparities, causing rural areas to be underserved. New ways of providing rheumatology care are needed to improve access, especially in rural areas, prevent physician burn-out, and reduce health inequities. This

study aimed to evaluate an inter-professional model of care implemented in rural Penticton, BC; to assess whether it improves access to rheumatologist care for inflammatory arthritis (IA) while providing high quality care.

**Methods:** We assessed access to, process and outcome of care, using Arthritis Alliance of Canada's IA system-level performance measures. Electronic medical records data were extracted on all IA patients seen in 2019 (ie, pre-COVID-19). The model consists of rheumatology nurses seeing patients first, taking histories, performing joint counts, addressing issues from nursing perspective, and identifying what the rheumatologist should address. This allows rheumatologists to focus on the most relevant or complex medical issues and on discussing management, with the aim of providing quality care more time-efficiently. Measures included: no. new/follow-up patients seen, wait time from referral to new consultation, continuity of care (% RA patients seen in yearly follow-up), extent and timeliness of DMARDs in RA; % RA patients meeting DAS-28 disease activity target and good physical function (HAQ < 1.0).

**Results:** In 2019, 3952 visits occurred in 1175 IA patients, including 214 new patients (RA: 568/72, PsA: 499/132, AS: 77/4, IBD-arthritis: 31/5), yielding a mean 32.3 follow-up visits and 3.5 new consults per clinic day worked. Median (25th;75th percentile) wait time for new consults was 104 (50;222) days in RA, 121 (62;281) in PsA, and 107 (44;1416) in AS. Only 7% of RA patients met the 28-day wait time alliance benchmark. Of RA patients seen in 2013-2018, yearly follow-up occurred in 69.4%. Of RA patients seen in 2019, 89.8% were prescribed a DMARD. In new RA patients, DMARDs were prescribed at initial consultation visit in most [median (25th;75th;90th percentile) no. days from RA diagnosis: 0 (0;1;97)], with 83.9% meeting the 14-day benchmark for starting DMARDs. Disease activity, calculated in 476 RA patients, met target in 86.3% (remission: 53.1%, low disease activity: 33.2%). Mean (SD) HAQ (n = 566 RA), was 0.77 (0.67), with 67% having good physical function.

**Conclusion:** This inter-professional nursing model of care allows greater access to care in underserved areas while maintaining high quality care, thus improving efficiency of service delivery where rheumatology workforce is sparse and reducing inequities in access to arthritis care. Despite greater efficiency of care delivery, wait times for new consults in IA patients in this rural underserved area remain suboptimal.

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### Telehealth: Enhancing the Role of Rheumatology Nursing Support

Arwa Nemir (University of British Columbia, Vancouver); Jason Kur (University of British Columbia, Vancouver); John Gurmin (Artus Health Centre, Vancouver)

**Objectives:** COVID-19 has precipitated a necessary and rapid shift away from the traditional and predominant model of care delivery for rheumatology patients in British Columbia (BC). Rheumatologists in the province have had to adapt to offer telehealth, now viewed as a safe medium, to provide care for their patients. Moreover, telehealth is considered to be an effective medium for follow-up visits that do not require procedures and immediate physical examination. The discipline has thus pivoted towards a hybrid model of in-person and virtual care. Prior to the COVID-19 pandemic, nurses played an essential role in the education and teaching of rheumatology patients. With the prompt switch to virtual platforms, nurses continue to offer similar support. The objective of this study is to explore the attitudes and perceptions of patients and nurses regarding the expansion of telehealth nursing care to gain a better understanding on the current and potential enhanced role of nurses in virtual rheumatology care.

**Methods:** This qualitative study was conducted in January 2021. The study included virtual semi-structured interviews with six rheumatology patients from four Canadian provinces, Alberta, British Columbia, Ontario, and Saskatchewan, and one virtual focus group composed of six rheumatology nurses based in BC. Data analysis was iterative, occurring as interviews proceeded and used a thematic approach.

**Results:** Most nurses reported using telehealth to provide care for their patients during the pandemic, with some nurses having in-person visits for

first-time appointments, unstable patients, or administering injections. The nurses described their experience with telehealth as evolving and changing over time. Attending to the mental health needs of patients, performing physical assessment, time constraints, language barriers, and patients' technology literacy were perceived by participating nurses as challenges during care provision via telehealth. Patients were most comfortable with telehealth nursing support for responding to email questions, counselling virtually, reviewing laboratory results and recommending in-person or allied health assessments. Patients were least comfortable with nurses altering advanced therapies or disease modifying drugs.

**Conclusion:** This study serves as a framework to support the improvement of rheumatology telehealth nursing in BC, and it establishes suggestions on the best ways to integrate virtual nursing care. Furthermore, activities that are suitable for nursing telehealth care in rheumatology practice are outlined, specifically those that are highly acceptable to rheumatology nurses and patients.

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### Effectiveness Outcomes Reported in Rheumatology Transition

#### Literature: A Scoping Review

Heather Bollegala (McMaster University, Hamilton); Avanti Patel (McMaster University, Hamilton); Adi Gasner (McMaster University, Hamilton); Mark Matsos (McMaster University, Hamilton); Michelle Batthish (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton)

**Objectives:** Young people with pediatric-onset rheumatic disease continue to experience active disease and associated morbidities in adulthood. Transition programs can help prepare young people for transfer to adult care and ensure that care is maintained through adulthood. However, transition literature measures "success" of transition programs and transfers to adult care with different definitions and outcomes. A scoping review of rheumatology transition literature was conducted with the objectives of: 1) identifying these outcomes, and 2) the frequency with which they are used.

**Methods:** A review was performed in duplicate by adapting a previously published search strategy. Six databases (CINAHL, EMBASE, HaPI, MEDLINE, PsychINFO and Web of Science) were searched. The inclusion criteria were: 1) Primary study design, 2) Full-text articles, 3) Transition clinics focused on pediatric to adult care, 4) Rheumatic conditions, 5) Outcomes measured and reported 6) English language articles. Of 803 abstracts, 35 full-text articles were reviewed and 13 met the inclusion criteria.

**Results:** Of 13 studies, 8 (61.5%) studies reported outcomes of health-care-related self-management skills. Quality of life or overall health assessment was used as an outcome in 7 (53.8%) studies, while 6 (46.2%) studies measured patient-reported experience/satisfaction outcomes. Transfer success/completion was used as an outcome in 4 (30.8%) studies. Disease activity was reported in 4 (30.8%) studies. There were no studies that reported transition readiness scales. Healthcare-related self-management skills can be further broken down into specific skills that were reported as outcomes. Of the 8 studies, 5 (62.5%) looked at medication management, 2 (25%) noted medication adherence, and 2 (25%) looked at managing medical appointments.

**Conclusion:** This review identified several categories of outcomes used to determine successful transition programs and transfers. The variability between outcomes used to measure success makes comparisons between transition programs difficult. Future studies should determine which category of outcome best correlates with a successful transition to allow for standardization in rheumatology transition clinics.

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### Supply and Services of the Pediatric Rheumatology Workforce in Ontario

Jennifer Lee (University of Toronto, Toronto); Roberta Berard (Children's Hospital, LHSC, London); Deborah Levy (Division of Rheumatology, SickKids Hospital; Faculty of Medicine, University of Toronto, Toronto);

Vicki Ling (Institute for Clinical Evaluative Sciences, Toronto); Jodi Gatley (ICES, Toronto); Jessica Widdifield (Sunnybrook Research Institute, ICES, University of Toronto, Toronto)

**Objectives:** The purpose of this study was to evaluate the annual supply and services of pediatric rheumatologists in Ontario between 2010 and 2019.

**Methods:** This was a retrospective population-based study using repeated cross-sections of outcome data on population denominators of the pediatric population (aged  $\leq 18$  years). Pediatric rheumatologists were identified and verified across two administrative databases, the ICES Physician Database and the Corporate Provider Database. We identified all patients with pediatric rheumatology encounters within the Ontario Health Insurance Plan (OHIP) Claims Database, which includes all fee-for-service and shadow billing claims, diagnoses, and dates of services associated with each encounter. Using annual population denominators, we determined the percentage of Ontario children with encounters annually, as well as rates of total encounters expressed per 1,000 children. Patient demographic characteristics were described including sex and travel distance in kilometres (km) to the nearest pediatric rheumatologist. Diagnosis codes from outpatient encounters were used to assess the case mix of patients.

**Results:** From April 1, 2010, to March 31, 2019, the number of pediatric rheumatologists increased from 15 to 27, with a corresponding supply increase from 0.51 to 0.91 pediatric rheumatologists per 100,000 children. Across the same period, the annual number of patients seen by pediatric rheumatologists increased from 9,688 to 13,811 total patients (53% female), representing 0.33% to 0.47% of all children. The number of new consultations each year during the study period ranged between 6,015 and 8,595 patients, which corresponds to 2-3 new consultations per 1,000 children. The annual total number of patient visits (new and repeat encounters) increased from 19,462 to 32,670 visits across the study period. Shadow billing claims comprised a large proportion of patient billing claims, reflecting services from tertiary centers; 7,915 (41%) were shadow claims in 2010, and 10,922 (33%) were shadow claims by 2019. Across all years, 29-33% of all encounters were associated with a systemic inflammatory disease diagnosis code. In 2018, 794 (5.8%) patients travelled  $> 100$  km to see their pediatric rheumatologist.

**Conclusion:** The annual supply and services of pediatric rheumatologists has increased in Ontario over the past decade. Our findings provide additional information for rheumatology workforce planning. Furthermore, the volume of shadow billing claims provides some reassurance on the use of administrative data for research purposes.

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### Economic Evaluation of Hydroxychloroquine Use in an International SLE Inception Cohort

Megan Barber (University of Calgary, Calgary); Yan St. Pierre (McGill University, Montreal); John Hanly (Dalhousie University and Nova Scotia Health Authority, Halifax); Murray Urowitz (University of Toronto, Toronto); Ann Clarke (University of Calgary, Calgary); SLICC Systemic Lupus International Collaborating Clinics (SLICC, Pittsburgh)

**Objectives:** While there is overwhelming evidence for the beneficial role of hydroxychloroquine (HCQ) in SLE, little is known about its economic impact. We estimated annual direct, indirect, and total costs (DC, IC, TC) associated with HCQ use.

**Methods:** A subset of patients from the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) inception cohort were assessed annually between 2014 and 2019 for health resource use, lost workforce/non-workforce productivity and concurrent HCQ use. Resource use was costed using 2021 Canadian prices and lost productivity using Statistics Canada age- and-sex specific wages. At each assessment, HCQ dose over the past year and weight were documented and patients were stratified into 1 of 3 HCQ dosage groups: non-users (0 mg/kg/day), low-intensity users ( $\leq 5$  mg/kg/day), or high-intensity users ( $> 5$  mg/kg/day). Costs associated with HCQ dose were calculated by averaging all observations within each dosage group. Multiple random effects linear regressions adjusted for the possible confounding of age at diagnosis, sex, race/ethnicity, disease dura-

**Table 1:** Unadjusted and adjusted mean annual direct, indirect, and total costs (in 2021 Canadian dollars) stratified by HCQ dose. Values are the mean (95% CI).

|                               | Non-users<br>(0 mg/kg/day) | Low-intensity users<br>(≤5 mg/kg/day) | High-intensity users<br>(>5 mg/kg/day) | Difference between non-users<br>and high-intensity users |
|-------------------------------|----------------------------|---------------------------------------|----------------------------------------|----------------------------------------------------------|
| Unadjusted DC                 | 10116                      | 5682                                  | 6466                                   | 3650 (3362, 5938)                                        |
| Hosp                          | 1415                       | 1081                                  | 1527                                   | -112 (-1254, 1031)                                       |
| Med                           | 2364                       | 1694                                  | 2047                                   | 317 (-673, 1307)                                         |
| Physicians and other services | 3089                       | 2649                                  | 2624                                   | 464 (-198, 906)                                          |
| Dialysis                      | 3249                       | 258                                   | 268                                    | 2981 (1540, 4422)                                        |
| Unadjusted IC                 | 37610                      | 32480                                 | 31418                                  | 6193 (806, 11579)                                        |
| Unadjusted TC                 | 47726                      | 38162                                 | 37884                                  | 9983 (3905, 15780)                                       |
| Adjusted DC*                  | 9599                       | 6344                                  | 6333                                   | 3266 (844, 5687)                                         |
| Adjusted IC**                 | 36558                      | 32914                                 | 31301                                  | 5257 (-1133/11647)                                       |
| Adjusted TC                   | 46157                      | 39257                                 | 37634                                  | 8523 (1223, 15823)                                       |

Boldface indicates significant results

Abbreviations: DC: direct costs; IC: indirect costs; TC: total costs

\*Adjusted for age at diagnosis as the other predictors (sex, race/ethnicity, disease duration, geographic region, education, alcohol use, and smoking) were not significant

\*\* Adjusted for disease duration, geographic region, and education as the other predictors (age at diagnosis, sex, race/ethnicity, alcohol use, and smoking) were not significant

tion, geographic region, education, alcohol use, and smoking on the association between annual DC and IC and HCQ dose. A possible mediating effect of disease damage (SLICC/ACR DI) on these associations was also investigated.

**Results:** 661 patients (89.4% female, 59.3% non-Caucasian race/ethnicity, mean age and mean disease duration at the start of economic assessments was 42.1 years and 9.5 years, respectively) were followed over a mean of 2.8 years. Across 1536 annual assessments, 36.1% of observations were provided by HCQ non-users, 43.1% by low-intensity users (mean dosage 3.4 mg/kg/day), and 20.8% by high-intensity users (mean dosage 5.9 mg/kg/day). Annual adjusted DC were higher in non-users (\$9599) versus low-intensity users (\$6344) and high-intensity users (\$6333) (Table 1). When disease damage was included in the regression, there were no significant differences in DC between dosage groups. While unadjusted IC were higher in non-users (\$37,610) versus low-intensity users (\$32,480) and high-intensity users (\$31,418), adjusted IC did not differ. Adjusted TC were higher in non-users (\$46,157) versus low-intensity users (\$39,257) and high-intensity users (\$37,634).

**Conclusion:** SLE patients reported higher adjusted annual DC and TC during periods of HCQ non-use versus periods of use, regardless of the intensity of use. There was no additional cost savings in those using high intensity dosages. The cost-savings effect of HCQ could potentially be partially mediated through reduced damage. In addition to its well-established therapeutic potential, there may be an economic imperative for HCQ use in SLE patients.

## 76 Accessing Care for Rheumatoid Arthritis: A Critical Interpretive Synthesis

Sharon Koehn (Simon Fraser University, Burnaby); Anh Pham (University of Alberta, Edmonton); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary); Cliff Lindeman (University of Alberta, Edmonton); Neil Drummond (University of Alberta, Edmonton); Allyson Jones (University of Alberta, Edmonton)

**Objectives:** We conducted a Critical Interpretive Synthesis (CIS) of the literature to answer the following questions about how individuals living with rheumatoid arthritis (RA) seek care: - How do individual characteristics, the nature of the disease, and its presentation influence help-seeking and their acceptance of services offered? - How do interactions with their primary care providers influence ability to secure appropriate treatment or referral? - How does the configuration of health services influence their perception of the accessibility of appropriate care? - How do environmental factors influence access to care?

**Methods:** CIS combines systematic review search strategies with adapted ethnographic review design and grounded theory analysis. Its outcome is a coherent theoretical framework that describes the complexity in timely

access to care. Using a systematic review search strategy, 708 abstracts were screened, and 97 full articles reviewed. The findings of included articles were coded into themes and subthemes using NVivo. A Framework Analytic Approach was adopted to code inductively, and deductively using dimensions of the Candidacy Approach to understand patient access to care.

**Results:** Our principal finding was that access to RA care was delayed on several levels. From a patient level, people struggled to identify their symptoms as abnormal and in need of professional attention. From a healthcare level, the configuration of the healthcare system (eg, mode of delivery, lack of linguistic sensitivity, staff unavailability) may impede navigation through the care continuum. Once in the physician's office, individual patient characteristics, such as their socioeconomic status, gender, experience with the healthcare system, and sense of identity all influenced their presentation to care. The physician's appraisal of patient need may also depend on the patient's characteristics; physician decision-making is also contingent on their approach to care, training, and the availability of rheumatologists. The availability of resources such as medications or physiotherapy is also salient, as is the extent to which outcomes are monitored and communication between providers is fostered. At an environmental level, the geographic and physical location can have profound effects on access especially in rural or remote communities.

**Conclusion:** Improving access to care for RA requires a multipronged approach to increase general population knowledge about the condition, and to ensure that all physicians are trained to apply person-centered, holistic approaches which respond to the social determinants of health. Interdisciplinary care teams with superior communication, role clarity, and flexible modes of delivery are essential. Staffing and resources to support timely access are crucial.

## 77

**Can a Questionnaire Reliably Identify Improvement and Worsening in the RA Disease Activity? Implications for use of RA-FQ for Telehealth**  
Susan Bartlett (McGill University, Montreal); Vivian Bykerk (Hospital for Special Surgery, New York); Orit Schieir (McGill University, Montreal); Marie-France Valois (McGill University, Montreal); Louis Bessette (Laval University, Quebec); Gilles Boire (Université de Sherbrooke, Sherbrooke); Glen Hazlewood (University of Calgary, Calgary); Carol Hitchon (University of Manitoba, Winnipeg); Edward Keystone (University of Toronto, Toronto); Janet Pope (University of Western Ontario, London); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (The Arthritis Program Research Group, Newmarket); Clifton Bingham (Johns Hopkins Arthritis Center, Baltimore); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

**Objectives:** The RA-FQ is a patient-reported measure that can be used to identify disease flares in RA. The RA-FQ asks about pain, physical function, fatigue, stiffness, and participation and yields a score from 0-50. We previously reported on reliability, validity, and responsiveness. In the era of COVID where in-person visits are not always feasible, our goal was to identify the score changes for RA-FQ associated with minimal and meaningful improvement or worsening as judged by patients, treating rheumatologists, and in relation to disease activity indices.

| Domain                | A Lot Better<br>(N=346; 43%) |              | The Same<br>(N=174; 21%) |             | A Lot Worse<br>(N=62; 8%) |             |
|-----------------------|------------------------------|--------------|--------------------------|-------------|---------------------------|-------------|
|                       | Δ                            | 95% CI       | Δ                        | 95% CI      | Δ                         | 95% CI      |
| RA-FQ Total (0-50)    | -6.0                         | (-7.1, -4.9) | -0.1                     | (-1.3, 1.1) | 8.9                       | (5.1, 12.7) |
| CDAI*                 | -5.3                         | (-6.3, -4.3) | -0.8                     | (-2.0, 0.5) | 6.8                       | (3.7, 9.8)  |
| DAS28-CRP             | -0.7                         | (-0.8, -0.6) | -0.2                     | (-0.4, 0.0) | 0.5                       | (0.2, 0.9)  |
| Patient Global (0-10) | -1.3                         | (-1.5, -1.0) | -0.1                     | (-0.4, 0.2) | 2.9                       | (2.1, 3.6)  |
| MD Global (0-10)      | -1.2                         | (-1.4, -1.0) | -0.1                     | (-0.4, 0.2) | 0.7                       | (0.0, 1.5)  |
| Swollen Joints (28)   | -1.4                         | (-1.7, 1.0)  | -0.4                     | (-0.9, 0.0) | 1.3                       | (0.2, 2.5)  |
| Tender Joints (28)    | -1.5                         | (-1.9, -1.1) | 0.0                      | (-0.7, 0.6) | 2.2                       | (0.8, 3.5)  |



**Methods:** We used data from adults with early RA (symptoms < 1 year) enrolled in the CATCH (Canadian Early Arthritis Cohort), a prospective study of real-world patients treated across Canada. Participants completed the RA-FQ, Patient Global, and RA Global Change Impression item (a little vs. a lot better or worse or same) at 3- and 6-month visits. Rheumatologists recorded joint counts and MD Global. We compared mean change across categories of improvement and worsening disease activity using patient, physician and CDAI anchors.

**Results:** The 808 adults were mostly white (84%) women (71%) with a mean (SD) age of 55 (15) and moderate-high disease activity (85%) at enrollment. At the second visit, 79% of patients reported that their RA had changed; 59% were better and 20% worse. Patients who were a lot worse had a mean increase of 8.9 points whereas those who rated themselves as a lot better had a -6.0 decrease on the RA-FQ (Table). Minimal worsening and improvement were associated with 4.7 and -1.8 change on the RA-FQ, respectively, while patients who rated their RA unchanged had stable RA-FQ scores. Physicians and CDAI classified more patients as worse than using patients' self-ratings, and minimal and meaningful RA-FQ thresholds differed by group. Similar changes were evident in CDAI, SDAI, and DAS indices (Table). Larger differences were observed with patient vs. physician global scores and tender vs. swollen joints. Across measures, the change associated with worsening was greater than for improvement. Results supported all prespecified hypotheses.

**Conclusion:** In this large ERA cohort, the RA-FQ was responsive to change and generally distinguished between minimal and meaningful improvement and worsening. These data add to growing evidence demonstrating robust psychometric properties of the RA-FQ and contribute new evidence supporting its use in RA care and research when in-person visits may not be feasible. Results also offer initial guidance about the amount of change associated with minimal and meaningful improvement or worsening in RA.

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### Key Factors for the Development and Implementation of a Patient Dashboard in Rheumatology: Review of Literature

Terezia Pirhalova (University of Calgary, Calgary); Namneet Sandhu (University of Calgary, Calgary); Susanne Benseler (Section of Rheumatology, Department of Paediatrics, Alberta Children's Hospital/University of Calgary, Calgary); Deborah Marshall (University of Calgary, Calgary); Marinka Twilt (University of Calgary, Calgary); Inelda Gjara (University of Calgary, Calgary); Martina Stevenson (University of Calgary, Calgary); Oladoyin Olaosebikan (University of Calgary, Calgary); Dianne Mosher (University of Calgary, Calgary); Rheum4U Team (Calgary)

**Objectives:** To identify key factors to inform patient dashboard content, design, development, and implementation in Rheum4U Precision Health Registry. Inflammatory arthritis (IA) affects approximately one million Canadians who, if untreated, can experience irreparable joint damage, pain, and disability. The cost of IA in Canada is estimated to reach over \$257 billion by 2040. Despite significant improvements in therapies and Treat-to-Target strategies, remission rates and low disease activity could be improved. Patient dashboards visualize individual patient disease data over time and are proven to successfully support the management of many chronic conditions. Patient-centered care incorporating shared decision making that facilitates patient-physician interaction about adherence, understanding of disease, and outcomes considered important by patients, still lacks. Patient-dashboards, co-designed by patients and health-care providers, can alleviate this gap and improve the overall quality of care. Such dashboards can be particularly helpful for patients having difficulty reaching or sustaining remission or low-disease activity.

**Methods:** A rapid review of scientific and gray literature was conducted for publications up to July 2021. Research questions and search terms were identified, and queried databases included MEDLINE, Science Direct. Search terms included: rheumatology, patient dashboard, patient-reported outcomes, shared decision making, patient reported outcomes,

human-centered design. Dashboard development for other chronic conditions like diabetes, was also queried.

**Results:** The literature search yielded 21 relevant articles. Physician/patient co-design analyzes user needs to determine distinct preferences for patient-facing dashboards. Dashboard content included: disease activity over time, outcomes, composite scores, demographics, and after visit summary, and clinic notes. Patients expressed interest in dashboards to also include holistic measures such as diet and stress. A combination of simple graphics and descriptions, with minimal cognitive load, is preferred by patients to help them easily understand the measures represented. Linking each measure to literacy level-appropriate educational materials has further enhanced use for patients. Human-centered design principles, including assessing user needs, prototyping design concepts, testing concepts with user, and pilot testing, supports successful dashboard development. User engagement incorporating motivational strategies, such as progress tracking and goal setting, further enhances dashboard use.

**Conclusion:** Several key factors can increase the likelihood of successful implementation of a patient dashboard including a user-centered approach to co-design, simple graphics with descriptions of the measures, a broad range of holistic measures, and the application of motivational strategies.

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### Impact of Early Antimalarial Adherence on Future Acute Care Utilization in Patients With Newly Diagnosed Rheumatoid Arthritis and Systemic Lupus Erythematosus: A Population-based Study

Rashedul Hoque (Faculty of Health Sciences, Simon Fraser University; Arthritis Research Canada, Richmond); Antonio Avina-Zubieta (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Richmond); Mary De Vera (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver); Yi Qian (Sauder School of Business, University of British Columbia, Vancouver); John Esdaile (University of British Columbia (Division of Rheumatology)/Arthritis Research Canada, Richmond); Hui Xie (Arthritis Research Canada/Faculty of Health Sciences at Simon Fraser University, Richmond)

**Objectives:** To examine the association between antimalarial (AM) adherence and acute care utilization among newly diagnosed rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients.

**Methods:** We used administrative databases for British Columbia, Canada, to conduct a retrospective, population-based propensity score (PS) matched study of incident cohorts of RA and SLE with incident AM use. The incident RA and SLE cases first met previously published RA and SLE criteria for administrative data between January 1997 and March 2014. Follow-up started on the first day of having AM and either RA or SLE, and only subjects with at least one year of follow-up were retained. In the first year ("baseline year"), we calculated AM adherence using proportion of days covered (PDC) and categorized as adherent (PDC  $\geq$  0.90) or non-adherent (0  $\leq$  PDC < 0.90). We computed PS for AM adherence using baseline variables (age, cohort entry year, sex, residence, income quintile, RA or SLE duration, prior AM use duration at cohort entry date, medication use, numbers of hospital admissions and hospitalized days, outpatient visits and related costs and Charlson comorbidity index) evaluated in 12 months before the cohort

**Table 1: Risk of acute care utilization**

| Adherence levels                | Event rate per person-year | Crude RRs <sup>§</sup> (95%CI) | Adjusted RRs <sup>§</sup> (95%CI) |
|---------------------------------|----------------------------|--------------------------------|-----------------------------------|
| <b>Hospital admissions</b>      |                            |                                |                                   |
| <b>Non-adherent (Reference)</b> | 0.42                       | 1                              | 1                                 |
| <b>Adherent</b>                 | 0.39                       | 0.91(0.85-0.97)                | 0.87(0.82-0.93)                   |
| <b>Hospitalized days</b>        |                            |                                |                                   |
| <b>Non-adherent (Reference)</b> | 2.66                       | 1                              | 1                                 |
| <b>Adherent</b>                 | 2.18                       | 0.82(0.71-0.95)                | 0.78(0.69-0.89)                   |

Abbreviations: RR, rate ratio; CI, confidence interval; PDC, proportion of days covered. Non-adherent: 0  $\leq$  PDC < 0.90, Adherent: PDC  $\geq$  0.90. <sup>§</sup>Obtained from quasi-Poisson regression with robust standard errors.

entry date. Each AM adherent patient was PS matched with up to two AM non-adherent patients using the greedy matching algorithm. Our outcomes include the numbers of hospital admissions and hospitalized days assessed in the following year ("follow-up year"). We used quasi-Poisson regression models with robust standard errors to examine the impact of AM adherence at the baseline year on these two outcomes in the follow-up year, adjusting for above baseline variables.

**Results:** We identified 6151 baseline AM adherent (mean age 56.6 years, 74.7% were women) and 11624 matched baseline non-adherent (mean age 55.4 years, 75.6% were women) incident RA and SLE patients. The crude rates for hospital admissions were 0.39 and 0.42 per person-year for adherent and non-adherent patients in the follow-up year, respectively. The respective crude rates for hospitalized days were 2.18 and 2.66 per person-year. Using the quasi-Poisson models, the adjusted rate ratios (RRs) of hospital admissions and hospitalized days obtained for AM adherent patients were 0.87 (95% CI: 0.82-0.93) and 0.78 (95% CI: 0.69-0.89), respectively, compared to AM non-adherent patients (Table 1).

**Conclusion:** RA and SLE patients adhering to AM therapy are associated with a lower risk of future acute care utilization (13% reduction in the risk of hospital admission and 22% reduction in the number of hospitalized days) than non-adherent patients.

### 80 Investigating the Determinants of Accessing Social and News Media and Experiencing Negative Impacts During COVID-19 in an International SLE Sample

Francesca Cardwell (University of Waterloo, Waterloo); Susan Elliott (University of Waterloo, Waterloo); Ricky Chin (University of Calgary, Calgary); Leigha Rowbottom (Alberta Health Services, Calgary); Yvan St. Pierre (McGill University, Montreal); May Choi (University of Calgary, Calgary); Murray Urowitz (University of Toronto, Toronto); Guillermo Ruiz-Irastorza (Biocruces Health Research Institute, Hospital Universitario Cruces, Bizkaia); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Michelle Petri (Johns Hopkins University School of Medicine, Baltimore); Christine Peschken (University of Manitoba, Winnipeg); Rosalind Ramsey-Goldman (Northwestern University Feinberg School of Medicine, Chicago); Paul Fortin (Department of Rheumatology, CHU de Québec-Université Laval, Québec); Sang-Cheol Bae (Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul); Anselm Mak (National University Hospital Singapore, Singapore); John Hanly (Dalhousie University and Nova Scotia Health Authority, Halifax); Anca Askanase (Columbia University, New York City); Juanita Romero-Diaz (Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City); Bernardo Pons-Estel (Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR), Rosario); Ian Bruce (University of Manchester, Manchester); Daniel Wallace (Cedaus-Sinai Medical Centre, West Hollywood); Ann Clarke (University of Calgary, Calgary)

**Objectives:** We assessed the determinants of SLE patients accessing health information in social and news media, and self-reporting negative health impacts associated with accessing health information through these sources.

**Methods:** SLE patients were recruited from 15 patient cohorts and five advocacy organizations. They completed an online survey (06/2020-04/2021) about sources of health information accessed preceding (pre-03/11/2020) and during (post-03/11/2020) COVID-19. Multivariate logistic regression was used to explore factors associated with: 1) accessing social media, 2) news media, and 3) self-reporting negative impacts from health information accessed through these sources, adjusting for region, sociodemographics, SLE characteristics, and access to/trust in sources.

**Results:** 1935 patients (Asia n = 201, Canada n = 845, Europe n = 324, Latin America (LA) n = 118, US n = 447) completed the survey (27.1% response rate): 92.7% female, 35.2% non-white race/ethnicity, mean age at diagnosis 32.0 years (SD 13.3), and mean disease duration 16.6 years (SD 12.0). 21.6% and 37.0% reported accessing health information often/always through social and news media, respectively, and 17.0% reported being negatively

impacted by information accessed through these sources. Respondents in Europe and LA vs Canada were more likely to access social (Europe: OR:1.46, 95% CI: 1.03-2.07; LA: OR: 2.19, 95% CI: 1.36-3.56) and news media (Europe OR:1.77, 95% CI: 1.26-2.49; LA OR:1.71, 95% CI: 1.03-2.83), and those in the US were less likely to access social media (OR: 0.58, 95% CI: 0.40-0.84). Females were more likely (OR: 2.02, 95% CI: 1.17-3.49), while older participants were less likely to access this source (OR: 0.98, 95% CI: 0.97-0.99). Patients accessing family physicians post-03/11/2020 were less likely to access social (OR: 0.70, 95% CI: 0.54-0.92) and news (OR: 0.64, 95% CI: 0.50-0.80) media, and those reporting trust in social (OR: 3.18, 95% CI: 2.45-4.14) and news media (OR: 4.33, 95% CI: 3.40-5.52) were more likely to access each, respectively. Those in Asia vs Canada (OR: 0.34, 95% CI: 0.17-0.66) and older participants (OR: 0.97, 95% CI: 0.96-0.99) were less likely to be negatively impacted, and females (OR: 2.27, 95% CI: 1.15-4.47) were more likely to be negatively impacted. While individuals with post-secondary education were less likely to be negatively impacted (OR: 0.60, 95% CI: 0.40-0.90), those with post-secondary education in Europe (OR: 3.56, 95% CI: 1.75-7.30) and LA (OR: 4.37, 95% CI: 1.44-13.30) were more likely to report negative impacts.

**Conclusion:** Region, age, gender, access to family physicians, and education are determinants of accessing social/news media and/or self-reporting negative impacts of accessing health information through these sources. This study emphasizes the need for targeted health messaging based on demographics and geography.

### 81 Health Information Use by SLE Patients Pre and During COVID-19

Francesca Cardwell (University of Waterloo, Waterloo); Susan Elliott (University of Waterloo, Waterloo); May Choi (University of Calgary, Calgary); Ricky Chin (University of Calgary, Calgary); Yvan St. Pierre (McGill University, Montreal); Leigha Rowbottom (Alberta Health Services, Calgary); Murray Urowitz (University of Toronto, Toronto); Guillermo Ruiz-Irastorza (Biocruces Health Research Institute, Hospital Universitario Cruces, Bizkaia); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal); Michelle Petri (Johns Hopkins University School of Medicine, Baltimore); Susan Manzi (West Penn Allegheny Health System, Allegheny General Hospital, Pittsburgh); Christine Peschken (University of Manitoba, Winnipeg); Rosalind Ramsey-Goldman (Northwestern University Feinberg School of Medicine, Chicago); Paul Fortin (Department of Rheumatology, CHU de Québec-Université Laval, Québec); Sang-Cheol Bae (Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul); Anselm Mak (National University Hospital Singapore, Singapore); John Hanly (Dalhousie University and Nova Scotia Health Authority, Halifax); Anca Askanase (Columbia University, New York City); Juanita Romero-Diaz (Instituto Nacional de Ciencias Médicas y Nutrición, Mexico City); Bernardo Pons-Estel (Centro Regional de Enfermedades Autoinmunes y Reumáticas (CREAR), Rosario); Ian Bruce

**Table 1: Difference in Health Information Source Frequency of Access\*, Pre and Post March 11, 2020**

|                                | Post-Pre % Difference, 95% CI |                   |
|--------------------------------|-------------------------------|-------------------|
|                                | Canada                        | International     |
| Family Physicians              | -11.1 (-14.6, -7.7)           | -3.5 (-6.4, -0.6) |
| Lupus Specialists              | -14.2 (-17.7, -10.7)          | -5.1 (-7.6, -2.7) |
| Pharmacists                    | -7.5 (-10.8, -4.1)            | -4.2 (-6.8, -1.6) |
| Alternative Care Providers     | -9.0 (-11.7, -6.3)            | -4.4 (-6.3, -2.6) |
| Peers                          | -1.2 (-4.4, 2.1)              | 3.8 (1.0, 6.5)    |
| Patient Advocacy Organizations | -2.5 (-5.3, 0.3)              | 3.2 (0.8, 5.7)    |
| News Media                     | 7.6 (3.9, 11.0)               | 9.1 (6.1, 12.0)   |
| Social Media                   | 1.5 (-1.3, 4.4)               | 2.8 (0.3, 5.4)    |

\*Respondents who reported health information source access sometimes/often/always

**Boldface indicates differences which are significant as the 95% CI does not include 0.**

(University of Manchester, Manchester); Daniel Wallace (Cedars-Sinai Medical Centre, West Hollywood); Ann Clarke (University of Calgary, Calgary)

**Objectives:** We conducted an online survey to assess how SLE patients access and trust health information pre and during COVID-19.

**Methods:** Canadian and international patients were recruited from 15 patient cohorts and five advocacy organizations. Participants completed an online survey from 06/2020-04/2021 regarding the sources of health information they accessed in the 12 months preceding (pre-03/11/2020) and during COVID-19 (post-03/11/2020). We calculated the percentage of patients accessing each source, their preferred sources, and the level of trust in each source. McNemar tests were used to compare frequencies pre and post 03/11/2020 in both samples.

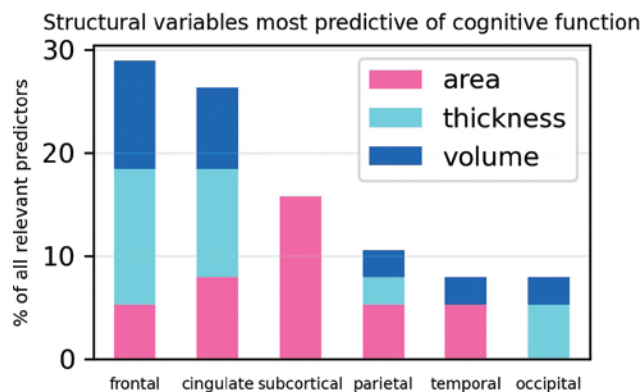
**Results:** 845 Canadian and 1090 international (Asia n = 201, Europe n = 324, Latin America n = 118, US n = 447) patients completed the survey (40.4% and 21.0% response rates, respectively); 78.0% were recruited through SLE research cohorts, 92.7% were female, 76.6% had completed post-secondary education, 35.2% reported non-white race/ethnicity, mean age at diagnosis was 32.0 years (SD 13.3) and mean disease duration was 16.6 years (SD 12.0). Canadian and international patients accessed news media more frequently during vs pre pandemic (44.6% of Canadians accessed sometimes/often/always pre vs 52.1% during; 59.8% of international participants accessed pre vs 68.9% during), while access to family physicians (Canada: 59.6% pre vs 48.5% during; international 53.4% pre vs 49.9% during) and lupus specialists (Canada: 72.0% pre vs 57.8% during; international 82.8% pre vs 77.7% during) decreased in both samples during the pandemic (Table 1). Lupus specialists (1st) and family physicians (2nd) were ranked the most preferred sources in both samples pre and during the pandemic. News media was more preferred post (3rd) vs pre-03/11/2020 (4th) in both samples, yet was considered less trustworthy in Canada (44.5% rated online news media as somewhat/very trustworthy pre vs 41.8% post) and internationally (43.0% pre vs 40.2% post) during COVID-19. In both samples, advocacy organizations were accessed less frequently pre (Canada: 31.1%; international: 40.9%) and during COVID-19 (Canada: 28.6%; international: 44.1%) than other less preferred and trusted sources (eg, peers, social media), and trust in advocacy organizations decreased during the pandemic in both Canadian and international samples by 4.1% and 5.0%, respectively.

**Conclusion:** Although lupus specialists and family physicians were ranked as the most preferred sources, patients accessed these sources less frequently during the pandemic and accessed news media, a less trusted source, more frequently. To increase accessibility to preferred and trusted sources, virtual visits should be promoted where not already in place. This research will improve existing information dissemination pathways valued by patients.

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### Potential Biomarkers of Cognitive Impairment in the Context of Childhood-onset Systemic Lupus Erythematosus

Santiago Arciniegas (Neurosciences and Mental Health, Research Institute, The Hospital for Sick Children; Institute of Biomedical Engineering, University of Toronto, Toronto); Sarah Mossad (Department of Psychology, The Hospital for Sick Children, Toronto); Tala El Tal (Division of Rheumatology, The Hospital for Sick Children, Toronto); Lawrence Ng (University of Toronto, The Hospital for Sick Children, Toronto); Paris Moaf (The Hospital for Sick Children, Toronto); Helen Branson (Department of Diagnostic Imaging, The Hospital for Sick Children, University of Toronto, Toronto); Adrienne Davis (Division of Emergency Medicine, Hospital for Sick Children, Toronto); Linda Hiraki (Division of Rheumatology, The Hospital for Sick Children; Division of Genetics, SickKids Research Institute; Faculty of Medicine, University of Toronto, Toronto); Deborah Levy (Division of Rheumatology, SickKids Hospital; Faculty of Medicine, University of Toronto, Toronto); Ashley Dangucean (Department of Psychology, The Hospital For Sick Children, Toronto); George Ibrahim (The Hospital for Sick Children, Toronto); Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto)



**Objectives:** 23%-60% of children with childhood-onset systemic lupus erythematosus (cSLE) report cognitive complaints, yet neuropsychiatric lupus (NPSLE) remains challenging to diagnose and treat. To increase understanding of mechanisms underlying this disease, we examined the quantitative association between cognitive function, demographic and disease measures, and structural neuroimaging metrics.

**Methods:** We examined a cross-sectional sample of 27 patients with cSLE (ages 12-17) meeting ACR or SLICC classification criteria. Patients completed standardized traditional neurocognitive tests quantifying domains of attention, working memory, and cognitive flexibility. From these three scores, we quantified the cognitive function of each patient as a point in 3-dimensional space. Cognitive impairment was defined as a score 1.5 standard deviations below the mean in any domain. T1-weighted brain magnetic resonance images (MRI) were obtained using a 3T scanner. Volume, cortical thickness, and surface area metrics were extracted for 101 brain segments. Demographic and disease measures were extracted from medical records. We used Partial Least-Squares Regression (PLS2) to examine the association between cognitive function and its potential predictors: structural brain metrics as well as disease and demographic measures. PLS2 enables linear regressions between multidimensional data with a relatively small sample size. Each predictor's relevance criteria (ie, stability and significance) were based on the bootstrapped sample distribution of its variable importance in projection (VIP) value, which summarizes the weight of a predictor in the linear model.

**Results:** Cognitive impairment was present in 41% (11/27) of patients; only one subject had a diagnosis of NPSLE. In PLS2 (Figure 1), 38 predictors were found to be relevant in the estimation of cognitive function (CI = 95%, VIP > 1). Of these, 37 were brain structure variables deriving from the frontal lobe (n = 11), cingulate cortex (n = 10), subcortical structures (n = 6), parietal lobe (n = 4), temporal lobe (n = 3) and occipital lobe (n = 3). The only non-structural measure found to be significantly predictive of cognitive function was the SLICC damage index (SDI).

**Conclusion:** Objective cognitive impairment was prevalent in > 40% of patients with cSLE. Impairment was strongly associated with several structural brain metrics, most of which derived from the frontal lobe and cingulate cortex. Only one disease-related factor (SDI) was found to be a relevant predictor of cognitive function. Our results suggest that computational models quantifying the relationship between brain metrics and clinical measures have the potential to enhance diagnosis of NPSLE. Further study is needed to identify robust biomarkers of NPSLE that can be linked to brain metrics with the use of machine learning models.

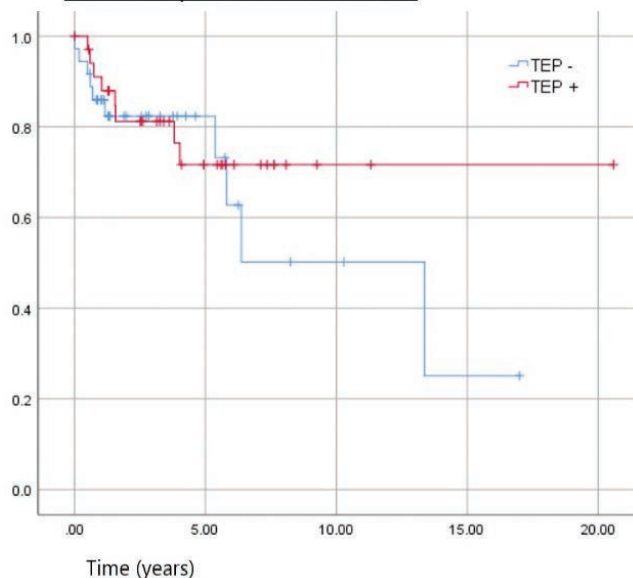
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### Do Patients With Giant Cells Arteritis (GCA) at CHUS Hospital From 2008 to 2020 With an Increased Vascular Uptake at Fluorodeoxyglucose-positron Emission Tomography (FDG-PET) Scan Have a Higher Incidence of Aortic Complications in Comparison With the Ones With a Negative Test?

Charles Pagé (Université de Sherbrooke, Sherbrooke); Patrick Liang (Université de Sherbrooke, Sherbrooke)



### Aortic complication - free survival



**Objectives:** Primary goal was to compare the incidence of aortic complications (aneurysm, dissection, rupture) of patients with giant cells arteritis (GCA) and Takayasu vasculitis (TAK) with FDG-PET scans with an increased vascular uptake with the ones with negative tests. Secondary goals were to describe the mortality rate, aortic surgery rate and the treatments adjustments after FDG-PET scans.

**Methods:** This is a descriptive retrospective cohort study of all consecutive GCA and TAK cases seen in the rheumatology outpatient clinic in our center, Centre Hospitalier Universitaire de Sherbrooke, from 2008 to 2021. Exclusion criteria were: prior aortic aneurysm, dissection or surgery and absence of FDG-PET scan. We formed two groups according to if they had or not at least one FDG-PET scan showing increased vascular uptake. We compared baseline cardiovascular risk factors and treatments. Kaplan-Meier curves for aortic complication-free survival was compared with log-rank test.

**Results:** There was 71 cases, of which 35 had at least one positive FDG-PET and 36 hadn't. Mean age at diagnosis was 68 years. Median follow-up time was 3,6 years. Baseline cardiovascular risk factors, age, CRP and erythrocyte sedimentation rate were similar between the two groups. There were 6 vs 8 aortic complications in TEP + and - groups, respectively. Complications were 13 aortic aneurysm and 1 aortic dissection, leading to 3 ascending thoracic aorta replacement surgeries. There was no significant difference in Kaplan-Meier curves for aortic complication-free survival comparing the two groups ( $P = 0,488$ ) (Figure). In 112 FDG-PET scans done during follow-up, having a positive vs a negative test was followed by these treatment modifications, respectively: starting prednisone in 16 vs 6% (mean dose 48,6 mg vs 21,3 mg); if already on prednisone: mean increase in dose of 14,6 mg vs 16,8 mg. There was no significant difference in all-cause mortality (6% vs 13%,  $P = 0,43$ ), with a total of 6 deaths (1 atherosclerotic cardiac disease, 1 head trauma, 4 cancers).

**Conclusion:** Aortic complications in GCA seemed similar regardless of FDG-PET scan results. Mortality rates were similar regardless of past FDG-PET results.

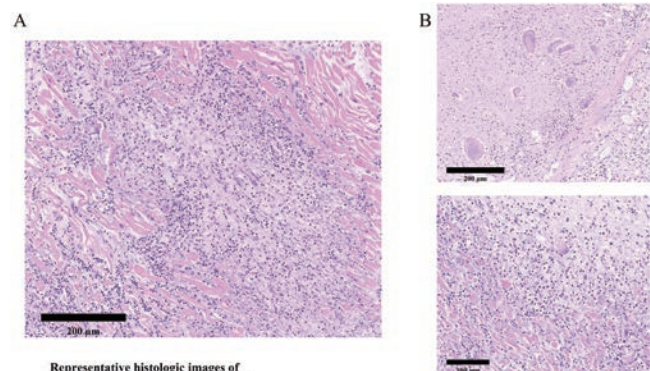
### 84 Fatal Myocarditis Following Immunization With an mRNA COVID-19 Vaccine in a Patient Receiving Immune Checkpoint Inhibition

Arjun Raghavan (University of Manitoba Faculty of Health Sciences, Winnipeg); Petra Rahaman (University of Manitoba Faculty of Health Sciences; Shared Health Manitoba, Winnipeg); Liam O'Neil (University of Manitoba Faculty of Health Sciences, Winnipeg); Jeffrey Graham (University of Manitoba Faculty of Health Sciences; CancerCare Manitoba, Winnipeg)

**Background:** Immune checkpoint inhibitors (ICI) are being used to treat several cancer subtypes. These drugs are associated with a spectrum of immune-based toxicities referred to as immune related adverse events (irAEs). Myocarditis is a rare irAE with high mortality. Cases of myocarditis have also been reported after immunization with mRNA vaccines against SARS-CoV-2. In this report, we describe a case of fatal myocarditis in a patient who received combination ICI therapy given in close temporal proximity to the first dose of an mRNA COVID-19 vaccine.

**Case Description:** This case involves a 52-year-old male receiving ipilimumab and nivolumab for advanced mesothelioma, who presented to hospital with symptoms of heart failure three days post cycle 2. He had received his first dose of the Pfizer-BioNTech vaccine 6 days prior to cycle 1. Upon presentation to hospital, bloodwork showed significantly elevated troponin T levels (8374 ng/L) and lactate (6.5 mmol/L). A chest x-ray showed a right sided pleural effusion and cardiomegaly. An ECG showed diffuse ST depression and ST elevation in leads V1 and V2. Following these investigations, the patient was sent for urgent coronary angiography which showed normal coronary vessels with no flow limiting lesions. An LVEDP of 25 mmHg was measured and LV angiography noted global LV dysfunction with an ejection fraction of 23%. The patient was then intubated for hypoxemic respiratory failure. An echocardiogram showed a small pericardial effusion, with biventricular failure and a dilated right ventricle with tricuspid regurgitation. He suffered multiple PEA arrests and unfortunately died despite maximal inotropic support, mechanical ventilation, as well as resuscitative measures (Figure).

**Conclusion:** Pathology of the heart after autopsy revealed widespread myocardial necrosis and inflammation, with mixed inflammatory infiltrates and numerous multinucleated giant cells consistent with fulminant myocarditis (these findings are inferred from the attached image). The temporal proximity of the vaccine exposure to ICI initiation in this case raises a suspicion for synergetic toxicity. Although causality cannot be proven, the rapid onset and severe presentation of this patient's myocarditis may warrant closer monitoring of patients receiving concurrent ICI therapy and mRNA vaccines.



Representative histologic images of hematoxylin and eosin (H&E) stained slides showing fulminant myocarditis with giant cells. (A) High power view of myocardium with evidence of myocyte damage secondary to involvement by dense mixed inflammation, including lymphocytes, plasma cells, a few multinucleated giant cells, and fibroblasts. (B) Upper Panel: High power view of several multinucleated giant cells within a milieu of fibroblasts and scattered predominantly lymphocytic inflammatory infiltrates. Lower Panel: Higher power view of myocardium with myocyte necrosis (bottom of image) and abundant mixed inflammatory infiltrates with a multinucleated giant cell in the center.

### 85 Precursors to Systemic Sclerosis and Systemic Lupus Erythematosus

Leonardo Martin Calderon (Western University, London); Janet Pope (University of Western Ontario, London)

**Objectives:** There are pre-morbid clinical states such as Undifferentiated

Connective Tissue Disease at risk for Systemic Sclerosis (UCTD-risk-SSc) which do not meet the scleroderma (SSc) ACR/EULAR 2013 criteria, but rather present with Raynaud's Phenomenon (RP) and either typical SSc capillaroscopic findings or serum marker antibodies. Patients diagnosed with UCTD-risk-SSc have a 35-50% risk of developing definite SSc. Moreover, prescleroderma, another entity of pre-clinical autoimmunity diagnosed in patients presenting with RP and either serum antibodies, avascular capillaroscopic changes or ANA positivity at 1:320 and avascular areas, has an even higher risk of developing SSc than UCTD-risk-SSc. Similarly, there are pre-clinical stages progressing to identifiable disease for Systemic lupus erythematosus (SLE). Commonly anti-nuclear antibodies will pre-date SLE diagnosis by years during undifferentiated pre-clinical stages previously dubbed "incomplete lupus" or "lupus-like syndrome" when ACR criteria for SLE are not met. However, as disease progression occurs, more specific antibodies for SLE such as anti-double stranded DNA and anti-Smith antibodies become positive. The purpose of this project is to describe the role of the innate and adaptive immune responses in the preclinical states of UCTD-risk-SSc and prescleroderma. Additionally, to discuss the evolution of SLE development as determined by antibodies predating the diagnosis and evolving from nonspecific antinuclear antibodies to specific antibodies shortly before diagnosis.

**Methods:** MEDLINE and EMBASE databases were searched for experimental and observational studies without language restriction from inception to the present. Reference lists of all primary studies and review articles were searched for additional references. Studies reported in full-text and abstract formats were included.

**Results:** Our search found 2286 studies of which 147 were included. Innate and adaptive immune pathways in pre-clinical SSc and SLE disease states encompass soluble vascular and intracellular adhesion molecules (sICAM-1, sVCAM-1), interleukins and cytokines (IL-12, IL-13, IL-35), and pro-fibrotic molecules (ANG-1, ANG-2, chitinase 3-like protein). Fibroblast dysfunction and pro-fibrotic gene expression is observed in dormant fibroblasts activation through macrophage induction by factors such as MyD88. Additionally, loss of invariant natural killer T cells is associated with decreased tolerance to nuclear antigens.

**Conclusion:** Ultimately, derangements in innate and adaptive immunity, as well as the dysregulation of inflammatory signal pathways have been observed to drive pathology in these pre-clinical stages with varying likelihood of progression to full-blown disease.

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### Identifying Lupus Flares From Electronic Clinical Notes in a Linked EMR-Claims Dataset

Laure Delbecq (Eli Lilly and Company, Brussels); Joseph Vasey (Veradigm Health, San Francisco); Dan O'Brien (Veradigm Health, San Francisco); Jianmin Wu (Eli Lilly and Company, Indianapolis); Alex Dean (Veradigm Health, San Francisco); Theresa Sudaria (Veradigm Health, San Francisco); Aisha Vadhariya (Eli Lilly & Co, Indianapolis); Julie Birt (Eli Lilly and Company, Indianapolis)

**Objectives:** Although algorithms have attempted to identify systemic lupus erythematosus (SLE) flares using large medical and pharmacy claims databases they have not been clinically validated. Important diagnostic information may not be available in structured data due to omission of details with common coding practices, leading to potential false negative classifications. Unstructured medical notes may provide the additional detail needed to accurately identify and classify a flare event. The purpose of this research was to explore the feasibility of using written clinical notes to identify flare episodes in patients with SLE.

**Methods:** A linked dataset of ambulatory electronic medical records (EMR) and administrative claims was used to identify SLE patients who had newly initiated selected immunosuppressants or advanced therapies. Adult patients were included if they had an index medication between 01 July 2015 and 30 June 2019 with a diagnosis of SLE on or before the date of therapy initiation. Natural language processing (NLP) was used to identify

key flare-related words or phrases from visit-level, unstructured, electronic clinical notes and to assist in developing rules to categorize notes. Three clinicians reviewed and classified the notes as indicative of a high-confidence flare, a probable flare, or not a flare. Fleiss kappa coefficient was calculated to determine inter-rater reliability on a random sample of notes. Time to first flare (if any) after initiation of the immunosuppressant was determined. **Results:** Among 801 eligible patients, 21.6% had initiated azathioprine, 11.0% belimumab, 35.2% methotrexate, and 32.2% mycophenolate. Of these 20% were identified as having at least one high-confidence or probable flare during the 12 months after initiation of immunosuppressant (azathioprine 23.1%, belimumab 19.3%, methotrexate 22.3%, mycophenolate 15.5%). Interrater agreement (Fleiss kappa = 0.68) was substantial. Among patients with a post-index flare the mean time to flare was 100.9 days (azathioprine 127.6 days, belimumab 158.4 days, methotrexate 67.6 days, mycophenolate 102.1 days).

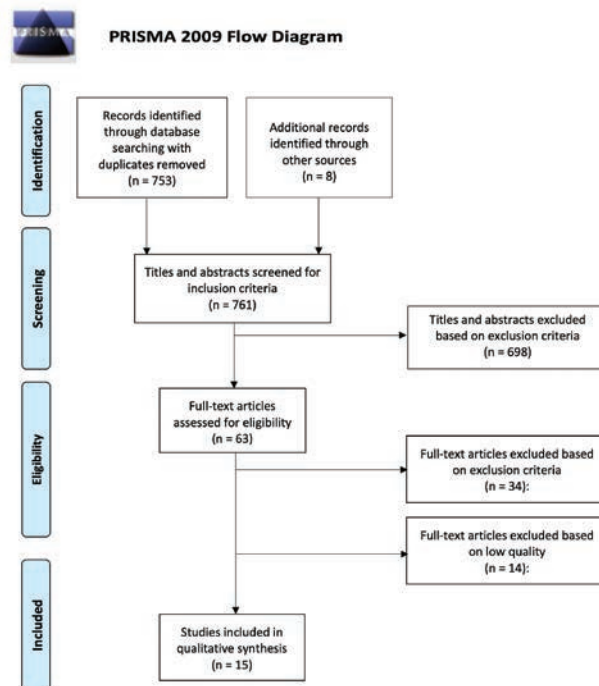
**Conclusion:** NLP combined with clinical review of unstructured notes was demonstrated to be a feasible approach to identifying SLE flares in a large EMR database. These results will be applied to a treatment and resource utilization study. Future work will investigate concordance between NLP and structured data approaches, and development of a machine learning algorithm for flare identification and severity.

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### Management of TMJ Arthritis; Eminence or Evidence

Jocelyne Beelen (University of Alberta, Edmonton); Peter Stoustrup (University of Aarhus, Aarhus); Thomas Pedersen (Aarhus University Hospital, Aarhus); Cory Resnick (Harvard University, Boston); Shelly Abramowicz (Emory University School of Medicine, Atlanta); Marinka Twilt (University of Calgary, Calgary)

**Objectives:** The temporomandibular joint (TMJ) is often affected in children with Juvenile Idiopathic Arthritis (JIA), with occurrence varying widely depending on factors like JIA type, diagnostic approaches, and study population. [1] Inflammation in the TMJs can result in joint deformity, dysfunction, and substantial morbidity in the pediatric arthritis population. [2] Management of TMJ arthritis is difficult due to the uniqueness of the joint and requires multidisciplinary care. This study will aim to develop



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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management recommendations based on expert consensus for TMJ arthritis in JIA by involving members of TMJaw and the Childhood Arthritis and Rheumatology Research Alliance (CARRA) TMJ interest group.

**Methods:** A scoping review of the literature was conducted until April 2021. Studies were deemed eligible if they met the following criteria: 1) treatment reported, 2) pediatric population, 3) disease of interest, TMJ arthritis in JIA, 4)  $\geq 4$  patients, 5) human studies, 6) English articles, 7) original research, and 8) full length articles. Studies were screened by reviewing titles and abstracts for relative content. Article quality was assessed using a modified version of Pasma et al Quality Assessment Tool. [3] Questions addressed patient recruitment through sampling method, participation, treatment and outcome measurements, and conflict declaration. Non-relevant questions were dropped from the tool. Three questions were deemed essential and a score of 1 was given to each question upon satisfaction. A study with a total score of 4 or higher and at least 2 of 3 essential questions was considered high-quality. Information on design, sample size, and patient demographics, management strategies and outcomes were aggregated. Management and outcomes were analyzed and discussed among TMJaw members and the CARRA TMJ interest group working group to suggest management recommendations.

**Results:** Of the 63 articles selected for full-text review, 15 articles were deemed high-quality from the fields of: dentistry (n = 1), imaging analysis and stereology (n = 3), rheumatology (n = 3), orthodontics (n = 5) and oral maxillofacial surgery (n = 3; Figure). No trials were available and therefore no meta-analysis was possible. Extrapolated evidence suggests that a multidisciplinary approach to care is necessary for diagnosis, interception, and management. Intervention with an orthodontic/orthopedic appliance may provide symptom relief and can minimize or correct developing deformity. Intraarticular TMJ injections generally result in symptom relief but may negatively influence TMJ growth and cause heterotopic bone formation. Joint reconstruction corrects dentofacial deformity and improves function when necessary.

**Conclusion:** Early diagnosis, monitoring, and treatment is necessary to reduce potential morbidity of TMJ arthritis. A multidisciplinary approach is recommended.

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### A Tale of Many Canadas: The Interplay of Ethnicity and Geographic Region as Modifiers of the Presentation to Care in Children With Juvenile Arthritis in Canada

Stephanie Wong (University of British Columbia, Vancouver); Lori Tucker (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Kristin Houghton (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); David Cabral (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Kimberly Morishita (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Mercedes Chan (University of British Columbia, Vancouver); Roberta Berard (Children's Hospital, LHSC, London); Andrea Human (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Ross Petty (British Columbia Children's Hospital, Vancouver); Rae Yeung (The Hospital for Sick Children, Toronto); Kiem Oen (Winnipeg); Ciaran Duffy (Children's Hospital of Eastern Ontario, Ottawa); Jaime Guzman (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); ReACCh-Out Investigators (Edmonton)

**Objectives:** To describe the relative proportion of juvenile idiopathic arthritis (JIA) disease categories, time from symptom onset to diagnosis and disease activity at presentation across major ethnic groupings and geographic regions in Canada.

**Methods:** Using data from 1479 participants in the Research in Arthritis in Canadian Children emphasizing Outcomes (ReACCh-Out) cohort study (children newly diagnosed with JIA between 2005-2010), we compared

Table 1: Comparison of characteristics at presentation to care of children with juvenile arthritis in 5 Canadian regions.

|                          | Mean (SD) weeks since onset to diagnosis | Mean (SD) JADAS score | JIA disease categories (%)                                                                                                                                     |
|--------------------------|------------------------------------------|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| British Columbia (n=257) | 39.7 (66.5)                              | 8.9 (6.3)             | Oligoarticular (40.9)<br>Poly RF- (17.1)<br>Poly RF+ (3.9)<br>Enthesitis related (19)<br>Psoriatic (4.3)<br>Systemic onset (9.3)<br>Undifferentiated (5.5)     |
| Prairies (n=257)         | 38.4 (59.3)                              | 9.3 (6.6)             | Oligoarticular (40.1)<br>Poly RF- (21.8)<br>Poly RF+ (5.8)<br>Enthesitis related (12.8)<br>Psoriatic (4.7)<br>Systemic onset (5.5)<br>Undifferentiated (9.3)   |
| Ontario (n=429)          | 42.6 (68.4)                              | 9.6 (7.2)             | Oligoarticular (36.4)<br>Poly RF- (21.4)<br>Poly RF+ (4.2)<br>Enthesitis related (14.4)<br>Psoriatic (6.8)<br>Systemic onset (7.2)<br>Undifferentiated (9.6)   |
| Quebec (n=331)           | 36.7 (70.9)                              | 7.3 (6.5)             | Oligoarticular (51.4)<br>Poly RF- (14.8)<br>Poly RF+ (3.3)<br>Enthesitis related (10.9)<br>Psoriatic (6)<br>Systemic onset (3.3)<br>Undifferentiated (10.3)    |
| Maritimes (n=196)        | 44.5 (76.4)                              | 10 (6.5)              | Oligoarticular (27.6)<br>Poly RF- (20.9)<br>Poly RF+ (2.6)<br>Enthesitis related (16.3)<br>Psoriatic (10.2)<br>Systemic onset (5.1)<br>Undifferentiated (17.3) |

the relative proportion of JIA categories, weeks from first symptom onset to diagnosis and the clinical Juvenile Arthritis Disease Activity Score (cJADAS10) scores (range from 0-30, including up to 10 active joints) across geographic regions and self-identified ethnic groups. Regions included British Columbia (BC), Prairies (Alberta, Saskatchewan, Manitoba), Ontario, Quebec, and Maritimes (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador). Ethnicity was analyzed per Statistics Canada groupings. We used chi-square tests and Kruskal-Wallis tests to identify statistically significant differences with a  $P < 0.05$ .

**Results:** There were significant differences in JIA categories across Canadian regions ( $P < 0.001$ ), oligoarthritis was most frequent in Quebec (51.4%) and least frequent in the Maritimes (27.6%); enthesitis related arthritis most frequent in BC (19.1%) and least frequent in Quebec (10.9%) (Table 1). Participants who self-identified solely as French had a different distribution of JIA categories relative to those self-identified solely as British. Participants who self-identified solely as Indigenous had the highest frequency of RF-positive polyarthritis (21.2%) of all ethnic groups. There were significant regional differences in time from symptom onset to diagnosis ( $P = 0.01$ ), from a mean of 36.7 weeks in Quebec, to a mean of 44.5 weeks in the Maritimes; and from 24.9 weeks among participants self-identified solely as South Asian, to 93.4 weeks among participants self-identified solely as Latin American. Participants who self-identified solely as Indigenous had an average of 25.9 weeks from symptom onset to diagnosis. The mean cJADAS10 score varied from 7.3 in Quebec, to 10 in the Maritimes; and from 5.9 in participants who self-identified solely as Latin American, to 11.7 in those self-identified solely as Indigenous. There were also significant differences in cJADAS10 scores across JIA categories ( $P < 0.001$ ), with a mean of 5.4 in oligoarthritis and 16.3 in polyarthritis RF-positive.

**Conclusion:** In this cohort, children with JIA across Canada had substantial differences in the distribution of JIA categories, time from onset to diagnosis and disease activity at presentation across Canadian regions and self-identified ethnicities. These differences should be accounted for in any comparisons of JIA treatments and outcomes across the country.

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### How Has the COVID-19 Pandemic Changed Care for Children With Rheumatic Diseases? A Family-Based Survey Study

Rafid Haq (BC Children's Hospital, Vancouver); Herman Tam (Department



of Pediatrics and Child Health, University of Manitoba, Winnipeg); Kristin Houghton (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver); Lori Tucker (Division of Rheumatology, Department of Pediatrics, BC Children's Hospital & University of British Columbia, Vancouver)

**Objectives:** To investigate changes to pediatric rheumatology healthcare delivery during the COVID-19 pandemic.

**Methods:** An anonymous survey was developed for online completion by patients and their families attending clinic visits at BC Children's Hospital (BCCH) Rheumatology Clinics from July-September 2021. The BCCH clinics care for children from the entire province of BC. The survey asks about the potential impact of the pandemic on pediatric rheumatic care, survey domains include 1) how the child's diagnosis affects family concern about COVID-19; 2) how the child's treatment and disease management has been affected; 3) how child and family mental health and security has been impacted. Patient demographic information was collected. Children aged 9-18 years were also asked to complete a modified version of the Pediatric Quality of Life Inventory Generic Core questionnaire, with an additional item asking if there was increased, decreased, or no change during the pandemic. Analysis is descriptive.

**Results:** Survey responses were obtained from 97 patients (60% female) and their families. A majority of parents (54%) reported moderate-extreme increase in concern about COVID-19 because of their child's disease or treatments. Many families reported a decrease of in-person clinical visits (42%), and a concurrent increase in virtual clinic visits (37%) (Table). These trends were less prominent in families living in the Greater Vancouver Area (30% more virtual visits and 34% less in-person visits) compared to those living in other BC regions (57% more virtual visits and 67% less in-person visits). A small number of families (17%) experienced difficulty in obtaining their medications and 30 (31%) reported limited access to healthcare due to a change or loss in employment, transportation issues, or a change in residence. 24 (40%) children and youth reported an increase in emotional health concerns. Of those children and/or parents eligible for a COVID-19 vaccine, 26 (28%) had not received it; of those, 14 (54%) stated they do not plan to get the vaccine or are unsure.

**Conclusion:** Pediatric rheumatology care in BC was significantly affected by the COVID-19 pandemic. Family concern about the pandemic related to their child's disease is high and families have reported limitations in access to healthcare due to personal circumstances. Children and youth also report an increase in mental health concerns related to COVID-19. Children with rheumatic diseases and their families require increased services and emotional support due to pandemic disruptions.

(McMaster University, Hamilton); Tania Cellucci (McMaster University, Hamilton); Stephanie Garner (McMaster University, Hamilton); Liane Heale (McMaster University and McMaster Children's Hospital, Hamilton); Mark Matsos (McMaster University, Hamilton); Michelle Batthish (McMaster University, Hamilton)

**Objectives:** The transition from pediatric to adult rheumatology care is associated with increased disease activity and morbidity. The parent-child relationship is a significant relationship in the transition journey and parents play a key role in promoting self-management skills in adolescent patients. Assessing both adolescents' and parents' perception of the adolescent's independence and self-management skills are important to identifying discordant views and developing strategies to improve transition. Thus, we compared transition readiness assessment scales from both perspectives and analyzed their level of agreement.

**Methods:** Adolescents aged 14-18 years old with JIA or *s*SLE and their parents were recruited in our multidisciplinary rheumatology transition clinic. The patient and one parent both independently completed the TRANSITION-Q during clinic appointments. The TRANSITION-Q is a 14-item, validated, self-administered questionnaire assessing healthcare self-management skills where higher scores (max. 100) indicate greater transition readiness. Total scores and frequencies of responses to each question ("never", "sometimes" or "always") were recorded and the proportion of agreement between their responses were determined. Pearson correlation analyses determined the correlation between adolescent and parent total transition scores and agreement was analyzed using a Bland-Altman plot.

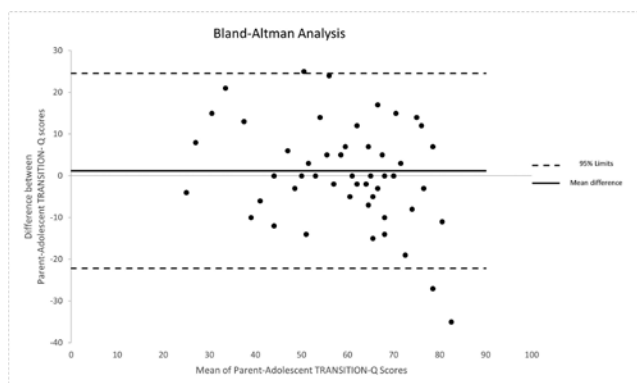
**Results:** Among 57 patient/parent dyads, the Pearson correlation coefficient between parents' and adolescents' total scores was 0.71 ( $P < 0.001$ ). Bland-Altman analysis illustrated generally good agreement with a mean difference of 1.2 which indicates a slight underestimation of parental scores compared to patient scores (Figure). For each question, dyads agreed an average of 70% of the time. The majority of disagreement was mild (ie, sometimes/always or sometimes/never). Most frequent disagreements pertained to adolescents' discussion with people about their health condition and asking questions regarding their health. Extreme disagreements (i.e. always/never) were rare and only occurred 7% of the time in relation to whether adolescents contact the doctor when they need to, and 9% of the time in relation to seeing the doctor/nurse on their own.

**Conclusion:** Adolescents and parents generally agree on the level of the adolescent's transition readiness, however there is occasional disagreement in specific domains. Identifying items more prone to disagreement can help identify areas to target future interventions to improve self-management skills in adolescent patients and successful transition to adult care.

Table: Changes in pediatric rheumatic disease care during COVID-19 pandemic (N, %)

| Type of care; region           | Increased | Decreased | No change or N/A |
|--------------------------------|-----------|-----------|------------------|
| <b>In person clinic visits</b> | 4 (4.3)   | 39 (42.4) | 49 (53.3)        |
| GVA (n=65)                     | 3 (4.6)   | 22 (33.9) | 40 (61.5)        |
| Other BC (n=24)                | 1 (4.7)   | 16 (66.7) | 7 (29.2)         |
| <b>Virtual clinic visits</b>   | 32 (37.2) | 6 (7.0)   | 48 (55.8)        |
| GVA (n=60)                     | 18 (30.0) | 4 (6.7)   | 38 (63.3)        |
| Other BC (n=23)                | 13 (56.5) | 2 (8.7)   | 8 (34.7)         |
| <b>Laboratory test visits</b>  | 7 (8.0)   | 22 (25.3) | 58 (66.6)        |
| <b>Infusion visits</b>         | 3 (3.4)   | 4 (4.6)   | 80 (92.0)        |
| <b>Joint injection visits</b>  | 0         | 4 (4.8)   | 80 (95.2)        |

Abbreviations: GVA, Greater Vancouver Area



## 90 Self-reported Transition Readiness of Adolescent Patients With Rheumatologic Disease: Do the Parents Agree?

Christina Ma (McMaster University, Hamilton); Molly Dushnicky (McMaster University, Burlington); Habeba Talaat (McMaster University, Hamilton); Steffy Thomas (McMaster University, Hamilton); Karen Beattie

## 91 Transition Readiness Before Versus After Adolescents With Rheumatic Disease Transition to Adult Care

Christina Ma (McMaster University, Hamilton); Habeba Talaat (McMaster University, Hamilton); Alessana Carmona (McMaster University, Hamilton); Julie Herrington (McMaster University, Hamilton); Tania Cellucci (McMaster University, Hamilton); Stephanie Garner (McMaster

University, Hamilton); Mark Matsos (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Michelle Bathish (McMaster University, Hamilton)

**Objectives:** The transition from pediatric to adult rheumatology care is associated with increased disease activity and morbidity. Consequently, there has been increasing focus on transitional programs involving multidisciplinary teams to improve self-management skills and other transition-related outcomes. Unfortunately, there is a lack of research surrounding the final stage of transition that occurs immediately after the patient transitions to adult care. Thus, our study aimed to better characterize transition readiness and assess how transition readiness may compare pre-transfer to adult care to post-transfer in a cohort of young adults who were seen in a multidisciplinary rheumatology transition program.

**Methods:** Adolescents aged 17-18 years old with juvenile idiopathic arthritis (JIA) or juvenile onset systemic lupus erythematosus (jSLE) were recruited in our multidisciplinary pediatric rheumatology transition clinic and followed after they transitioned to adult care at age 18 years. Upon transfer to adult care, young adult patients are seen by an adult rheumatologist and an Advanced Clinical Practitioner in Arthritis Care (ACPAC) physiotherapist who sets goals and coaches patients on self-management skills and strategies. Prior to and after the transfer to adult care, all patients completed the TRANSITION-Q, a 14-item, validated, self-administered questionnaire assessing healthcare self-management skills where higher scores (max. 100) indicate greater transition readiness. Total scores and frequencies of responses to each question ("never", "sometimes" or "always") were recorded and changes in scores were assessed.

**Results:** Thus far, 15 patients have participated (n = 13 female, 87%) of whom 67% have JIA. The mean (SD) TRANSITION-Q score prior to transition to adult care was 67.7 (15.2) compared to 82.9 (17.0) after transfer. TRANSITION-Q scores increased in 14/15 (93%) of patients. Individual domains in which the greatest number of patients (53-60%) improved pertained to traveling to doctors' appointments on their own, contacting the doctor when they need to, booking their own doctor's appointments, and seeing the doctor on their own during appointments.

**Conclusion:** Young adult patients with pediatric-onset rheumatic disease who were seen as adolescents in our multidisciplinary transition clinic show improved self-management skills after transitioning to adult care as measured by improved TRANSITION-Q scores. The reasons for improvement are likely multifactorial and related to our transition program, patient maturation and the involvement of an ACPAC after transfer to adult care. Future work will involve increasing our sample size and comparing with patients who did not have access to an ACPAC after transfer.

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### Physician Perception of Ambulatory Rheumatology Care Using Telemedicine During a Global Pandemic

Glynis Byrne (University of British Columbia, Vancouver); Fergus To (University of British Columbia, Division of Rheumatology, Vancouver); Rylan Egan (Queen's University, Kingston)

**Objectives:** The COVID-19 pandemic has been a catalyst to widespread uptake of telemedicine in ambulatory rheumatology care. In Canada, across British Columbia (BC), health authorities encouraged rheumatologists to provide care using telemedicine, including both telephone and video-based platforms, in place of traditional in-person visits when possible. Our aim was to assess how telemedicine has impacted BC rheumatologists' clinical care, relationships with patients, and ambulatory practice processes including administrative workload for both physicians and support staff.

**Methods:** A survey was created and distributed to all adult rheumatologists in BC. Data collected included both quantifiable metrics and qualitative data from free text answers. One-way ANOVA with post-hoc Bonferroni analysis was used for parametric data, and independent samples Kruskal-Wallis test was used for non-parametric data.

**Results:** Of the 85 practicing rheumatologists in BC, 38 (45%) responded to the survey. The majority (76%) of respondents agreed or strongly agreed that history was adequate via telemedicine. This differed significantly based

on years in practice, with a higher percentage of those in the first 4 years of practice in agreement when compared with those with 11 or more years in practice. The majority (86%) of respondents disagreed or strongly disagreed that a physical examination performed by telemedicine was adequate. When respondents were asked to agree or disagree with statements regarding adequacy of history, physical examination, diagnosis and treatment of common rheumatologic conditions (gout, inflammatory arthritis, systemic lupus erythematosus, vasculitis, positive serology without rheumatologic disease, non-inflammatory musculoskeletal conditions and other connective tissue diseases), the percentage of respondents in agreement differed based on the condition. The mean percentage of instances where patients required a subsequent in-person appointment because telemedicine was felt to be inadequate was 25%. The majority (69%) of respondents agreed or strongly agreed that patient satisfaction was high using telemedicine and 94% felt they could effectively communicate with patients. The majority (57%) felt workload was unchanged using telemedicine. Respondents stated that they planned to conduct a mean of 46% of future appointments via telemedicine, with the most common reasons being for patients in rural locations, those with physical limitations and those who find telemedicine more convenient.

**Conclusion:** Our data suggests that rheumatologists are satisfied with the history obtained from telemedicine. However, solutions to facilitate an adequate physical exam remain an area to be explored. Workload is not significantly increased and rheumatologists plan to continue using telemedicine beyond the pandemic.

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### Anakinra Treatment of Multisystem Inflammatory Syndrome in an Adult (MIS-A) With Fulminant Myocarditis Following COVID-19 Infection and mRNA Vaccination: A Case Report and Literature Review.

Chance McDougall (University of Calgary, Calgary); Susan Barr (University of Calgary, Calgary)

**Objective:** Multisystem Inflammatory Syndrome in Adults (MIS-A) is a novel syndrome that has emerged during the COVID-19 pandemic. It is related to its pediatric counterpart, MIS-C, which shares features of Kawasaki Disease and Toxic Shock Syndrome. There is no clear consensus on treatment of these novel syndromes, however case reports have described success with IVIg, glucocorticoids and biologics, including tocilizumab and anakinra. Although mRNA vaccines are considered safe and effective against COVID-19, myocarditis has been reported after vaccination in young adults. We report a case of MIS-A and fulminant myocarditis following asymptomatic COVID-19 infection and mRNA vaccine (Moderna), with clinical response to anakinra.

**Methods:** A case report and literature review on treatment of MIS-A and myocarditis are presented.

**Results:** A previously healthy, 21-year-old Haitian Canadian female received an mRNA vaccine 28 days following an asymptomatic COVID-19 (B.1.1.7 variant) infection. She presented to emergency 17 days post-vaccine with a 7-day history of nausea, vomiting, headache, rash, arthritis, fever, chest pain and dyspnea. She took prednisone 50 mg x 5 days prior to admission. Labs revealed WBC 17.7, CRP 315.5, ferritin 668, NT-proBNP 1641, Troponin T 808, and normal serology (ANA, RF, C3, C4). She was admitted to ICU for cardiogenic shock secondary to myocarditis and received IV vasopressors, heparin, IVIg 2 gm/kg and pulse methylprednisolone. Her ejection fraction decreased to < 5% (NT-proBNP 27,699) and she was moved to CV-ICU for ECMO. She received anakinra 100 mg IV BID, titrated up to q6h the following day. After 7 days of biologic therapy, she was extubated and taken off ECMO. The anakinra was tapered off over 1 week (14 days total), with normalization of cardiac function. Her course was complicated by cardioembolic left cerebellar, pontine and mid brain stroke, thrombosed right common femoral artery secondary to ECMO, and polyneuropathy requiring extensive rehabilitation.

**Conclusion:** There is a growing body of literature supporting treatment of MIS-A and myocarditis with IL-1 antagonist therapy. This is the first report of a vaccine-related MIS-A/myocarditis treated with IL-1 antago-

nist therapy that we are aware of. Advantages of anakinra over tocilizumab may include safety (lower risk of infection and leukopenia, shorter  $t_{1/2}$ ) and efficacy in idiopathic myocarditis. Also, anakinra does not blunt CRP and ferritin levels which are useful disease activity markers. More evidence is needed to support a consensus on the treatment of MIS-A. Finally, this case raises questions concerning the safe timing of mRNA vaccination after COVID-19 infection.

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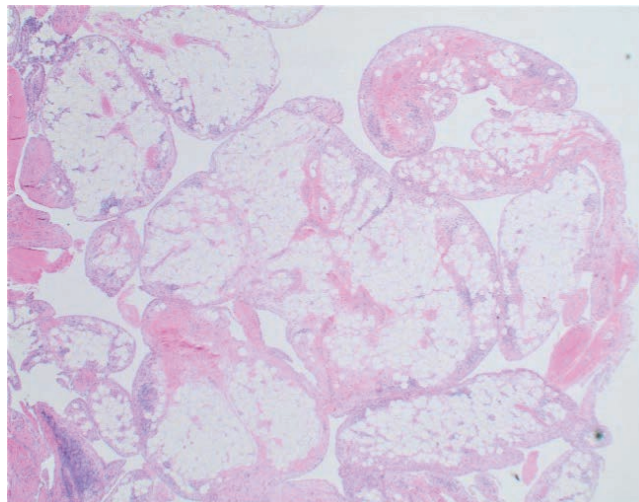
#### **Bilateral Lipoma Arborescens in a Patient With Crohn's Disease: A Diagnostic and Treatment Dilemma**

Daksh Choudhary (University of British Columbia - Division of Rheumatology, Vancouver); Marcia Clark (Department of Surgery, Section of Orthopedics, University of Calgary, Calgary); Dianne Mosher (University of Calgary, Calgary)

**Background:** Lipoma arborescens (LA) is a rare intra-articular disorder of the synovium. It is characterized by lipomatous proliferation of the synovial tissue and presents clinically with progressive and recurrent joint effusions. These benign tumors are most commonly found in the knee and can be painful or painless. Diagnosis is made via MRI or synovial biopsy.

**Case Description:** We report a rare case of bilateral LA and the first case of LA reported in a patient with history of IBD (Figure).

**Conclusion:** The case is valuable because it delineates the difficulties in diagnosing and treating LA.



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#### **Transient Perivascular Inflammation of the Carotid Artery (TIPIC) Syndrome: A Precursor to Giant Cell Arteritis?**

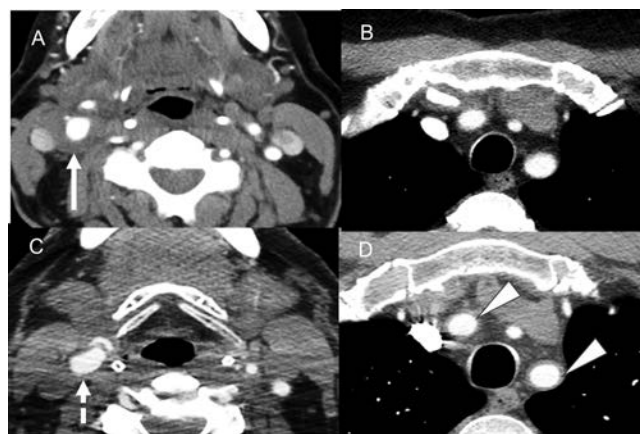
Deborah Koh (McMaster University, Hamilton); Ryan Rebello (McMaster University, Hamilton); Sankalp Bhavsar (McMaster University, Hamilton)

**Cases:** An 84-year-old male presented with a 2-day history of right-sided neck pain with no constitutional symptoms, headaches, or vision changes. His C-reactive protein (CRP) was 155 mg/L. CT scan showed perivascular inflammation (PVI) around the right common carotid artery with extension (Figure). Temporal artery biopsy was negative. He was started on high-dose prednisone with rapid resolution of pain. His prednisone was tapered, and his CRP normalized. CT imaging 3 weeks later showed complete resolution of the PVI, consistent with TIPIC syndrome. There were never signs of large vessel vasculitis (LVV) on imaging. Approximately 1 month later, he developed a temporal headache and his inflammatory markers rose. He was diagnosed with giant cell arteritis (GCA) and his prednisone dose was increased with resolution of the headache. He was weaned off prednisone without the use of steroid-sparing therapies and remains in remission. Another 68-year-old male presented with repeated short episodes of neck pain that self-resolved. He described associated earache and sore throat. He

ultimately presented during an episode with CRP 100.1 mg/L and ESR 97 mm/hr. CT scan showed PVI around the right common and internal carotid arteries with no other vascular changes. He was treated with aspirin. Two weeks later, CT showed shrinkage of the PVI. The PVI resolved 6 months later, consistent with TIPIC. Eighteen months later, he developed neck pain, pleuritic chest pain and right foot synovitis with an elevated CRP. He now had CT evidence of LVV affecting large arteries in the chest, pelvis and lower extremities. He was started on high dose prednisone with good response and began tocilizumab 1 month later.

**Discussion:** TIPIC syndrome is a poorly known condition that has recently gained attention. TIPIC causes acute neck pain and pericarotid inflammation on imaging. NSAIDs and aspirin are both proposed treatments. TIPIC may be a form of vasculitis. This is supported by increased glucose uptake by the PVI in FDG-PET CT scans, which is also seen in affected areas of LVV. Furthermore, patients with vasculitis have increased levels of s-intracellular adhesion molecule-1 (sICAM-1), a molecule used to support the inflammatory response. Patients with TIPIC also have elevated levels of sICAM-1, suggesting similar pro-inflammatory pathways.

**Conclusion:** We propose that TIPIC syndrome acted as a precursor to GCA in our patient cases, heralding more significant disease akin to palindromic rheumatism and rheumatoid arthritis. To our knowledge, there is no existing report of this nature in the literature.



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#### **Nailfold Videocapillaroscopy Alterations in Idiopathic Inflammatory Myopathies: A Prospective Study**

Thaisa Cotton (McGill University, Montreal); Valérie Leclair (McGill University, Montreal); Mianbo Wang (Lady Davis Institute for Medical Research, Montreal); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal); Geneviève Gyger (McGill University, Jewish General Hospital, Montreal)

**Objectives:** Nailfold videocapillaroscopy (NVC) alterations have been described in idiopathic inflammatory myopathies (IIM) classified using Bohan and Peter criteria. The aim of this study was to describe NVC abnormalities in IIM subsets using updated sero-clinico-pathological integrated criteria and to determine change in response to treatment.

**Methods:** We studied IIM subjects in the Canadian Inflammatory Myopathy Study (CIMS), an early onset cohort followed prospectively. NVC images were acquired using the DS MEDICA Videocap (X200 magnification). The nailfolds of the second, third, fourth and fifth fingers of both hands were photographed and scored by an experienced rheumatologist. Microhemorrhages, giant capillaries, ectasias and ramified capillaries were scored using a standardized semi-quantitative scale (0 = no, 1 =  $\leq 33\%$ , 2 = 33–66%, and 3 =  $\geq 66\%$  abnormalities per linear millimeter). Capillary density was scored semi-quantitatively (0 if  $\geq 7$ , 1 if 4–6, or 2 if  $\leq 3$  capillaries/mm) and quantitatively (mean number of capillaries/mm). Each NVC parameter, as well as giant-ramified capillaries, were scored as present or absent. Finally, the propor-



Table 1 Nailfold videocapillaroscopic (NVC) patterns in IIM at baseline and follow up (n=39)

| NVC patterns | Dermatomyositis (n=22) |            | Anti-synthetase syndrome (n=8) |           | Scleromyositis (n=9) |           |
|--------------|------------------------|------------|--------------------------------|-----------|----------------------|-----------|
|              | Baseline               | Follow up  | Baseline                       | Follow up | Baseline             | Follow up |
| SSc          | 3 (13.6%)              | 1 (4.6%)   | 2 (25%)                        | 0         | 2 (22.2%)            | 3 (33.3%) |
| SSc-like     | 8 (36.4%)              | 6 (27.3%)  | 1 (12.5%)                      | 1 (12.5%) | 6 (66.7%)            | 3 (33.3%) |
| Non-specific | 8 (36.4%)              | 5 (22.7%)  | 1 (12.5%)                      | 5 (62.5%) | 0                    | 3 (33.3%) |
| Normal       | 3 (13.6%)              | 10 (45.4%) | 4 (50%)                        | 2 (25%)   | 1 (11.1%)            | 0         |

SSc: systemic sclerosis or scleroderma

tion of subjects with scleroderma (SSc), SSc-like, nonspecific, and normal patterns were compared.

**Results:** Thirty-nine patients were included: 22 dermatomyositis (DM), 8 anti-synthetase syndrome (ASS), and 9 scleromyositis (SM). Baseline capillaroscopy revealed decreased capillary density in DM (mean 5.55/mm) and SM (mean 5.50/mm), while ASS was normal (mean 7.15/mm). Ectasias were common at baseline in DM (87%) and SM (100%) patients, while only 50% ASS patients had this finding. Ramified capillaries were also common at baseline, seen in 86.4% DM, 62.5% ASS, and 88.9% SM patients. Giant capillaries were seen in 66.7% SM, but only 45.5% DM, and 37.5% ASS patients. Baseline NVC patterns in DM were more commonly SSc-like (36.4%) or nonspecific (36.4%), while 50% ASS were normal, and 66.7% SM were SSc-like. At follow-up, all capillaroscopy abnormalities in DM improved, except ramified capillaries which increased (Table 1). Capillaroscopy abnormalities also improved in ASS, except ramified and ectasias, which increased, while in SM there was no improvement.

**Conclusion:** This is the first study of NVC using integrated criteria for IIM. Although ASS and SM are often classified together as overlap myositis, these findings highlight NVC differences between these two subsets, suggesting that NVC can refine IIM phenotyping. Treatment may improve capillaroscopy abnormalities in DM and ASS but not in SM. NVC might be a potential biomarker for disease monitoring in certain IIM subsets.

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### A Survey of Treatment Satisfaction With Intravenous Immunoglobulin Among Patients With Inflammatory Myositis

Alan Zhou (University of Ottawa, Department of Medicine, Ottawa); Nancy Maltez (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Catherine Ivory (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa)

**Objectives:** Intravenous Immunoglobulin (IVIg) is used to treat rheumatic conditions such as Inflammatory Myositis. Home-based subcutaneous Immunoglobulin (SCIg) is an alternative route of administering Immunoglobulin that is cost-effective with similar outcomes and less adverse events. Our objective was to characterize patient satisfaction regarding IVIg treatment of their myositis, and to explore their perceptions of SCIg and interest in transitioning to SCIg.

**Methods:** Adult patients (age 18+) receiving IVIg for Inflammatory Myositis at a Tertiary Centre in Ottawa were approached and provided informed consent to participate. An adaptation of the validated Treatment Satisfaction Questionnaire for Medication was administered to collect data on patient satisfaction across 4 domains (effectiveness, convenience, side effect burden, and global satisfaction) and to gauge interest in SCIg. Data was collected using a 5 or 7-point Likert scale. Results were anonymized and summarized descriptively with means reported. Ethics approval was obtained from the Ottawa Health Science Network Research Ethics Board.

**Results:** 9 patients responded to our survey. Indications for IVIg included Dermatomyositis (55.6%), Polymyositis (11.1%), Anti-Synthetase Syndrome (11.1%), and other Inflammatory Myositis (22.2%). 55.6% of participants had received IVIg for more than 3 years, 33.3% for less than 1 year, and 11.1% for 1-3 years. On average, participants were satisfied with the effectiveness of IVIg (5.8/7) but somewhat dissatisfied with the overall convenience (4.4/7). 88.9% of participants reported side effects including headache (77.8%), fatigue (33.3%), nausea (33.3%), chills (22.2%), cramps (11.1%), and minor chest pain (11.1%). Side effects were rated as neutral to somewhat bothersome. Overall, participants were satisfied with their experience (5.1/7). Scores across all 4 domains were similar regardless of diagnosis or treatment duration. 88.9% of participants were unfamiliar with

SCIg. Participants were somewhat uncomfortable with the idea of SCIg (4.1/7) with 33.3% citing lack of knowledge. 44.4% were willing to switch to SCIg, 11.1% were not, and 44.4% were unsure. Those willing to switch had on average received IVIg for a shorter duration.

**Conclusion:** Participants were satisfied with the effectiveness of IVIg in treating their myositis but somewhat dissatisfied with the inconvenience and side effect burden. This discrepancy has been reported in other diseases treated with IVIg, with the inconvenience being attributed to the frequency and duration of infusions. SCIg may offer a solution to this, though unfamiliarity is a barrier to patient buy-in. Further patient education on SCIg, as well as larger controlled studies to validate its use in Inflammatory Myositis, are required.

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### Understanding Perceived Barriers and Facilitators to Engaging in Care for Knee Osteoarthritis in Persons With Type 2 Diabetes Mellitus: A Qualitative Study Using the Theoretical Domains Framework

Owen Krystia (University of Toronto, Toronto); Lauren King (University of Toronto, Toronto); Esther Waugh (University of Toronto, Toronto); Crystal Mackay (University of Toronto, Toronto); Ian Stanaitis (Women's College Research Institute, Women's College Hospital, Toronto); Noah Ivers (Women's College Hospital, Toronto); Lorraine Lipscombe (University of Toronto, Toronto); Gillian Hawker (University of Toronto, Toronto)

**Objectives:** Symptomatic knee osteoarthritis (OA) frequently co-occurs in individuals with type 2 diabetes mellitus (T2DM) and may lead to worse T2DM outcomes, yet it remains undertreated. Studies suggest health care providers often assign OA a lower priority relative to other chronic conditions like T2DM, but there is no published literature on barriers and facilitators to OA care from the perspectives of persons living with T2DM. With view to developing an intervention to improve both diagnosis and treatment of knee OA in persons with T2DM, we sought to understand the perceived barriers and enablers to the behavior of seeking and engaging in knee OA care in persons with T2DM.

**Methods:** We conducted semi-structured telephone interviews with 18

Table 1. Theoretical Domains Framework analysis with inductively developed belief statements

| TDF Domain                          | Belief statements                                                                              | Quotes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|-------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Knowledge                           | When I have a strong understanding of what OA is, I am better able to engage in its management | "I guess the education point, but then I felt like I was left with okay, now what do I do. I don't know what to do about it." - P11                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|                                     |                                                                                                | "I guess I ignored my pain] because I have a high pain threshold, I was, yeah, it's just another ache and pain growing old." - P17                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Beliefs about capabilities          | I believe that joint pain stops me from engaging in exercise for OA treatment                  | "I just couldn't exercise; I was in a tremendous amount of pain" - P2<br>"I'm unable to do anything now." - P6                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Optimism                            | I do not expect that OA treatments will significantly help my symptoms                         | "I think I'm just to the point where I'm almost beyond hope." - P14<br>"I mean, I'm not expecting utopia, I'm not expecting to have the same mobility and lack of pain that I had when I was in my teen years or 20s." - P13                                                                                                                                                                                                                                                                                                                                                          |
| Reinforcement                       | I continue to engage with the OA treatments if they improve my OA symptoms                     | "It seems like if I do the exercise then the joints will not be as stiff if I'm not doing the exercise. If I miss one day exercise, I feel the joints are very stiff and very painful. That's why it's kind of a push that I have to do exercise every morning, no matter how tired I will be." - P18<br>"[Walking is] to keep muscle tone, and muscle tone always helps. By the end of it I feel it, but it's a price worth paying." - P8                                                                                                                                            |
| Environmental context and resources | Negative experiences with health care providers limit how I manage my OA                       | "I don't think [my family doctor] knew what to do, I think she did some simple examinations and checked to see if my hips were involved and I don't think she knew what else to do... The osteoarthritis, I don't think she had a clue." - P5<br>"He [surgeon] says, well, what can I tell you, he says I'm not going to touch you [operate for knee OA] unless you lose another 50 pounds." - P1<br>"I think the problem is a lot of people when they age, and they get aches and pains, and they're told [by health care providers], oh, it's part of aging, be more active." - P16 |
|                                     | Access to relevant facilities, programs, or resources enables management of my OA              | "I'm not covered, insurance-wise, so I couldn't go for physio and things like that" - P4<br>"At Parks and Rec, they have a heated pool, so I was going there two and three times a week, basically walking back and forth in the water because the warm water and walking I found it helpful." - P17                                                                                                                                                                                                                                                                                  |
| Social influences                   | Having social supports help me to stay engaged with OA treatments                              | "My wife is the go-getter here. She would say, let's go down and give it a whirl and try [pool exercise] out, so we did. I don't know how she thought of it, but we just did and it seemed to work." - P15<br>"No, I'm alone. And I said, the loneliness is the mother of all evil that I'm alone." - P6                                                                                                                                                                                                                                                                              |
|                                     | I listen to peers about how to manage OA                                                       | "And you learn more from other people. You learn how to cope with other people. And that's what I like                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

individuals with a physician diagnosis of T2DM and symptomatic knee OA recruited from an urban family medicine practice and the Arthritis Society rehabilitation program in Ontario, Canada. Recruitment was guided by saturation of themes. Transcripts were deductively coded using the Theoretical Domains Framework (TDF), an implementation science framework that incorporates a range of theoretical constructs to comprehensively identify determinants of behavior which can be mapped systematically to behavior change techniques. Within each of the 14 TDF domains, data were thematically analyzed to generate belief statements.

**Results:** Of the 18 individuals interviewed, nine (50%) were women, nine (50%) were over the age of 70 years, and 9 (50%) had been diagnosed with T2DM more than 10 years prior. Mean WOMAC pain was 8.17/20 (SD 4.84) and 13 (72%) had at least “some difficulty” walking outdoors on flat ground due to their OA. Seven of the TDF domains were identified to prominently influence the behavior to seek and engage in OA care: knowledge, beliefs about capabilities, reinforcement, environmental context and resources, social influences, and behavioral regulation. Belief statements constructed within these domains are presented in Table 1. Important barriers include insufficient OA knowledge to fully engage in care (knowledge), feeling incapable of participating in physical activity/exercise due to joint pain (beliefs about capabilities), lack of guidance from health care providers and insufficient access to community programs/supports (environmental context and resources). Key facilitators were strong social support (social influences) and sources of accountability (behavioral regulation). Concomitant T2DM was not seen to limit engagement in OA care.

**Conclusion:** Among individuals with symptomatic knee OA and T2DM, we identified multiple barriers and facilitators to seeking and engaging in knee OA that will be used in developing an implementation intervention.

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### Understanding Barriers and Facilitators to Health Care Providers Assessing and Treating Knee Osteoarthritis in Persons with Type 2 Diabetes Mellitus: A Qualitative Study Using the Theoretical Domains Framework

Owen Krystia (University of Toronto, Toronto); Lauren King (University of Toronto, Toronto); Esther Waugh (University of Toronto, Toronto); Crystal Mackay (University of Toronto, Toronto); Ian Stanaitis (Women's College Research Institute, Women's College Hospital, Toronto); Noah Ivers (Women's College Hospital, Toronto); Lorraine Lipscombe (University of Toronto, Toronto); Gillian Hawker (University of Toronto, Toronto)

**Objectives:** Symptomatic knee osteoarthritis (OA) commonly co-exists in persons with Type 2 diabetes (T2DM) and, if left untreated, may impede diabetes self-management, including engaging in physical activity. Evidence-based therapies for OA are underutilized. Studies suggest health care providers may pay less attention to diagnosis and management of OA in the context of other competing chronic conditions. To inform the development of an implementation intervention to improve guideline-concordant management of symptomatic knee OA in persons with T2DM, we examined the perspectives of diabetes health care providers regarding barriers and enablers to diagnosing and treating knee OA in persons with T2DM.

**Methods:** We conducted 18 semi-structured telephone interviews with healthcare providers who treat persons with T2DM (family physicians, endocrinologists, and diabetes educators) purposefully selected to represent a range of practice settings and years of experience. Recruitment was guided by saturation of themes. Transcripts were deductively coded using the Theoretical Domains Framework (TDF), an implementation science framework that incorporates a range of theoretical constructs to comprehensively identify determinants of behavior which can be mapped systematically to behavior change techniques. Within each of the 14 TDF domains, data were thematically analyzed to generate belief statements. We then compared represented domains and belief statements across the different health care providers.

**Results:** Eighteen providers were interviewed (8 endocrinologists, 7 family physicians, 3 diabetes educators). Of the 14 TDF domains, 6 were featured prominently in the interviews: knowledge, skills, professional role and identity, intentions, environmental context and resources, and social influ-

Table 1. Theoretical Domains Framework analysis with inductively developed belief statements

| TDF Domain                            | Belief Statements and Illustrative Quotes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|---------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                       | Endocrinologists and diabetes educators                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Family physicians                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <b>Knowledge</b>                      | <p>I lack sufficient knowledge about OA to diagnose or make treatment recommendations</p> <p><i>"And in terms of the latest treatments in arthritis care, I'm not fully up to date on that literature..." - P2 (Endo)</i></p> <p><i>"I don't even remember getting any education on osteoarthritis." - P12 (DM educator)</i></p>                                                                                                                                                                                                                                                                                       | ---                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>Skills</b>                         | <p>I am not comfortable performing a joint examination</p> <p><i>"It's hard to tackle [joint assessment] in great detail, especially when it's not something that we necessarily have tonnes of direct training on." - P9 (Endo)</i></p>                                                                                                                                                                                                                                                                                                                                                                               | <p>• I am comfortable performing a joint assessment</p> <p><i>"Yeah, I feel comfortable assessing joint pain." P10</i></p>                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <b>Professional role and identity</b> | <p>I do not see OA as a comorbidity that diabetes specialists manage</p> <p><i>"I think most of my patients, they know that the way we run this is a very focused practice, very much the metabolic and cardiovascular implications of diabetes is what we focus on." - P4 (Endo)</i></p> <p>I believe joint pain should be evaluated and managed by the patient's family physician</p> <p><i>"I feel like [joint pain] doesn't [fit into my professional role]. I'm going to be perfectly honest." - P8 (Endo)</i></p> <p><i>"I always tell them their first stop should be their family doctor." - P4 (endo)</i></p> | <p>I believe that joint pain should be evaluated by the family physician, but prescription and monitoring exercise therapy should be managed by other professions</p> <p><i>"If we had access to, not an exercise physiologist, but even a physio that could spend the time to go through with someone, to really sit down and figure out what they have access to, what they're willing to do, all that sort of stuff, to come up with a reasonable plan with them that they'll actually do, and follow up with them. That would be really great." - P10</i></p> |
| <b>Intentions</b>                     | <p>I prioritize assessment of diabetes control and complications and do not seek to address joint pain</p> <p><i>Everything is focused on the A1C. Get an A1C every three months, see your doctor, whether it's a family doctor or an endocrinologist for your diabetes visit every three months. There's just too much to cover in a 15-minute visit every three months." - P8 (Endo)</i></p>                                                                                                                                                                                                                         | <p>I prioritize assessment of diabetes control and complications and do not seek to address joint pain</p> <p><i>"In my mind, we probably get to the osteoarthritis last, and that would mean that there's less time." - P16</i></p>                                                                                                                                                                                                                                                                                                                              |

ences. Belief statements within these domains are presented in Table 1. For all health care providers, important barriers include not seeing joint pain as a priority (intention), and the perceived insufficient supports that are available to refer to (environmental context and resources). As seen in Table 1, compared to family physicians, endocrinologists and diabetes educators perceived having less sufficient knowledge and skills to assess OA (knowledge, skills), did not consider it within their professional role to address OA (professional role and identity), and perceived other physicians would not want to receive a referral for OA care (social influences).

**Conclusion:** Using the TDF, we identified several domains that featured prominently in health care providers' behavior of assessing and treating knee OA in persons with T2DM. These will guide the development of a complex intervention to address the deleterious impact of underdiagnosed and undertreated knee OA on T2DM management.

100

### A Case of Rhabdomyolysis Following Vaccination Against COVID-19 in a Patient With Pathogenic Ryanodine Receptor Gene Variant

Matthew Jessome (McMaster University, Hamilton); Brittany Salter (McMaster University, Hamilton); Mark Tarnopolsky (McMaster University, Hamilton); Haroon Yousuf (McMaster University, Hamilton); Faiza Khokhar (McMaster University, Hamilton)

**Background:** Rhabdomyolysis has a broad range of etiologies, and the rheumatologist may be expected to exclude immune-mediated myopathies as a

| Laboratory Test (Reference Range)       | 8 days post-vaccine | 11 days post-vaccine | 7 weeks post-vaccine |
|-----------------------------------------|---------------------|----------------------|----------------------|
| Creatinine (58-110 µmol/L)              | 69                  | 67                   | -                    |
| Creatine Kinase (30-150 U/L)            | <b>203,088</b>      | <b>586,647</b>       | 88                   |
| Hemoglobin (115-165 g/L)                | 129                 | 126                  | 118                  |
| Platelets (150-400 x10 <sup>9</sup> /L) | 236                 | 282                  | 201                  |
| Leukocytes (4-11 x10 <sup>9</sup> /L)   | 9.6                 | 10.8                 | 5.2                  |
| AST (18-34 U/L)                         | <b>673</b>          | <b>1376</b>          | 26                   |
| ALT (0-34 U/L)                          | <b>68</b>           | <b>191</b>           | 21                   |
| ALP (38-126 U/L)                        | 96                  | 96                   | -                    |
| Total Bilirubin (<21 µmol/L)            | 8                   | 11                   | -                    |

Table 1: Relevant laboratory values at presentation, at time of peak CK value, and during period of clinical improvement. Abnormal values bolded.



cause. We herein present a case of rhabdomyolysis following COVID-19 vaccination in a patient with ryanodine receptor (RYR1) gene mutation.

**Case Summary:** A 30-year-old female presented to hospital with progressive bilateral upper and lower extremity myalgia and weakness, starting 3 days after second dose of Moderna COVID-19 vaccine. She has known pathologic RYR1 gene mutation at the canonical splice site (c.12624+1\_124+2insT), with 5 prior episodes of rhabdomyolysis, most triggered by viral infections. Medical history included schizoaffective disorder, latent tuberculosis treated 5 years prior, polycystic ovarian syndrome, iron deficiency anemia, and obstructive sleep apnea. Medications included atorvastatin, clozapine, lithium, flupentixol, ferrous gluconate, and vitamin D. There was no recent strenuous exercise, trauma, prolonged exposure to heat, alcohol or recreational drug consumption, or sick contacts. Review of systems revealed flu-like symptoms 1 day after vaccination, resolving within 2 days, but otherwise negative for connective tissue disease, mucocutaneous, cardiovascular, respiratory, gastrointestinal, neurologic, or additional musculoskeletal abnormalities. Physical examination was notable for symmetric 4/5 strength globally, with normal mental status, tone, reflexes, joints, and skin. Investigations (Table 1) demonstrated initial CK of 203,088 U/L and AST greater than ALT elevation. Creatinine, urea, electrolytes, albumin, glucose, venous blood gas, lactate, and complete blood count were normal except for mild hypokalemia and mild hyperphosphatemia. Urinalysis revealed no protein, and 3+ blood. ANA, pANCA, cANCA, Anti-HMGCR, and 15 antibody myositis panel were negative. Thigh MRI revealed diffusely heterogeneous symmetric intramuscular and intermuscular edema. Upon presenting 8 days post-vaccination, she received aggressive intravenous fluids, and oral dantrolene 25 mg TID. Atorvastatin was discontinued. Her myalgia and weakness initially worsened, with peak CK at 586,647 U/L 11 days post-vaccination. Rheumatology was consulted to exclude inflammatory myopathy, particularly given statin exposure for 2 years. By day 14 post-vaccination, the patient began improving clinically with normalization of CK 1 month post discharge, without receiving immunosuppressive therapy.

**Conclusion:** In summary, we present a case of severe rhabdomyolysis without evidence of immune-mediated myopathy. Other diagnostic considerations such as malignant hyperthermia, or neuroleptic malignant syndrome, were not clinically compatible. Given the close temporal relationship, we hypothesize that COVID-19 vaccination likely triggered an inflammatory response that precipitated rhabdomyolysis in this patient who was susceptible due to an underlying pathogenic RYR1 gene mutation, with concomitant risk factors including statin and antipsychotic drug exposure.

## 101

### JIA Polyarthritis as a Misdiagnosis for Farber Disease: A Case Report

Paul Dancy (Jewish Children's Hospital and Rehabilitation Centre, St. John's); John Mitchell (Montreal Children's Hospital, Montreal); Alexander Solyom (Aceragen, Basel); Kathleen Crosby (Aceragen, Durham)

**Background:** Farber disease is an ultra-rare lysosomal storage disease caused by mutations in the *ASAHI* gene. The resulting deficiency of the acid ceramidase enzyme leads to accumulation of the pro-inflammatory sphingolipid ceramide. Three cardinal symptoms of Farber disease include joint disease (polyarticular arthritis and contractures), subcutaneous nodules, and a hoarse voice. There is a broad spectrum of severity with classic disease presenting in infancy and attenuated forms that may not be recognized until adulthood. In this report we describe a patient diagnosed with JIA prior to the diagnosis of Farber disease through genetic testing.

**Case Description:** A one-year-old boy of Syrian descent was referred to the rheumatology clinic for progressive pain and stiffness in his hands over the preceding 6 months. There was no history of fever or rash. He was born full-term, had normal growth and no known health problems. The family described a gross motor delay attributed to pain when using his hands. Family history was negative for rheumatological diagnoses. Consanguinity through great-grandparents was later reported. The physical exam revealed painful joint contractures in his fingers, wrists, knees, hips, ankles, and elbows, with joint swelling in his first toes, wrists, second and third MCP joints,

and thumbs. He had one small nodule on the dorsal aspect of a finger. The remainder of the physical exam was normal. Preliminary testing revealed a normal CBC and CRP, and negative ANA and RF. X-rays of the joints did not reveal any bone changes. Ophthalmology exam and a mucopolysaccharidosis screen were normal. He was diagnosed with RF negative JIA polyarthritis and started on naproxen and methotrexate. His parents reported a good response to naproxen with improved mobility and pain reduction, however nodules and joint disease progressed. Subsequent genetic testing identified a homozygous mutation in the *ASAHI* gene consistent with a diagnosis of Farber disease. The patient is now 4 years old and has developed voice hoarseness and more significant developmental delay over time. Methotrexate was discontinued and he is now receiving tocilizumab without a clear response. Due to poor feeding, a g-tube is being considered. **Conclusion:** There is no cure for Farber disease and current treatment strategies including DMARDs and hematopoietic stem cell transplantation have significant limitations. The diagnosis should be considered in patients with chronic joint contractures who also develop subcutaneous nodules, neurologic symptoms, or dysphonia, or fail to respond to standard arthritis treatments. Future treatments options may include enzyme replacement or gene therapy.

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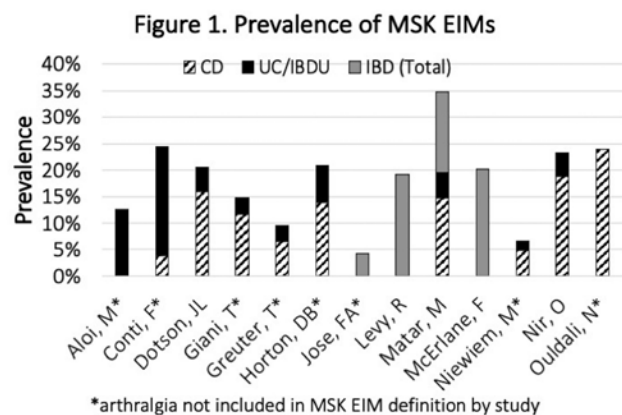
### Epidemiology of Musculoskeletal Manifestations in Pediatric Inflammatory Bowel Disease: A Systematic Review

Aaisham Ali (Schulich School of Medicine & Dentistry, Western University, London); Melanie Schmidt (Lawson Health Research Institute, London); David Piskin (Lawson Health Research Institute, London); Eileen Crowley (Children's Hospital, LHSC, London); Roberta Berard (Children's Hospital, LHSC, London)

**Objectives:** Paediatric inflammatory bowel disease (p-IBD) is a chronic and relapsing gastrointestinal disorder of childhood with associated long-term morbidity. Several extraintestinal manifestations (EIMs) are described, the most common being joint pain and/or inflammation. In 1986, Passo et al. were the first to describe the association of arthritis in p-IBD patients. However, since then, data on the epidemiology, patient and disease factors associated with, treatments for, and outcomes of p-IBD associated musculoskeletal (MSK) disease are not well-established. Our study aims to summarize the literature on the epidemiology of MSK EIMs in p-IBD in the era of biologics.

**Methods:** A systematic review of the literature was performed. PubMed, Embase, Cochrane Library, Web of Science Core Collection, and CINAHL databases were searched with relevant keywords. Studies in English published from January 1, 2000, to December 21, 2020, were included. In total, 3893 papers were identified, and screening was performed by two independent reviewers (AA, MS). Conflicts were resolved by a third reviewer (EC, RB). Study and population characteristics were recorded. The primary outcomes of interest were MSK symptoms at presentation and their course, method of diagnosis and definitions used for MSK EIMs. Risk of bias assessment was performed using the JBI Critical Appraisal Tools.

**Results:** Thirteen studies were included for full review, which were





primarily single-centre observational studies with retrospective or cross-sectional design. The method of diagnosis for MSK EIMs varied across the studies, with only 4 studies stating the involvement of a rheumatologist in diagnosis. The definitions also varied, with MSK EIMs such as peripheral arthritis, axial arthritis, enthesopathy, and arthralgia included. Only 7 studies focused on MSK EIMs as their primary outcome, while the remainder reported on all p-IBD associated EIMs. There was a wide range in the prevalence of MSK EIMs from 2-35% (Figure 1). Four studies reported on the therapeutic response of MSK EIMs, and only 3 of those reported on biologic use. Risk of bias demonstrated heterogeneity in the quality of included studies.

**Conclusion:** This is the first systematic review of the literature for MSK EIMs in p-IBD. Analysis was limited due to variability in study design and data-reporting methods. Included studies reported prevalence of MSK EIMs, but the ascertainment of MSK EIMs, both method and definition varied with a clear lack in standardization. Our study demonstrates the need for further research to accurately define the MSK associations of p-IBD and explore optimal management to advance care for this group of children.

### 103

#### Mind the Gap: The Experience of Adolescents in a Rheumatology Transition Clinic

Claire Fine (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Tania Cellucci (McMaster University, Hamilton); Stephanie Garner (McMaster University, Hamilton); Liane Heale (McMaster University and McMaster Children's Hospital, Hamilton); Mark Matsos (McMaster University, Hamilton); Michelle Batthish (McMaster University, Hamilton)

**Objectives:** We aimed to assess the transition clinic experiences of 14-18 year-old patients with JIA and SLE and to identify areas where current transition care is not meeting patients' ideal standards.

**Methods:** The "Mind the Gap" validated questionnaire was administered to our Transition Clinic rheumatology patients aged 14-18 years old attending our Transition Clinic. The questionnaire assesses the transition clinic expectations and experiences and includes 22 questions covering 3 domains: management of environment, provider characteristics and process issues. Patients completed the questionnaire twice on a single occasion; first with respect to their "ideal" experience and second with respect to their current clinic experience. Responses ranged from strongly disagree (1) to strongly agree (7). For each question, a "gap" score was calculated by subtracting the current from the ideal score. A score of 0 signifies that the current experience is ideal; positive scores suggest current care is less than ideal, and negative scores suggest current care exceeds the ideal experience. The greater the positive gap score, the lower the level of satisfaction. Similarly, the greater the negative gap score, the greater the satisfaction. Descriptive statistics summarized our patients' responses.

**Results:** Of 63 patients (43 female), mean (SD) age 16.4 (1.2) years, 86% had JIA and 14% had SLE. For each domain, the mean gap score was between 0 and 1, indicating virtually no gap between current and ideal care (Table 1). The largest frequency of patients recording a gap score  $\geq 1$  was 45%, for the clinic's ability to communicate information to the patient's schoolteachers. When comparing gap scores for males and females, mean gap scores were similar for the environment and process issues. However, for provider characteristics, mean (SD) gap scores for females (0.41 (1.2)) appeared higher than males (0.0, (0.5)). Females were less satisfied with how well the staff knew them and the staff's "ability to understand the realities of being a teenager".

Table 1: Median (min, max) gap scores by domain

| Domain                        | Male (n=20)     | Female (n=43)   | Total (n=63)    |
|-------------------------------|-----------------|-----------------|-----------------|
| Management of the Environment | 0.0 (-1, 2.4)   | 0.4 (-3.8, 5.4) | 0.2 (-3.8, 5.4) |
| Provider Characteristics      | 0.2 (-0.9, 1.5) | 0.3 (-1.4, 6.9) | 0.2 (-1.4, 6.9) |
| Process Issues                | 0.2 (-1.5, 2)   | 0.5 (-1.7, 5.7) | 0.3 (-1.7, 5.7) |

**Conclusion:** Although overall Transition Clinic experiences appear to be meeting the expectations of the majority of our rheumatology patients, there is room for improvement within all three domains. Future directions should include developing standardized interventions to address the identified gaps, such as communication with schools and the provider's abilities to discuss sensitive issues.

### 104

#### Kawasaki and Kawasaki-like Illness During the Covid-19 Pandemic: A Single Centre Cohort Study

Justine Turmel-Roy (McGill University Health Centre, Montreal); Claire LeBlanc (McGill University Health Centre, Montreal); Gaëlle Chédeville (McGill University Health Centre, Montreal); Sarah Campillo (McGill University Health Centre, Montreal); Rosie Scuccimarrì (McGill University Health Centre, Montreal)

**Objectives:** The aim of this study was to describe our cohort of Kawasaki disease (KD) and Kawasaki-like illness (KLI) during the COVID-19 pandemic and to ascertain the incidence of multisystem inflammatory syndrome in children (MIS-C) among these.

**Methods:** Retrospective chart review was performed of patients diagnosed with KD and KLI at the McGill University Health Centre from March 1st 2020 to May 31st 2021. American Heart Association definitions were applied for complete/incomplete KD and coronary artery dilatations/aneurysms. MIS-C was defined as per CDC and WHO criteria. Information on clinical features, laboratory and cardiac investigations, treatment and outcomes were collected and analyzed. P-values were calculated using chi-square, Fisher's exact test or Wilcoxon rank-sum test.

**Results:** Fifty-five patients were included. Median age was 6.2 years; 50.9% were female; 36.4% were either of Afro-Caribbean or Hispanic ethnicities. All patients had fever and at least one other KD criteria. Complete and incomplete KD was diagnosed in 52.7% and 36.4% respectively. A third of patients fulfilled either MIS-C CDC (30.9%) or WHO criteria (34.5%). Acute gastrointestinal symptoms were seen in 81.8% with 6.7% undergoing laparoscopy. Neurological symptoms were common (29.1%). Features of shock were seen in 30.9%. Patients admitted to the ICU (16; 29.1%) were significantly older [median 10.4 vs 5.1 years (p-value: 0.0002)]; less likely to fulfill complete KD criteria (p-value: 0.034); more likely to have thrombocytopenia (p-value: 0.005) or increased troponin (p-value: < 0.0001). All patients had increased C-reactive protein; 87.3% had lymphopenia; 58.2% had neutrophilia; 40% had thrombocytopenia. Coagulation dysfunction was present among all tested patients and ferritin was > 500 mcg/L in 28%. Troponin was elevated in 39.1% when measured. Coronary dilatations/aneurysms developed in 34.5%, normalizing in 78.9% by 6-8 weeks. Other important echocardiogram findings were seen in 25.5%. Significant ECG abnormalities developed in 7.3% including ventricular tachycardia in one. Patients were treated with IVIG and antiplatelet medications (96.4%), steroids (56.4%), biologics (14.6%), respiratory support (23.6%) and vasopressors (18.2%). Overall, 32.7% had confirmed COVID-19 infections (either by PCR or serology) or a significant close household contact, with more positive COVID-19 cases admitted to ICU (52.6% vs 20.5%; p-value: 0.0026). There were no deaths; all recovered completely except for one with a myopathy and another with coronary aneurysms.

**Conclusion:** Despite only one third of patients fulfilling definition for MIS-C, the COVID-19 pandemic seems to have modified the presentation of KD and KLI. Patients were older, with the majority having gastrointestinal symptoms and lymphopenia. There was more severe disease, but outcomes were good overall.

### 105

#### An Unusual Presentation of Granulomatosis With Polyangiitis in a Pediatric Patient

Jessica Scott (McMaster University, Hamilton); Tania Cellucci (McMaster University, Hamilton); Evelyn Rozenblyum (The Hospital for Sick Children, Toronto); Rahul Chanchlani (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton)

**Background:** GPA is an ANCA-associated vasculitis that affects the small- to medium-sized vessels.

**Case Description:** A previously healthy 8-year-old female was found to have profound microcytic anemia (hemoglobin 65, mean corpuscular volume 74.1) in the context of a one-month history of decreased appetite, 5-kg weight loss, and worsening fatigue. On presentation, she also reported bilateral lower extremity weakness, accompanied by hyperreflexia and sustained ankle clonus. MRI of the brain and spine was unremarkable. She denied other complaints. On admission, urinalysis revealed moderate proteinuria (urine protein/creatinine ratio 179 mg/mmol) and hematuria, with normal blood pressure, renal function (creatinine 32 μmol/L), and complement. Although she had no cardiac complaints, an echocardiogram revealed severe dilation of multiple coronary arteries. Chest X-ray and abdominal CT were unremarkable. Bloodwork demonstrated overproduction of antibodies to proteinase 3 (> 8 IU/mL), rheumatoid factor (717 IU/mL), anti-tissue transglutaminase (55.8 U/mL) and anti-endothelial (20 U/L) antibodies. Testing for antibodies to myeloperoxidase, antinuclear antibodies and a panel of extractable nuclear antigens was negative. Renal biopsy showed focal segmental proliferative and necrotizing glomerulonephritis with active disease in 30% of glomeruli. Immunofluorescence and electron microscopy were consistent with pauci-immune glomerulonephritis with no IgA present, ruling out immune-complex mediated disease. Additionally, punch biopsy of a purpuric heel lesion revealed prominent vasculitis in multiple small vessels. Together with her clinical picture, these biopsy results confirmed granulomatosis with polyangiitis (GPA). Interestingly, CT head, sinuses and chest showed no inflammatory changes. She began an induction regimen of high-dose glucocorticoids and rituximab with good effect. She continues to be clinically well on azathioprine and a tapering dose of prednisone. Recent urinalysis showed persisting hematuria and mild proteinuria.

**Discussion:** While upper airway involvement is the most common manifestation of GPA, it was notably absent. Additionally, although renal involvement is common, our patient was normotensive and lacked significant renal abnormalities, despite active disease on biopsy. Equally unusual were our patient's neurological and cardiovascular manifestations. Neuropathy is rarely a presenting feature of GPA and we identified only one reported case of large coronary artery aneurysms in a child with GPA. Despite no inflammatory joint or gastrointestinal features, our patient's overproduction of multiple antibodies (including rheumatoid factor and antibodies associated with Celiac disease) is the first report of such biochemical abnormalities in pediatric GPA. This case represents a highly unusual presentation of GPA and highlights the importance of considering a broad differential diagnosis for children with multi-system involvement.

## 106

### Safety Profile of Ixekizumab for the Treatment of Psoriatic Arthritis and Axial Spondyloarthritis Up to 3 Years: an Updated Integrated Safety Analysis

Sergio Schwartzman (The Hospital for Special Surgery, New York); Atul Deodhar (Oregon Health and Science University, Portland); Bernard Combe (Hopital Lapeyronie, Montpellier); Ana Accioly (Eli Lilly and Company, Indianapolis); Andris Kronbergs (Eli Lilly and Company, Indianapolis); Boris Janos (Eli Lilly Canada Inc., Toronto); Danting Zhu (Eli Lilly and Company, Indianapolis); David Sandoval (Eli Lilly and Company, Indianapolis); Proton Rahman (Memorial University of Newfoundland, St. John's); Denis Poddubnyy (Charite Universitätsmedizin Berlin Campus Benjamin Franklin and German Rheumatism Research Centre, Berlin)

**Objectives:** We report a summary of ixekizumab (IXE) safety outcomes with over 2000 patient-years (PY) of exposure up to 3 years in patients with psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA).

**Methods:** Long-term safety of IXE was assessed from 8 randomized trials in patients with PsA or axSpA. Treatment-emergent adverse events (TEAEs) adjusted incidence rates (IRs) per 100 PY within 1-year time periods through 19 March 2021 were calculated for all patients treated with ≥ 1 dose of IXE. Safety outcomes included TEAEs, serious AEs (SAEs), discontinuations due to AEs, deaths, and selected safety topics of interest. Major

Table. Safety Outcomes

|                                         | Pooled PsA (IXE)<br>(N=1401) | Pooled axSpA (IXE)<br>(N=932) |
|-----------------------------------------|------------------------------|-------------------------------|
| n (IR)                                  | Py=2247.7                    | Py=2096.2                     |
| 95% CI                                  | 7.131 - (50.3)               | 7.988 - (38.1)                |
| TEAEs                                   | 47.5 - 53.3                  | 35.5 - 40.8                   |
| SAEs                                    | 134 (6.0)<br>5.0 - 7.1       | 101 (4.8)<br>4.0 - 5.9        |
| Discontinuations due to adverse events  | 115 (5.1)<br>4.3 - 6.1       | 66 (3.1)<br>2.5 - 4.0         |
| Infections                              | 759 (33.8)<br>31.4 - 36.3    | 540 (25.8)<br>23.7 - 28.0     |
| Serious infections                      | 28 (1.2)<br>0.9 - 1.8        | 23 (1.1)<br>0.7 - 1.7         |
| Opportunistic infections <sup>a</sup>   | 40 (1.8)<br>1.3 - 2.4        | 17 (0.8)<br>0.5 - 1.3         |
| Candida infections <sup>b</sup>         | 45 (2.0)<br>1.5 - 2.7        | 26 (1.2)<br>0.8 - 1.8         |
| Injection-site reactions                | 260 (11.6)<br>10.2 - 13.1    | 156 (7.4)<br>6.4 - 8.7        |
| Inflammatory bowel disease <sup>c</sup> | 3 (0.1)<br>0.0 - 0.4         | 17 (0.8)<br>0.5 - 1.3         |

axSpA, axial spondyloarthritis; IR, incidence rate per 100 patient-years; ODE, oxekizumab; n, number of patients in each category; PsA, psoriatic arthritis; SAEs, serious adverse events; TEAEs, treatment-emergent adverse events.  
<sup>a</sup>Adverse event (AE) terms were derived from MedDRA v21.1.  
<sup>b</sup>Opportunistic infections included esophagus candidiasis, oral candidiasis, hepatitis B reactivation, and herpes zoster.  
<sup>c</sup>Some Candida infections cases were also considered as opportunistic infections. All cases of Candida infections were localized. In PsA program, most cases were mild (34/45, IR=1.5 per 100 patient-years) to moderate (10/45, IR=0.4 per 100 patient-years) in severity, except 1 case of esophagus candidiasis considered severe. The patient who reported severe esophagus candidiasis did not discontinue the study drug due to this AE. In axSpA program, all cases were mild (16/26, IR=0.6 per 100 patient-years) or moderate (10/26, IR=0.5 per 100 patient-years) in severity. Across indications, no cases of systemic candidiasis were reported.  
<sup>d</sup>The data represents confirmed cases per external adjudication. Includes 1 cases confirmed as ulcerative colitis for PsA (IR=0.0) and 10 for axSpA (IR=0.5). 2 events were confirmed as Crohn's disease for PsA (IR=0.1) and 7 for axSpA (IR=0.3). In the PsA population, none of the patients with confirmed IBD per external adjudication had medical history of IBD. Three patients had events of IBD confirmed by adjudication. One patient had more than 1 event. In the axSpA population, of the 17 patients with adjudicated IBD, 5 patients had a history of IBD.

adverse cerebro-cardiovascular event (MACE) and inflammatory bowel disease (IBD) reported cases were adjudicated.

**Results:** A total of 1401 patients with PsA and 932 patients with axSpA with a cumulative IXE exposure of 2247.7 PY for PsA and 2096.2 PY for axSpA were included in this analysis (Table). The IRs per 100 PY for any TEAE were 50.3 for PsA and 38.1 for axSpA. Serious AEs were reported by 134 patients with PsA (IR = 6.0), and 101 patients with axSpA (IR = 4.8). A total of 9 deaths was reported, including 6 in PsA (IR = 0.3) and 3 in axSpA (IR = 0.1). The IRs per 100 PY of discontinuation from the study drug due to AE were 5.1 (PsA) and 3.1 (axSpA). IRs of serious infections were low (PsA: IR = 1.2, axSpA: IR = 1.1). IRs of opportunistic infections (PsA: IR = 1.8, axSpA: IR = 0.8) and Candida infections (PsA: IR = 2.0, axSpA: IR = 1.2) were low. There were no confirmed cases of reactivation of tuberculosis. Injection site reactions occurred with IRs of 11.6 (PsA) and 7.4 (axSpA). The IRs for allergic/hypersensitivity reactions were 4.5 (PsA) and 4.2 (axSpA). No confirmed events of anaphylaxis were reported. Across indications, IRs were low for cytopenia (≤ 2.5), malignancies (≤ 0.7), MACE (≤ 0.5), depression (≤ 1.6), and iridocyclitis (≤ 2.8). Per external adjudication, 20 patients had confirmed IBD (including 3 patients with PsA and 17 with axSpA) of which 1 was confirmed as ulcerative colitis for PsA (IR = 0.0) and 10 for axSpA (IR = 0.5); 2 events were confirmed as Crohn's disease for PsA (IR = 0.1) and 7 for axSpA (IR = 0.3). Across safety topics, IRs were decreased or remained constant over time.

**Conclusion:** In this updated analysis with 2247.7 PY for PsA and 2096.2 PY for axSpA, IXE maintained a safety profile consistent to that previously reported, with no new or unexpected safety events through exposure up to 3 years.

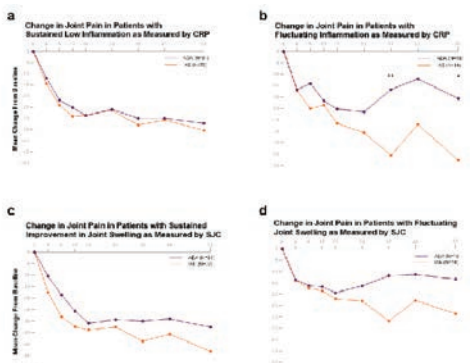
## 107

### Ixekizumab Shows a Pattern of Pain Improvement in Patients With and Without Measurable Inflammation in Psoriatic Arthritis

Kurt de Vlam (UZ Leuven, Leuven); Gaia Gallo (Eli Lilly & Company, Indianapolis); Philip Mease (University of Washington, Seattle); Proton Rahman (Memorial University of Newfoundland, St. John's); Venkatesh Krishnan (Eli Lilly and Company, Indianapolis); David Sandoval (Eli Lilly and Company, Indianapolis); Chen-Yen Lin (Eli Lilly and Company, Indianapolis); Danting Zhu (Eli Lilly and Company, Indianapolis); Rebecca Bolce (Eli Lilly and Company, Indianapolis); Philip Conaghan (University of Leeds, Leeds)

**Objectives:** The efficacy of ixekizumab (IXE) and adalimumab (ADA) in patients with psoriatic arthritis (PsA) has been previously reported using ACR 50 and Psoriasis Area and Severity Index (PASI) 100 responses. To minimize confounding effects, in this analysis we assessed the efficacy of either IXE or ADA monotherapy on reduction of pain beyond measurable inflammation in patients with active PsA and with low C-reactive protein (CRP) (< 5 mg/L) at baseline.

**Methods:** This post-hoc analysis of SPIRIT-H2H study (NCT03151551) included only patients treated with IXE or ADA as monotherapy and with low CRP (< 5 mg/L) at baseline. Changes in joint pain were measured using



**Figure 1.** All patients had low baseline CRP (CRP < 5 mg/L) and were treated with IXE or ADA as monotherapy. (a) Change in joint pain from baseline of patients with sustained low inflammation measured by CRP in IXE and ADA treatment groups. (b) Change in joint pain from baseline of patients with fluctuating inflammation measured by CRP in IXE and ADA treatment groups. (c) Change in joint pain from baseline of patients with sustained improvement in SJC in IXE and ADA treatment groups. (d) Change in joint pain from baseline of patients with fluctuating improvement in SJC in IXE and ADA treatment groups. \*p < 0.05, \*\*p < 0.01. Some patients were excluded from analyses due to missingness at visits.

PsA Patient's Assessment of Pain Visual Analog Scale (VAS). We stratified patients into four categories by two measures of inflammation: 1. Sustained low inflammation either by a. CRP < 5 mg/L during W4-24 or b. ≥ 50% improvement in swollen joint count (SJC) during W8-24. 2. Fluctuating inflammation either by a. CRP ≥ 5 mg/L at least once between W4-24 or b. < 50% improvement in SJC at least once between W8-24.

**Results:** Ninety-five monotherapy patients with a CRP < 5 mg/L at baseline were included in this analysis. In patients with fluctuating inflammation as measured by CRP, IXE-treated patients demonstrated a numerically greater mean improvement in joint pain VAS vs ADA-treated patients at W16 (IXE: -31.64, ADA: -25.33, Figure 1b) that was sustained up to W52 (IXE: -47.69, ADA: -20.67, Figure 1b). There was significance in favour of IXE at W32 (P = 0.0045) and W52 (P = 0.0288, Figure 1b). In patients with sustained low inflammation as measured by CRP, there was no difference in improvement in joint pain between IXE and ADA-treated patients (Figure 1a). In patients with sustained improvement in joint swelling as assessed by SJC, IXE-treated patients demonstrated a numerically greater mean improvement in joint pain VAS vs ADA-treated patients from W4 (IXE: -17.47, ADA: -10.42, Figure 1c) that was sustained through W52 (IXE: -43.16, ADA: -32.62, Figure 1c). In patients with fluctuating improvement in joint swelling as assessed by SJC, IXE-treated patients demonstrated a numerically greater mean improvement in joint pain VAS vs ADA-treated patients from W16 (IXE: -22.00, ADA: -19.31, Figure 1d) that was sustained through W52 (IXE: -28.57, ADA: -13.27, Figure 1d).

**Conclusion:** This analysis suggests a different pattern of pain improvement in patients with low baseline CRP treated with IXE or ADA monotherapy, with a favourable pain reduction outcome for IXE-treated patients, even when inflammation is fluctuating as measured by CRP or SJC improvement. This analysis supports the hypothesis that IXE improves joint pain in PsA patients with and without measurable inflammation.

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### The Effect of Ixekizumab Versus Adalimumab on Individual Components of the ACR Composite Score, With and Without Concomitant Methotrexate or Other Conventional Synthetic DMARDs at 52 Weeks in Patients With Psoriatic Arthritis

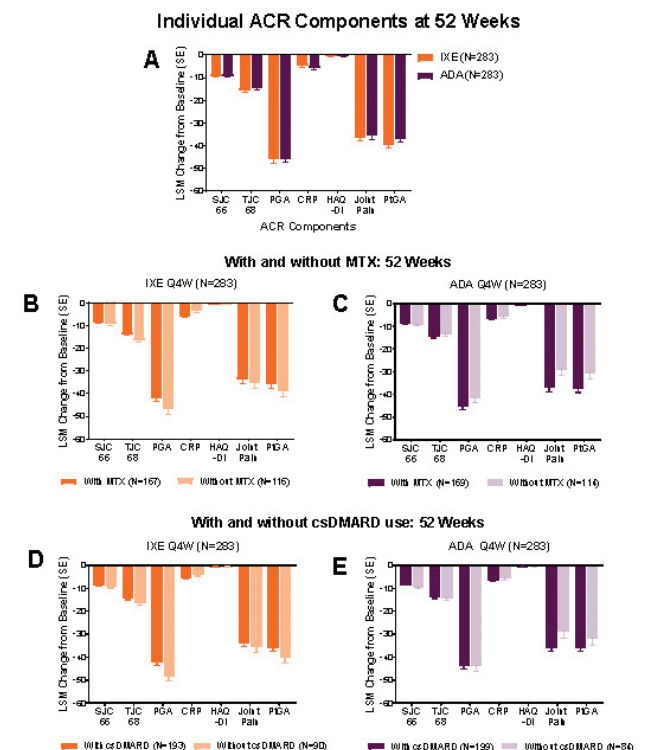
Elaine Husni (Cleveland Clinic, Cleveland); Sona Kamat (St. Louis University, St. Louis); Keri Stenger (Eli Lilly and Company, Indianapolis); Rebecca Bolce (Eli Lilly and Company, Indianapolis); Thorsten Holzkaemper (Eli Lilly and Company, Indianapolis); Cameron Helt (Eli Lilly and Company, Indianapolis); So Young Park (Eli Lilly and Company, Indianapolis); Jeffrey Lisse (Eli Lilly and Company, Indianapolis); Luca Idolazzi (University of Verona, Verona); Louis Bessette (Laval University, Quebec)

**Objectives:** This analysis describes the effect of ixekizumab (IXE) and adalimumab (ADA) on the individual American College of Rheumatology (ACR) components at week (W) 52 in patients with active psoriatic arthritis (PsA) from SPIRIT-H2H.

**Methods:** Patients from SPIRIT-H2H (NCT03151551, 52 W randomized

study) who met Classification Criteria for Psoriatic Arthritis (CASPAR) (N = 566), were randomized (1:1, stratified by baseline concomitant csDMARDs and moderate-to-severe psoriasis [PsO]) to IXE or ADA on-label PsA or PsO dosing. Patients were bDMARD-naïve with IR to csDMARDs, active PsA (≥ 3 tender joints [TJC] and ≥ 3 swollen joints [SJC]) and had PsO ≥ 3% BSA (body surface area). Patient's Global Assessment (PtGA) and Physicians Global Assessment (PGA), Health Assessment Questionnaire-Disability Index (HAQ-DI), and joint pain were assessed by visual analog scale, and TJC and SJC as well as C-reactive protein (CRP) were analyzed. All post-hoc analyses were performed on the intent-to-treat (ITT) population. Change from baseline (CFB) in individual ACR components was analyzed using an Analysis of Covariance (ANCOVA) model, for overall as well as with and without concomitant therapies (eg, MTX or csDMARD). Least square mean (LSM) and standard error (SE) are presented. Missing data were imputed using modified baseline observation carried forward (mBOCF). Nine patients with active PsO and BSA ≥ 3% were assessed as Psoriasis Area and Severity Index (PASI) = 0 at baseline, a medical inconsistency that was resolved using medical judgment. These patients were considered PASI100 responders if PASI = 0 and BSA = 0 at post-baseline visits.

**Results:** A total of 566 patients received either IXE (N = 283) or ADA (N = 283). Baseline values for individual ACR components were balanced between IXE and ADA. At W52, IXE demonstrated efficacy across all individual ACR components in the ITT population, specifically in PGA, PtGA and Joint Pain; ADA also demonstrated numerical efficacy (Figure A). Improvements from baseline for IXE were observed across ACR compo-



**Figure 2.** Change from baseline in the individual components of the ACR composite score at week 52 in patients treated with IXE or ADA (A) in the ITT population, (B and C) with and without MTX use at baseline and (D and E) with and without csDMARD use at baseline. Data presented as least square mean (LSM) change from baseline (mBOCF) + SE. Abbreviations: ACR, American College of Rheumatology; ADA, adalimumab; CRP, C-reactive protein; csDMARD, conventional synthetic disease modifying antirheumatic drug; HAQ-DI, health assessment questionnaire disability index; ITT, intent-to-treat; IXE, ixekizumab; mBOCF, modified baseline observation carried forward; MTX, methotrexate; PGA, physicians global assessment, PtGA, patients global assessment; SJC, swollen joint count; TJC, tender joint count.



nents, with or without MTX or csDMARD (Figure B-E). The effect of MTX (with or without) was notably different between IXE and ADA in TJC68, PGA, Joint Pain, and PrGA.

**Conclusion:** In this analysis, there was improvement with IXE in all components of the ACR composite score at W52, irrespective of MTX or csDMARD use. In the ITT population, IXE showed comparable efficacy to ADA at W52 in all ACR components, demonstrating improvement across musculoskeletal domains. These results may provide further confidence of the clinical benefits of IXE across musculoskeletal domains in patients with PsA, regardless of MTX or csDMARD use.

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**Achieving Treatment Targets and Treatment Satisfaction in Psoriatic Arthritis Patients Treated With Apremilast in Canada at 1 Year**

Vinod Chandran (Krembil Research Institute, Toronto Western Hospital, Toronto); Louis Bessette (Laval University, Quebec City); Carter Thorne (The Arthritis Program Research Group, Newmarket); Maqbool Sheriff (Nanaimo Regional General Hospital, Nanaimo); Proton Rahman (Memorial University of Newfoundland, St. John's); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital, Toronto); Sabeen Anwar (Windsor Regional Hospital, Windsor); Jennifer Jelley (Amgen Canada Inc., Mississauga); Anne-Julie Gaudreau (Mississauga); Manprit Chohan (Amgen Canada Inc, Mississauga); John Sampalis (McGill University and University of Montreal, JSS Medical Research, St. Laurent)

**Objectives:** To better understand the long-term effectiveness, tolerability, and overall satisfaction with apremilast (APR) for treatment of active psoriatic arthritis (PsA) in real-world Canadian clinical settings.

**Methods:** APPRAISE (NCT03608657) is a prospective, multicenter, observational study, enrolling adult patients with active PsA prescribed APR per routine care. Patients were followed from treatment initiation to 12 months, with follow-up visits suggested every 4 months. The primary outcome measure is achievement of low disease activity (LDA: cDAPSA score < 14). Baseline patient demographics were summarized descriptively. Continuous outcomes at Months 4, 8, and 12 were analyzed by paired Student's t-test or McNemar's test. Data are presented as observed.

**Results:** Between July 2018 and March 2020, 102 patients were enrolled. Mean (SD) age was 51.8 (11.7) and 5.5 (7.9) years, respectively, with the majority of patients female (56.9%) and white (96.1%). Overall, 74.3% of patients presented with ≥ 1 comorbidity, and 44.6% presented with ≥ 2; almost half had cardiometabolic disease, and one-quarter anxiety or depression. Baseline cDAPSA indicated moderate/high disease activity in 75.5% of patients. The proportion of patients with cDAPSA LDA increased from 24.5% of patients at baseline, to 53.8% of patients at Month 12; changes in cDAPSA score from baseline to all study visits were statistically significant (Table 1). A decrease over time in rates of enthesitis (34.0% at baseline) and dactylitis (18.2% at baseline) was observed, with SJC (0-66) and TJC (0-68) declining significantly from baseline to Months 4, 8, and 12 (Table 1). Mean TSQM Overall Satisfaction scores improved over 12 months (Table 1), and the proportion of patients achieving PASS increased significantly from baseline (26.3%) to Months 4 (53.5%), 8 (63.2%), and

Table 1. Changes From Baseline in Disease/Clinical Parameters and PROs at Month 4, Month 8, and Month 12

| Parameter                                   | Change or n (%) at Month 4 n = 93 | Change or n (%) at Month 8 n = 71 | Change or n (%) at Month 12 n = 56 |
|---------------------------------------------|-----------------------------------|-----------------------------------|------------------------------------|
| cDAPSA score, mean (SD)                     | -7.7 (12.0)*                      | -9.7 (12.9)*                      | -8.5 (14.2)*                       |
| SJC (0-66), mean (SD)                       | -3.0 (4.4)*                       | -3.0 (4.3)*                       | -3.4 (5.2)*                        |
| TJC (0-68), mean (SD)                       | -2.4 (6.2)*                       | -3.8 (5.0)*                       | -3.2 (7.5)*                        |
| PrGA VAS (0-100 mm), mean (SD)              | -10.2 (27.0)*                     | -9.6 (32.3)*                      | -6.4 (37.2)                        |
| Pain VAS (0-100 mm), mean (SD)              | -9.3 (26.3)*                      | -12.9 (29.1)*                     | -10.2 (26.0)*                      |
| PhGA VAS (0-100 mm), mean (SD)              | -19.3 (24.6)                      | -23.0 (24.8)                      | -19.8 (24.8)                       |
| Enthesitis, n (%)                           | 21 (24.4)                         | 10 (18.2)                         | 9 (18.8)                           |
| Dactylitis n (%)                            | 9 (10.5)                          | 5 (7.9)                           | 1 (2.0)                            |
| HAQ-DI (0-3), mean (SD)                     | -0.13 (0.50)*                     | -0.15 (0.56)*                     | -0.16 (0.63)                       |
| TSQM: Overall Satisfaction score, mean (SD) | 0.1 (29.7)                        | 4.4 (31.4)                        | 7.1 (29.4)                         |

The n represents the number of patients with data available for each parameter may vary. \*Denotes significant change from baseline (P < 0.05) from paired-sample t-tests or McNemar's test. BSA = psoriasis-involved body surface area; HAQ-DI = Health Assessment Questionnaire-Disability Index; PrGA = Physician's Global Assessment of PsA; PGA = Patient's Global Assessment of PsA; SJC = swollen joint count; TJC = tender joint count; TSQM = Treatment Satisfaction Questionnaire for Medication; VAS = visual analog scale.

12 (68.0%). Significant improvements from baseline were observed in additional clinical and patient-reported outcomes (Table 1). A total of 48 (47.1%) patients discontinued the study, with lack/loss of effectiveness (21 [43.8%]) and adverse events (AE) (21 [43.8%]) the most common reasons. In patients discontinuing treatment due to AEs, diarrhea (9/48 [18.8%]), nausea (4/48 [8.3%]), and migraine (4/48 [8.3%]) were the most common. COVID restrictions impacted in-office assessment visits, necessitating reliance on virtual visits.

**Conclusion:** In this real-world analysis, Canadian patients with PsA treated with APR over a 12-month period have achieved continuous improvements in clinical and patient-reported parameters, with the majority satisfied with their disease state. The observed safety profile of APR is consistent with previously reported clinical data.

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**What Influences Fatigue Improvement in Rheumatoid Arthritis? A Prospective Cohort Study**

Samar Aboulenain (University of Toronto, Toronto); Ellie Donath (University of Miami, West Palm Beach); Ozlem Pala (University of Miami, Miami)

**Objectives:** Fatigue is a common and debilitating complication in patients with rheumatoid arthritis (RA). Its mechanism is not fully elucidated, and when persistent, is often challenging to manage. Despite treatment with DMARDs, a proportion of patients will continue to have fatigue raising the necessity to investigate other non-DMARDs therapeutic options. This study aimed to explore characteristics that correlate with fatigue improvement in adult patients with RA.

**Methods:** A single-centered prospective cohort study of 111 adult patients with rheumatoid arthritis. Fatigue level was measured using fatigue numerical rating scale (NRS) ranging from 0 to 100. Fatigue was measured at the time of enrollment and 6, 12 and 24 months follow-up appointments. The minimal clinically important difference (MCID) for the fatigue NRS (6.7% change from baseline) was used to assess the change in fatigue level compared to baseline. Univariate and multivariate (adjusting for age, gender and BMI) logistic regression analyses were performed to examine the association between fatigue improvement at 12 months and baseline demographics and disease characteristics.

**Results:** The median (interquartile range [IQR]) for age was 55 (44-61) years and the majority were Caucasian (67%), females (88%), and with an above-average BMI (71%). The median (interquartile range [IQR]) of fatigue scores at enrollment and 12 months were 40 (8-70) and 38 (5-58), respectively. At 12 months, fatigue level improved in half of the population (Table 1). In a univariate analysis, several predictors were noted to be associated with improved fatigue scores. These included female gender (P < 0.001), non-smokers (P < 0.01) and increased baseline fatigue levels (P = 0.04). Several other variables, including depression, showed a trend towards significance. These variables were further investigated using a multivariate analysis (adjusting for age, gender and BMI). Non-smokers were found to be highly likely to improve fatigue levels at year-end (OR 7.63, 95% CI 1.11-52.63, P = 0.04) compared to smokers. In addition, baseline depression was found to be linked with a significantly lower likelihood of improving fatigue level (OR 0.17, 95% CI 0.03-0.82, P = 0.03). Many other variables were examined, and none were found to be associated with the outcome of interest including BMI, employment status, physical activity level, pain control, number of comorbidities, duration of RA, CDAI score, switching to biological DMARDs, or RF and CCP seropositivity.

**Conclusion:** We observed in this cohort study an improvement in fatigue level in half of the population. The female gender, non-smoking status and lack of depression were all associated with fatigue improvement at 12 months.

Table 1. Fatigue score and progression in the study participants at 6, 12 and 24 months compared to baseline.

|                       | Baseline  | 6 months  | 12 months | 24 months   |
|-----------------------|-----------|-----------|-----------|-------------|
| VAS-F [Median (IQR)]* | 40 (8-70) | 35 (5-60) | 38 (5-58) | 13 (5-52.5) |
| Improved %            | N/A       | 53%       | 50%       | 69%         |
| Worsened %            | N/A       | 31%       | 31%       | 21%         |
| Unchanged %           | N/A       | 16%       | 19%       | 10%         |

VAS-F, fatigue Visual Analog Scale. IQR, interquartile range. \*Scores reported on a scale of 0-100 mm on which higher numbers indicate greater fatigue.

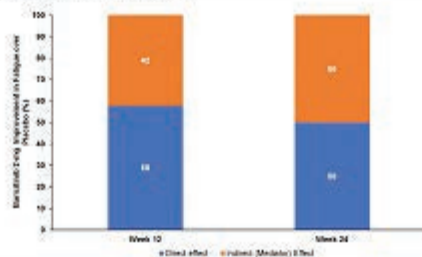
### An Independent Treatment Effect of Baricitinib in Reducing Fatigue After Adjusting for Clinical Disease Activity: Results From the RA-BEACON Phase 3 Trial

Janet Pope (University of Western Ontario, London); Jianmin Wu (Eli Lilly and Company, Indianapolis); Duzhe Wang (Eli Lilly and Company, Indianapolis); Ju Ji (Eli Lilly and Company, Indianapolis); Kirstin Griffing (Eli Lilly and Company, Indianapolis); Vibeke Strand (Division of Immunology/Rheumatology, Stanford University, Palo Alto)

**Objectives:** Fatigue is common in rheumatoid arthritis (RA) and impairs quality of life. Baricitinib improved fatigue, pain, and other patient-reported outcomes in patients with active RA and an inadequate response (IR) to  $\geq 1$  tumor necrosis factor inhibitors or other biological DMARDs (bDMARDs). The objective of this post-hoc analysis was to estimate the proportion of independent (direct) treatment effect of baricitinib on fatigue after adjusting for the indirect effect mediated by improvement in clinical disease activity in bDMARD-IR RA patients with data from the phase 3 trial, RA-BEACON (NCT01721044).

**Methods:** In RA-BEACON, all patients (N = 527) had a diagnosis of adult-onset RA, defined by ACR/EULAR 2010 Criteria. Fatigue was measured with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F). Disease activity was measured with the Clinical Disease Activity Index (CDAI). Spearman's rank correlation between FACIT-F and CDAI was calculated by pooling all visits up to Week 24 across baricitinib 2-mg and placebo arms. A longitudinal mediation analysis was implemented to evaluate whether and how much the effect of baricitinib 2-mg on FACIT-F was mediated through the improvement of CDAI. The independent variable in the mediation analysis was treatment (baricitinib 2-mg or placebo). The dependent variable was change in FACIT-F from baseline to Week 4, 8, 12, 16, 20, and 24, and the mediator was the change in CDAI from baseline to Week 4, 8, 12, 16, 20, and 24. The treatment effect of baricitinib 2-mg on FACIT-F over placebo that could be accounted for by changes in CDAI was the indirect effect, and that which could not be accounted for by changes in CDAI was the direct effect. Missing values were imputed by the modified last observation carried forward method.

**Figure.** Mediation analysis of the effect of CDAI and direct effect of non-CDAI variables on changes from baseline in FACIT-F after treatment with baricitinib at Weeks 12 and 24. The total treatment effect over placebo on changes in FACIT-F that could be accounted for by CDAI was the indirect effect. The total treatment effect over placebo that could not be accounted for by CDAI is the direct effect.



CDAI: Clinical Disease Activity Index; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue

**Results:** For placebo and baricitinib 2-mg, respectively, the least-squares mean change in FACIT-F was 5.2 and 8.3 ( $P < 0.01$ ) at Week 12 and 5.7 and 8.1 ( $P < 0.05$ ) at Week 24. Spearman's rank correlation coefficient between FACIT-F and CDAI was  $-0.5$  ( $P < 0.001$ ), implying that fatigue and disease activity were moderately correlated. Results of the mediation analyses indicated that less than 50% of improvement in the FACIT-F among the baricitinib 2-mg-treated patients was mediated through CDAI improvement (Figure). At Week 12 and Week 24, respectively, approximately 58% and 50% of the impact of baricitinib on FACIT-F was independent of effects mediated through CDAI.

**Conclusion:** In this bDMARD-IR patient population, a substantial effect of baricitinib 2-mg on fatigue is independent of its effect on disease activity improvement.

### Discontinuation Rate of Tofacitinib as Monotherapy is Similar Compared to Combination Therapy with Methotrexate in Rheumatoid Arthritis Patients: Pooled Data from Two Rheumatoid Arthritis Registries in Canada

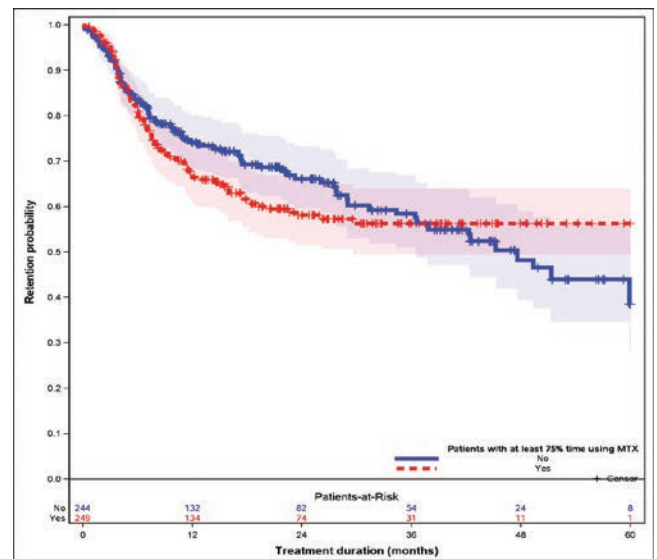
Mohammad Movahedi (University Health Network, Toronto); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal); Louis Coupal (Institut de Rhumatologie de Montréal, Montréal); Angela Cesta (University Health Network, Toronto); Xiuying Li (University Health Network, Toronto); Edward Keystone (University of Toronto, Toronto); Claire Bombardier (University of Toronto, Toronto); OBRI investigators (University Health Network, Toronto); Rhumadata investigators (Montreal)

**Objectives:** Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). TOFA can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi). We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX in comparison with TNFi, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).

**Methods:** RA patients enrolled in the OBRI initiating their TOFA between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2018 were included. Concurrent MTX use was defined as MTX use for more than 75% of the time while using TOFA. Time to discontinuation (due to any reason) were assessed using Kaplan-Meier survival (adjusted for propensity score using inverse probability of treatment weight) to compare patients with and without MTX use at initiation of TOFA. We used multiple imputation (N = 20) to deal with missing data for covariates at treatment initiation.

**Results:** A total of 493 patients initiated TOFA. Of those, 244 (49.5%) and 249 (51.5%) were treated with and without MTX, respectively. Compared to TOFA monotherapy, the TOFA with MTX group had a significantly lower mean HAQ-DI, fatigue score, and number of prior biologic use at the time of TOFA initiation. A lower proportion of positive ACPA (59% vs. 66%), prevalence of hypertension (31% vs 37%), and concomitant use of Leflunomide (11% vs. 23%) were also observed for patients using TOFA with MTX. Over a mean of 19.0 month follow-up, discontinuation was reported in 182 (36.9%) of all patients. After adjusting for propensity score quantile across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 1.12, 95% CI: 0.83-1.51;  $P = 0.49$ ) (Figure 1).

**Conclusion:** In this pooled real-world data study, we found that in patients with RA, the retention of TOFA is similar if it is used as monotherapy or in combination with MTX. MTX could be stopped if needed in a sub-population of patients with RA.





### Biologics Initiation in Moderate Vs Severe Rheumatoid Arthritis Patients: Prospective Observational Study From a Canadian Registry

Nancy Guo (University Health Network, Toronto); Mohammad Movahedi (University Health Network, Toronto)

**Objectives:** Prior studies have shown that in the real-world setting, rheumatoid arthritis (RA) patients have lower disease activity than those studied in clinical trials. However, randomized controlled trials for biologics continue to mainly recruit patients with severe disease. To assess the implications of this practice, our study investigated clinical responses to biologics in RA patients with moderate disease activity versus severe disease activity, after 12 months of starting the first biologic, and identifies baseline patient characteristics associated with biologic response.

**Methods:** This study included RA patients who have never been treated with a biologic and initiated their first biologic while enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, between 2008 and 2019. Patients selected had either moderate RA (DAS28  $\geq 3.2$  to  $\leq 5.1$ ) or severe RA (DAS28  $> 5.1$ ). Comparisons were made between the moderate and severe disease groups using the Student's *t*-test for continuous variables, and the chi-square test for categorical variables. Multivariate logistic regression was used to test characteristics associated with remission.

**Results:** 264 moderate RA patients and 219 severe RA patients were selected. In the moderate group, the mean age (SD) was 55.7 (13.1) and 80% were female. In the severe group, mean age (SD) was 58.4 (12.3) and 81% were female. At time of biologic initiation, the mean DAS28 for the moderate group was 4.1 (0.5), and 6.0 (0.6) for the severe group. After 12 months of starting a biologic, the proportion of patients achieving remission was 50% in the moderate group, and 23% in the severe group ( $P < 0.0001$ ). In contrast, the absolute improvement in DAS28 after 12 months was higher in the severe group at 2.2 (1.5), compared to 1.4 (1.3) in the moderate group ( $P < 0.0001$ ). Characteristics negatively associated with remission include female gender (odds ratio (OR), 0.54, 95% confidence interval (CI), 0.31-0.94;  $P = 0.0306$ ), RA disease duration (OR 0.96, 95% CI 0.93-0.995,  $P = 0.0272$ ), and higher HAQ-DI score (OR 0.51, 95% CI 0.32-0.80;  $P = 0.0001$ ). In turn, moderate disease at time of biologic initiation (OR 2.35, 95% CI 1.44-3.82;  $P = 0.0006$ ) was positively associated with remission.

**Conclusion:** This prospective cohort study found RA patients with moderate disease activity were more likely to reach target states (remission and low disease activity), whereas severe patients had greater absolute improvements in DAS28 and HAQ-DI. Moderate disease was positively associated with remission, whereas female sex, RA disease duration and higher HAQ-DI score were negatively associated with remission.

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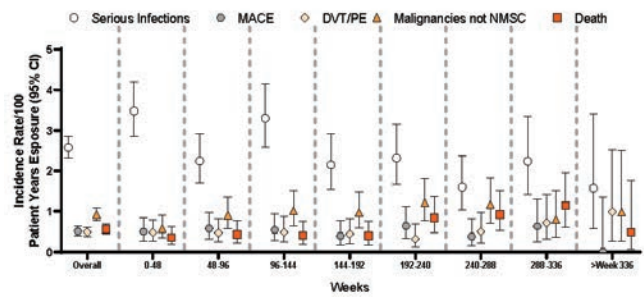
#### Safety Profile of Baricitinib for the Treatment of Rheumatoid Arthritis Up to 9.3 Years: An Updated Integrated Safety Analysis

Peter Taylor (University of Oxford, Oxford); Tsutomu Takeuchi (Keio University, Tokyo); Gerd Burmester (Charité - University Medicine Berlin, Free University and Humboldt University Berlin, Berlin); Patrick Durez (Cliniques Universitaires Saint-Luc, Brussels); Josef Smolen (Medical University of Vienna, Vienna); Walter Deberdt (Eli Lilly and Company, Indianapolis); Jinglin Zhong (IQVIA, Morrisville); Jorge Ross Teres (Eli Lilly and Company, Indianapolis); Natalia Bello (Eli Lilly and Company, Indianapolis); Kevin Winthrop (Oregon Health Sciences University, Portland); Janet Pope (University of Western Ontario, London)

**Objectives:** To report baricitinib's (bari) safety profile with data up to 9.3 years of treatment.

**Methods:** Pooled data from 9 randomized (5 Phase 3, 3 Phase 2, 1 Phase 1b) and 1 long-term extension (LTE) study were assessed. Incidence rates (IR) per 100 patient-years at risk (PYR) were calculated for all patients treated with  $\geq 1$  dose of bari (All-bari-RA). Adverse events (AEs) of interest were assessed over time in 48-month intervals. Major adverse cardiovascular events (MACE) were adjudicated in 5 Phase 3 studies and the LTE. Incidence rates for MACE were also evaluated in subgroups of patients

Figure: Incidence rates by 48-week exposure intervals.



CI=confidence interval; DVT=deep vein thrombosis; MACE=positively adjudicated major adverse cardiovascular events; NMSC=non-melanoma skin cancer; PE=pulmonary embolism

age  $\geq 50$  years and presenting with  $\geq 1$  cardiovascular risk factor (current smoker, hypertension, high-density lipoprotein cholesterol  $< 40$  mg/dL, diabetes, or arteriosclerotic cardiovascular disease). Exposure adjusted IRs (EAIRs) for deep vein thrombosis (DVT), pulmonary embolism (PE), and DVT and/or PE (DVT/PE) were also calculated for groups of patients while receiving bari 2-mg or bari 4-mg within All-bari-RA.

**Results:** A total of 3770 patients received bari for 14,744.4 PYE with a median exposure of 4.6 years and a maximum exposure of 9.3 years; 80.5% of PYE were bari 4-mg and 18.1% of PYE were bari 2-mg. Overall, EAIRs per 100 PYE for any treatment-emergent AE and serious AE (including death) were 22.6 and 7.4, respectively. Overall IRs per 100 PYR were 2.58 for serious infections; 0.35 for DVT, 0.26 for PE, 0.49 for DVT/PE, 0.51 for MACE, and 0.92 for malignancy; IRs remained stable over time (Figure). The IR (95% CI) of MACE for patients age  $\geq 50$  years was 0.68 (0.52-0.88). In patients age  $\geq 50$  with  $\geq 1$  of the cardiovascular risk factors, IR (95% CI) of MACE was 0.77 (0.56-1.04). EAIRs (95% CI) for patients while receiving bari 2-mg (PYE = 2678) and bari 4-mg (PYE = 11,872) were DVT 2-mg 0.41 (0.21-0.73) and 4-mg 0.35 (0.25-0.48); PE 2-mg 0.26 (0.11-0.54) and 4-mg 0.27 (0.18-0.38); and DVT/PE 2-mg 0.49 (0.26-0.83) and 4-mg 0.51 (0.39-0.66).

**Conclusion:** In this report with 14,774 PYE, bari maintained a safety profile similar to that previously reported with no increase of IRs across safety events through exposures up to 9.3 years.

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#### Consistency in Time to Response With Upadacitinib as Monotherapy or Combination Therapy and Across Patient Populations With Rheumatoid Arthritis

Andrea Rubbert-Roth (Klinik fuer Rheumatologie, Kantonsspital St. Gallen, St. Gallen); Bernard Combe (Hopital Lapeyronie, Montpellier); Zoltan Szekanez (University of Debrecen, Debrecen); Stephen Hall (Cabrini Medical Centre, Malvern); Boulos Haraoui (Institut de Rhumatologie de Montréal, Montreal); Suzan Attar (King Abdulaziz University Hospital, Mirabel); Anna-Karin Ekwall (University of Gothenburg, Gothenburg); Yanna Song (AbbVie, North Chicago); Tim Shaw (AbbVie, Maidenhead); Orsolya Nagy (AbbVie, North Chicago); Ricardo Xavier (Av. Brigadeiro Luís Antônio, São Paulo)

**Objectives:** Upadacitinib (UPA) has demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) across patient populations. This post hoc analysis aimed to evaluate the consistency in time to achieving meaningful clinical response with UPA 15 mg + conventional synthetic (cs) DMARDs in biologic (b) DMARD-inadequate responder (IR) versus csDMARD-IR patients with RA as well as with UPA 15 mg monotherapy versus UPA 15 mg + csDMARDs in csDMARD-IR patients.

**Methods:** Patients randomized to UPA 15 mg from four Phase 3 trials were included in this analysis: SELECT-BEYOND and SELECT-CHOICE (UPA 15 mg + csDMARDs in bDMARD-IR patients), SELECT-NEXT (UPA 15 mg + csDMARDs in csDMARD-IR patients), and SELECT-

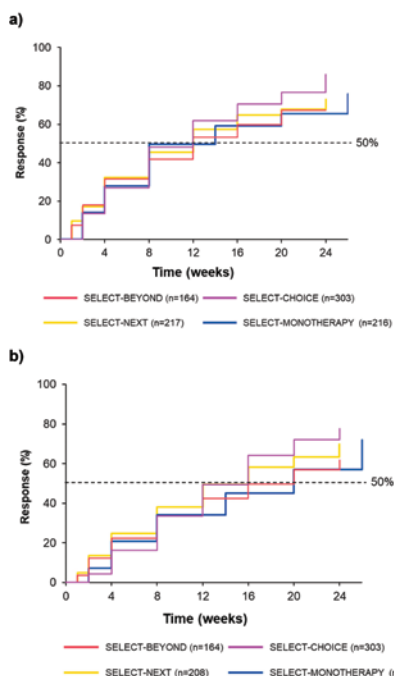


MONOTHERAPY (UPA 15 mg in methotrexate-IR patients). Time to response was estimated using Kaplan–Meier method for clinical outcomes over 24/26 weeks. Clinical outcomes included achievement of 28-joint Disease Activity Score with C-reactive protein (DAS28[CRP])  $\leq$  3.2; low disease activity (LDA) defined as Clinical Disease Activity Index (CDAI)  $\leq$  10 and Simple Disease Activity Index (SDAI)  $\leq$  11; and 50% improvement in American College of Rheumatology (ACR) core components and morning stiffness (MS) duration/severity. Data presented as observed.

**Results:** 905 patients were included (SELECT-BEYOND: n = 164; SELECT-CHOICE: n = 303; SELECT-NEXT: n = 221; SELECT-MONOTHERAPY: n = 217). csDMARD-IR patients had mean disease duration of 7.3 (SELECT-NEXT) or 7.5 years (SELECT-MONOTHERAPY); bDMARD-IR patients had mean disease duration of 12.4 years, with a more refractory population ( $\geq$  3 prior bDMARDs) in SELECT-BEYOND (23%) than SELECT-CHOICE (10%). The median time to DAS28(CRP)  $\leq$  3.2, CDAI LDA, 50% improvement in ACR core components, and 50% improvement in MS duration/severity were consistent across studies. For SELECT-BEYOND, SELECT-CHOICE, SELECT-NEXT, and SELECT-MONOTHERAPY, median (95% CI) time to achieve DAS28(CRP)  $\leq$  3.2 was 12 (12-16), 12 (8-12), 12 (8-12), and 14 (8-14) weeks (Figure 1a), and median time to achieve CDAI LDA was 20 (12-24), 16 (12-16), 16 (12-16), and 20 (14-20) weeks, respectively (Figure 1b). A longer median (95% CI) time to achieve SDAI LDA was observed with UPA monotherapy (20 [14-20] weeks) versus UPA + csDMARDs (12 [12-16] weeks) in csDMARD-IR patients. Among bDMARD-IR patients, median (95% CI) time to 50% improvement in pain was longer in SELECT-BEYOND versus SELECT-CHOICE (16 [12-20] versus 8 [8-12] weeks).

**Conclusion:** In diverse patient populations with RA, patients treated with UPA 15 mg, as monotherapy or with csDMARDs, demonstrated consistent time to achieving DAS28(CRP)  $\leq$  3.2, CDAI LDA, and 50% improvement in clinical outcomes.

**Figure 1.** Kaplan–Meier plot of a) time to first achievement of DAS28(CRP)  $\leq$  3.2, and b) time to first achievement of CDAI  $\leq$  10 (LDA)



DAS28(CRP), 28-joint Disease Activity Score with C-reactive protein  
CDAI, Clinical Disease Activity Index; LDA, low disease activity

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### Characteristics and Outcomes of Rheumatoid Arthritis Patients Treated With Upadacitinib in Real-world Canadian Clinical Practice

Tom Appleton (St. Joseph's London Rheumatology Centre and Western University, London); Jayesh Patel (AbbVie, North Chicago); Tanya Girard (AbbVie Canada, Saint Laurent); Fiona Bailey (Adelphi Real World, Bollington); Hannah Jones (Adelphi Real World, Bollington); Caylib Durand (University of Calgary, Calgary)

**Objectives:** Upadacitinib (UPA) is a selective Janus Kinase 1 receptor inhibitor, approved for the treatment of rheumatoid arthritis (RA) in Canada in January 2020. Our objective was to describe clinical usage and outcomes of Canadian RA patients receiving UPA.

**Methods:** The Adelphi RA Disease Specific Programme™ is a point-in-time survey conducted amongst rheumatologists. Physicians completed online record forms for RA patients who had received upadacitinib for at least 6 months. We report here the interim demographic and clinical outcomes data of an ongoing survey.

**Results:** Current data was provided by 8 rheumatologists for 47 patients (expected total: 20 rheumatologists, 200 patients). The mean age of these patients was 49.6 (SD 11.3), 74% were female and mean RA duration of 4.2 years (SD 3.8, n = 46). Mean Charlson Comorbidity Index was 1.2 (SD 0.7). Patients were receiving upadacitinib for an average of 10.5 months (SD 3.5). UPA was the first advanced therapy in 51% of patients and as a second or later line therapy after a JAKi (28%), a TNFi (21%), and/or other modes of action (9%) in the remaining patients. UPA was initiated predominantly in combination with background csDMARDs (74%) and after  $\geq$  6 months of UPA use, this combination decreased to 23%. 11% of patients received UPA in combination with a steroid, dropping to 2% after  $\geq$  6 months of UPA use. Disease activity measures were documented inconsistently. Physician-perceived disease severity improved in 62% of patients with  $\geq$  6 months of UPA use. At UPA initiation, mean tender joint count was 12.0 (SD 3.0, n = 34), mean swollen joint count was 9.0 (SD 4.0, n = 44) and mean CDAI score was 30.7 (SD 7.4, n = 21). After  $\geq$  6 months of UPA use, this had reduced to 1.8 (SD 2.1, n = 26), 0.6 (SD 1.1, n = 33) and 3.8 (SD 3.5, n = 18) respectively, with 44% (n = 8) of patients with reported CDAI scores (n = 18) in remission (0.0-2.8) and 44% (n = 8) with low disease activity (2.9-10.0) (Table 1).

**Conclusion:** Interim analysis of real-world data in Canadian RA patients demonstrates expected rates of improvement in disease activity after  $\geq$  6 months of treatment with UPA. In addition,  $\geq$  6 months of treatment with UPA led to a reduction in combination csDMARD and steroid therapy use. Full analysis is planned when data collection is complete. Rheumatologists may need better tools for documenting routine disease activity measures in the real world.

|                                                                                    |                                                            |                   |
|------------------------------------------------------------------------------------|------------------------------------------------------------|-------------------|
| Physician-perceived disease severity change (based on mild/moderate/severe) (n=47) | Improved, n (%)                                            | 29 (62%)          |
|                                                                                    | No change, n (%)                                           | 18 (38%)          |
| 28 Tender joint count                                                              | Mean at initiation (SD) (n=34)                             | 12.0 (SD 3.0)     |
|                                                                                    | Mean after $\geq$ 6 months of UPA use (SD) (n=26)          | 1.8 (SD 2.1)      |
| 28 Swollen joint count                                                             | Mean at initiation (SD) (n=44)                             | 9.0 (SD 4.0)      |
|                                                                                    | Mean after $\geq$ 6 months of UPA use (SD) (n=33)          | 0.6 (SD 1.1)      |
| CDAI score at initiation (n=21)                                                    | Mean (SD)                                                  | 30.7 (SD 7.4)     |
| CDAI score after $\geq$ 6 months UPA (n=18)                                        | Mean (SD)                                                  | 3.8 (SD 3.5)      |
|                                                                                    | Remission (0.0-2.8)/Low Disease Activity (2.9-10.0), n (%) | 8 (44%) / 8 (44%) |
|                                                                                    | Moderate Disease Activity (10.1-22.0), n (%)               | 2 (11%)           |

Table 1. Clinical outcomes of RA patients with  $\geq$  6 months of UPA use.

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### Assessing the Relationship of Patient Global Assessment of Disease Activity and Health Related Quality of Life by SF-36 with Other Patient-Reported Outcomes in Rheumatoid Arthritis: Post Hoc Analyses of Data from Phase 3 Trials of Baricitinib

Vibeke Strand (Division of Immunology/Rheumatology, Stanford University, Palo Alto); Anthony Sebba (Department of Rheumatology, University of South Florida, Tampa); Savannah Scardo (Eli Lilly and Company, Indianapolis); Amanda Quebe (Eli Lilly and Company, Indianapolis); Liliana Zaremba-Pechmann (HaaPACS GmbH, Schriesheim); Peter Taylor (University of Oxford, Oxford); Dalton Sholter (University of Alberta, Edmonton)

**Objectives:** To examine the relative importance of patient reported outcomes (PROs) on the Patient Global Assessment of Disease Activity (PtGA) and health-related quality of life (HRQoL) and whether these differ in patients with good disease control vs. those not in low disease activity (LDA) or remission in different patient populations in baricitinib (bari) phase 3 studies.

**Methods:** We report post-hoc analyses of: RA-BEGIN (conventional synthetic DMARD-naïve patients [n = 588]); RA-BEAM (MTX-inadequate response (IR) patients [n = 1307]); and RA-BEACON (biologic DMARD-IR patients (n = 527)). PtGA was measured by a visual analog scale (VAS, 0-100 mm) and HRQoL was measured by SF-36 physical component summary (PCS) and mental component summary (MCS) scores. PROs included pain (VAS, 0-100 mm), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration of morning joint stiffness (AMJtS), and Health Assessment Questionnaire-Disability Index (HAQ-DI). Good disease control was defined as either LDA or remission by Clinical Disease Activity Index (CDAI,  $\leq 10$  and  $\leq 2.8$ , respectively). Within each RCT, treatment-agnostic correlation analyses at all time points from baseline to Week 24 were performed. Multiple regression analyses for the overall population and for patients in LDA, remission or nonresponse were conducted; we present standardized parameter estimates from the regression analyses for each PRO to assess their relative importance on the PtGA, PCS score and MCS score.

**Results:** Across RCTs, pain strongly correlated with PtGA (r: 0.9); FACIT-F moderately correlated with PtGA, PCS, and MCS scores (r: 0.6 to 0.7; FACIT-F and PtGA are negatively correlated); and HAQ-DI moderately-to-strongly correlated with PtGA and PCS score (r: 0.6 to 0.8; HAQ-DI and PCS are negatively correlated). Duration of AMJtS was weakly correlated with the other PROs (r: -0.2 to -0.3 for PCS and MCS and 0.3 to 0.4 for PtGA). In regression analyses across RCTs at baseline and Week 24 for the overall populations, the most significant factors were pain with PtGA, HAQ-DI with SF-36 PCS score, and FACIT-F with SF-36 MCS score. Similar results were observed in patients in LDA, remission, or nonresponse.

**Conclusion:** These results confirm prior findings, such as high correlations of pain with PtGA. We, however, observed that the relationships between other PROs with PtGA, PCS, or MCS scores were stable across time points over the first 6 months of treatment in differing patient populations, ranging from early to later disease. PtGA, PCS, and MCS scores were each associated with different PROs, indicating the importance of collecting multiple PROs in RCTs and real-world clinical practice.

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### Rapid Clinical Response in Patients with Moderately to Severely Active Rheumatoid Arthritis Treated with Baricitinib

Dalton Sholter (University of Alberta, Edmonton); Jianmin Wu (Eli Lilly and Company, Indianapolis); Duzhe Wang (Eli Lilly and Company, Indianapolis); Amanda Quebe (Eli Lilly and Company, Indianapolis); Kirstin Griffing (Eli Lilly and Company, Indianapolis); Vivian Bykerk (Hospital for Special Surgery, New York)

**Objectives:** To investigate the speed of response to baricitinib (BARI) across disease measures in patients (pts) with rheumatoid arthritis who had an inadequate response (IR) to conventional synthetic DMARDs (csDMARDs) and biological DMARDs (bDMARD).

**Methods:** Data were assessed from two phase 3 studies, RA-BUILD (NCT01721057; csDMARD-IR pts) and RA-BEACON (NCT01721044; bDMARD-IR pts). Time to first achievement of each of the following responses over 24 weeks were evaluated: ACR 20% and 50% improvement (ACR20 and ACR50), DAS28-CRP low disease activity (DAS28-CRP

Table 1. Summary of hazard ratios and median time to achieve clinical responses from RA-BUILD and RA-BEACON

| RA-BUILD (csDMARD-IR pts) | Treatment        | Sample Size | Median (wk) | HR (95% CI) vs. Placebo, P-value |
|---------------------------|------------------|-------------|-------------|----------------------------------|
| ACR20                     | Placebo          | 228         | 8.0         | 1.53 (1.25, 1.87), <0.001        |
|                           | Baricitinib 2-mg | 229         | 4.0         |                                  |
| ACR50                     | Placebo          | 228         | NE          | 1.84 (1.41, 2.42), <0.001        |
|                           | Baricitinib 2-mg | 229         | 16.0        |                                  |
| DAS28-CRP LDA             | Placebo          | 228         | 24.9        | 1.90 (1.46, 2.48), <0.001        |
|                           | Baricitinib 2-mg | 229         | 14.0        |                                  |
| CDAI LDA                  | Placebo          | 228         | NE          | 1.54 (1.19, 1.99), <0.001        |
|                           | Baricitinib 2-mg | 229         | 14.9        |                                  |
| SJC66 50% Reduction       | Placebo          | 228         | 4.0         | 1.27 (1.05, 1.53), 0.013         |
|                           | Baricitinib 2-mg | 229         | 2.3         |                                  |
| TJC68 50% Reduction       | Placebo          | 228         | 8.0         | 1.29 (1.06, 1.57), 0.011         |
|                           | Baricitinib 2-mg | 229         | 4.0         |                                  |
| RA-BEACON (bDMARD-IR pts) | Treatment        | Sample Size | Median (wk) | HR (95% CI) vs. Placebo, P-value |
| ACR20                     | Placebo          | 176         | 12.0        | 1.62 (1.25, 2.09), <0.001        |
|                           | Baricitinib 2-mg | 174         | 4.9         |                                  |
| ACR50                     | Placebo          | 176         | NE          | 1.90 (1.33, 2.71), <0.001        |
|                           | Baricitinib 2-mg | 174         | NE          |                                  |
| DAS28-CRP LDA             | Placebo          | 176         | NE          | 1.95 (1.35, 2.84), <0.001        |
|                           | Baricitinib 2-mg | 174         | 24.9        |                                  |
| CDAI LDA                  | Placebo          | 176         | NE          | 1.66 (1.14, 2.39), 0.007         |
|                           | Baricitinib 2-mg | 174         | NE          |                                  |
| SJC66 50% Reduction       | Placebo          | 176         | 8.1         | 1.17 (0.93, 1.49), 0.183         |
|                           | Baricitinib 2-mg | 174         | 4.1         |                                  |
| TJC68 50% Reduction       | Placebo          | 176         | 8.4         | 1.13 (0.89, 1.44), 0.313         |
|                           | Baricitinib 2-mg | 174         | 8.0         |                                  |

RA-BUILD (csDMARD-IR pts), RA-BEACON (bDMARD-IR pts); Hazard ratio and p-value from Cox proportional hazards model; NE: not estimable as the response was not reached within 24 weeks. All subjects received csDMARDs as background therapy.

LDA)  $\leq 3.2$ , Clinical Disease Activity Index (CDAI) LDA  $\leq 10$ , and 50% reduction in 68 Tender Joint Count (TJC68) or 66 swollen joint count (SJC66). Hazard ratios (HR) between BARI 2-mg and placebo (PBO) and the corresponding p-values were obtained using Cox proportional hazards model adjusted for treatment group and main stratification factors (RA-BUILD: region and baseline joint erosion status; RA-BEACON: region and history of bDMARD use). All analyses were based on observed data without imputation.

**Results:** In the csDMARD-IR population, BARI 2-mg treated pts were significantly more likely to achieve ACR20 (HR: 1.53,  $P < 0.001$ ), ACR50 (HR: 1.84,  $P < 0.001$ ), DAS28-CRP LDA (HR: 1.90,  $P < 0.001$ ), CDAI LDA (HR: 1.54,  $P < 0.001$ ), SJC66 50% reduction (HR: 1.27,  $P = 0.013$ ) and TJC68 50% reduction (HR: 1.29,  $P = 0.011$ ) compared with PBO (Table 1). Median time to first achievement of ACR20, DAS28-CRP LDA, SJC66 50% reduction and TJC68 50% reduction with BARI 2-mg was 4 weeks, 10.9 weeks, 1.7 weeks, and 4 weeks faster than PBO, respectively. Median time to first achievement of ACR50 with BARI 2-mg was 16 weeks and 14.9 weeks for CDAI LDA, whereas the median did not occur for PBO during the 24 weeks. In the bDMARD-IR population, BARI 2-mg-treated pts were significantly more likely to achieve ACR20 (HR: 1.62,  $P < 0.001$ ), ACR50 (HR: 1.90,  $P < 0.001$ ), DAS28-CRP LDA (HR: 1.95,  $P < 0.001$ ), and CDAI LDA (HR: 1.66,  $P = 0.007$ ) and had numerical quicker response in SJC66 50% reduction and TJC68 50% reduction compared with PBO (SJC66: HR: 1.17,  $P = 0.183$ ; TJC68: HR: 1.13,  $P = 0.313$ ). As for the median time to achieve clinical response, similar trends were observed between the csDMARD-IR and bDMARD-IR populations.

**Conclusion:** In csDMARD and bDMARD-IR patient populations, treatment with BARI was more likely to achieve quicker clinical response than PBO. Time to achieve clinically meaningful responses was faster in pts treated with BARI than those who received PBO.

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### Rheumatoid Arthritis and Oral Health Associations in the Canadian Longitudinal Study of Aging

Vivianne Cruz de Jesus (University of Manitoba, Winnipeg); Shubleen Sidhu (University of Manitoba, Winnipeg); Philip St John (University of Manitoba, Winnipeg); Chrysi Stavropoulou (University of Manitoba, Winnipeg); Carol Hitchon (University of Manitoba, Winnipeg)

**Objectives:** Periodontal disease (PD) is a frequent but neglected comorbidity of rheumatoid arthritis (RA) and may contribute to RA development or persistent disease activity. The Canadian Longitudinal Study of Aging (CLSA) collected data from community-residing older individuals including medical history, medication use, function assessments and oral health symptoms and habits. The aim of this study was to evaluate the association between RA and oral health using the CLSA data.

**Methods:** The CLSA baseline data from 300,097 individuals was analyzed. Individuals who self-reported an RA diagnosis and taking DMARDs were considered to have RA. Individuals who self-reported having at least one

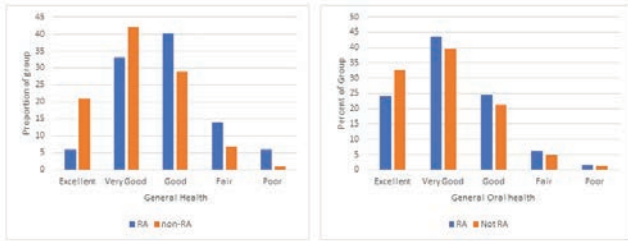


Figure: Self-reported general health and general oral health

symptom of loose natural teeth, sore or bleeding gums around natural teeth were considered to have PD. Maximum grip strength was considered a surrogate of upper extremity function relevant to RA. Descriptive statistics are reported.

**Results:** We identified 268 individuals with RA (cohort prevalence 0.9%; 73% female with average (standard deviation) age of 64.3 (10.2) years, > 95 % White). For individuals with oral health data (N = 28692), compared to non-RA (n = 28435), RA participants (n = 257) reported worse general physical health (excellent general physical health for RA 0.06% versus non-RA 21%; P < 0.0001) but similar oral health (Figure). No significant differences in the cohort prevalence of diabetes, osteoarthritis of hands, knee and hips, other arthritis, and smoking were observed between the groups. Compared to non-RA, a greater proportion of RA participants reported edentulism (35% vs. 25%), uncomfortable eating sometimes (17% vs. 5%), avoiding eating sometimes (9% vs. 5%) and issues chewing adequately (15% vs. 8%), all P < 0.0001, and a greater proportion reported swelling in the mouth, dry mouth, burning mouth, jaw muscle pain, and jaw joint pain (all P < 0.05). Only 42% of non-RA and 31% of RA participants reported no oral health concerns (P < 0.0001). The cohort prevalence of at least one PD symptom was 20% for RA and 19% for non-RA participants (P = NS). Compared to non-RA, RA participants had poorer grip strength (mean difference; 95% CI -8.8; -10.2, -6.9; P < 0.0001). Multivariable modelling identified age and grip strength but not RA or sex to associate with PD symptoms.

**Conclusion:** In this cohort of elderly Canadians, RA participants had worse self-reported oral health symptoms than non-RA participants. Although PD symptoms were common and associated with upper extremity function, dental examination is required to determine true PD cohort prevalence. Greater attention to and management of the oral health needs of elderly RA patients is needed.

## 120 Evaluating Frailty in Rheumatoid Arthritis: A Scoping Review

Alexandra Legge (University of British Columbia (Division of Rheumatology)/Arthritis Research Canada, Vancouver); Diane Lacaille (Arthritis Research Canada, University of British Columbia, Vancouver)

**Objectives:** Frailty is emerging as a useful construct for understanding the heterogeneous outcomes observed among patients with rheumatic diseases. This scoping review aimed to 1) Identify measures/tools used to characterize frailty in individuals with rheumatoid arthritis (RA); and 2) Compare estimates for the prevalence of frailty among RA patients across the identified measures/tools.

**Methods:** This review was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses extension for Scoping

Reviews. MEDLINE, EMBASE, and CINAHL were searched from database inception to September 15, 2021, using keywords and Medical Subject Headings for “rheumatoid arthritis” and “frailty”, as well as additional search terms related to known frailty instruments. Full-text, English language articles of any study design that described the development, application, or validation of frailty measures/tools in patients with RA were included. Pertinent data were extracted from the included articles, which were also assessed for risk of bias using NHLBI Study Quality Assessment Tools.

**Results:** The search yielded 199 articles for title/abstract review, of which 52 underwent full text review. Twenty articles (15 cross-sectional studies, 4 cohort studies, and 1 meta-analysis of individual patient data from RCTs) met the inclusion criteria. All included studies were published in 2017 or later and received overall ratings of “fair” in the risk of bias assessment. Frailty was assessed using 13 different instruments, including 3 measures developed specifically for RA patients. While 10 of 13 instruments assessed multiple health domains, all were heavily weighted towards physical deficits. The frailty phenotype and the Kihon Frailty Checklist were the most frequently used measures (4 studies each). The frailty index (FI) approach was used in three studies (Table 1). Eighteen studies reported the prevalence of frailty among RA patients, with estimates ranging from 10% to 73%. In 11 studies, the prevalence of pre-frailty ranged from 20.4% to 71%. Three studies comparing individuals with versus without RA reported a significantly higher prevalence of frailty among RA patients (16.6-37.6% for RA vs. 3.4-15.7% for non-RA). Most studies (7/12) reported increasing prevalence of frailty with older age, although this relationship was attenuated when compared to individuals without RA. In 7/9 studies, the prevalence of frailty was higher among females when compared to males.

**Conclusion:** While different measures/tools used to assess frailty in patients with RA produce a wide range of estimates for its prevalence, studies have consistently demonstrated an increased prevalence of frailty among RA patients when compared to individuals without RA.

## 121 Transient Temporal Arteritis Post-COVID-19 Vaccination

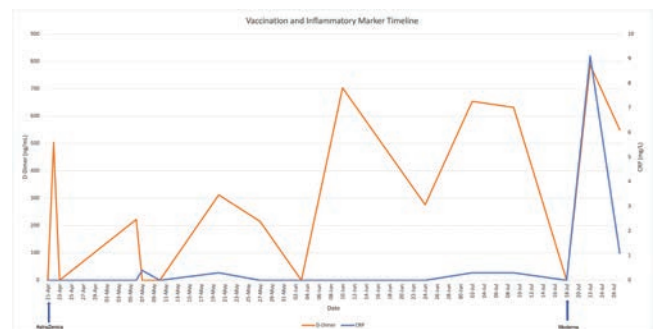
Joanne Wang (University of British Columbia, Vancouver); Mohammad Bardi (University of British Columbia, Division of Rheumatology, Vancouver)

**Background:** Giant Cell Arteritis (GCA) is a primary vasculitis affecting medium to large vessels in people over 50. Temporal arteritis describes the common clinical subtype affecting the cranial arteries. However, inflammation of the temporal arteries can occur due to infections and other inflammatory conditions. Untreated, GCA can lead to complications, including blindness and stroke.

**Case Description:** A 49-year-old woman with known homozygous factor V Leiden developed greater saphenous vein superficial thromboembolism two days after receiving the AstraZeneca vaccine. Sixteen days post-vaccine, she developed pulsatile, non-painful, right temporal artery swelling with new-onset headaches. She had no other GCA symptoms (ie, scalp tenderness, jaw claudication or visual symptoms). CRP and

Table 1. Studies using the frailty index (FI) approach to evaluate frailty among individuals with rheumatoid arthritis (RA).

| Publication (first author, year) & dataset used for FI derivation                                                                 | Data sources used to define health deficits                                                    | Number of health deficits & health domains addressed                                  | Prevalence of frailty in RA                                                                                         |
|-----------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| Li G, et al. (2019)<br>Ontario Best Practices Research Initiative (OBRI) clinical registry of patients with RA in Ontario, Canada | Self-report questionnaires, healthcare provider report of comorbidities and medications        | 32 health deficits, including physical (31 items) and psychological (3 item) domains  | FI scores evaluated as a continuous variable only and therefore frailty prevalence not reported.                    |
| Hanson P, et al. (2020)<br>Meta-analysis of individual patient data from eight randomized controlled trials (RCTs) of RA patients | Self-report questionnaires, medical chart review, objective physical tests, laboratory results | 40 health deficits, including physical (36 items) and psychological (4 items) domains | Prevalence of frailty in RA ranged from 33% to 73% across the 8 RCTs (frailty defined as an FI score $\geq 0.24$ ). |
| Cook MJ, et al. (2021)<br>United Kingdom (UK) Biobank, a population-based prospective cohort of adults aged 40-69 years           | Patient self-report from questionnaires and research interviews                                | 45 health deficits, including physical (40 items) and psychological (5 items) domains | FI scores evaluated as a continuous variable only and therefore frailty prevalence not reported.                    |





D-dimer remained normal at 0.4 mg/L ( $N < 4.8$ ) and 222 ng/mL ( $N < 500$ ), respectively. On day 2, her family physician suspected GCA and initiated prednisone 30 mg with the resolution of headaches by day 3. On day 4, when seen at the GCA Fast Track clinic, she had resolution of temporal artery swelling. Physical exam and ultrasound assessment of the cranial vessels were unremarkable [DE1]. Day 5-17, prednisone was rapidly tapered from 30 to 5 mg with mild transient temporal swelling at 5 mg lasting less than 48 hours. By day 22, she tapered off prednisone without reoccurrence of symptoms. Moderna vaccine was administered 12 weeks later with mild recurrence of right temporal artery swelling three days post-vaccination without any other GCA symptoms; however, CRP and D-dimer increased to 9.1 mg/L ( $N < 4.8$ ) and 786 ng/mL ( $N < 500$ ), respectively (Figure). Given the patient's previous self-resolving course, she was monitored closely without initiation of prednisone. The temporal artery swelling resolved over five days with normalization of the CRP to 1.1 mg/L. She has not had any recurrent symptoms since.

**Discussion:** This case illustrates the potential to develop transient temporal arteritis after COVID vaccination. Influenza vaccines containing adjuvants have resulted in reactions mimicking GCA. Given that COVID vaccines do not contain adjuvants, this represents a novel finding that has not been reported to date in COVID vaccines.

**Conclusion:** Awareness of transient temporal arteritis as a vaccine reaction is vital to recognize to prevent over-treatment with corticosteroids in patients as this could interfere with vaccine response.

## 122

### I Simply Cannot See What the Problem Is

Ali Shams (University of Saskatchewan, Saskatoon)

**Background:** The rate of infectious syphilis in Canada is on the rise at an incidence of 11.2 per 100,000 in 2017, almost four times the incidence of GPA. Secondary syphilis can present very similarly to systemic vasculitis. However, retinal involvement is an exceedingly rare manifestation of GPA and should point to another disease process.

**Case Description:** A 29-year-old female is referred to Rheumatology by Internal Medicine for progressive bilateral vision loss on a presumed diagnosis of granulomatosis with polyangiitis (GPA) made in the community. On review of systems, the patient endorsed a rash, joint pain and swelling as well as oral and nasal ulcers. Investigations were notably positive for ANCA atypical neutrophil staining but MPO and PR3 were negative. CRP was 17.3. The rest of the autoimmune workup was negative. Ophthalmology assessment yielded differential diagnoses of fungal endophthalmitis, systemic inflammatory disease, and other infectious processes. There was retinal involvement seen on ophthalmoscopy. As the patient's visual loss worsened to near blindness, Rheumatology elected to initiate pulse steroids and intravenous cyclophosphamide. Upon follow-up four days later, there was no improvement in the patient's visual symptoms. The patient's serum then tested positive for syphilis. A course of appropriate intravenous antibiotics was completed but the patient's vision never recovered.

**Conclusion:** The following case presentation explores a challenging diagnosis of secondary syphilis closely mimicking systemic vasculitis.

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### A Novel Syndrome...Hiding in Plain Sight

Medha Soowamber (University of Toronto, Toronto)

**Background:** VEXAS (Vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a novel adult-onset autoinflammatory syndrome, discovered using a unique genotype-driven approach. The clinical features of VEXAS bridge rheumatologic and hematologic conditions and as such, rheumatologists should be aware of its unique presentation. The objective of this case report is to describe the clinical features of VEXAS.

**Case Description:** A 61-year-old male, with a history of diabetes, was referred to rheumatology for a third opinion in context of having a 3-year history of the diffuse rashes, recurrent DVTs and polyarthritides not responsive to a plethora of immunosuppressive medications. His symptoms

began with erythematous plaques and papules throughout his body with a skin biopsy showing a neutrophilic dermatosis (working diagnosis of Sweet's syndrome) (Figure). The rash was only responsive to high doses of prednisone and would recur on moderate doses of prednisone, approximately 20 mg. He then developed 2 unprovoked DVTs for which he was anticoagulated and soon after, developed symmetrical polyarthritides involving his wrists, MCPs and MTPs on a background of also developing constitutional symptoms of fever, chills and night sweats that were also only responsive to high dose of prednisone. He was diagnosed as having concomitant seronegative rheumatoid arthritis and was placed on several conventional disease modifying antirheumatic drugs including methotrexate, sulfasalazine and leflunomide and thereafter, treatment was escalated to biologics with no improvement of his symptoms. His rashes, inflammatory arthritis and constitutional symptoms would recur on 20 mg of prednisone despite immunosuppression. On blood work, he had a progressive macrocytic anemia and bone marrow biopsy only showed a hypercellular bone marrow with no evidence of dysplasia. He was also evaluated by infectious disease and underlying infectious trigger was not identified. He was seen for the first time in the vasculitis 3 months after the initial description of VEXAS syndrome and we recognized that the patient had the following features of this syndrome: neutrophilic rashes, polyarthritides, constitutional symptoms, recurrent unprovoked DVTs and progressive macrocytic anemia. As a result, DNA sequencing was done on his blood, which found the somatic mutation (pMet14Leu) on the UBA1 gene characteristic of VEXAS syndrome. Reanalysis of his previous bone marrow found multiple vacuoles in the cytoplasm of the myeloid and erythroid precursor cells, which are part of the VEXAS syndrome.

**Conclusion:** To our knowledge, this is the first case of VEXAS described in Ontario and rheumatologists should be aware of its various clinical phenotype.



### TNF- $\alpha$ Inhibitors in the Treatment of Neurobehçet Syndrome: A Case Series and Literature Review

Ashley Yip (University of Alberta, Edmonton); Mohammed Osman (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton); Alison Clifford (University of Alberta, Edmonton)

**Objectives:** Behçet's syndrome is a systemic inflammatory endothelialopathy which can result in a variable vessel vasculitis. It is characterized by recurrent mucocutaneous ulcers, ocular disease, skin lesions, gastrointestinal involvement, neurologic disease, vascular disease and/or arthritis. Neurobehçet syndrome (NBS) occurs in 5% of cases. NBS is associated with parenchymal or vascular involvement, with parenchymal imaging changes accounting for 75-80% of cases. There is a paucity of evidence supporting treatment of NBS. Our objective was to review the course of two patients with parenchymal NBS who were treated with TNF- $\alpha$  inhibitors.

**Methods:** Two cases of NBS treated first line with TNF- $\alpha$  inhibitors are presented.

**Results:** Case 1. A 28-year-old Chinese male with a prior left midbrain and pons ischemic stroke (February 2020) and right basal ganglia intracerebral hemorrhage (January 2021) presented to the outpatient rheumatology clinic with new visual symptoms in June 2021. Ophthalmologic evaluation revealed retinal vasculitis with periphlebitis. Cerebrospinal fluid (CSF) revealed increased cells but negative for typical and atypical infection. Further history revealed intermittent oral ulcers since childhood. HLA-B\*51 was positive. He was diagnosed with NBS and started on pulse methylprednisolone, azathioprine, and adalimumab. At 4 months, his disease remains in remission, with improvement of ocular inflammation. Repeat CSF analysis demonstrated normalization of cell count and protein. Case 2. A 45-year-old Caucasian female with suspected Behçet's syndrome presented to hospital with dyspnea, anemia and diplopia. A few weeks prior, she started azathioprine, which was thought to be the cause of anemia and was held. She described a history of intermittent oral and vaginal ulcers. Physical exam confirmed oral ulcers, ulcerating cutaneous lesions, and cranial nerve 6th palsy. CT PE revealed multiple bilateral pulmonary embolisms. MRI brain revealed cranial nerve VI enhancement and bilat-

Table 1. Summary of case series evidence for treatment of NBS with TNF- $\alpha$  inhibitors

| Reference                     | # Patients, Study Design | TNF- $\alpha$ , Dose                                                               | Outcome                                                                                                                                                                |
|-------------------------------|--------------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Van Laar et al., 2007         | 2, case series           | IFX 3-5 mg/kg q4-12w then ADA 40 mg sc q2w                                         | Complete remission 2/2                                                                                                                                                 |
| Pipitone et al., 2008         | 8, case series           | IFX 5 mg/kg weeks 0, 2, 6 then q4-8w                                               | Clinical improvement: 8/8<br>Clinical remission: 7 of 8<br>MRI improvement: 5 of 5                                                                                     |
| Kikuchi et al., 2008          | 5, case series           | IFX 5 mg/kg weeks 0, 2, 6, 14                                                      | Clinical improvement: 3 of 5                                                                                                                                           |
| Borhani Haghighi et al., 2011 | 4, case series           | IFX 3 mg/kg (n=2) or 5 mg/kg (n=2)                                                 | Clinical response, first month: 4 of 4<br>Radiologic response, first month: 4 of 4                                                                                     |
| Giardina et al., 2011         | 5, case series           | IFX<br>Dose unknown                                                                | Complete remission: 5 of 5                                                                                                                                             |
| Vallet et al., 2015           | 13, case series          | IFX 5 mg/kg week 0, 2, 6 then q4-6 weeks (n = 10) or ADA (n = 3) 40 mg sc q2 weeks | Infliximab: response in 9/10<br>Adalimumab: response in 3/3                                                                                                            |
| Desbois et al., 2015          | 17, case series          | IFX 5 mg/kg (n = 13) or ADA 40 mg (n = 4)                                          | Infliximab: response 12/13<br>• Partial response: 8/13<br>• Complete response: 4/13<br>Adalimumab: response 4/4<br>• Partial response: 3/4<br>• Complete response: 1/4 |
| Zeydan et al., 2016           | 16, case series          | IFX 5 mg/kg weeks 0, 2, 6 then q8w                                                 | Response in 15/16                                                                                                                                                      |
| <b>Total</b>                  | <b>70</b>                | <b>61 IFX<br/>9 ADA</b>                                                            | <b>Overall: response 65/70 (92.8%)<br/>IFX: response 56/61<br/>ADA: response 9/9</b>                                                                                   |

Legend: NBS (NeuroBehçet's), IFX (infliximab), ADA (adalimumab)

eral pontine enhancing lesions. CSF analysis demonstrated elevated protein with normal cell count. HLA-B\*51 was negative. She was diagnosed with NBS and started on pulse methylprednisolone and infliximab 5 mg/kg IV. Treatment response is too premature to assess at time of abstract submission.

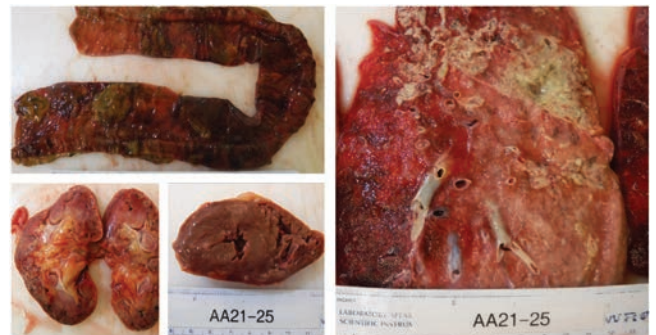
**Conclusion:** NBS is a rare manifestation of an uncommon disease. Parenchymal NBS may be treated with glucocorticoids and azathioprine, however TNF- $\alpha$  inhibitors may be considered in those with severe or refractory disease, and ongoing studies may provide additional insight into their utility. We summarize the case series evidence for treatment of NBS with TNF- $\alpha$  inhibitors in Table 1.

### The Devil in the Details

Matthew Anacleto-Dabarno (McGill University, Montreal); Elizabeth Hazel (McGill University, Montreal)

**Case Description:** A 78-year-old female ex-smoker with a past medical history of bronchiectasis and osteoporosis presents to a community hospital with 4 weeks of intermittent cough, scant hemoptysis, and fatigue. She had significant muscle wasting. Initial investigations were significant for elevated inflammatory markers, elevated high-sensitivity troponins, microscopic hematuria, and hyponatremia consistent with syndrome of inappropriate anti-diuretic hormone. Imaging showed multiple bilateral pulmonary cavitary lesions, and right perihilar mass encasing the right upper lobe bronchus. Previous imaging was significant for biapical sub-centimetric nodules which with no interval follow-up. The patient was treated and investigated for infectious etiologies before undergoing positron-emission tomography and transthoracic needle biopsy to exclude malignancy. Late in her hospital course, the patient developed bilateral lower extremity palpable purpura. This prompted measurement of creatine which had not been verified serially as it was normal in her early hospital course. After a near-tripling of the patient's creatinine, she was transferred to an academic center for renal biopsy. The patient died shortly after arrival having been started on treatment for presumptive ANCA vasculitis. An autopsy was performed which showed extensive multi-organ granulomatous necrosis involving the gastrointestinal tract, myocardium, kidneys, uterine and left ovarian tissue, bilateral lungs, skin, liver, spleen and adrenal glands (Figure). The cause of death was extensive granulomatosis with polyangiitis (GPA).

**Discussion:** This case presents several unusual features of GPA. While subglottic stenosis is well described in ANCA vasculitis,[1,2,3] radiological encasement of the proximal airway tree is more commonly associated with malignancy. Encasement of other anatomical structures[4] and endobronchial disease[1,5,6] have been described, but remain uncommon findings in GPA or ANCA vasculitis more broadly. The distribution of organ involvement is also unusual, particularly ovarian disease and splenic involvement, which have both been only rarely described.[7,8,9] The case also presents diagnostic pitfalls that in this case, may have contributed to a significant adverse outcome. There is a well-known inverse relationship between muscle mass and serum creatinine [10] that lead to false reassurance of the patient's renal function. An initial absence of extrapulmonary disease and several clinical and radiological features indicating malignancy caused vasculitis to be overlooked as a potential diagnosis until evidence mounted in its support. This is an example of a "premature closure" cognitive bias, a common and problematic error in judgment in medicine.[11,12,13] References: [1.] Quinn KA. Rheumatology 2019;58:2203-2211. [2.] Sacoto G. Presse Med 2020;49:104039. [3.] Vartiainen E. Ear Nose Throat J 1992;71:423-424;427-428. [4.] Salvi F. Neurol Sci 2010;31:639-641. [5.] Daum TE. Am J Respir Crit Care Med 1995;151:522-526. [6.] Grygiel-Górniak B. Postgrad Med 2018;130:581-596. [7.] Saleh Farghaly HR. Indian J Nucl Med 2019;34:153-156. [8.] Bottomley MJ. BMC Nephrol 2019;20:84. [9.] Bielejewska A. Sarcoidosis Vasc Diffuse Lung Dis 2020;37:179-183. [10.] Kashani K. Eur J Intern Med 2020;72:9-14. [11.] Blissett S. Med Educ 2017;51:1095-1096.





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**A Systematic Review and Meta-analysis of Models to Predict the Diagnosis of Giant Cell Arteritis**

Mats Junek (McMaster University, Hamilton); Angela Hu (University of British Columbia, Vancouver); Matthew Jessome (McMaster University, Hamilton); Deborah Koh (McMaster University, Hamilton); Farid Foroutan (University of Toronto, Toronto); Stephanie Garner (McMaster University, Hamilton); Nader Khalidi (McMaster University, St Joseph's Healthcare Hamilton, Hamilton)

**Objectives:** The diagnosis of giant cell arteritis (GCA) can be difficult in individuals with inconclusive symptoms and inflammatory markers. Temporal artery biopsy (TAB), while often thought of as the gold standard, may miss a proportion of diagnoses. As such, many diagnostic models incorporating various predictors have been developed to assist clinicians in predicting a diagnosis of GCA with varying utility. This systematic review seeks to analyze these models to understand common and stable predictors of a diagnosis of GCA, understand their rigor, and determine how different criteria can alter the diagnosis of GCA.

**Methods:** We performed a literature review from January 1990 to May 2020 for studies that used a model to diagnose giant cell arteritis. Studies with models that had fewer than three variables or 30 people were excluded. Abstract screening, data extraction, and risk of bias were performed by two independent reviewers for each study. Study characteristics, patient characteristics, method of and criteria for diagnosis, and model details were extracted and summarized. Meta-analysis of individual signs and symptoms was performed using generic inverse variance. The PROBAST tool was used to assess risk of bias in each individual study.

**Results:** We screened 1 446 abstracts and included 34 studies using data from 11 countries. 42 diagnostic models were identified. A total of 13 388 patients, 12 570 TABs, and 3 718 diagnoses of GCA were included. 22 studies required TAB positivity to diagnose GCA, 7 diagnosed using a composite of clinical and investigative findings, and 4 only required clinical findings. Rates of diagnosis of GCA were 25.0%, 39.0%, and 44.9% in each group respectively; Rates of TAB positive diagnoses were 98.2%, 53.7%, and 69.8%. There were 82.9% more diagnoses of GCA when using composite criteria over TAB positivity alone. Jaw claudication and Temporal changes were most associated with a diagnosis of GCA, however there were more predictive of TAB positive GCA than a clinical diagnoses, whereas headache and vision loss were more associated with non-TAB based diagnoses of GCA (Table 1). studies were at high risk of model bias and 4 were low risk.

**Conclusion:** Models used to predict a diagnosis of GCA are of variable methodological quality and are largely dependent on using TAB positivity as a gold standard for a diagnosis of GCA. Despite this, predictors of GCA are consistent. Future models should focus on validation and use diagnostic standards that include composite criteria that reflect current practice.

**Table 1:** Meta-odds ratios and 95% confidence intervals of predictors of a diagnosis of GCA, stratified based on including all studies, including studies that diagnosed GCA based on a positive TAB, and studies that diagnosed GCA using clinical and/or composite criteria to diagnose GCA.

| Predictor                            | All models predicting GCA | TAB to diagnose GCA | Clinical/Comp for GCA |
|--------------------------------------|---------------------------|---------------------|-----------------------|
| Age                                  | 1.04 (1.02-1.05)          | 1.04 (1.01-1.05)    | 1.04 (1.02-1.05)      |
| Headache                             | 2.96 (1.75-5.02)          | 2.55 (1.63-4.00)    | 3.60 (1.78-7.28)      |
| Temporal artery and/or scalp changes | 2.60 (1.75-3.85)          | 2.80 (1.71-4.59)    | 2.07 (1.35-3.18)      |
| Jaw Claudication                     | 3.73 (2.48-5.63)          | 4.05 (2.38-6.91)    | 2.62 (1.89-3.64)      |
| PMR                                  | 1.58 (0.68-3.66)          | 1.53 (0.33-7.08)    | 1.59 (0.76-3.31)      |
| Vision Loss                          | 2.09 (1.50-2.92)          | 1.93 (1.23-3.04)    | 2.51 (1.35-4.69)      |
| ESR (mm/hr)                          | 1.03 (1.01-1.04)          | 1.03 (1.01-1.05)    | 1.18 (0.81-1.72)      |
| CRP (mg/dl)                          | 1.36 (1.04-1.78)          | 1.36 (1.24-1.49)    | 1.58 (0.63-3.96)      |
| Platelets (10 <sup>9</sup> /L)       | 1.01 (1.01-1.01)          | 0.95 (0.90-1.00)    | 1.43 (1.07-1.90)      |

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**Probable Hughes-Stovin Syndrome Presenting with Recurrent Massive Hemoptysis**

Gabriel Jeyasingham (Western University, London); Tom Appleton (St. Joseph's London Rheumatology Centre and Western University, London)

**Background:** Vasculitic syndromes like Behcet's syndrome can cause pulmonary aneurysms and thrombosis. However, isolated pulmonary vascular manifestations without other features of systemic vasculitis may suggest a rarer diagnosis of Hughes-Stovin syndrome (HSS) that carries high mortality. We report a case of probable HSS presenting with recurrent massive hemoptysis.

**Case Description:** An otherwise healthy 32-year-old man presented with pleurisy and dyspnea secondary to left-sided pulmonary embolisms with parenchymal infarcts. Despite oral anticoagulation, he developed progressive and ultimately massive hemoptysis. He was afebrile and hemodynamically stable. Computed tomography (CT) of the chest revealed progressive left-sided pulmonary embolisms and a 39-millimetre ill-defined soft-tissue mass surrounding a dilated lingular segmental artery and left lower lobe pulmonary artery. Review of his imaging confirmed several left-sided pulmonary arterial aneurysms. Several surgical biopsies of the mass were negative for malignancy but showed non-specific inflammation. Abdominal CT imaging was negative for other masses. He developed recurrent hemoptysis despite changes in anticoagulation. Further investigations revealed an elevated C-reactive protein (86 mg/L), anemia, thrombocytosis, and normal liver enzymes and renal function. Infectious workup was unremarkable including blood cultures and viral serology. Antiphospholipid antibody and inherited thrombophilia testing were negative, and he had no peripheral thrombosis. He had no other systemic features of connective tissue disease or vasculitis, and autoimmune serology including anti-neutrophil cytoplasmic antibodies was unremarkable. For probable HSS, the patient received induction therapy with high-dose intravenous methylprednisolone followed by oral prednisone and 6 doses of monthly cyclophosphamide. Full-dose anticoagulation was stopped after consultation with a thrombosis specialist. The patient's hemoptysis resolved, and his pulmonary aneurysms improved on repeated imaging. Azathioprine was used for maintenance therapy and the patient completed a prednisone taper. He subsequently developed a new pulmonary embolism, requiring re-induction with high-dose prednisone and transition from azathioprine to methotrexate and infliximab.

**Discussion:** Our case adds to 57 published cases of HSS, a possible variant of Behcet's syndrome primarily affecting young men. Clinical manifestations include arterial or venous thrombosis and pulmonary vasculitis manifesting as pulmonary arterial aneurysms or pseudoaneurysms with in-situ thrombosis. Bronchial arterial aneurysms can occur, and aneurysmal wall enhancement on CT imaging may identify underlying vasculitis. Following the European League Against Rheumatism's recommendations for pulmonary vasculitis in Behcet's syndrome, treatment of HSS requires high-dose glucocorticoids and cyclophosphamide due to high mortality. Tumor necrosis factor alpha inhibitors may be considered in refractory cases. Our case supports observations that early recognition and aggressive immunosuppression may improve outcomes in HSS.

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**Giant Cell Arteritis with Recurrent Strokes: A Case Report and Review of Literature**

Angela Hu (University of British Columbia, Vancouver)

**Background:** Giant cell arteritis (GCA) resulting in strokes is an infrequent (3-5%) complication. We present a challenging case with severe occlusive disease and recurrent cerebrovascular events despite immunosuppression.

**Case Description:** Ms. F is a 70F who developed cranial GCA symptoms in April 2021 (severe headache, scalp tenderness, fevers and polymyalgia rheumatica symptoms). In August she had right eye blurriness and came to ED. CRP 41mg/L (N < 3). CTA arch to vertex showed severe mural thickening and multifocal stenoses throughout bilateral vertebral arteries, and diffuse irregularity and mild stenosis of intracranial arteries. She was started on low dose ASA, methotrexate 20 mg SC weekly and 3 days of IV pulse steroids, with subsequent slow taper. Ophthalmological examination was normal. She had a temporal artery biopsy on Aug 10, results consistent with GCA. She returned Sept 14 with left arm weakness, dysarthria and right



perioral numbness, consistent with transient ischemic attack (TIA). Repeat CTA head/neck showed progression of severe bilateral stenoses of cavernous ICAs, and similar occlusion of the vertebral arteries. MRI showed acute R PICA infarct. Given this rapid progression, the changes were felt to be secondary to GCA. Her cranial GCA symptoms had resolved, and CRP normalized (0.2 mg/L). Another pulse of methylprednisolone was given for 5 days. The stroke team-initiated anticoagulation with IV heparin, transitioned to apixaban. Sept 16 repeat CTA head/neck showed still mildly worsening stenoses in the cavernous ICAs and left intracranial vertebral artery; she also had recurrent TIA symptoms. As a result, cyclophosphamide induction per EUVAS protocol at 10 mg/kg was initiated. She subsequently stabilized and was discharged Sept 22.

**Conclusion:** There is a paucity of literature for treatment of strokes related to GCA. Lower mortality is reported in patients who receive combination therapy compared to corticosteroid (CS) monotherapy (40% vs 58%, respectively). In a retrospective review of 45 patients from 2016, 69% received CS alone, 4% CS + methotrexate or azathioprine, and 18% CS + cyclophosphamide. The GiACTA trial (NEJM 2017) examined the efficacy of tocilizumab, but specifically excluded patients with recent major ischemic events such as stroke. One case report discusses a patient who initially responded to cyclophosphamide but subsequently had refractory strokes when switched to tocilizumab. Another case report describes successful treatment with tocilizumab for stroke in the internal carotid territory related to GCA.

Lack of research limits our understanding of optimal therapies in intracranial GCA. Overall experience favours use of cyclophosphamide in conjunction with corticosteroid.

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### The Anatomy of Severe Neuropsychiatric Systemic Lupus Erythematosus: A Single Center Experience

James Haigney (Beth Israel Deaconess Medical Center, Boston); Stefanie Wade (Beth Israel Deaconess Medical Center, Vancouver); Vasileios Kyttaris (Beth Israel Deaconess Medical Center, Boston)

**Objectives:** Severe neuropsychiatric systemic lupus erythematosus (NPSLE) is one of the least characterized SLE manifestations. In this study we describe features of severe NPSLE at our institution and analyze the manifestations and outcomes according to anatomical region involved and mechanisms of disease.

| Neurologic Region Effected                                        | Exclusive CNS    | Exclusive PNS    | p value |
|-------------------------------------------------------------------|------------------|------------------|---------|
| Number of subjects                                                | 20               | 4                |         |
| Female %                                                          | 80%              | 80%              | 0.822   |
| Race                                                              |                  |                  |         |
| Black                                                             | 50%              | 75%              | 0.357   |
| White                                                             | 30%              | 25%              | 0.841   |
| Other                                                             | 20%              | 0%               | 0.327   |
| Median age (years) of SLE diagnosis (Q1, Q3)                      | 33 (23.5, 43.25) | 36 (29.75, 44.5) | 0.288   |
| Onset of NPSLE relative to SLE diagnosis (years), median (Q1, Q3) | 3 (0, 7)         | 6.5 (2.0, 11.75) | 0.655   |
| Severity                                                          |                  |                  |         |
| No admission                                                      | 15%              | 50%              | 0.116   |
| Hospitalization                                                   | 85%              | 50%              | 0.116   |
| ICU Stay                                                          | 25%              | 0%               | 0.372   |
| Mechanisms                                                        |                  |                  |         |
| Demyelination                                                     | 25%              | 25%              | 1.000   |
| Vasculitis                                                        | 25%              | 75%              | 0.053   |
| Thrombosis                                                        | 35%              | 0%               | 0.160   |
| Myasthenia                                                        | 0%               | 25%              | 0.022*  |
| Other                                                             | 45%              | 0%               | 0.089   |
| Treatment before NP flare                                         |                  |                  |         |
| Prednisone                                                        | 40%              | 100%             | 0.029*  |
| CYC                                                               | 5%               | 0%               | 0.548   |
| HCQ                                                               | 50%              | 50%              | 1.000   |
| Antimetabolite                                                    | 5%               | 75%              | >0.001* |
| Immune modulators (IVIG, interferon)                              | 5%               | 0%               | 0.648   |
| TNF Inhibitor                                                     | 0%               | 0%               |         |
| NPSLE treatment                                                   |                  |                  |         |
| Pulse steroids                                                    | 50%              | 50%              | 1.000   |
| Prednisone > 0.5 mg/kg                                            | 10%              | 100%             | 0.029*  |
| Prednisone > 0.5 mg/kg                                            | 60%              | 0%               | >0.001* |
| CYC                                                               | 40%              | 50%              | 0.772   |
| HCQ                                                               | 60%              | 25%              | 0.200   |
| Antimetabolite                                                    | 15%              | 25%              | 0.624   |
| Immune modulators (IVIG, interferon)                              | 20%              | 50%              | 0.206   |
| AC/ASA                                                            | 25%              | 0%               | 0.327   |
| Clinical Outcome                                                  |                  |                  |         |
| Patients with follow up data                                      | 19               | 4                |         |
| No improvement                                                    | 21%              | 25%              | 0.822   |
| Partial improvement                                               | 52%              | 75%              | 0.459   |
| Complete improvement                                              | 21%              | 0%               | 0.327   |

**Table 1: Demographics and characteristics of NPSLE**  
Anatomy of Patients with "other" disease mechanisms had disease processes that could not be entirely attributed to vasculitis, thrombosis, myasthenia, or demyelination. p values refer to the comparison between the exclusive CNS to exclusive PNS groups.

**Methods:** This is a retrospective medical record review. Cases were identified by cross referencing ICD9/10 codes for SLE with psychosis, delirium, organic brain syndrome, seizures, CVA, aseptic meningitis, transverse myelitis, peripheral neuropathy, cranial nerve neuropathy, and lupus headache from 1990-2020. Demographics, details of SLE and NP disease, and serologies were extracted. Patients were classified by anatomic manifestations: central nervous system (CNS), peripheral nervous system (PNS), or combined CNS/PNS. Data was analyzed with NCSS 2021 software.

**Results:** Of the 714 records identified, a total of 26 patients fulfilled inclusion criteria. The median follow-up interval was 6 (IQR: 4-10) months. 20 had exclusive CNS, exclusive 4 PNS, and 2 had CNS/PNS (Table 1). Within CNS, 5 had demyelinating disease, 8 thrombotic, 5 vasculitis, and 10 other manifestations. Within PNS 1 had demyelinating disease, 4 had vasculitis, and 2 had myasthenia. The median age of SLE diagnosis for the cohort was 33.68 (IQR: 26-43) years. NPSLE manifestations occurred after an established diagnosis of SLE at a median of 4 (IQR: 0-7) years. Importantly though, patients with demyelinating disease presented with CNS lesions that antedated SLE diagnosis by a median of 11 years (IQR: 0-22). Overall, 80.8% of our cohort required hospitalization. Most CNS patients (85%) required hospitalization with 25% of them, admitted to the ICU. Both categories received pulse steroids; however, CNS patients received higher doses on average. Cyclophosphamide was administered to less than half of our patients. The rest were treated with a variety of anti-metabolites, IVIG, and interferon in patients with demyelinating disease. Remission within the follow-up interval was achieved in only 21% of CNS and 25% of PNS patients.

**Conclusion:** Most patients with severe NPSLE presented several years after being diagnosed with SLE, apart from those with demyelinating disease who generally presented before establishing a diagnosis of SLE. Generally, patients with CNS disease had a more severe disease course, with most requiring hospital admission, high dose steroids, and immune suppression. Clinical remission was achieved in a small minority of patients, a fact that calls for rigorous studies on prevention and treatment of this severe complication of SLE.

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### Hospitalizations for COVID in Canadian SLE Patients Followed in Clinical Cohorts in the Pre-vaccination Period.

Jia Li Liu (McGill University, Montreal); Christian Pineau (McGill University Health Centre, Montreal); John Hanly (Dalhousie University and Nova Scotia Health Authority, Halifax); Ann Clarke (University of Calgary, Calgary); Christine Peschken (University of Manitoba, Winnipeg); Paul Fortin (Université Laval, CHU de Québec, Québec); Évelyne Vinet (Department of Medicine, Division of Rheumatology, McGill University Health Centre, McGill University, Montreal); Carol Hitchon (University of Manitoba, Winnipeg); Sasha Bernatsky (McGill University Health Centre, Department of Medicine, Division of Rheumatology, Montreal)

**Objectives:** To capture the number of serious COVID cases (defined as those requiring hospitalization) reported in pre-vaccination period at five clinical SLE cohort registries in Canada.

**Methods:** Our study combined data from five clinical SLE cohort registries in Canada (Montreal, Quebec City, Halifax, Winnipeg, and Calgary). The cohorts enroll unselected patients aged 18 years or older who meet American College of Rheumatology (ACR) criteria for SLE. Patients are evaluated yearly, and report detailed clinical information including hospitalization for

| SITE     | Active patients in cohort | Cohort Female N(%) | Cohort Caucasian race/ethnicity N(%) | Cohort Mean age (SD) |
|----------|---------------------------|--------------------|--------------------------------------|----------------------|
| Montreal | 432                       | 388 (89.8)         | 258 (59.7%)                          | 53.3 (17.3)          |
| Calgary  | 270                       | 250 (92.6%)        | 145 (53.7%)                          | 52.7 (15.5)          |
| Halifax  | 313                       | 277 (88.5)         | 283 (90.4%)                          | 58.1 (15.5)          |
| Winnipeg | 234                       | 220 (94%)          | 159 (68.0%)                          | 56.3 (14.0)          |
| Quebec   | 126                       | 107 (84.9%)        | 118 (93.7%)                          | 54.5 (15.0)          |

any reason. We used this sampling reference to determine the number of SLE patients from these cohorts who were hospitalized for COVID from March 31, 2020, to April 1st, 2021 (which included the first and second pandemic waves). During this time in Canada, vaccination against COVID was available primarily to nursing home residents and health care workers only.

**Results:** During March 31, 2020, to April 1, 2021, in the Canadian cohorts there were 432 patients from Montreal, 270 from Calgary, 313 from Halifax, 234 from Winnipeg, and 126 from Quebec (Table). Most (1242/1375, 90%) were female and in their 50s. White race/ethnicity ranged from 93.7% (Quebec City) to 53.7% (Calgary). Out of these 1,375 Canadian SLE patients followed in clinical cohorts, no hospitalizations for COVID had been recorded between March 31, 2020, and April 1, 2021. Potential limitations: These data are limited by the fact that these represent only patients from academic centres, and we relied on active reporting of patients to their physicians, in combination with annual assessments of (all-cause) hospitalization, which may have missed some events. Also, we are focused on COVID hospitalizations, not COVID infections, which did occur in some cohort members over this period. Our findings may not reflect COVID infections in the post-Delta variant era.

**Conclusion:** These data are interesting to consider given contrasting findings of COVID hospitalizations in SLE patients (in US and other jurisdictions) during the first wave [1] of the pandemic. Differences may in part be due to variations in race/ethnicity, urban-versus-rural residence, health care access, and potentially clinical variables (eg, drugs, disease control). As well, sociological differences (eg, public and personal health measures and other factors) are likely important. Despite the very limited nature of these data, they provide a snapshot of hospitalizations for COVID in Canadian SLE patients followed in clinical research cohorts in the pre-vaccination period. References: [1.] Fernandez-Ruiz R. <https://onlinelibrary.wiley.com/doi/full/10.1002/art.41450>

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#### SARS-CoV-2 Seroprevalence, Seroconversion and Neutralizing Antibodies in a Systemic Lupus Erythematosus Cohort and Comparison to Controls

Katherine Buhler (University of Calgary, Calgary); Hannah Matthew (University of Calgary, Calgary); May Choi (University of Calgary, Calgary); Ksenia Gukova (University of Calgary, Calgary); Francesca Cardwell (University of Waterloo, Waterloo); Heather Waldhauser (University of Calgary, Calgary); Ann Clarke (University of Calgary, Calgary); Marvin Fritzier (University of Calgary, Calgary)

**Objectives:** At the outset of the SARS-CoV-2 pandemic, it was speculated that systemic lupus erythematosus (SLE) patients may be at significant risk of COVID-19 due to underlying immune dysregulation and immunosuppressive therapies. We examined the prevalence of SARS-CoV-2 antibodies, RT-PCR positivity, and neutralizing antibodies in a local SLE cohort prior to vaccination compared to controls.

**Methods:** Pre-pandemic serum samples biobanked prior to 01/01/2020 and intra-pandemic samples collected from 03/15/2020-01/31/2021 were tested for SARS-CoV-2 antibodies using an ELISA measuring IgA and IgG anti-spike 1 (S1) protein (Euroimmun AG, Lübeck, Germany) and an assay detecting IgG antibodies to nucleocapsid (N), S1 receptor binding domain (RBD), and S1 (Luminex Corporation, Austin, TX). 100 pre-pandemic and 148 intra-pandemic sera (ie, 248 unique individuals) from unselected ambulatory individuals undergoing autoantibody testing served as controls. Pre-pandemic and intra-pandemic SLE and control samples with antibodies to at least one SARS-CoV-2 antigen were tested for neutralizing antibodies using the Surrogate Virus Neutralization Test (GenScript Biotech Corporation, Piscataway, NJ). RT-PCR tests were performed on the SLE cohort if clinically indicated and results retrospectively collected until 01/31/2021.

**Results:** 173 SLE patients were included (94.8% female, mean age 48.5 years, 83.2% prescribed hydroxychloroquine, 28.9% corticosteroids, and 43.9% other immunomodulators). None of the SLE patients had pre-pandemic SARS-CoV-2 antibodies versus 6% of controls (difference -6.0%, 95% CI: -10.7%, -1.4%; Table 1). Comparable proportions of SLE patients and controls had at least one intra-pandemic SARS-CoV-2 antibody (3.5% versus 4.7%, difference -1.2%, 95% CI: -5.6%, 3.2%). Intra-pandemic seroprevalence of anti-N IgG in SLE patients was lower than in the general population (Calgary, AB) over a similar observation interval (0.6% vs 2.9%, difference -2.3%, 95% CI: -3.6%, -1.0%). 7.5% (6/80) of SLE patients had a positive RT-PCR. None of the nine SLE patients with either intra-pandemic SARS-CoV-2 antibodies and/or positive RT-PCR were hospitalized. Two of six SLE patients with at least one SARS-CoV-2 intra-pandemic antibody developed neutralizing antibodies; both had anti-RBD IgG antibodies. None of six pre-pandemic and 4/7 intra-pandemic controls with at least one antibody to SARS-CoV-2 had neutralizing antibodies.

**Table 1.** SLE cohort patients and controls with pre- and/or intra-pandemic SARS-CoV-2 antibodies.<sup>1</sup>

|                                      |                                                  | SLE, n (%)<br>(n = 173)   | Controls, n (%)<br>(pre-pandemic, n = 100; intra-pandemic, n = 148) | Difference between cohort and controls, % (95% CI) |                   |
|--------------------------------------|--------------------------------------------------|---------------------------|---------------------------------------------------------------------|----------------------------------------------------|-------------------|
| Pre-Pandemic                         | ELISA                                            | Anti-S1 IgA <sup>2</sup>  | 0 (0.0)                                                             | 3 (3.0)                                            | -3.0 (-6.3, 0.3)  |
|                                      |                                                  | Anti-S1 IgG <sup>3</sup>  | 0 (0.0)                                                             | 4 (4.0)                                            | -4.0 (-7.8, 0.1)  |
|                                      | xMAP <sup>4</sup>                                | Anti-N IgG <sup>5</sup>   | 0 (0.0)                                                             | 2 (2.0)                                            | -2 (-4.7, 0.7)    |
|                                      |                                                  | Anti-RBD IgG <sup>6</sup> | 0 (0.0)                                                             | 0 (0.0)                                            | 0 (-0.0, 0)       |
|                                      |                                                  | Anti-S1 IgG <sup>4</sup>  | 0 (0.0)                                                             | 0 (0.0)                                            | 0 (-0.0, 0)       |
|                                      | Patients with at least one antibody <sup>7</sup> | 0 (0.0)                   | 6 (6.0)                                                             | -6.0 (-10.7, -1.4)                                 |                   |
| Neutralizing Antibodies <sup>8</sup> | 0 (0.0 <sup>9</sup> )                            | 0 (0.0 <sup>9</sup> )     | NA                                                                  |                                                    |                   |
| Intra-Pandemic                       | ELISA                                            | Anti-S1 IgA <sup>2</sup>  | 1 (0.6)                                                             | 3 (2.0)                                            | -1.4 (-3.9, 1.1)  |
|                                      |                                                  | Anti-S1 IgG <sup>3</sup>  | 5 (2.9)                                                             | 5 (3.4)                                            | -0.5 (-4.3, 3.3)  |
|                                      | xMAP <sup>4</sup>                                | Anti-N IgG <sup>5</sup>   | 1 (0.6)                                                             | 5 (3.4)                                            | -2.8 (-5.9, 0.3)  |
|                                      |                                                  | Anti-RBD IgG <sup>6</sup> | 2 (1.2)                                                             | 3 (2.0)                                            | -0.8 (-3.6, 2.0)  |
|                                      |                                                  | Anti-S1 IgG <sup>4</sup>  | 0 (0.0)                                                             | 1 (0.7)                                            | -0.7 (-1.1, -0.2) |
|                                      | Patients with at least one antibody <sup>7</sup> | 6 (3.5)                   | 7(4.7)                                                              | -1.2 (-5.6, 3.2)                                   |                   |
| Neutralizing Antibodies <sup>8</sup> | 2 (33.3)                                         | 4 (57.1)                  | Not done <sup>9</sup>                                               |                                                    |                   |
| RT-PCR (+/-)                         | 6 (7.5 <sup>9</sup> )                            | NA                        |                                                                     |                                                    |                   |

Bolded differences indicate statistical significance.

Abbreviations: ELISA, enzyme-linked immunosorbent assay; IgA, immunoglobulin A; IgG, immunoglobulin G; N, nucleocapsid; NA, not applicable; RBD, receptor binding domain; RT-PCR, reverse transcription-polymerase chain reaction; S1, spike 1 protein; SLE, systemic lupus erythematosus.

<sup>1</sup> None of the SLE patients received a COVID vaccination prior to intra-pandemic testing. None of the controls received a COVID vaccination prior to pre-pandemic sampling. We were unable to verify the vaccination status of the intra-pandemic control samples, but there was very limited vaccine available in Canada prior to January 31, 2021.

<sup>2</sup> Cut-off for positivity: 1.9 OD ratio

<sup>3</sup> Cut-off for positivity: 0.8 OD ratio

<sup>4</sup> Cut-off for positivity: 700 MFI

<sup>5</sup> Identified by either ELISA or xMAP assays

<sup>6</sup> Cut-off for positivity: 20%

<sup>7</sup> Only patients positive for SARS-CoV-2 antibodies pre- and/or intra-pandemic were assessed for neutralizing antibodies (pre-pandemic, n = 6

controls, n=0 SLE; intra-pandemic, n=7 controls, n=6 SLE)

<sup>8</sup> 80 patients had a RT-PCR performed.

<sup>9</sup> Statistical testing not done due to low n.

demographic SARS-CoV-2 antibodies versus 6% of controls (difference -6.0%, 95% CI: -10.7%, -1.4%; Table 1). Comparable proportions of SLE patients and controls had at least one intra-pandemic SARS-CoV-2 antibody (3.5% versus 4.7%, difference -1.2%, 95% CI: -5.6%, 3.2%). Intra-pandemic seroprevalence of anti-N IgG in SLE patients was lower than in the general population (Calgary, AB) over a similar observation interval (0.6% vs 2.9%, difference -2.3%, 95% CI: -3.6%, -1.0%). 7.5% (6/80) of SLE patients had a positive RT-PCR. None of the nine SLE patients with either intra-pandemic SARS-CoV-2 antibodies and/or positive RT-PCR were hospitalized. Two of six SLE patients with at least one SARS-CoV-2 intra-pandemic antibody developed neutralizing antibodies; both had anti-RBD IgG antibodies. None of six pre-pandemic and 4/7 intra-pandemic controls with at least one antibody to SARS-CoV-2 had neutralizing antibodies.

**Conclusion:** Our SLE cohort had a lower rate of seropositivity pre-pandemic and a slightly lower to similar rate of seropositivity intra-pandemic compared to controls. It is unclear which factors influence SARS-CoV-2 infection in SLE, but as no pre-pandemic SARS-CoV-2 IgG antibodies were observed in our SLE cohort, this seems an unlikely explanation for protection against COVID-19. Future efforts should focus on vaccine responses in SLE.

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#### Screening for Cognitive Impairment with the Automated Neuropsychological Assessment Metrics in Patients with Systemic Lupus Erythematosus

Ruyi Pan (University of Toronto, Toronto); Juan Diaz-Martinez (Division of Rheumatology, Toronto Western Hospital, University Health Network; University of Toronto, Toronto); Jessica Gronsbell (University of Toronto, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** The American College of Rheumatology Neuropsychological Battery (ACR-NB) is the standard screening test for cognitive impairment (CI) in systemic lupus erythematosus (SLE). While the ACR-NB is validated for classifying definite, indeterminate, or non-CI, the Automated Neuropsychological Assessment Metrics (ANAM) is an accessible alter-

Table 1: ANAM subtests selected for prediction of ACR-NB CI status from the proportional odds cumulative logits model.

| ANAM Domain                    | Subtest                       | Score     |
|--------------------------------|-------------------------------|-----------|
| Fine Motor Processing          | Tapping right                 | CV        |
|                                | Tapping left                  | MR<br>CV  |
| Attention and Processing Speed | Simple reaction time          | MR        |
|                                | Procedural reaction time      | MR<br>PCT |
|                                | Simple reaction time-repeated | MR        |
|                                |                               | CV        |
|                                | Two choice reaction time      | MR        |
|                                |                               | PCT       |
|                                | Running memory                | CV        |
| MR                             |                               |           |
| PCT                            |                               |           |
| Visual-Spatial Perception      | Spatial processing            | CV        |
|                                |                               | MR        |
| Language Processing            | Logical relations             | PCT       |
|                                |                               | CV        |
| Learning Memory                | Code substitution learning    | MR        |
|                                |                               | PCT       |
|                                | Matching to sample            | CV        |
|                                |                               | MR        |
|                                | Code substitution delayed     | PCT       |
|                                |                               | CV        |
| Executive Functioning          | Math processing               | MR        |
|                                |                               | PCT       |
|                                | Go no go                      | CV        |
|                                |                               | MR        |
|                                | Tower puzzle                  | PCT       |

native for the ACR-NB. Since one third of SLE patients are classified as indeterminate CI in practice and didn't be considered in previous study, our objectives in this study were to: (i) identify ANAM subtests predictive of CI, (ii) develop an initial approach for classifying definite, indeterminate, or non-CI, (iii) evaluate performance relative to the ACR-NB.

**Methods:** 211 adult SLE patients were given the ACR-NB and ANAM on the same day at a single center in 2016-2018. The ACR-NB scores across the 6 domains are standardized by age and gender to define CI as: definite: z-score  $\leq -1.5$  in  $\geq 2$  domains, indeterminate: z-score  $\leq -1.5$  in 1 domain, or non: z-scores in all domains  $> -1.5$ . The ANAM has 7 domains with 15 subtests scored with the mean reaction time (MR), percentage correct responses (PCT), the coefficient of variation of the MR (CV), and/or throughput (TH). To classify ACR-NB CI status with the ANAM subtests, we fit 6 models with all subtests: 4 with one score each, one with MR, CV, and PCT, and one with MR, CV, PCT, and TH. In each setting, we fit a proportional odds cumulative logit model with the adaptive elastic net penalty using the log transformed ANAM subtest scores. The penalized fitting identifies relevant subtests by shrinking coefficients of irrelevant subtests to zero. Performance estimates relative to the ACR-NB were obtained with weighted 3-fold cross-validation.

**Results:** The best performing model included the MR, CV, and PCT scores. The selected 36 subtest scores are presented in Table 1. Overall accuracy for classifying the ACR-NB CI status is: 33.8% for non-CI, 41.2% for indeterminate, and 77.4% for definite. The model performs well for definite CI compared to ACR-NB. Used as a screening test for CI relative to indeterminate or non-CI, the model has a sensitivity of 0.62 (95% confidence interval: 0.48-0.76), specificity of 0.72 (0.60-0.88), and area under the curve of 0.76 (0.69-0.80).

**Conclusion:** This is the first study to evaluate the ANAM in discriminating definite, indeterminate, and non-CI in a real world SLE population. The ANAM holds promise as a CI screener and warrants further assessment.

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### The New EULAR/ACR 2019 SLE Classification Criteria: A Predictor of Long-term Outcomes

Laura Whittall-Garcia (University Health Network, Toronto); Dafna Gladman (Krembil Research Institute, Toronto Western Hospital,

Toronto); Murray Urowitz (University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto); Sindhu Johnson (Toronto Scleroderma Program, Mount Sinai Hospital; Division of Rheumatology, Toronto Western Hospital; Department of Medicine, and Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** We recently demonstrated that a EULAR/ACR classification Criteria score  $\geq 20$  predicts a higher disease activity throughout the first 5 years after diagnosis. A score of 20 was used as a threshold based on ROC analysis. We aimed to determine the ability of a EULAR/ACR score  $\geq 20$  to predict damage accrual and mortality.

**Methods:** 867 SLE patients from the Toronto Lupus Clinic were included (all recruited in the first year after diagnosis). For each patient, the EULAR/ACR score was calculated based on baseline information. Patients were divided into 2 groups depending on their score  $< 20$  or  $\geq 20$ . The following outcomes were assessed: - Time to first damage accrued: First increase in SDI from 0 to  $\geq 1$  within the first 10 years after SLE diagnosis. - Time to any increase in damage: Any increase in the SDI within the first 10 years after SLE diagnosis. - Time to death within the first 10 years after SLE diagnosis. - Mean SDI score at the 10th year of follow-up.

**Results:** Of 867 patients included, 87.5% were woman. At baseline the mean age was 36.2 years, the mean disease duration was 0.2 years, and the mean SDI score was 0.1, which was the same for both groups ( $P = 0.13$ ). The proportion of patients who accrued damage within the first 10 years was significantly higher in the group with the higher score, 46% vs 40%, score  $\geq 20$  vs  $< 20$  respectively ( $P = 0.02$ ). On multivariable regression analysis, after adjusting for age and ethnicity, a score  $\geq 20$  continued to significantly predict accrual of first damage and any increase in SDI throughout the first 10 years of follow-up. (Table 1). The mean SDI at 10 years was significantly higher in the group with a score of  $\geq 20$ , 1.28 vs 0.97, score  $\geq 20$  vs  $< 20$  respectively ( $P = 0.03$ ). When looking at the specific domains, the group with a score  $\geq 20$  at the 10th year had significantly more renal damage ( $P = 0.006$ ) and a higher percentage of diabetes ( $P = 0.01$ ). In total 68 patients (7.8%) died within the first 10 years of follow-up. The percent of deaths was higher in the group with a score  $\geq 20$ , 9.7% vs 5.8% score  $\geq 20$  vs  $< 20$  respectively ( $P = 0.03$ ). Individuals in the group with a score of  $\geq 20$  had twice the probability of dying (Table 1).

**Conclusion:** A EULAR/ACR score  $\geq 20$  is a predictor of damage accrual and mortality in SLE.

| Table 1: Univariate and Multivariable Cox Regression analysis. Factors associated with damage accrual and death within 10 years of follow-up. |                           |         |                              |         |
|-----------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|---------|------------------------------|---------|
|                                                                                                                                               | Univariate Cox Regression |         | Multivariable Cox Regression |         |
| First damage accrued (Initial SDI* >0) <sup>†</sup>                                                                                           |                           |         |                              |         |
| VARIABLE                                                                                                                                      | Hazard Ratio (95% CI)     | P value | Hazard Ratio (95% CI)        | P value |
| Age at first visit                                                                                                                            | 1.02 (1.01-1.03)          | <0.001  | 1.02 (1.02-1.03)             | <0.001  |
| Caucasian vs non-caucasian                                                                                                                    | 0.88 (0.71-1.10)          | 0.27    | 0.91 (0.73-1.14)             | 0.42    |
| EULAR/ACR score < or $\geq 20$                                                                                                                | 1.25 (1.01-1.54)          | 0.04    | 1.33 (1.07-1.64)             | 0.009   |
| Any increase in SDI <sup>†</sup>                                                                                                              |                           |         |                              |         |
| Age at first visit                                                                                                                            | 1.02 (1.01-1.03)          | <0.001  | 1.02 (1.01-1.03)             | <0.001  |
| Caucasian vs non-caucasian                                                                                                                    | 0.88 (0.71-1.08)          | 0.22    | 0.89 (0.72-1.11)             | 0.31    |
| EULAR/ACR score < or $\geq 20$                                                                                                                | 1.21 (0.98-1.48)          | 0.07    | 1.3 (1.04-1.57)              | 0.02    |
| Mortality                                                                                                                                     |                           |         |                              |         |
| Age at first visit                                                                                                                            | 1.05 (1.03-1.06)          | <0.001  | 1.05 (1.03-1.07)             | <0.001  |
| Caucasian vs non-caucasian                                                                                                                    | 1.46 (0.84-2.57)          | 0.17    | 1.48 (0.84-2.62)             | 0.17    |
| EULAR/ACR score < or $\geq 20$                                                                                                                | 1.66 (1.01-2.73)          | 0.04    | 2.13 (1.28-3.54)             | 0.003   |

\* 57 patients who had damage at entry were excluded for the analysis

<sup>†</sup> SLICC/ACR Damage Index

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### Factors Associated With Employment and Work Disability in Patients With SLE: A Nested Case-control Study

Connor Maddock (University College Dublin, Dublin); Behdin Nowrouzi-Kia (University of Toronto, Toronto); Jiandong Su (Toronto



Western Hospital, Toronto); Zahi Touma (Centre for Prognosis Studies, Division of Rheumatology, Toronto Western Hospital, University Health Network, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto)

**Objectives:** Systemic lupus erythematosus (SLE) can range in severity, resulting in some patients being unable to continue working while others can remain employed. This study aimed to analyze and compare factors including disease activity between work disabled and employed SLE patients to elucidate variables associated with unemployment.

**Methods:** This is a cross-sectional study focused on the status of last employment reported on 1110 adult SLE patients followed at a single centre where 746 patients were categorized as “Employed” and 364 as “Unemployed” (work disability or Sick Leave). In the employed group, 478 patients were matched to 297 patients in the unemployed group by 2:1 matching based on gender, inception status (first seen at clinic within 12 months of SLE diagnosis), disease duration at last visit ( $\pm$  3 years), ethnicity (Caucasian/non-Caucasian) and education level. Associations between variables and employment status were assessed using univariable and multivariable logistic regressions in a nested case-control study. Greedy matching algorithm was used to assemble cases and controls. Patients’ characteristics were compared by paired t-test and McNemar’s test, and a logistic regression was performed to examine patients’ demographics, disease activity, organ damage, disease burdens and treatment to the last employment status. Step-down variable selection method was adopted in the multivariable model building with Akaike Information Criterion (AIC) used as the model fitting statistics.

**Results:** Of the 775 patients those in the unemployed group showed significantly greater disease activity (higher adjusted mean SLEDAI-2K and SLEDAI-K Glucocorticoid index (SLEDAI-2KG) in the past five years and greater damage (by SDI). Patients were found to have a significantly higher prevalence of myocardial infarction, stroke, fibromyalgia, hypertension, and higher daily and cumulative glucocorticoid use. In the multivariable analysis (Table 1), age at SLE diagnosis (OR 95% CI: 1.04, 1.02-1.06), adjusted mean SLEDAI-2KG in past five years (OR 95% CI: 1.07, 1.03-1.12), SDI (OR 95% CI: 1.59, 1.40-1.80) and fibromyalgia (OR 95% CI: 3.84, 2.52-5.86) were associated with the increased risk of unemployment. Additional modeling where adjusted mean SLEDAI-2KG was substituted by adjusted mean SLEDAI-2K and cumulative glucocorticoid dose in the past five years, showed similar results to the previous model.

**Conclusion:** High disease activity, damage and use of glucocorticoids were associated with an increased likelihood of patients being unemployed. Similarly, fibromyalgia was strongly associated with a patient being unemployed. Employment status may be improved by better control of SLE disease activity and management of fibromyalgia and other risk factors.

Table 1: Univariate and multivariate conditional logistic regression analyses to assess the association with unemployment

|                                                                                  | Univariate Conditional Logistic Regression |                                          |                                          |                | Multivariate Conditional Logistic Regression with SLEDAI-2K + Glucocorticoids |                                          |                                          |                | Multivariate Conditional Logistic Regression with SLEDAI-2K |                                          |                                          |                |
|----------------------------------------------------------------------------------|--------------------------------------------|------------------------------------------|------------------------------------------|----------------|-------------------------------------------------------------------------------|------------------------------------------|------------------------------------------|----------------|-------------------------------------------------------------|------------------------------------------|------------------------------------------|----------------|
|                                                                                  | ORs Ratio Estimate                         | Lower 95% Confidence Limit for ORs Ratio | Upper 95% Confidence Limit for ORs Ratio | P > Chi-Square | ORs Ratio Estimate                                                            | Lower 95% Confidence Limit for ORs Ratio | Upper 95% Confidence Limit for ORs Ratio | P > Chi-Square | ORs Ratio Estimate                                          | Lower 95% Confidence Limit for ORs Ratio | Upper 95% Confidence Limit for ORs Ratio | P > Chi-Square |
| Age at SLE diagnosis                                                             | 1.04                                       | 1.02                                     | 1.06                                     | <0.001         | 1.04                                                                          | 1.02                                     | 1.06                                     | 0.0002         | 1.04                                                        | 1.02                                     | 1.06                                     | 0.0001         |
| Adjusted Mean SLEDAI-2K in last five years                                       | 1.08                                       | 1.04                                     | 1.13                                     | 0.0008         | 1.06                                                                          | 1.00                                     | 1.12                                     | 0.07           | 1.07                                                        | 1.03                                     | 1.12                                     | 0.002          |
| Adjusted Mean SLEDAI-K in last five years                                        | 1.09                                       | 1.05                                     | 1.13                                     | <0.001         |                                                                               |                                          |                                          |                | 1.07                                                        | 1.03                                     | 1.12                                     | 0.002          |
| Last SDI score                                                                   | 1.60                                       | 1.40                                     | 1.79                                     | <0.001         | 1.58                                                                          | 1.39                                     | 1.79                                     | <0.0001        | 1.58                                                        | 1.40                                     | 1.80                                     | <0.0001        |
| Myocardial infarction within last five years                                     | 3.80                                       | 1.43                                     | 9.58                                     | 0.0009         |                                                                               |                                          |                                          |                |                                                             |                                          |                                          |                |
| History of stroke within last five years                                         | 3.68                                       | 1.41                                     | 9.48                                     | 0.0007         |                                                                               |                                          |                                          |                |                                                             |                                          |                                          |                |
| Fibromyalgia within last five years                                              | 3.67                                       | 2.42                                     | 5.96                                     | <0.001         | 3.88                                                                          | 2.54                                     | 5.84                                     | <0.0001        | 3.88                                                        | 2.52                                     | 5.86                                     | <0.0001        |
| Hypertension <sup>1</sup> within last five years                                 | 2.69                                       | 1.52                                     | 4.89                                     | <0.001         |                                                                               |                                          |                                          |                |                                                             |                                          |                                          |                |
| Dyslipidemia <sup>2</sup> within last five years                                 | 2.26                                       | 1.62                                     | 3.14                                     | <0.001         |                                                                               |                                          |                                          |                |                                                             |                                          |                                          |                |
| Cumulative dose of glucocorticoids within last five years in the last 5 years    | 1.13                                       | 1.13                                     | 1.14                                     | <0.001         | 1.07                                                                          | 1.06                                     | 1.08                                     | 0.044          |                                                             |                                          |                                          |                |
| Average dose taken on glucocorticoids within last five years in the last 5 years | 1.07                                       | 1.04                                     | 1.09                                     | <0.001         |                                                                               |                                          |                                          |                |                                                             |                                          |                                          |                |

<sup>1</sup> Hypertension defined as blood pressure  $\geq$ 140/90 mmHg or treated with antihypertensive

<sup>2</sup> Dyslipidemia defined as abnormal total cholesterol or low-density lipoprotein levels or treated with antidiyslipidemic agents

### 135 Cerebral Vasculitis as an Initial Presentation of Systemic Lupus Erythematosus

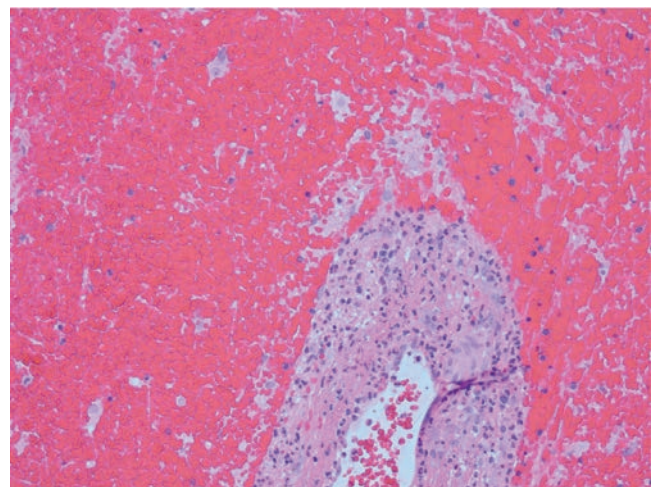
Siobhan Deshauer (McMaster, Hamilton); Haonan Mi (Queen’s University,

Kingston); John Provias (McMaster University, Hamilton); Konstantinos Tselios (University of Toronto, Toronto)

**Background:** Cerebral vasculitis is a rare manifestation of SLE, with a post-mortem incidence of < 10%. Symptoms range from headache to psychosis or seizures. While imaging modalities can be helpful in the diagnosis, brain biopsy remains the gold standard.

**Case Description:** A previously healthy 29-year-old Black male presented to hospital with a 3-day history of fever, and a 1-day history of vomiting, ataxia and right sided weakness. Laboratory investigations showed hemolytic anemia (Hb = 81 g/l), severe thrombocytopenia (PLT = 6000/ $\mu$ l), lymphopenia (300/ $\mu$ l) and acute kidney injury (creatinine = 263  $\mu$ mol/l); the remaining tests were normal. Brain MRI showed a left frontal intracranial mass (diameter 4.2 cm) with extensive vasogenic edema causing a 1-cm rightward midline shift. After 24 hours, the patient had a rapid decline in his level of consciousness following an episode of emesis and an urgent CT scan revealed an intrasubarachnoid hemorrhage. He underwent a decompressive craniotomy and evacuation of the hemorrhage. Pathology from a brain biopsy showed fibrinoid necrosis, perivascular and transmural mononuclear infiltration (predominantly T cells and macrophages), consistent with vasculitis (Figure). His autoimmune profile was positive for antinuclear antibodies, anti-dsDNA antibodies (559 IU/ml, normal range < 10), positive anti-Sm, anti-SSA/Ro and anti-RNP antibodies. Antiphospholipid antibodies (including lupus anticoagulant, anticardiolipin and anti-b2GPI antibodies) were negative. A diagnosis of deficiency of adenosine deaminase 2 (DADA2) was ruled out with urine purine and pyrimidine. The patient was diagnosed with cerebral vasculitis secondary to systemic lupus erythematosus (SLE). He was treated with intravenous pulses of glucocorticoids (methylprednisolone 1000 mg/day for 3 consecutive days), cyclophosphamide (750 mg/m<sup>2</sup> of body surface area) and hydroxychloroquine 400 mg daily. His level of consciousness, renal function, anemia and thrombocytopenia improved rapidly, and he was discharged after 2 weeks without any residual neurologic deficits.

**Conclusion:** This case report highlights this rare SLE manifestation and the successful treatment with corticosteroids and cyclophosphamide.



### 136 A Rare Case of Scleroderma Renal Crisis in a Patient with Systemic Sclerosis-Systemic Lupus Erythematosus (SSc-SLE) Overlap

Amanda Hu (St. Joseph’s Health Care London, London); Surosh Rouhani (Department of Medicine, Western University, London); Sherry Rohekar (Western University, London)

**Objectives:** Scleroderma (systemic sclerosis; SSc) is an immune disorder characterized by inflammation, vasculopathy, and fibrosis. Scleroderma has high morbidity and mortality, often cited to have reduced quality of life.[1] There are associated complications including scleroderma renal crisis (SRC).

SRC occurs in 5% of patients with SSc and is characterized by malignant hypertension and acute renal failure.[2] Furthermore, increased age at scleroderma onset is strongly associated with cancer risk.[3-5] In an already rare disease entity, there is a cohort of people who also have an overlap syndrome with systemic lupus erythematosus (SSc-SLE). Little is known about the epidemiology, clinical characteristics and survival of these patients. We aim to describe a case of an 82-year-old female who presented with scleroderma renal crisis and rapidly progressive diffuse SSc with features meeting EULAR/ACR classification criteria for SLE.

**Methods:** We obtained informed consent from the patient's Power of Attorney for the use of photography and description of the patient's case, omitting any identifiers, for educational purposes.

**Results:** Our patient presents to hospital with hypertensive emergency, chest pain, and shortness of breath. She had multiple bloodwork abnormalities including hemolytic anemia and thrombocytopenia, as well as elevated cardiac enzymes, prompting admission. The question of scleroderma was raised when a trainee recognized the characteristic skin tightening and digital ulcers. Rheumatologic assessment concluded that she had rapidly progressive diffuse SSc with significant skin tightening in the hands, arms past the elbows, chest, and lower limbs, digital ulcers, and dilated nailfold capillaries. She was diagnosed with Raynaud's phenomenon three years ago but only started to have skin tightening in the last three months. During this time, she also had sicca symptoms, dysphagia, and oral ulcers. During admission, captopril was promptly initiated with other antihypertensives. Other investigations yielded an organized pericardial effusion, pleural effusion, and ascites. Her blood work was significant for strongly positive ANA 1:1280, Scl70, anti-RNP/Anti-Smith, Anti-Ro 52. She had low complements and creatinine of 500  $\mu\text{mol/L}$  with oliguria.

She met the ACR/EULAR classification criteria for SSc, as well as the EULAR/ACR criteria for SLE. In a bid to avoid dialysis, the decision was made to initiate oral cyclophosphamide, as pulsed prednisone would likely exacerbate her SRC.

**Conclusion:** Rapidly progressive diffuse scleroderma with SLE overlap carries a poor prognosis as therapeutic decisions are not clear cut. In addition, late age of presentation is worrisome for underlying malignancy. References: [1.] Almeida C. *Autoimmun Rev* 2015;14:1087-96. [2.] Mouthon L. *Clin Rev Allergy Immunol* 2011; 40:84-91. [3.] Steen VD. *Am J Med* 1984;76:779-86. [4.] Hudson M. *J Rheumatol* 2007; 34:2218-23. [5.] Shah AA. *Arthritis Rheumatol* 2015;67:1053-61.

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### Early Systemic Sclerosis: Mitochondria, Fatigue and Fibromyalgia

Charmaine van Eeden (University of Alberta, Edmonton); Naima Mohazab (University of Alberta, Edmonton); Desiree Redmond (University of Alberta, Edmonton); Arthur Jones (University of Alberta, Edmonton); Andrew Mason (University of Alberta, Edmonton); Jan Willem Cohen Tervaert (University of Alberta, Edmonton); Mohammed Osman (University of Alberta, Edmonton)

**Objectives:** Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and Fibromyalgia (FM) are commonly described in patients with systemic sclerosis. Previous studies have not described this in patients with early Systemic Sclerosis (eSSc) (< 2 years of disease onset, without skin fibrosis). There are also no biomarkers that can distinguish patients with CFS/ME from patients with FM. To address this, we aimed to assess the frequency of mitochondrial transcripts in different patient groups.

**Methods:** All eSSc patients met the 2013 ACR/EULAR classification criteria. Rates of ME/CFS, FM, anxiety, depression and sleep disturbances were assessed through validated questionnaires. Expression of various mitochondrial electron transport chain (ETC) genes from blood was determined through qPCR. Relative frequency of oxidative phosphorylation was estimated by measuring the proportion of active (dephosphorylated) pyruvate dehydrogenase (PDH) in PBMCs which reflects its activity, and the rate limiting step controlling aerobic respiration.

**Results:** We found 48% of our eSSc patients fulfilled the diagnostic criteria for ME/CFS, with 75% of those patients having co-morbid FM. eSSc patients with fatigue were not distinguishable from idiopathic FM patients based on clinical evaluation for ME/CFS ( $P = 1.0$ ) and FM ( $P = 0.2$ ). eSSc patients with fatigue could be distinguished from FM patients through ETC gene analysis. Expression of ND4 ( $P = 0.002$ ) and CyB ( $P = 0.04$ ) were reduced in eSSc and Cox7C elevated ( $P = 0.04$ ) when compared to FM patients. Relative oxidative phosphorylation frequencies, as measured by the ratio of phosphorylated Pyruvate Dehydrogenase/Pyruvate Dehydrogenase, was not found to be significantly different between the disease groups.

**Conclusion:** A large proportion of eSSc patients suffer from co-morbid ME/CFS and FM. These symptoms may be linked to a novel mitochondrial signature affecting the efficiency of the electron transport chain. Further studies are needed to determine whether functional loss is also evident. These findings may lead to the development of pivotal clinical interventions for eSSc patients suffering from ME/CFS and FM and a deeper understanding. Funding: Our work was supported by an unrestricted research grant from Boehringer Ingelheim through an unrestricted investigator-initiated study, the Dutch Kidney Foundation (17PhD01); and Arthritis Society (19-0558).

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