

Canadian Rheumatology Association Meeting Virtual Congress February 24 – 26, 2021

The 75th Annual Meeting of The Canadian Rheumatology Association was held virtually on February 24–26, 2021. The program consisted of presentations covering original research, symposia, awards, and lectures. Highlights of the meeting include the following 2021 Award Winners: Distinguished Rheumatologist, Rachel Shupak; Distinguished Investigator, Sasha Bernatsky; Distinguished Teacher-Educator, Elaine Yacyshyn; Emerging Investigator, Zahi Touma; Ian Watson Award for the Best Abstract on SLE Research by a Trainee, Raffaella Carlomagno; Phil Rosen Award for the Best Abstract on Clinical or Epidemiology Research by a Trainee, Kimberley Yuen; Best Abstract by a Rheumatology Resident, Ariane Barbacki; Best Abstract on Basic Science Research by a Trainee, Andrew Kwan; Best Abstract by a Post-Graduate Research Trainee, Luiza Grazziotin; Best Abstract on Quality Care Initiatives in Rheumatology, Nadia Luca; Best Abstract by a Medical Student, Daniel Levin; Best Abstract by an Undergraduate Student, Anson Lee; Best Abstract by a Rheumatology Post-Graduate Research Trainee, Jennifer Lee; Best Abstract on Research by Young Faculty, Lihi Eder; Best Abstract on Spondyloarthritis Research, Sandeep Dhillon; Practice Reflection Award, Gold, Stephanie Gottheil; CRA Master Awards, Ciarán M. Duffy, Mary-Ann Fitzcharles, James M. Henderson. Lectures and other events included: Keynote Lecture by Danielle Martin: Delivering on What Matters: Lessons from Canada's Response to the COVID-19 Pandemic; State of the Art Lecture by Michael Libman: Vaccination and Travel: Should I or Shouldn't I?; Dunlop-Dottridge Lecture by Dan Kastner: Rheumatic Disease and the Human Condition; and the Great Debate: Be it Resolved that Telemedicine Allows Rheumatologists to Provide Excellent Care to Patients with Autoimmune Rheumatic Diseases. Arguing for: Alexandra Saltman and Tommy Gerschman, and against: Brent Ohata and Jocelyne Murdoch. 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*.

1

Retinal Toxicity in a Multinational Inception Cohort of Systemic Lupus Patients on Hydroxychloroquine

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Objectives: Despite the beneficial effects of hydroxychloroquine (HCQ) in systemic lupus erythematosus (SLE), retinal toxicity is a concern. Factors associated with retinal toxicity have been studied among long-term HCQ users but have not been described for incident SLE patients. We evaluated the incidence of HCQ-related retinal toxicity in a large, international, inception cohort of SLE patients, and assessed factors potentially associated with this event.

Methods: We analyzed prospective data from the Systemic Lupus International Collaborating Clinics (SLICC) cohort, that includes SLE patients from 33 sites in Europe, Asia, and North America, enrolled within 15 months of diagnosis. Using annual study visits between 1999-2019, we followed patients from first visit on HCQ (time zero/baseline) up to the time of retinal toxicity documentation (outcome) or death, loss to follow-up, or censoring at end of study interval. Retinal toxicity was identified based on the SLICC/ACR damage index item for retinal damage and cases were confirmed with chart review. Multivariable Cox regression was used to estimate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for baseline factors potentially associated with retinal toxicity (i.e., sex, race/ethnicity, age at SLE onset, HCQ daily dose/kg, body mass index, and smoking). We also plotted a Kaplan-Meier curve for probability of retinal toxicity related to total duration of HCQ therapy.

Results: A total of 1460 patients (89% female, 52% Caucasian) were included. Mean SLE duration at time zero (HCQ initiation) was 2.4 (standard deviation, SD 2.2) years and patients remained on HCQ an average of 6.4 (SD 4.2) years. Retinal toxicity was confirmed for 11 patients (incidence 1.0 per 1000 person-years) at a mean of 8.8 (SD 4.0) years. Our hazards regression model identified greater risk in patients who were older at SLE diagnosis, and non-significant trends for greater risk in black patients, those receiving more than 5 mg per kg at baseline, and overweight patients. In the Kaplan-Meier curve, the crude probability of retinal toxicity was less than

1% until 10 years of cumulative HCQ use, but increased around 1% each year after that, reaching 5% after 14 years.

Conclusion: In recent-onset SLE patients receiving HCQ, the probability of retinal toxicity increases after 10 years of cumulative use. We observed higher risks among those older at SLE onset and there were non-significant trends for greater risk in black patients, those receiving more than 5 mg/kg at baseline, and overweight patients. More sophisticated analyses with time-dependent variables are under way.

2

Risk of Serious Infections in Offspring Exposed In Utero to Ustekinumab

Jonah Gorodensky (McGill University, Montreal); Sasha Bernatsky (McGill University Health Centre, Montreal); Yvan St. Pierre (McGill University, Montreal); Kristian Filion (McGill University, Montreal); Evelyne Vinet (McGill University Health Centre, Montreal)

Objectives: Ustekinumab and other biologics, which harbour an Fc portion, are actively transported across the placenta, often reaching higher fetal than maternal levels. Ustekinumab, an IL-12/23 inhibitor, is indicated for use among patients with psoriasis (PsO), psoriatic arthritis (PsA), and inflammatory bowel disease (IBD), but there is currently little evidence regarding its safety in pregnancy. We compared the risk of serious infections in offspring exposed to ustekinumab, tumour necrosis factor inhibitors (TNFi), non-TNFi biologics, and non-biologic immunosuppressives versus offspring unexposed during pregnancy among women with PsO, PsA, or IBD.

Methods: We conducted a retrospective cohort study using the US MarketScan database, an employment insurance database. We included live (01/2011-12/2018) births among women with PsO, PsA, and/or IBD and a randomly selected group of unaffected mothers matched 10:1 on age, geographic location and year of delivery. Drug exposure was defined as ≥ 1 filled prescription or infusion procedure code during or within 3 months prior to pregnancy. In offspring, we evaluated serious infections within the first year of life. We performed multivariate analyses using logistic regression, adjusting for maternal age, co-morbidities, corticosteroids use, and preterm birth.

Results: We included 16,130 offspring born to 7,623 women with PsO/PsA, 8,319 with IBD, 188 with PsO/PsA and IBD, and 160,762 matched controls. A total of 52 women were exposed to ustekinumab, 51 to other non-TNFi biologics (mostly vedolizumab, $n = 36$), 1,588 to TNFi, 1,861 to non-biologic immunosuppressives alone, and 12,578 unexposed to any drug. The percent of serious infections in children exposed to ustekinumab (3.9%; 95% CI 0.5-13.9) was identical to that observed among children exposed to other non-TNFi biologics (3.9%; 95% CI 0.5-14.2). The risk was 2.6% (95% CI 1.9-3.6) in children exposed to TNFi, 2.4% (95% CI 1.8-3.3) among those exposed only to non-biologic immunosuppressives, and 2.6% (95% CI 2.3-2.9) among those unexposed to any drug. The percent of serious infections in children born to control mothers was 2.0% (95% CI 1.9-2.1). In multivariate analyses of children exposed to ustekinumab or non-TNFi biologics versus unexposed offspring born to affected mothers, our point estimates were consistent with increased risk, but the CIs were wide, including the null value [OR for ustekinumab 1.47 (95% CI 0.35-6.1); OR for non-TNFi biologics 1.38 (95% CI 0.34-5.54)].

Conclusion: In a large cohort of inflammatory disease offspring, we observed a potential trend for more serious infections in children exposed to ustekinumab or non-TNFi biologics versus unexposed offspring, although the CIs were wide, precluding strong conclusions.

3

Genome-wide Sequencing Identified Rare Genetic Variants for Childhood-onset Monogenic Systemic Lupus Erythematosus

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Andrea Knight (The Hospital for Sick Children/University of Toronto, Toronto); Daniela Dominguez (The Hospital For Sick Children, Toronto); Jingjing Cao (The Hospital for Sick Children, Toronto); Declan Webber (University of Toronto, Toronto); Deborah Levy (Division of Rheumatology, SickKids Hospital; Faculty of Medicine, University of Toronto, Toronto); Andrew Paterson (The Hospital for Sick Children, Toronto); Earl Silverman (Division of Rheumatology, The Hospital for Sick Children; Divisions of Translational Medicine and Genetics, SickKids Research Institute; 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)

Objectives: Our aim was to calculate the burden of rare variants in monogenic systemic lupus erythematosus (SLE) genes, in children suspected of monogenic SLE or lupus-like disease.

Methods: From our multiethnic cohort of cSLE patients at SickKids, Toronto, we examined demographic and clinical features, comparing groups with t-tests for continuous variables, and Fisher's exact test for categorical variables. We completed paired end whole genome sequencing (WGS) or whole exome sequencing (WES) in patients suspected of monogenic SLE. We prioritized rare (MAF < 1%) nonsynonymous variants (frameshift, missense and stop-gain) in 36 monogenic SLE genes and compared allele frequencies in our cohort to population frequencies in gnomAD (Chi-squared tests (Bonferroni correction $P < 7 \times 10^{-4}$)). We further prioritized predicted deleterious variants using Polyphen (> 0.446), SIFT (< 0.05) and/or CADD scores (≥ 15). We then considered zygosity and predicted mode of inheritance. We filtered for copy number variants (CNVs) > 1 kb in 36 monogenic SLE genes. Participants also underwent genotyping on the Illumina multiethnic MEGA or GSA array. Additive non-HLA and HLA SLE genetic risk scores (GRS) were calculated using common risk alleles. We tested the association between GRSs and the burden of nonsynonymous variants with logistic (0 vs. ≥ 1 variant) and multivariate analyses (0 vs. > 1), adjusted for sex (female, male), ancestry (Admixed, African, Amerindian, East Asian, Middle Eastern, South Asian) and age at diagnosis.

Results: The cohort included 71 patients (80% female), with a mean age at diagnosis of 8.5 years (SD ± 2.9) and 42% of patients with kidney or neuropsychiatric disease. We identified predicted disease-causing variants in 9 patients (13%) who were significantly younger at SLE diagnosis compared to those without a rare disease-causing variant (6.9 years (SD ± 2.1) vs. 8.8 years (SD ± 3.0), $P = 0.048$). We did not identify disease causing CNVs > 1 kb. We did not find a significant association between non-HLA GRS and carrying 1 or more rare nonsynonymous variants (OR = 1.42; 95% CI = 0.73, 2.91; $P = 0.32$), nor between HLA GRS and rare nonsynonymous variants (OR = 1.28; 95% CI = 0.12, 14.8; $P = 0.89$), in univariate and multivariable adjusted models. We also did not find a significant association between GRSs and rare nonsynonymous variant count in multivariate analyses.

Conclusion: We identified a likely causal genetic variant for monogenic SLE in 13% of patients sequenced. We did not detect a significant association between SLE-GRSs comprised of common SLE risk variants, and the number of rare nonsynonymous variants. Additional studies are needed to validate our findings.

4

Marijuana (Herbal Cannabis) Use in Patients Attending Outpatient Rheumatology Clinics after Cannabis Legalization

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Objectives: Following recreational cannabis legalization in Canada, increased interest in medical marijuana is anticipated among rheumatology

patients. There are limited data regarding cannabis for the treatment of rheumatic diseases, and little Canadian data regarding the prevalence of cannabis use in these patients. Furthermore, doses and routes are not standardized, product concentrations are not regulated, and physicians do not have control over how patients use cannabis after it is prescribed. Our aim is to assess the prevalence of marijuana use in a hospital-based rheumatology clinic patient population and to examine factors associated with the use of marijuana including perceived benefits and harms, associations with patient demographics, diagnoses, and severity of disease.

Methods: This is an observational study involving one thousand consecutive patients attending the Health Sciences Centre (HSC) Rheumatology Clinic. Patients are provided a questionnaire regarding cannabis use. Questions include whether cannabis use was recreational/for pleasure, or for medical reasons/symptom relief, previous and/or current use, specific symptoms relieved or side effects experienced and form, route and dose and source of cannabis. Rheumatologists complete a questionnaire to provide information regarding patients' diagnosis, demographics, comorbidities, rheumatologic medications and physician global disease severity.

Results: Preliminary data was analyzed from 675 initial patient surveys. A history of medical cannabis use was reported in 170 patients (25.2%), with 106 patients (15.7%) reporting current medical use. A history of recreational use was reported in 440 patients (65.2%), with current recreational use in 83 patients (12.3%). Sixty percent ($n = 305$) of patients with no history of medical cannabis use reported that they would consider it. The most common symptoms reported to be alleviated by marijuana among the 170 patients that had used medical cannabis were joint pain (141, 82.9%), poor sleep (117, 68.8%), anxiety (72, 42.4%), other pain (64, 37.6%), and fatigue (37, 21.8%).

Conclusion: These preliminary data suggest that a significant proportion of patients followed at the HSC Rheumatology Clinic use medical cannabis for symptom management. Our prevalence appears to be much higher than the 8.2% ever /6.5% current medical cannabis use reported (Fitzcharles et al, 2020) at McGill. This may indicate growing popularity of medical cannabis as the McGill study was conducted one year earlier, demographic factors such as age (mean age 53 vs 64 at McGill), or regional differences. Further completion of patient and physician surveys will improve our understanding of patterns of use and perceived harms and benefits.

5

Barriers and Facilitators to Physical Activity for People with Scleroderma: A Scleroderma Patient-centered Intervention Network (SPIN) Cohort Study

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Objectives: Regular physical activity is important to enhance health for people with systemic sclerosis (SSc; scleroderma), but there are barriers to engagement in activity. We previously identified physical activity barriers and facilitators via group interviews; however, the proportion of people with SSc experiencing barriers, their importance, and likelihood of using facilitators are not known. Our objectives were to determine the (1) prevalence and importance of barriers to physical activity experienced by people with SSc and (2) likelihood of using barrier-specific and general facilitators to physical activity.

Methods: We invited 1,707 participants enrolled in the Scleroderma

Patient-centered Intervention Network cohort to complete a separate survey to rate (4-point Likert scale): (1) importance of experienced barriers; (2) likelihood of using corresponding barrier-specific facilitators and general facilitators and whether they have previously tried them.

Results: Among 721 respondents, 13 barriers (12 medical-related, 1 motivation-related) were experienced by $\geq 25\%$ of total participants. Fatigue and Raynaud's phenomenon were considered 'important' or 'very important' by $\geq 50\%$ of participants; 7 other barriers, addressing limited hand function, activity restrictions due to various pathologic changes, and low motivation were considered 'important' or 'very important' by 26-50%. Overall, 23 of 103 facilitators were rated by $\geq 75\%$ as 'likely' or 'very likely' to use among those who experienced corresponding barriers; these facilitators focused on adapting exercise, taking care of one's body, keeping warm, and protecting skin. All facilitators were considered 'likely' or 'very likely' to use by $\geq 50\%$ of those who experienced the corresponding barrier and had tried them versus 12 of 103 among those with the barrier who had not tried them.

Conclusion: Medical-related barriers to activity were most commonly experienced and considered important; Raynaud's phenomenon and fatigue were the most commonly experienced. Facilitators widely considered likely to be used addressed adapting exercise type or setting, using health behaviours to take care of the body, and using clothing or materials to protect the skin or to keep warm. Participants who had tried facilitators were generally more likely to use them again compared to participants who had never tried them.

6

Are Patients with Immune Medicated Inflammatory Diseases More Likely to Receive COVID-19 Tests and Test Positive for SARS-CoV-2? A Matched Population-based Study

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Objectives: To investigate the probability of being tested and the risk of being found positive for COVID-19 in patients with immune mediated inflammatory diseases (IMIDs) compared with matched non-IMID comparators from the general population in Ontario.

Methods: A population-based, matched cohort study was conducted using health administrative data from adult Ontario residents from January to September 2020. Ten cohorts of the following IMIDs were assembled: rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, systemic autoimmune rheumatic diseases (including systemic lupus, scleroderma, Sjogren's, dermatomyositis/polymyositis, undifferentiated connective tissue disease), multiple sclerosis, iritis, inflammatory bowel disease (IBD), polymyalgia rheumatica (PMR) and vasculitis (including giant cell arteritis and other types of vasculitides). Each patient was matched with 5 non-IMIDs comparators based on age, sex, area of residence and living in long-term care (LTC). Between IMIDs and non-IMIDs, we compared the proportion tested for COVID-19, as well as those testing positive. Multivariable logistic regression analyses assessed sociodemographic factors associated with COVID-19 testing and positivity.

Results: A total of 505,302 IMID patients and 2,525,958 non-IMID comparators were assessed. Significantly more IMIDs patients versus non-IMIDs were tested for COVID-19 (18.3% vs. 14.6%), while the proportion of those who tested positive for COVID-19 was identical (0.3% of all patients in both groups). The age- and sex-standardized rate of COVID-19 testing was significantly higher in IMIDs than non-IMIDs (1,737.1 vs. 1,397.4 tested patients per 10,000 population, respectively). Overall, testing

rates were significantly higher across all IMIDs groups versus their respective matched non-IMID comparators, being highest in vasculitis, PMR and SARDs. The standardized rate of positive COVID-19 tests was similar in IMIDs and non-IMIDs patients (30.5 and 29.2 per 10,000 population). Overall, IMIDs patients were more likely to undergo COVID-19 testing (adjusted odds ratio, (adjusted-OR) 1.22, 95% CI 1.21, 1.23) and highest in vasculitis (adjusted-OR 1.56), PMR (adjusted-OR 1.36) and SARDs (adjusted-OR 1.33). While no association was observed between being found positive for COVID-19 and all IMIDs, vasculitis patients were more likely to have positive COVID-19 tests (adjusted-OR 1.19) while IBD patients were less likely to have positive tests (adjusted-OR 0.75). The strongest association with COVID-19 testing and positive testing was residence in LTC. Additional factors associated positive COVID-19 testing were multimorbidity, urban residence, and lower socioeconomic status.

Conclusion: Patients across all IMIDs were more likely to be tested for COVID-19 versus non-IMIDs patients, but their risk of being found positive for COVID-19 was not elevated overall.

7

Patient-Reported Outcome Response and Safety Profile in Patients With Moderately to Severely Active Rheumatoid Arthritis Treated With Baricitinib 2-mg

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Objectives: Baricitinib improved patient-reported outcomes (PROs) in patients with active rheumatoid arthritis (RA) and an inadequate response (IR) to ≥ 1 tumor necrosis factor inhibitors or other biological DMARDs (bDMARDs) [1], or to conventional synthetic DMARDs (csDMARDs) [2]. The objective of this post-hoc analysis was to describe the PRO response of baricitinib 2-mg versus placebo at Week 24 among patients who achieved minimally clinically important difference (MCID) improvement at Week 4 and Week 12, in addition to long-term safety of baricitinib 2-mg.

Methods: Data were assessed from two phase 3 studies, RA-BEACON (NCT01721044; bDMARD-IR patients) and RA-BUILD (NCT01721057; csDMARD-IR patients). PROs included pain by visual analog scale, HAQ-DI, Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration of morning joint stiffness (MJS), and Short-Form 36 physical component score (SF-36 PCS). MCID was defined as ≥ 10 mm reduction for pain, ≥ 0.22 -unit reduction for HAQ-DI, ≥ 3.56 -point improvement for FACIT-F, ≥ 30 -minute improvement for MJS duration, and ≥ 5 -unit improvement for SF-36 PCS. For each PRO, the proportion of patients who continued to report improvement \geq MCID at Week 24 were calculated based on those with MCID improvements at Week 4 and Week 12. An integrated long-term safety analysis of baricitinib 2-mg was reported.

Results: Among bDMARD-IR patients who achieved MCID in a specific PRO at Week 4, the proportion who continued improvement \geq MCID at Week 24 with baricitinib 2-mg vs. placebo were 66.3% vs. 40.5% ($P \leq 0.001$) for pain, 70.9% vs. 48.7% ($P \leq 0.01$) for HAQ-DI, 61.5% vs. 52.3% for FACIT-F, 71.8% vs. 40.4% ($P \leq 0.001$) for MJS duration, and 63.0% vs. 40.4% ($P \leq 0.05$) for SF-36 PCS; and among csDMARD-IR patients were 81.5% vs. 61.9% ($P \leq 0.001$) for pain, 75.4% vs. 61.2% ($P \leq 0.05$) for HAQ-DI, 72.1% vs. 57.8% ($P \leq 0.05$) for FACIT-F, and 73.1% vs. 49.3% ($P \leq 0.01$) for SF-36 PCS. A similar trend was observed among patients who achieved MCID in each PRO at Week 12. An integrated long-term safety analysis up to 6.9 years showed a safety profile for baricitinib 2-mg consistent with earlier analyses in RA [3].

Conclusion: Early clinically meaningful improvements in pain, physical function, fatigue, morning joint stiffness duration, and quality of life (physical component) continued to Week 24 with baricitinib 2-mg versus

placebo in patients with active RA. Baricitinib 2-mg maintained a similar safety profile with longer exposure. No new safety signals were identified. [1.] Smolen et al. *Ann Rheum Dis*. 2017;76(4):694-700. [2.] Emery et al. *RMD Open*. 2017;3(1): e000410. [3.] Genovese et al. *Lancet Rheumatol*. 2020;2(6):E347-E357.

8

Leveraging a Behaviour Change Model to Inform Key Elements for a National Implementation Plan of an Early Rheumatoid Arthritis (RA) Patient Decision Aid.

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Objectives: Despite the evidence to support the use of patient decision aids (PtDAs) to facilitate shared-decision making (SDM), they are rarely used in rheumatology practice. The objective of the study was to understand barriers to the use of PtDAs in rheumatoid arthritis (RA) within a behaviour change model to inform implementation strategies to improve SDM.

Methods: A qualitative approach was used to obtain perspectives from healthcare providers (HCPs) and patients living with RA on a PtDA for patients with newly diagnosed RA. Participants reviewed the PtDA and provided their perspectives on perceived facilitators and barriers to PtDA implementation. Data was collected through semi-structured interviews which were transcribed and analyzed by inductive thematic analysis. The Themes were then mapped to the Behaviour Change Wheel COM-B system ("capability = C", "opportunity = O", and "motivation = M") by the researchers, an implementation scientist and 2 patient partners to inform key elements of a national implementation strategy for the PtDA.

Results: A total of 15 HCPs and 15 people living with RA participated in the qualitative interviews. Inductive thematic analysis yielded 5 major themes presented as "lessons learned" (COM-B mapping denoted for each "lesson" as C, O, M). Lesson 1 was that paternalistic decision-making is a dominant practice in early RA (C, M). Lesson 2 was that the current decision-making model was unable to address all of the needs of people living with RA at diagnosis (C, O). Lesson 3 was that implementing PtDAs at diagnosis to facilitate SDM may be difficult without reform of arthritis models of care (C, O). Lesson 4 was that flexibility was necessary for successful implementation given diversity of models of care (C, O) and Lesson 5 was that HCPs had limited interest in further training opportunities about PtDAs (M, O). Five main elements were identified for potential inclusion in a national PtDA implementation strategy: 1) making the PtDAs directly available to patients through patient-accessible websites and educational material; 2) creating a SDM rheumatology curriculum; 3) leveraging allied health resources as "decision coaches"; 4) linkage of PtDAs to "living" rheumatology guidelines; 5) designing future trials of SDM in rheumatology to evaluate patient-important outcomes.

Conclusion: A multifaceted strategy is suggested to improve uptake of SDM through the use of PtDAs and future work is ongoing in innovative SDM trial development. Supported by a CIORA grant.

9

The Effect of the Shared Epitope on an Animal Model of Atherosclerosis

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Objectives: Rheumatoid arthritis (RA) is associated with HLA-DR4 alleles encoding major histocompatibility II molecules containing a consensus

sequence known as the Shared Epitope. The Shared Epitope binds strongly to citrullinated peptides leading to the production of anti-citrullinated protein/peptide antibodies (ACPA), which are highly specific for RA. Patients expressing ACPA are more likely to have joint erosions and RA complications, including cardiovascular disease (CVD). RA patients are at 1.5 times the risk of CVD compared to the general population and the risk is higher for patients who express HLA-DR4 and ACPA. The mechanisms by which HLA-DR4 and ACPA contribute to CVD risk in RA are unknown. The objective of this study is to generate a novel mouse model to study the role of HLA-DR4 in atherosclerosis.

Methods: Mice transgenic for human HLA-DR4 were cross-bred for 5 generations with LDL receptor knock-out (LDLR^{-/-}) mice that are known to develop atherosclerosis when fed a high-fat high-cholesterol (HFHC) diet. Genotype was confirmed by PCR. Male and female DR4tgLDLR^{-/-} mice (N = 24) and controls: DR4tg (N = 12), LDLR^{-/-} (N = 12) and wild-type B6 mice (N = 12) were fed a HFHC diet or regular chow for 12 weeks and monitored for weight gain and joint swelling. Blood samples were analysed for serum lipoproteins using a colorimetric assay. Heart, aorta, liver and limbs were collected, and sections stained by haematoxylin and eosin. Aortic plaque surface area was assessed by staining en face preparations of the aortas with SUDAN IV (stains lipids red).

Results: When fed a HFHC diet vs. regular chow, LDLR^{-/-} and DR4tgLDLR^{-/-} mice gained weight (P < 0.05) and had evidence of fatty liver on histopathology. Serum LDL levels were significantly higher in HFHC-fed LDLR^{-/-} vs. DR4tgLDLR^{-/-} (1602 mg/dL vs. 905.3 mg/dL, respectively; P = 0.0056), but the aortic plaque burden was similar for these two strains. B6 and DR4tg mice did not have any significant atherosclerotic plaque detected. None of the mice had detectable inflammatory arthritis.

Conclusion: In a mouse model of atherosclerosis, expression of HLA-DR4 led to lower levels of circulating LDL but a similar burden of atherosclerotic plaque, analogous to the RA lipid paradox where patients with lower LDL levels have high risks of CVD events.

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Perceptions, Facilitators and Barriers of Physical Activity in Axial Spondyloarthritis: Results from a Qualitative Study

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Objectives: The benefits of physical activity (PA) are well known for preventing chronic disease, improving function, and increasing musculoskeletal and cardiorespiratory fitness. Despite these benefits, most Canadians fall short of PA targets. It is well established that PA is fundamental in the management of axial spondyloarthritis (axSpA); however, evidence indicates that people with axSpA are not adhering to recommended guidelines for sufficient PA participation. Given the importance of PA in managing axSpA, the objectives this study were to: 1) determine axSpA patients' definition of PA; 2) identify facilitators and barriers to PA engagement and 3) explore the importance of PA in the context of axSpA.

Methods: Semi-structured, key informant interviews were conducted with axSpA patients attending an urban academic outpatient rheumatology clinic. Interviews were conducted by telephone, audio recorded and transcribed verbatim. Data were analyzed using a thematic approach: two study investigators independently assigned themes and codes to the data set according to study objectives. Key informant recruitment continued until saturation of emergent themes was reached. Themes were presented to the investigative team to allow for comparison and reconciliation. Systematic labeling of the dataset was completed using an inductive approach. QSR NVivo V8 was used for data management and aggregation of codes into common themes.

Results: In total, 12 interviews were conducted. Most respondents were

male (83.3%); mean age 45.5 (\pm 12.5) years; mean disease duration 21.5 (\pm 14.9) years. Approximately half were receiving biologic treatment (58.3%), mean Bath Ankylosing Spondylitis Disease Activity Index 2.5 (\pm 1.4) and mean Bath Ankylosing Spondylitis Functional Index 1.8 (\pm 1.9). Participants defined PA as any activity involving physical exertion including exercise and other activities (i.e., transportation, employment, housework and seasonal activities). Facilitators for PA engagement included intrinsic factors (symptom relief, impact on health and self-efficacy) and extrinsic factors (social support networks and facility access). Similarly, barriers to PA engagement included intrinsic factors (disease-related, fear of injury, and presence of comorbidities) and extrinsic factors (life demands, availability/time and environmental restrictions). The role of PA in axSpA management was well recognized and included symptom relief, the evolution of benefits and the impact on mental and physical health.

Conclusion: The results of this study provide insight into patients' understanding of PA within the context of axSpA in terms of definition, facilitators/barriers, and its role in disease management. The above findings will be informative when applied to education and self-management programs aimed at increasing PA engagement in patients with axSpA. Supported by a CIORA grant.

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The Long-Term Cardiac and Non-Cardiac Prognosis of Kawasaki Disease (KD): A Systematic Review

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Objectives: To examine long-term mortality, cardiac and non-cardiac prognosis of children following a diagnosis of Kawasaki Disease (KD).

Methods: A systematic literature search of Ovid Medline, Embase, Cochrane, and Clinicaltrials.gov was performed to identify studies from inception to June 2020. Included search terms were relevant to KD and prognosis, including mortality, major adverse cardiovascular events (myocardial infarctions (MI), stroke, and revascularization interventions), chronic cardiac conditions (hypertension, hyperlipidemia), and non-cardiac disease (including allergic diseases, infections, and systemic autoimmune diseases). Studies were eligible for data extraction if they met the following inclusion criteria: 1) human participants with KD, diagnosed < 18 years old, 2) controlled trials or observational studies, 3) reported mortality or clinically relevant cardiac or non-cardiac outcome at least one year following KD, and 4) English studies. Extracted data included study design, population characteristics, follow-up duration and outcomes.

Results: From 4621 abstracts, we included 71 studies from 13 countries for full extraction. The majority of studies (76%) originated from East Asian countries. Fifty-seven (80%) studies were retrospective cohort studies, 6(9%) were case-control studies, 2(3%) were prospective cohort studies, and 6(9%) were cross-sectional studies. Twenty-three studies (32%) had 1-5 years follow-up, 22(31%) had 5-10 years follow-up, 17(24%) had 10-15-year follow-up, and 9(13%) reported > 15-year follow-up. Thirty-one studies (44%) described mortality in 29,587 patients. Nine studies evaluated survival over time, with the mean 10-year, 20-year, and 30-year survival at 92% (SD: 7), 89% (SD: 7), and 81% (SD: 14), respectively. Eight studies, derived from one cohort, compared the overall mortality rate of KD patients to the general population, and found no difference. Fifty studies (70%) described a cardiac outcome in 44,377 patients, of which the most frequently evaluated outcomes were MI (60%) and cardiovascular revascularization (44%). The prevalence of MI was 9% and the mean 10-year MI event-free probability was 73% (SD: 24). Seven studies evaluated hypertension, of which 1 study suggested increased risk; 11 studies evaluated hyperlipidemia, of which 5 reported increased risk. Eleven studies (15%) described a non-cardiac outcome in 17,068 patients, including allergic diseases (n = 5), infections (n = 1), pregnancy (n = 1), malignancy (n = 1), ADHD (n = 2), exercise performance (n = 1), and vision (n = 1). Four

studies reported an increased risk of allergic diseases and 1 study reported an increased risk of malignancy.

Conclusion: Overall survival after KD appears to be favourable over a 30-year period. The majority of long-term studies evaluated major cardiac events like MI. There is insufficient evidence on the risk of chronic cardiac and non-cardiac comorbidities such as hypertension, hyperlipidemia, and malignancy in KD. Several studies reported an increased risk of allergic diseases after KD diagnosis. Best Abstract By A Rheumatology Post-Graduate Research Trainee.

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Disentangling the Web of Costs Associated with Juvenile Idiopathic Arthritis

Luiza Grazziotin (University of Calgary, Calgary); Marinka Twilt (Alberta Children's Hospital, Calgary); Gillian Currie (University of Calgary, Calgary); Michelle Kip (University of Twente, Enschede); Maarten Ijzerman (University of Melbourne, Melbourne); Deborah Marshall (University of Calgary, Calgary); UCAN CAN-DU Investigators Understanding Childhood Arthritis Network (Toronto)

Objectives: Juvenile idiopathic arthritis (JIA) is a chronic rheumatic disease affecting 1 in 1,000 children. The multifaceted care path for JIA can lead to significant expenditure for the healthcare system. There is a lack of real-world cost estimates for children diagnosed with JIA in Canada and we aim to assess these overall and JIA-associated costs.

Methods: A single center cohort of newly diagnosed JIA patients, attending the pediatric rheumatology clinic from 2011-2019 was identified using a validated JIA case ascertainment algorithm. Clinical variables were extracted from medical records and resource use was estimated from six administrative health databases, including hospital admission, emergency visits, ambulatory visits, practitioners' visits, drugs dispensation, and laboratory and imaging tests. Costs were assigned to each dataset using appropriate sources. We used descriptive statistics to summarise the overall and JIA-associated costs (JIA code as the main reason for the visit or procedure requested by the rheumatologist) as mean cost per patient (with 95% confidence intervals), standardized for a period of one year and stratified by subtype. Costs were adjusted for inflation and expressed in 2019 CAD.

Results: A total of 390 patients met the eligibility criteria. Oligoarticular and polyarticular JIA were the most common subtypes (36% and 36%, respectively), 60% female, and the median age was 10.9 years. The mean total overall and JIA-associated cost per patient for one-year time period was \$10,465 (95% CI: \$9,579-11,351) and \$5,477 (95% CI: \$4,901-6,053), respectively. Dispensed drugs, driven by use of biologic therapies, and outpatient visits were the greatest contributor to the total cost. The overall mean cost was constant over a six-year period from the first visit to the pediatric rheumatologist with practitioners and ambulatory care visits as the main cost drivers early on and then shifting with an increase in the proportion of drugs costs over time. Finally, systemic onset JIA had the highest mean overall cost (\$20,172, 95% CI: \$9,722-30,621), while oligoarticular arthritis had the lowest cost (\$6,952, 95% CI: \$5,946-7,959).

Conclusion: The care pathway for children diagnosed with JIA can be expensive, long, and complex - and varies by JIA subtype. Although the mean overall cost was stable, the change in the distribution of costs over time is explained by the introduction of biologic therapies later in the care pathway. This study provides better understanding of the JIA expenditure profile using a healthcare system perspective and can help inform future economic studies. Best Abstract By A Post-Graduate Research Trainee.

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Implementation and Evaluation of a Pediatric Musculoskeletal Examination Curriculum for Pediatric Residents

Kate Neufeld (University of Saskatchewan, Saskatoon); Piya Lahiry (The Hospital for Sick Children, Toronto); Herman Tam (BC Children's Hospital, Vancouver); Shirley Tse (The Hospital for Sick Children, Toronto)

Objectives: Pediatric musculoskeletal (MSK) physical examination is underemphasized during resident training. Previous needs assessment

demonstrates resident discomfort in performing MSK exams. A standardized, interactive approach with learner engagement, such as the pGALS (pediatric Gait Arms Legs Spine), has been suggested as ideal for MSK physical exam learning. The objective of this study was to assess whether a standardized pGALS curriculum would improve knowledge and confidence in performing a comprehensive screening pediatric MSK examination and improve detection of common MSK abnormalities in rheumatologic conditions at the PGY2 resident level.

Methods: Learners were second year pediatric residents on their rheumatology rotation between September 2019 to May 2020 at The Hospital for Sick Children. Educators were three pediatric rheumatology fellows. Self-efficacy (2 questions on a 10-point Likert scale) and knowledge (assessing detection of MSK abnormalities in 3 short answer questions, expressed as a percentage) were assessed using questionnaires pre- and post-rotation. Differences between mean pre- and post-rotation scores were examined using paired t-test with statistical significance of $P \leq 0.05$. The educational tools utilized were a standardized 15-minute pGALS instruction video and a modified pGALS checklist (scored out of 19) with 3 screenings questions and 16 physical exam maneuvers. Learners practiced pGALS throughout the rotation and were evaluated using the pGALS checklist. Competence-based evaluations (Elentra) were optional. Qualitative feedback was collected using open-ended questions.

Results: The curriculum was delivered to 9 learners (2 evaluated prior to creation of checklist). Pre-rotation ($n = 9$) mean self-efficacy score was 4.2 and mean content knowledge score was 96.3%. Post-rotation ($n = 9$) mean self-efficacy score was 7.8 and mean content knowledge score was 95.8%. Self-efficacy improved between pre- and post-rotation (difference of 3.6; $P = 0.0002$), but mean content knowledge was not significantly different (-3.0%; $P = 0.59$). The average pGALS checklist score post-rotation was 16.3/19 (85.5%, $n = 7$). Additionally, 5 learners were evaluated using Elentra and 4 achieved 'autonomy' competence levels. Qualitatively, residents reported the teaching was effective, interactive, and they enjoyed the hands-on approach.

Conclusion: This novel implementation and evaluation of a standardized MSK teaching curriculum in a Canadian pediatric resident cohort demonstrates that a standardized pGALS curriculum improves learner self-efficacy in MSK physical examinations. Lack of difference in pre/post knowledge scores may be due to low level of difficulty of knowledge questions. This study suggests standardized and interactive MSK learning, and assessment should be incorporated into pediatric resident curriculums. Future directions may include increasing difficulty of knowledge questions, using a larger cohort and control group comparison.

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Palliative Care for the Rheumatologist: An Educational and Patient Care Intervention

Charles Serapio (University of Toronto, Toronto); Leah Steinberg (University of Toronto, Toronto); Colman Rebecca (University of Toronto, Toronto); Alexandra Saltman (University of Toronto, Toronto)

Objectives: Patients with advanced systemic rheumatic diseases such as systemic sclerosis, inflammatory myositis and vasculitis often have a high burden of symptoms and limited life expectancy. However, these patients have limited access to palliative care (PC). The results of a survey sent out by the Canadian Rheumatology Association revealed that rheumatologists self-report discomfort with, and inadequate knowledge of, palliative care topics including how to engage in advance care planning and goals of care (ACP and GOC) conversations suggesting a gap in training. This study assesses the impact of an education session designed for rheumatologists and trainees.

Methods: A group of rheumatologists and trainees participated in a didactic session and hands on practice with standardized patients based on a structured ACP and GOC Conversation Guide. A post-workshop survey assessed participants' practice patterns and the workshop's impact on participants' comfort with these conversations. Results were analyzed using descriptive statistics.

Results: 12 rheumatology faculty and trainees participated in the workshop and 8 completed the post-workshop survey. Of the participants who completed the survey, 63% ($n = 5$) reported that 5% or more of inpatients that they cared for had advanced rheumatologic diseases with significant functional limitation and/or an estimated prognosis of less than 1 year. 88% ($n = 7$) felt that the workshop was useful to their clinical practices. 75% ($n = 6$) reported that they will be more comfortable in engaging in goals of care conversations with patients following the workshop. 63% ($n = 5$) reported that the workshop raised awareness of the importance of PC for patients with life-limiting systemic rheumatic diseases. 63% ($n = 5$) reported that the insights acquired will facilitate challenging aspects of patient care.

Conclusion: We piloted and evaluated a rheumatology-specific advance care planning and goals of care conversation training module delivered to rheumatology residents and faculty. Preliminary results point to participants' increased comfort with these conversations and increased awareness of PC's role for patients with end-stage rheumatologic conditions. Further study on a larger scale is required to better assess the value of such educational interventions.

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Effective, Efficient, and Convenient: Examiner and Examinee Experiences with a National Virtual Objective Structured Clinical Examination (OSCE) in a Rheumatology Competence By Design Curriculum

Leah Ellingwood (University of British Columbia, Vancouver); Azin Ahrari (UBC, Vancouver); Raheem Kherani (University of British Columbia, Richmond); Shahin Jamal (Division of Rheumatology, University of British Columbia, Vancouver)

Objectives: To assess feasibility and resident examinee and faculty examiner experiences of a national virtual Objective Structured Clinical Exam (OSCE) of Canadian Rheumatology residents.

Methods: In July 2020 during the COVID-19 pandemic, we administered a virtual OSCE for incoming Rheumatology residents using Zoom technology following a 3-day virtual Rheumatology Basic Skills Course. The virtual OSCE was comprised of four history, counselling, or management stations assessing Competence by Design curriculum Entrustable Professional Activities. Post-OSCE, we distributed voluntary anonymous online surveys to resident examinees and faculty examiners with 5-point Likert scale questions on experiences of the virtual OSCE as a method of learning and assessment and free-text questions on the advantages and limitations of virtual versus in-person OSCEs. Likert responses were analyzed using descriptive statistics, and open-ended questions were analyzed with thematic analysis.

Results: Twenty-two resident examinees ($N = 22$) and six faculty examiners ($N = 6$) completed the surveys. All residents (100%, $n = 22$) and faculty (100%, $n = 6$) strongly agreed that the online technology was easy to use. All residents (100%, $n = 22$) and most faculty (83%, $n = 5$) somewhat or strongly agreed that the virtual OSCE was helpful preparation for telehealth appointments. The majority of residents (95%, $n = 21$) and all faculty (100%, $n = 6$) somewhat or strongly agreed that they were able to effectively demonstrate/evaluate clinical skills and knowledge in a virtual setting. Most residents (95%, $n = 21$) and faculty (83%, $n = 5$) either somewhat or strongly agreed that compared to an in-person OSCE, a virtual OSCE is a practical and useful evaluation tool. Most residents (77%, $n = 17$) somewhat or strongly agreed that their performance was comparable to how they would have performed on an in-person OSCE. Responses to whether it would be easy to cheat on this virtual exam varied, with 54% ($n = 12$) of residents and 33% ($n = 2$) of faculty somewhat or strongly disagreeing; half of faculty ($n = 3$) neither agreed nor disagreed. Qualitative feedback from residents and faculty emphasized the convenience, efficiency, comfort, and accessibility of the virtual format. Perceived limitations included inability to evaluate physical exam skills and potentials for cheating or technical issues.

Conclusion: Rheumatology residents and faculty perceived the virtual OSCE to be an effective, convenient, and practical evaluation tool. Virtual OSCEs thus may enable formal evaluation when physical distancing is required for public health reasons or when geographic proximity is

challenging or unfeasible. Further research into approaches to mitigate cheating and facilitate physical examination skills assessment in the virtual format would be beneficial.

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National Burden of Rheumatoid Arthritis in Canada 1990-2017: Findings from the Global Burden of Disease Study 2017

Nejat Hassen (University of British Columbia, Arthritis Research Canada, Richmond); Diane Lacaille (University of British Columbia (Division of Rheumatology)/Arthritis Research Canada, Richmond); Nizal Sarrafadegan (University of British Columbia, Vancouver); Alice Xu (University of British Columbia, Vancouver); Sophia Sidi (University of British Columbia, Vancouver); Amani Alandejani (University of British Columbia, Vancouver); Marjan Mansourian (Isfahan University of Medical Sciences, Isfahan); Jacek Kopec (Arthritis Research Canada, Richmond)

Objectives: According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017, over 120,000 individuals currently have rheumatoid arthritis (RA) in Canada, yet a study that evaluates the combined effect of RA on the longevity and quality of life in the country is lacking. The objectives of this study are three: 1) to describe burden of RA levels and trends from 1990-2017 using GBD data, 2) to describe age and sex differences, and 3) to compare Canada RA burden to other countries.

Methods: We obtained publicly available data from GBD Study 2017 from the Institute for Health Metrics and Evaluation interactive visualization tool (<http://vizhub.healthdata.org/gbd-compare>). Disease burden indicators include prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs). Estimates were presented as non-age-standardized and age-standardized rates per 100,000 population. GBD estimated mortality and prevalence using published literature, survey data, patient records, and health insurance claims. YLLs measure premature death calculated as the sum of each death multiplied by the standard life expectancy at each age. YLDs measure amount of time in a year an individual lives with a short- or long-term health condition, calculated by combining RA prevalence with disability weights for each age/sex/year. DALYs were calculated as the sum of YLLs and YLDs. DALYs for Canada were compared to DALYs of countries with similar socio-demographic index (SDI) values. SDI combines income per capita, average educational attainment, and fertility rates. Data were analysed by DisMod-MR 2.1, a Bayesian meta-regression tool.

Results: In Canada, RA mortality (mortality and YLLs) has improved over time, with a steeper decline after the year 2002. However, the population burden of quality of life (YLDs and DALYs) has increased due to increasing prevalence. The disease burden was higher in females (prevalence, mortality, YLLs, YLDs, DALYs), and DALY rates were higher among older populations. Compared to other countries, Canada had a greater improvement in mortality and YLLs over time and had a lower age standardized DALYs rate compared to countries of similar SDI values. A weak association was found between global age standardized DALYs and SDI ($R^2 = 0.0138$).

Conclusion: RA is a major public health challenge. Canada fares better than other countries with regards to national RA burden. Early identification and management are critical to reducing the overall burden of RA in Canada, especially in women. More data from multiple provincial RA databases would increase the accuracy of our estimates for Canada.

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The Effect of Targeted Rheumatoid Arthritis Therapeutics on Systemic Inflammation and Anemia

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Objectives: Anemia and inflammation associated with RA may have considerable impact on patient functionality and quality of life. We evaluated the effects of the TNF inhibitors (TNFi), IL-6 receptor inhibitors (IL-6Ri), and Janus kinase inhibitors (JAKi) on the levels of hemoglobin

(Hb) and CRP after 6 months of therapy in adults enrolled in Corrona, a large US RA registry.

Methods: We selected patients who initiated a TNFi, IL-6Ri, or JAKi during or after January 2010, had valid Hb and CRP measurements at both baseline and 6 (± 3) months of follow-up, and had continued therapy until at least that follow-up visit. For both parameters, outcomes included mean concentration changes and proportions of patients who switched from abnormal (Hb: < 12 g/dL (women) or < 13 g/dL (men); CRP: ≥ 0.8 mg/L) to normal levels, and vice versa, from baseline to Month 6. We also assessed the proportions of patients who had a mild (≤ 1.5 g/dL) or moderate or worse (> 1.5 g/dL) Hb decrease. Differences in these outcomes were evaluated using covariate-adjusted multivariable regression models.

Results: This analysis included 2772 patients (TNFi, 65%; IL-6Ri, 17%; JAKi, 17%). Overall, 17% patients had low Hb and 38% had elevated CRP. By Month 6, 32-34% patients across the three groups discontinued treatment. The IL-6Ri group had the highest Hb increase (0.44 ± 1.06 g/dL), which was significantly greater than those observed with TNFi (0.12 ± 0.95 g/dL) and JAKi (-0.09 ± 0.94 g/dL), regardless of Hb status at baseline. In addition, IL-6Ri was associated with significantly higher odds of attaining normal Hb than TNFi or JAKi (odds ratios 3.25 and 3.85, respectively) and with significantly lower odds of experiencing mild (0.55 and 0.36) or moderate or worse Hb decrease (0.67 and 0.36). Similarly, IL-6Ri was associated with a significant improvement from baseline to Month 6 in CRP level over TNFi and JAKi and with significantly higher odds of attaining a normal CRP. Greater improvements in Hb and CRP with IL-6Ri compared with TNFi and JAKi were also observed for patients with low Hb or high CRP at baseline.

Conclusion: In this real-world completer analysis of patients with RA, continuous 6-month therapy with IL-6Ri was associated with improvements in Hb and CRP, which were significantly greater than those with continuous 6-month therapy with TNFi or JAKi. These results align with the mechanism of IL-6R inhibition and may be useful when considering treatment options for patients with RA.

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What are the Real-World Predictors of Initiating Different Advanced Therapies in Early RA? Data from the Canadian Early Arthritis Cohort (CATCH) Group.

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Objectives: Compare the characteristics of real-world early RA (ERA) patients who are starting TNFi, non-TNFi, and JAKi post failure of conventional synthetic disease modifying antirheumatic drugs (csDMARDs).

Methods: Prospective cohort data analyzed from early RA patients (symptoms < 1 year) enrolled in CATCH starting TNFi, non-TNFi or JAKi as first line advanced therapy between January 2014 (when JAKi were first approved in Canada) to December 2019. Descriptive statistics, t-tests and chi-square tests summarized and compared secular trends and patient characteristics initiating each class of therapy. Multinomial logistic regression identified predictors of starting non-TNFi vs TNFi, or JAKi vs TNFi as first advanced therapeutic.

Results: 246 participants started advanced therapy during the study period, mean (SD) age 50 (14) years, 75% female, and 79% Caucasian. The proportion of JAKi used as first-line therapy increased over time (0% to 33% from 2014-2019) and TNFi decreased (87% to 61%). The following findings are from the visit just prior to starting advanced therapy. Those starting

JAKi, had the lowest DAS28 (mean [SD]: 3.6[1.4]; $P = 0.001$), CDAI (16.5[13.7]; $P \leq 0.009$), MD global (3.2[2.7]; $P = 0.003$), ESR (median [IQR]: 12[13]; $P \leq 0.05$), and tender joint count (median [IQR]: 2 [6]; $P = 0.02$). Reciprocally, those starting non-TNFi had the highest DAS28 (mean [SD]: 4.8 [1.5]; $P = 0.001$), CDAI (24.8[14.9]; $P \leq 0.009$), MD global (4.8 [2.8]; $P = 0.003$), ESR (median [IQR]: 28 [23.5]; $P \leq 0.05$), and tender joint count (median [IQR]: 6 [9]; $P = 0.02$). Those starting TNFi had the shortest disease duration in months (mean [SD]: 32.5 [29.1]; $P = 0.0006$), and the highest proportion of non-Caucasian participants (26%; $P = 0.02$). There were no statistically significant differences between the groups for proportion of women, annual household income, employment status, private medical insurance, or RF positivity in the first year. Comparing JAKi vs TNF, the strongest predictor of initiating JAKi was province of Ontario where access is preferential for JAKi and TNFi, versus Quebec (OR [95% CI]: 0.44 [0.20, 0.94]), or Western Canada (0.11 [0.01, 0.99]). Comparing non-TNFi to TNFi, those prescribed non-TNFi were associated with grade 12 or higher education (2.92 [1.28, 6.63]). Non-TNFi were also associated with more comorbidities at baseline (1.35 [1.01, 1.81] and trended towards older age (1.01 [0.97, 1.05]).

Conclusion: Both patient-related factors and physician-related factors were associated with different choices of advanced DMARD. Patient formal education beyond high school was the strongest predictor of starting non-TNFi compared to TNFi. Physician practice location within Ontario was the strongest predictor of starting JAKi compared to TNFi. Finally, JAKi use is increasing as first-line advanced therapy after csDMARD failure.

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Patient Characteristics and Treatment Patterns Across Four Canadian Rheumatoid Arthritis Cohorts

Glen Hazlewood (University of Calgary, Calgary); Claire Bombardier (University of Toronto, Toronto); Xiuying Li (University Health Network, Toronto); Mohammad Movahedi (University Health Network, Toronto); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal); Louis Coupal (Institut de Rhumatologie de Montréal, Montréal); Vivian Bykerk (Hospital for Special Surgery, New York); Orit Schieir (University of Toronto, Notre-Dame-de-Grace); Dianne Mosher (University of Calgary, Calgary); Deborah Marshall (University of Calgary, Calgary); Sasha Bernatsky (McGill University Health Centre, Montreal); Nicole Spencer (University of Calgary, Calgary); Claire Barber (University of Calgary/Arthritis Research Canada, Calgary); OBRI (University Health Network, Toronto); RHUMADATA* (Montreal); CATCH Canadian Early Arthritis Cohort (Toronto); on behalf of the Rheum4U Team (Calgary)

Objectives: To describe and compare the clinical characteristics and treatment patterns of patients with rheumatoid arthritis (RA) across 4 Canadian cohorts.

Methods: We used data from four RA Canadian longitudinal cohorts in our analyses: The Canadian Early Arthritis Cohort (CATCH), a national inception cohort of patients with early RA ($n = 2878$); Ontario Biologics Registry Initiative (OBRI), an Ontario cohort of patients with RA enrolled at the time of a treatment switch to either a non-biologic DMARD or advanced therapy (biologic of JAK inhibitor) ($n = 3734$); the Quebec cohort RHUMADATA* ($n = 2890$), and The Calgary Rheum4U Precision Health Registry ($n = 709$), which both enroll patients with RA at any stage of disease. Each cohort conducted their own analyses, which were supervised and standardized through a central team. All data was complete up to Jan-Sept 2020. Clinical characteristics and treatment patterns were summarized descriptively and compared between the cohorts.

Results: A total of 10,213 patients with RA were included across the 4 cohorts. Overall, the percentage of patients who entered the cohort with early RA was 63% but ranged from 29% (Rheum4U) to 100% (CATCH), depending on the eligibility criteria. Mean age (55 years), gender (75% female) and seropositivity (69%) were similar between cohorts. At the time of initial DMARD, disease activity scores (DAS-28) varied, ranging from 3.00 (Rheum4U) to 5.17 (CATCH), but were more similar at the time of the first DMARD switch (range: 3.54-4.93), first advanced therapy

(range: 4.23-4.62) and second advanced therapy (range: 3.59-4.32). The initial DMARD was most commonly methotrexate, either in monotherapy (32%, range: 18%-40%), dual therapy (34%, range: 32%-46%), or triple therapy (3%, range: 1%-10%). Hydroxychloroquine monotherapy as initial DMARD varied from 14% (OBRI) to 29% (RHUMADATA*). The first DMARD switch was to another DMARD monotherapy in 20% (range: 10%-22%), dual therapy in 49% (range: 39%-56%) triple therapy in 6% (range: 2%-20%) and advanced therapy in 24% (range: 15%-28%). The first advanced therapy was a TNF inhibitor in 80% (range: 78%-82%). Of the 2892 patients who ever started an advanced therapy across the 4 cohorts, 52% were on their first, 22% on their second and 12% on their third and 13% on their fourth or greater.

Conclusion: Canadian RA cohorts that include over 10,000 patients across a range of settings demonstrate some heterogeneity in treatment patterns. This project is a first step towards future efforts to conduct harmonized analyses across Canadian RA cohorts.

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Biologic Refractory Rheumatoid Arthritis: A Report From the Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT) Database

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Objectives: Advances in therapy have provided more options for patients with rheumatoid arthritis (RA) who do not improve on initial therapy. However, there still remains a significant proportion of patients with refractory RA, defined as those who progress to a third class of advanced therapy (biologic or targeted synthetic DMARD). Previous studies have estimated that between 6-20% of patients are refractory, thus early identification of this population could alter initial treatment strategy and help focus resources. Our objective was to identify baseline characteristics of patients who later developed refractory RA.

Methods: The Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT) registry is a prospective inception cohort in Northern Alberta that captures data on RA patients since 2000 starting advanced therapy after at least 4 months of exposure to conventional synthetic DMARDs. We compared baseline demographic and disease characteristics of patients with and without refractory RA. We then performed time-to-event multivariate hazard ratio (HR) analyses to compare the outcomes of the two groups.

Results: We observed 2341 patients for 14012 patient-years (mean follow-up 6.0 years, median follow-up 5.1 years; IQR: 2.2, 9.2), 274 (11.7%) of patients were refractory. Baseline characteristics were similar between the non-refractory and refractory RA groups: mean age (years) (SD) 44 (15) vs 43 (14), female 73% vs 75%, mean RA duration (years) (SD) 10 (10) vs 10 (11), ever smokers 58% vs 58%, BMI > 30 23% vs 25%. The number of patients with severe functional loss on HAQ was 30% vs 36% and high disease activity on DAS28-CRP was 31% vs 41%. Multivariate HR analyses of baseline characteristics showed higher rates of unemployment (HR 1.45; 95% CI 1.03, 2.06), prednisone use (HR 1.76; 95% CI 1.18, 2.63) and entry into the RAPPORT database after 2011 (HR 2.26; 95% CI 1.52, 3.35). There were no significant differences in ethnicity, smoking status, seropositivity, type of b/tsDMARD, or objective markers of active disease including HAQ, CDAI, or DAS28-CRP.

Conclusion: At the point of b/tsDMARD initiation, we identified very few robust predictors of refractory disease. There was a significant shift after 2011 in the number of patients with refractory RA. This may reflect a change in practice patterns toward treat-to-target or simply the wider variety of treatment options available. Further work to evaluate the impact of switching between b/tsDMARDs according to evolving definitions of refractory disease on patients and society is planned.

Characterization of Remission in Patients with Psoriatic Arthritis Treated with Upadacitinib: Post-hoc Analysis from Two Phase 3 Trials

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Objectives: To assess the rates of patients achieving remission or low disease activity (LDA) based on very low/minimal disease activity (VLDA/MDA) measures, DAPSA and PASDAS scores at Weeks 12 and 24 using data from the SELECT-PsA 1 and SELECT-PsA 2 Phase 3 studies. Individual MDA components among patients who did or did not achieve MDA criteria at Week 24 were also assessed.

Methods: This is a post-hoc analysis of 2 randomized controlled trials. In SELECT-PsA 1, patients with PsA and prior inadequate response (IR) or intolerance to ≥ 1 non-biologic DMARD (N = 1705) were randomized to once daily upadacitinib (UPA) 15mg (UPA15), UPA 30mg (UPA30), adalimumab (ADA) 40mg every other week, or placebo (PBO). In SELECT-PsA 2, patients with prior IR or intolerance to ≥ 1 biologic DMARD (N = 642) were randomized to UPA15, UPA30, or PBO. Remission and LDA were assessed using VLDA/MDA, DAPSA scores of $\leq 4/\leq 14$, and PASDAS scores of $\leq 1.9/\leq 3.2$, at Weeks 12 and 24.

Results: Overall, 2345 patients were analyzed. In both studies, higher rates of remission and LDA were observed with both UPA doses vs PBO at Weeks 12 and 24 (nominal P-values < 0.05). Generally, higher rates of remission and LDA were also observed with UPA30 vs ADA in non-biologic DMARD-IR patients (nominal P-values < 0.05). Greater rates of MDA/VLDA were observed at Weeks 12 and 24 with UPA15 and UPA30 vs PBO in both studies and with UPA30 vs ADA in non-biologic DMARD-IR pts (nominal P-values < 0.05 for all comparisons). The proportion of responder or non-responder patients receiving UPA15 or UPA30 was similar for each of the MDA components in both studies. At Week 24, more responder and non-responder patients in both studies achieved SJC $66 \leq 1$, PASI ≤ 1 or BSA-Psoriasis $\leq 3\%$, and Leeds Enthesitis Index (LEI) ≤ 1 . Conversely, the proportion of patients Achieving TJC $68 \leq 1$ and Patient's Global Assessment of Pain ≤ 1.5 tended to be lower.

Conclusion: Regardless of previous biologic DMARD failure, patients treated with UPA15 or UPA30 achieved a higher rate of remission or LDA measured by various disease activity measures vs PBO at Weeks 12 and 24; higher rates of response were observed in most of the remission and LDA measures with UPA30 vs ADA in non-biologic DMARD-IR patients. Among patients who did or did not achieve MDA criteria at Week 24, a greater proportion of UPA-treated patients achieved physician derived measures such as SJC ≤ 1 , PASI ≤ 1 or BSA-Ps $\leq 3\%$, and LEI ≤ 1 .

22

Shared Decision-Making for Inflammatory Arthritis Treatment Decisions: Preferences of Indigenous Patients

Valerie Umaefulam (University of Calgary, Calgary); Terri-Lynn Fox (University of Calgary, Calgary); Cheryl Barnabe (University of Calgary, Calgary)

Objectives: Decision making for treatment of inflammatory arthritis is complex, with multiple beneficial medication options and approaches available, but with the potential for treatment-related adverse effects and economic considerations. Shared decision-making (SDM) is a process where health professionals and patients use specific tools and approaches in working together to make informed healthcare decisions and choices and is associated with improved patient involvement and satisfaction with

care. Indigenous patients experience a significant burden of inflammatory arthritis, both in increased prevalence and differential treatment outcomes relative to the general population. Treatment decisions reflect an interplay of clinical, family, and societal factors. SDM may represent an approach to support these decisions in a culturally congruent and safe manner. The study aimed to identify aspects of inflammatory arthritis care that Indigenous patients find relevant for shared decision-making and explore preferences for shared decision-making strategies.

Methods: A purposive sampling process from rheumatology clinics that provide services to Indigenous patients in Calgary was used to recruit patients to participate in semi-structured interviews. Interview guides were developed to discuss patient's perceptions about the potential role of SDM in arthritis care, priorities for application of SDM, and preferences for SDM strategies. The interviews were reviewed and coded by two individuals, including a First Nations patient with inflammatory arthritis, and the data was analyzed via thematic analysis using NVivo software.

Results: Seven participants were recruited to reach content saturation. They were all women aged 37-61 years, living with rheumatoid arthritis. Participants supported that SDM would be beneficial, primarily to support decisions around treatment plans and medication changes, managing arthritis comorbidities and complications, and the inclusion of traditional modes of healing in care plans. SDM would need to reflect specific content areas, such as available treatments for arthritis and side effects, which medication options would be covered by the federal formulary (Non-Insured Health Benefits), and how the treatment decisions would impact quality of life, especially while living with other comorbidities and social realities. All participants were interested in a SDM strategy that involved having a decision coach and preferred an approach that used a combination of paper and electronic resources and support groups.

Conclusion: Indigenous patients' value active engagement in decision making for arthritis care. This study advances knowledge in the priority areas and specific content needed in the SDM process, and the preferences of SDM strategies relevant and appropriate for Indigenous patients living with inflammatory arthritis.

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Secukinumab Dose Escalation for the Treatment of Ankylosing Spondylitis in Canada: Retrospective Analysis Using Real-World Data from the XPOSE Patient Support Program

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Objectives: Secukinumab is a fully human monoclonal antibody targeting interleukin-17A, approved for AS treatment. At the recommended dose of 150 mg monthly, secukinumab showed a 5-year sustained improvement in signs/symptoms and favorable safety profile in the MEASURE trials. Dose escalation (DE), defined as an increase in dose and/or shortening of dose interval vs. initial dosage, has been previously described for biologics in AS. It constitutes a patient-centric approach to treatment optimization before considering therapy switch. The current analysis leverages the Patient Support Program (PSP) data to describe the demographics, baseline disease characteristics, drug retention rate (DRR) and effectiveness of secukinumab in AS patients who underwent DE.

Methods: The XPOSE[®] PSP is available to Canadian AS patients initiated on secukinumab. Patient demographics, previous biologic therapy, dosage/dates and BASDAI were collected to support reimbursement. We present a retrospective analysis in patients who received ≥ 1 dose of secukinumab between 20-Apr-2016 and 2-May-2019, and for whom dosage/dates were adequately captured. We report DRR at 12-month post-DE and BASDAI responses in different DE cohorts.

Results: Among 1,895 qualifying patients, 642 received DE. The mean

(SD)/median times to DE were 227.7 (179.6)/160 days post-secukinumab initiation. In DE patients, mean age was 45.4 years, 13.9% were biologic-naïve and 54.8% female. The corresponding figures in non-DE patients were 46.1 years, 22.2% and 50.0%. For patients with recorded BASDAI scores (n = 1,483), mean (SD)/median baseline BASDAI were 7.1 (1.60)/7.4 in DE patients (n = 490) vs. 6.9 (1.69)/7.0, in non-DE patients (n = 993). Most frequently prescribed DE regimens were 300 mg monthly (68.9%), 150 mg every 2 (17.6%) and every 3 weeks (9.4%). In DE patients, DRR 12-month post-DE was 67.4% (196/291). A similar DRR was observed in non-DE biologic-naïve patients (71.2%, 74/104) 12-month post-initiation. In a DE cohort (n = 68) with BASDAI available pre-secukinumab initiation and post-DE (mean time to post-DE F/U = 188.9 (77.0) days), BASDAI decreased from 7.18 (1.36) to 4.43 (1.76). In another DE cohort with BASDAI available pre-DE (within 3 months) and post-DE (n = 23), DE was associated to a 1.32 points reduction (from 5.60 (1.95) to 4.28 (1.86)).

Conclusion: We herein report a characterization of DE practices amongst Canadian physicians treating AS with secukinumab. Looking at baseline characteristics, DE patients were more frequently bio-experienced and had slightly higher BASDAI scores. For post-intervention outcomes, when deemed clinically relevant by the physician, DE was successful in a majority of cases, leading to appreciable disease activity improvement and 12-month retention in over 2/3 of patients.

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Can Relapses after 12 Month Follow-up be Predicted using Disease Status and Characteristics at Month 12 in Patients with Granulomatosis with Polyangiitis?

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Objectives: Previous studies have identified proteinase 3 (PR3)-antineutrophil cytoplasmic antibody (ANCA) positivity at diagnosis and remission, and persistent hematuria at remission as risk factors for relapse in ANCA-associated vasculitis, but with more controversial results in granulomatosis with polyangiitis (GPA). This study sought to analyze the predictive value of positive ANCA status and persistent microhematuria at 12-month follow-up on subsequent relapses in a cohort of GPA patients followed at the Toronto vasculitis clinic.

Methods: Data from patients with GPA followed at the Toronto vasculitis clinic were extracted from the CanVasc database and included demographics, clinical, and biological data at diagnosis and follow-up month 12 \pm 3 (M12). Relapse was defined as recurrence or new onset of disease due to active vasculitis after a period of remission, requiring a change in dose of glucocorticoids and/or the addition of another immunosuppressant. The association between independent parameters and relapses after M12 were assessed using Cox proportional hazard models.

Results: Of the 234 GPA patients in the database, 113 patients were included (118 patients had no ANCA serology at 12 \pm 3 months follow-up and 3 patients had follow-up period of less than 24 months). The demographics and disease characteristics of the 50 ANCA+ and 63 ANCA- patients at M12 were similar, including the treatments used for induction and at M12. A significantly higher proportion of patients who were ANCA- at M12 had a previous relapse (prior to M12) compared to patients ANCA+ at M12 (P = 0.03). However, between the two groups there was no significant difference in the number of patients experiencing a relapse after M12. In multivariate analyses, MPO-ANCA positivity at M12 was the strongest of the only two identified parameters predictive of subsequent relapses after M12 (HR 3.54, P = 0.01), along with the presence of microhematuria at M12 (HR 1.91, P = 0.04). Elevated serum creatinine levels at M12 were associated with a decreased risk of relapse after M12 (HR 0.99, P = 0.04).

Conclusion: These findings suggest that in GPA patients, the presence of MPO-ANCA positivity at M12 or microhematuria at M12 are associated with more subsequent relapses, and thus are important parameters to follow.

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Radiological Validation of a Novel MRI Reporting System for Axial Spondyloarthritis

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Objectives: The diagnosis of axial spondyloarthritis (SpA) can be challenging, resulting in increasing use of magnetic resonance imaging (MRI). Often, however, bone marrow edema (BME) on MRI alone, rather than a global radiologic assessment, is mistakenly used to arrive at an imaging diagnosis. Given this, our group proposed a novel classification system for MRI reporting of the sacroiliac joints (SIJ) in a recent publication (O'Neill J, Carmona R, Maksymowych W. Clinical Radiology, 2019). Beyond standardising MRI reporting, the novel system reminds radiologists and clinicians that BME alone does not constitute a diagnosis of axial SpA, allows room for uncertainty, and provides a framework for communication between physicians. This study aims to validate this novel reporting system. A separate study is being conducted to assess the impact on clinical practice.

Methods: In this retrospective review we identified 100 patients \geq 18 years old, who had spondylitis MRI protocol (n = 5 for initial pilot study, n = 95 for full analysis) ordered by two rheumatologists for suspected SpA from 2012 to 2018. Two rheumatologists retrospectively applied the novel classification system to the original MRI reports. Two MSK radiologists, blinded to initial imaging diagnosis, 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 and quantify the effect on imaging diagnosis and change in classification.

Results: All MRIs have been re-interpreted using the new system. Of the 5 pilot study patients, the original MRI reports of 2/5 patients were interpreted as class 4C (acute-on-chronic sacroiliitis) by the rheumatologists. Utilizing the new classification system, the radiologists re-classified 1 of these as class 2, indicating an alternate diagnosis. In the patient who remained as 4C, cervical imaging aided in the diagnosis. Of 4 patients without sacroiliitis utilizing the new system, spinal imaging helped in arriving at an alternate diagnosis. The full data set will be presented at the CRA-ASM in February 2021.

Conclusion: We present a new MRI classification system for reporting in axial SpA. Our preliminary assessment revealed a reclassification of MRI diagnosis of 1/5 (20%) patients. Adding spinal imaging contributed to the diagnosis of these patients. The full data set validating this new reporting system, as well as data describing the utility of adding spinal MRI to MRIs of the SI joints will be examined and presented at the CRA meeting. Best Abstract on Spondyloarthritis Research Award.

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Changes in Disease Features Do Not Differ Between SSc Patients Who Did versus Did Not Undergo Annual PAH Screening: Data from the Canadian Scleroderma Research Group Registry

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Objectives: Pulmonary arterial hypertension (PAH) has a high mortality in systemic sclerosis (SSc) patients despite available therapies. Guidelines recommend annual echocardiograms to assess for PAH. However, it is unknown whether annual screening improves disease progression and

outcomes. Using data from the Canadian Scleroderma Research Group (CSRG) database, we compared characteristics in pulmonary function, cardiac function and skin manifestations between SSc patients who did versus did not undergo annual echocardiograms for PAH screening over the duration of registry follow-up.

Methods: Data was obtained from the CSRG, a national longitudinal registry of SSc patients > 18 years old. All patients with ≥ 3 visits (baseline plus ≥ 2 follow-ups) were included. We considered a patient to have annual echocardiograms if an echocardiogram was performed within 18 months of baseline and follow-up visits. Those who did not undergo annual screening were those for whom ≥ 1 screening was missed. We compared baseline diffusion capacity for carbon monoxide (DLCO), right ventricle systolic pressure (RVSP) and modified Rodnan skin scores (mRSS) between groups after controlling for gender, age at diagnosis, total number of visits, tobacco use and prevalence of peripheral vascular disease, diabetes mellitus and rheumatoid arthritis using regression analyses. Regression analyses also compared changes in each of DLCO, RVSP and mRSS between groups after controlling for covariates.

Results: Of 1223 individuals who had ≥ 3 visits, 360 (29.4%) underwent annual echocardiograms for the duration of their registry follow-up. Of these, 83.1% were female while 88.7% of those who did not have annual echocardiograms were female. At entry into CSRG, DLCO, RVSP, and mRSS were similar between those who did versus did not have annual echocardiograms after accounting for covariates. Over the course of follow-up, there was no significant difference in the absolute changes in DLCO, RVSP or mRSS between groups. Throughout the follow-up, 19.7% of those with annual echocardiograms had a right heart catheterization (RHC), of whom 35.2% had PAH on RHC. Of those who did not have annual echocardiograms, 17.6% had an RHC, of which 21.1% were found to have PAH.

Conclusion: Results suggest that changes in DLCO, RVSP and mRSS do not differ between those who do versus do not undergo annual echocardiograms. Similarly, there was no difference between the proportion of patients who received a diagnosis of PAH between groups. These results support previous CSRG data questioning the appropriateness of annual screening recommendations for all patients.

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The New EULAR/ACR 2019 SLE Classification Criteria: Defining Ominosity in SLE

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Objectives: Determine the ominosity of the 2019 European League Against Rheumatism/American College of Rheumatology classification criteria (EULAR/ACR) by determining its predictive role for disease severity in the first 5-years following diagnosis.

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. To determine disease severity in the first 5-years after diagnosis, adjusted mean SLEDAI-2K (AMS), flares, remission and use of immunosuppressive treatment were used as outcomes. Based on receiver Operating Characteristic analysis a EULAR/ACR score of 20 was used as a threshold to compare demographic, clinical characteristics and outcomes between groups.

Results: A total of 867 inception patients were included, 87.5% were woman, with a mean age of 36.2 years at baseline. Most patients were Caucasians (66.7%), followed by Blacks (14.2%). The mean disease duration (time between diagnosis and first visit) was 0.2 years, the median time between the first visit and the second visit was 3.3 months. Blacks more frequently

presented with a score ≥ 20 compared to Caucasians. At baseline patients with a score ≥ 20 were younger, had higher SLEDAI-2K scores and were more likely to receive immunosuppressive therapy. In the first 5 years of disease course patients with a score ≥ 20 had higher AMS scores ($P < 0.001$) and were more likely to ever experience a flare ($P < 0.001$). Every increase of 10 points in the score increased the AMS by 2.2 units (Univariate Linear regression, $\beta = 0.22$, $P < .0001$) and the risk of a flare by 32% (RR: 1.32 95% CI: 1.173, 1.485, $P < .0001$). Also, individuals with a score ≥ 20 had lower probabilities of achieving remission, (including all 4 DORIS definitions of remission), of at least 15% compared to individuals with a low score, the Hazard ratios with significant P values confirmed this finding. The higher score group were also characterized by higher requirements for immunosuppressive therapy.

Conclusion: A EULAR/ACR score ≥ 20 is an indicator of ominosity in SLE. Patients with a score ≥ 20 were characterized by a more active disease course throughout the first 5 years. Thus, these new classification criteria could also provide prognostic information regarding disease severity in the first 5 years following diagnosis.

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Assessment of the Impact of Interferon Levels on Cognitive Dysfunction in Patients with SLE

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Objectives: Cognitive impairment (CI) is among the earliest and most prevalent manifestations of SLE. Previous studies have demonstrated that increased levels of interferon (IFN)-induced gene expression in SLE are positively correlated with SLE disease activity and severity. The aim of this study is to examine the relationship between IFN levels and cognition as measured by the American College of Rheumatology neuropsychological battery (ACR-NB).

Methods: 301 consecutive consenting SLE patients (18-65 years old) attending a single center between Aug 2017 and Jan 2019 were enrolled in the study. IFN-induced gene expression was quantified by nano String on RNA isolated from whole peripheral blood archive in TEMPUS tubes. The log2 transformed normalized levels of five IFN-induced genes were summed to produce the IFN5 score. Cognition was measured using the ACR-NB (19 tests) representing manual dexterity, processing speed, language, simple attention, memory and executive function domains. Using age and gender stratified normative data, patients were classified on the ACR NB as having CI if a z-score of ≤ -1.5 was observed in ≥ 2 domains or $z \leq -2.0$ in ≥ 1 domain. Principal Component Analysis (PCA) was used to explore the relationships among cognitive tests, interferon levels and SLE disease duration. IFN levels and SLE disease duration were used as supplementary variables.

Results: Of 301 patients, 89.0% were women, mean age 40.9 ± 12.1 and mean disease duration 14 ± 10.1 years at study entry. PCA cognitive tests loaded onto 2 dimensions explained 39.6% of the variance in neuropsychological performance. The 1st dimension (explained 28.3% of the total variance) was correlated mainly with more complex cognitive tests and primarily

explained CI status of participants. The second dimension (11.3%) was mainly explained by measures of simple information processing or motor speed. The 1st dimension splits CI and non-CI patients, and no clustering was observed when participants were categorized based on interferon level. No relationship was found between the cognitive tests and IFN levels or disease duration. A weak negative correlation was observed between interferon levels and The Rey Complex Figure Task and hand tapping domains, though this was not significant.

Conclusion: This study assessed the relationship between IFN levels and cognitive function in patients with SLE. Using PCA analysis, we found no association between IFN levels and any cognitive tests, even after considering factors such as SLE disease duration. Best Abstract On Basic Science Research By A Trainee.

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Medical Cannabis Use in Patients Attending Rheumatology Clinics in Ontario

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Objectives: To determine the prevalence of medical cannabis use and the symptoms being treated in patients attending rheumatology clinics in Ontario.

Methods: Eight rheumatology clinics, currently participating in the Ontario Best Practices Research Initiative (OBRI), each recruited approximately 100 consecutive patients to complete a medical cannabis survey. Regardless of their diagnosis, patients were eligible to participate if they were 18 years of age or older and English speaking. The Student's t-test and Chi-square test were used to compare medical cannabis users (currently or within the past two years) to patients who reported never having used medical cannabis.

Results: A total of 858 surveys were completed. 179 (21%) patients reported ever medical cannabis use of whom 163 (19%; 95% CI: 16.5%-21.8%) were either currently using medical cannabis or had used it within the past two years. No significant differences were observed between medical cannabis users and non-users in mean (SD) age (56.7 (14.2) vs 59.5 (15.3)) and gender (% female) (72.8% vs 71.0%). The most common rheumatologist assigned diagnoses amongst users were osteoarthritis (40.5%) and rheumatoid arthritis (37.4%). Compared to the never used group, patients reporting medical cannabis use were more likely to be currently taking opioids (16.0% vs 7.2%, $P = 0.0005$) and anti-depressants (25.8% vs 13.5%, $P = 0.0001$), and have psychiatric (23.9% vs 10.9%, $P < 0.0001$) and gastrointestinal disorders (30.7% vs 21.2%, $P = 0.01$). Mean (SD) physician and patient global scores (0-10 VAS) were higher in medical cannabis users (2.9 (1.8) vs 2.1 (2.0), and 6.0 (2.6) vs 4.2 (3.0), $P < 0.0001$) as were mean (SD) pain scores (0-10 VAS) (6.2 (2.5) vs 4.7 (3.0), $P < 0.0001$). Amongst medical cannabis users, pain was the most common symptom being treated (73.0%), followed by anxiety (49%) and difficulty sleeping (49%). Overall,

less than half the users (44.8%) reported medical cannabis to be effective or very effective in treating their symptoms. When asked whether changes had been made to their prescribed medications while using medical cannabis, 9.2% reported that they had their prescribed medications lowered and 6.1% that they had their prescribed medications stopped.

Conclusion: Based on our findings, it is not uncommon for patients being seen by rheumatologists to use medical cannabis and most are using it to reduce their pain symptoms. Less than half of the patients reporting medical cannabis use found it to be effective in relieving their symptoms and only 15% reported changes to their prescribed medications.

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Does Statin Use have an Effect on Progression of Knee Osteoarthritis on Magnetic Resonance Imaging: The Vancouver Longitudinal Study of Early Knee Osteoarthritis (VASEKO)

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Objectives: Recent in vitro and epidemiologic research has suggested a potential beneficial effect of statins on knee osteoarthritis (OA). The aim of this study was to evaluate the effect of statin use on progression of cartilage damage, joint effusion, osteophytes and bone marrow lesions (BML) on magnetic resonance imaging (MRI) in a population-based cohort with predominantly pre-radiographic knee OA.

Methods: Subjects were recruited at random from the population and assessed at baseline and 7-year follow up. Inclusion criteria: 1) age 40-79 years; 2) pain/discomfort in/around the knee on most days of the month at any time in the past; 3) any pain/discomfort in/around the knee in the past 12 months. Exclusions were inflammatory arthritis, recent knee surgery or injury, inability to undergo MRI. Current statin use was ascertained at baseline. Subjects completed the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index version VA 3.1 (scale 0-100). Radiographs were graded using the Kellgren Lawrence (KL) 0-4 scale. MRIs were read for cartilage (0-4; 0/1 were collapsed), osteophytes (0-3), BML (0-3), and effusion (0-3). Each outcome was defined as an increase ≥ 1 in any of the compartments graded. The primary outcome was cartilage progression. Logistic regression was used to assess the association between baseline statin use and progression of MRI outcomes after 7 years. Analyses were adjusted for age, sex, and BMI. To obtain population-based estimates, analyses were performed using age decade-gender stratum sampling weights.

Results: Of 122 subjects, 7.7% were statin users, 55.7% were female, mean age was 55.5, mean BMI 26.1, mean WOMAC pain 19.1. KL grades 0 to 4 was seen in 40.8%, 19.7%, 22.5%, 11.3% and 5.8%, respectively. Statin users, compared to non-users, had reduced cartilage progression, although this was not statistically significant (OR 0.56; 95% CI 0.13, 2.36). Similarly, there was no statistically significant association of statin use with progression of osteophytes (OR 2.00; 95% CI 0.28, 14.05), BML (OR 0.94; 95% CI 0.22, 3.97), or effusion (OR 1.20; 95% CI 0.27, 5.31).

Conclusion: In this population-based longitudinal cohort of early knee OA, statin use did not have an effect on MRI progression of cartilage, BML, osteophytes or effusion over 7 years. Despite recent evidence that statins might be beneficial in OA, we were unable to confirm such beneficial effects in this cohort with early disease.

1

Reduction of Anterior Uveitis Flares in Patients With Axial Spondyloarthritis During Certolizumab Pegol Treatment: 96-Week Results from the C-VIEW Study

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Objectives: Acute anterior uveitis (AAU) is the most common extra-articular manifestation in axial spondyloarthritis (axSpA), affecting up to 40% of patients and causing significant burden. Previous studies have shown that tumor necrosis factor inhibitors (TNFi) can reduce the incidence of AAU flares in patients with radiographic axSpA (ankylosing spondylitis), but few have focused on patients across the full axSpA spectrum. We report 2-year outcomes from the phase 4, open-label CVIEW study (NCT03020992), which investigated the impact of certolizumab pegol (CZP) treatment on AAU in patients with active axSpA and a recent history of AAU.

Methods: C-VIEW prospectively investigated patients with active axSpA who were HLA-B27 positive and had recurrent AAU, with a history of ≥ 1 AAU flare in the year prior to baseline (additional study criteria and study design are described elsewhere). The primary efficacy variable was the incidence of AAU flares during 96 weeks of CZP treatment versus the 2-year pre-baseline period. AAU incidence was evaluated using Poisson regression adjusted for duration of time in each period, with period (pre- and post-baseline) and axSpA disease duration as covariates. Secondary efficacy variables were Assessment of Spondyloarthritis international Society 20%/40% (ASAS20/40) response rates, as well as mean Ankylosing Spondylitis Disease Activity Score (ASDAS) and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) over time to Week 96.

Results: Of 115 enrolled patients, 89 initiated CZP treatment; 83 completed Week 96. The primary analysis revealed an 82% reduction in the incidence of AAU flares during CZP treatment compared with pre-baseline (rate ratio [95% CI]: 0.18 [0.12, 0.28], $P < 0.001$). The percentage of patients experiencing ≥ 1 and ≥ 2 AAU flares reduced from 100% and 59.6% pre-baseline to 20.2% and 11.2% during treatment. There were also improvements in axSpA disease activity: by Week 96, 75.6% and 58.5% of patients had achieved ASAS20 and ASAS40 responses, respectively. ASDAS and BASDAI also improved substantially over the 96-week treatment period: baseline mean ASDAS and BASDAI was 3.5 and 6.5, respectively and by Week 96, it was 1.9 and 3.0, respectively. No new safety signal was identified, compared to previous reports.

Conclusion: These data support the use of CZP for the treatment of patients with axSpA and a history of recurrent AAU. During 96 weeks' CZP treatment, there was a significant reduction of 82% in the AAU flare rate compared to pre-baseline. There were also substantial improvements in patients' axSpA disease activity.

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Filgotinib Treatment Results in Reduction of Biomarkers Associated With Disease in Patients With Ankylosing Spondylitis

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Objectives: Ankylosing spondylitis (AS) is a chronic, immune-mediated disease characterized by inflammation of the sacroiliac joints and spine. In the TORTUGA study, Filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, significantly reduced AS disease activity versus placebo (PBO). Selective JAK1 inhibition by FIL has the potential to block multiple inflammatory pathways simultaneously. We evaluated the impact of selective JAK1 inhibition with FIL on circulating biomarkers of AS disease activity in adult patients from TORTUGA.

Methods: TORTUGA (NCT03117270) was a 12-week, randomized, double-blind, placebo-controlled, phase 2 study. Patients were randomized 1:1 to FIL 200 mg ($n = 58$) or PBO ($n = 58$) once daily. Serum samples (FIL $n = 56$; PBO $n = 53$) were collected at baseline and weeks 1, 4 and 12, and analyzed for 135 biomarkers using the Meso Scale Discovery immunoassay platform (Meso Scale Diagnostics, Rockville, MD, USA). Change from baseline in biomarker concentration was computed for paired patient data at each timepoint and subject to clustering analysis. Correlations between biomarkers and select clinical scores at baseline were assessed by Spearman rank correlation.

Results: FIL significantly reduced the concentration of biomarkers associated with AS disease activity. Five clusters of biomarker response were identified based on the kinetics and magnitude of percent change from baseline. These clusters also represented discrete biological functions: cluster 1 (rapid, strong $> 50\%$ decrease at all three timepoints) included systemic inflammation biomarkers e.g., CRP, SAA; cluster 2 ($> 20\%$ decrease at least one timepoints) included immune cell biomarkers e.g., MIP3B, IL12p40; cluster 3 ($< 20\%$ decrease at all three timepoints) included cellular adhesion biomarkers e.g., ICAM-1, VCAM-1; cluster 4 (delayed decrease) included matrix remodeling biomarkers e.g., MMP1, TIMP1; and cluster 5 included biomarkers with gradually increasing concentration during FIL treatment. Spearman rank correlation analyses showed that at baseline, biomarkers of systemic inflammation, CRP and SAA, and a number of others, including ICAM-1 and MMP3, were positively correlated with AS disease activity score (ASDAS). Biomarkers showing a negative correlation with baseline ASDAS were few and included cytokine receptor FLT3 and chemotactic cytokine fractalkine (FRACTAL).

Conclusion: In patients with active AS, FIL significantly decreased levels of circulating biomarkers associated with active disease, including proinflammatory cytokines and chemokines, cell adhesion molecules, and markers of matrix remodeling. Clustering analysis revealed early, and late biomarker changes associated with disease. These data are consistent with reduced AS disease activity in TORTUGA and suggest that FIL treatment leads to a rapid and sustained reduction of inflammation in AS.

3

Impact of Filgotinib on Structural Lesions in the Sacroiliac Joints at 12 Weeks in Patients With Active Ankylosing Spondylitis: Correlation With Clinical Endpoints

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Objectives: In TORTUGA, Filgotinib—an oral, selective Janus kinase 1 inhibitor—reduced inflammation in patients with active ankylosing spondylitis (AS), as measured by Spondyloarthritis Research Consortium of Canada (SPARCC) MRI scores. In this post-hoc analysis, we examined the effect of Filgotinib on MRI measures of structural change in the sacroiliac joint (SIJ) versus clinical parameters.

Methods: TORTUGA (NCT03117270) was a 12-week, randomized, phase 2 trial. Patients with active AS (per modified New York classification; sacroiliitis confirmed by central reading) were randomized to Filgotinib

200 mg (n = 58) or placebo (n = 58) once daily. Baseline and Week (W) 12 MRI scans were re-evaluated post-hoc by blinded experts for SPARCC SIJ Structural Scores (SSS; erosion, backfill, ankylosis, fat lesions). Changes from baseline SPARCC SSS measures were evaluated using analysis of covariance with factors for treatment, baseline value, and randomization stratification. Least-squares mean (LSM) changes from baseline and between-group differences with 95% confidence intervals were calculated; p-values were nominal. Data were compared with clinical outcomes. Pearson correlations to assess intra-subject relationships were determined for changes in structural lesions from baseline to W12 versus changes in C-reactive protein, Ankylosing Spondylitis Disease Activity Score, Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Functional Index, and SPARCC MRI SIJ and spine inflammation scores.

Results: Evaluable MRI scans (baseline and W12) were obtained from 87 patients (Filgotinib, n = 48; placebo, n = 39). At baseline, there were no differences in MRI structural lesions between Filgotinib and placebo. From baseline to W12, erosion scores decreased with Filgotinib and increased with placebo (LSM change from baseline, -0.46 [95% CI, -1.31, 0.40] versus 0.56 [95% CI, -0.31, 1.42], respectively; P = 0.02 for between-group difference). Backfill scores increased with Filgotinib but not placebo (LSM change from baseline, 0.76 [95% CI, 0.07, 1.45] versus -0.26 [95% CI, -0.97, 0.45], respectively; P = 0.005). There were no between-group differences in change from baseline for ankylosis (P = 0.46) or fat lesions (P = 0.17). At W12, changes in erosion scores were moderately positively correlated with changes in SPARCC MRI SIJ inflammation scores (Filgotinib: r = 0.35921, P = 0.0132; placebo: r = 0.56043, P = 0.0002), suggesting changes in inflammation and structural score occurred in the same individuals. A moderate negative correlation was observed for backfill (Filgotinib: r = -0.41479, P = 0.0037; placebo: r = -0.37483, P = 0.0187). No correlations were observed for any clinical endpoint with ankylosis or fat lesion scores.

Conclusion: In TORTUGA, Filgotinib was associated with reduced SIJ inflammation versus placebo as assessed by MRI, correlating with a reduction in SIJ erosions and increased backfill.

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Effects of Filgotinib on Spinal Lesions in Patients With Ankylosing Spondylitis: Magnetic Resonance Imaging Data from the Placebo-Controlled, Double-Blind, Randomized TORTUGA Trial

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Objectives: In the phase 2 TORTUGA study (NCT03117270), Filgotinib (FIL) - oral, selective JAK1 inhibitor-significantly improved Spondyloarthritis Research Consortium of Canada (SPARCC) spine and sacroiliac joint MRI inflammation scores versus placebo (PBO) in patients with active ankylosing spondylitis (AS). This post-hoc analysis evaluated FIL on Canada-Denmark (CANDEN) MRI measures of spinal inflammation and structural lesions in TORTUGA patients.

Methods: TORTUGA was a PBO-controlled, multi-center, double-blind trial. Patients with active AS (modified New York classification criteria, with sacroiliitis confirmed by central reading) were randomized to FIL 200 mg (n = 58) or PBO (n = 58) once-daily for 12 weeks. Total spine MRIs were conducted at baseline and end of treatment. Scans were re-evaluated post-hoc by blinded, independent experts according to the detailed anatomy based CANDEN method and inter-reader discrepancies resolved by independent adjudicator. Changes from baseline (CFB) were evaluated using covariance analysis with factors for treatment, baseline value, and randomization stratification by prior TNF-inhibitor use. Least-squares

mean (LSM) CFB, and between-group differences were calculated; p-values are nominal.

Results: MRI scans (47 FIL, 41 PBO) with evaluable MRI at baseline and Week 12 (or early termination visit) were re-evaluated. Baseline characteristics were similar between subjects with and without MRI scan. Of those with MRI scans, mean total spine inflammation score was higher in FIL versus PBO (18.0 [standard deviation (SD), 21.35] versus 11.8 [SD, 17.05]) and mean ankylosis score was lower in FIL versus PBO (15.4 [SD, 42.11] versus 31.1 [SD, 54.99]) at baseline. Total spine inflammation scores decreased from baseline with FIL but not PBO (LSM, -4.40 [95% CI, -6.65, -2.15] versus 0.09 [95% CI, -2.17, 2.34], respectively; P = 0.0003). [GW1] [KP2] [GW3] Cumulative probability plots favored FIL over PBO for CFB in subregion inflammation scores, including postero-lateral elements (i.e. sum of lesions in ribs, transverse processes, spinous processes, soft tissue inflammation and posterolateral vertebral body), facet joint, and vertebral body. Total spine fat lesion scores numerically increased from baseline with FIL but decreased with PBO (LSM, 1.09 [95% CI, -0.22, 2.40] versus -0.09 [95% CI, -1.40, 1.21]; P = 0.0878). There were no statistically significant differences between groups for changes in erosion (P = 0.1956) or ankylosis (P = 0.2203) scores.

Conclusion: FIL decreased inflammation, including in postero-lateral elements of spine and facet joints, which has not been demonstrated previously in a PBO-controlled trial. No changes in erosion or ankylosis were seen. Due to imbalance in MRI measures at baseline and post-hoc analysis, our findings need to be confirmed in a large trial.

5

The Role of e-Health Technology in Physical Activity for Patients With Axial Spondyloarthritis: Results from a Qualitative Study

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Objectives: Physical activity (PA) is fundamental in the management of axial spondyloarthritis (axSpA); however, evidence suggests that patients with axSpA are not adhering to PA recommendations. The literature suggests enhanced social support systems, health care professional monitoring, and technology support may improve adherence to PA targets. Several approaches to increasing PA in the general population and in patients with chronic disease have demonstrated that e-health technology (e.g., telephone reminders, mobile text messaging and web-based interventions) can effectively influence PA participation. The aim of this study was to explore the role of e-health technology to increase PA engagement among patients with axSpA with respect to: 1) smartphone habits; 2) technology design; 3) electronic reminders; 4) performance feedback and 5) virtual support.

Methods: Semi-structured key informant interviews were conducted with axSpA patients attending an urban academic outpatient rheumatology clinic. Interviews were conducted by telephone, audio recorded, and transcribed verbatim. Data was analyzed using a thematic approach: two study investigators independently assigned themes and codes to the data set according to study objectives. Key informant recruitment continued until saturation of emergent themes was reached. Themes were presented to the investigative team to allow for comparison and reconciliation. Systematic labeling of the dataset was completed using an inductive approach. QSR NVivo V8 was used for data management and aggregation of codes into common themes.

Results: In total, 12 interviews were conducted. Most respondents were male (83.3%); mean age 45.5 (± 12.5) years; mean disease duration 21.5 (± 14.9) years. Participants indicated high confidence using technology, mean 8.1 (± 1.7) on a 10-point scale. One third (33.3%) of participants reported to have their smartphone on their person when engaging in exercise or PA. The design of e-health technology was considered important in the context

of PA and should incorporate simple layout, easy operation and intuitive function. The role of technological reminders to encourage PA participation included the risk of apathy, concern regarding interruptions, and emphasis on the ability to customize reminders. Feedback was an important component of e-health technology to increase PA engagement with respect to knowledge of progress and goal acquisition. Virtual support networks with peers, mentors and health care providers were considered important to provide encouragement and accountability.

Conclusion: The results of this study provide a foundation to guide development of a patient-centered e-health technology intervention to increase PA uptake in patients with axSpA and thereby improve disease-related outcomes and quality of life in this patient population. Supported by a CIORA grant.

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Response to Ixekizumab by C-reactive Protein Level in Patients With Radiographic Axial Spondyloarthritis: Results from the COAST-V (Biological-Naïve) and COAST-W (TNF- α Inhibitor-Experienced) Trials at 52 Weeks

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Objectives: To evaluate the efficacy of ixekizumab (IXE), a selective interleukin-17A inhibitor, compared to placebo (PBO) in patients (pts) with radiographic axial spondyloarthritis (r-axSpA) at 52 weeks (wks) stratified based on non-elevated (≤ 5 mg/L) and elevated (> 5 mg/L) baseline (BL) C-reactive protein (CRP) as measured by the Assessment of Spondyloarthritis International Society 40% response (ASAS40). Additional analysis was done with BL CRP ≤ 10.0 mg/L vs > 10.0 mg/L.

Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were phase 3, randomized, double-blind, PBO-controlled trials investigating efficacy of 80-mg IXE every 4 wks (Q4W) and every 2 wks (Q2W) in pts who met ASAS criteria for r-axSpA, had radiographic sacroiliitis according to mNY criteria, and were biological disease-modifying antirheumatic drug (bDMARDs)-naïve (COAST-V) or tumor necrosis factor inhibitor (TNFi)-experienced (COAST-W). Data from 157 COAST-V pts and 188 COAST-W IXE-treated pts (Wk 0-52) were analyzed. Efficacy was assessed by ASAS40, $\geq 50\%$ improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50) and change in Short Form 36 Physical Component Summary (SF36 PCS) score. Missing data were imputed by nonresponder imputation for binary measures and modified BL observation carried forward for continuous measure. Wk 16 data are presented for comparison.

Results: BL CRP levels in IXE-treated pts through Wk 52 in COAST-V/-W were, ≤ 5.0 mg/L: 34.4%/33.0%, > 5.0 mg/L: 65.6%/67.0%, ≤ 10.0 mg/L: 61.8%/55.9%, and > 10.0 mg/L: 38.2%/44.1%, respectively. At Wk 16, ASAS40 response in COAST-V was numerically higher with IXE in the ≤ 5 mg/L group (Q4W/Q2W/PBO, respectively: 34.5%/42.9%/19.2%) and significantly higher with IXE in the > 5 mg/L group (55.8%*/56.4%*/18.0%, * $P < 0.001$ vs PBO), and was significantly higher with IXE in the ≤ 10 mg/L (43.4%†/42.9%†/16.7%, † $P < 0.01$ vs PBO) and > 10 mg/L groups (57.1%†/64.7%*/20.5% vs PBO). Results were similar in COAST-W and significant in the > 5 mg/L (27.1%/31.9%†/15.4%, † $P < 0.05$ vs PBO) and ≤ 10 mg/L (20.6%/26.4%†/9.8%) groups. At Wk 52, among IXE-treated patients, $> 45\%$ (48.5%-63.3%) COAST-V pts and $> 35\%$ (35.5%-37.3%) COAST-W pts achieved an ASAS40 response, $> 40\%$ (40.7%-58.3%) COAST-V pts and $> 25\%$ (27.4%-32.5%) COAST-W pts achieved a

BASDAI50 response, and change from BL in SF-36 PCS score was > 5 points in both studies regardless of the BL CRP cutoffs evaluated.

Conclusion: A higher proportion of ASAS40 responders was observed in IXE-treated arms vs PBO among bDMARD-naïve and TNFi-experienced pts with r-axSpA when the CRP cutoff of 10 mg/L was evaluated, and the responses were consistent through Wk 52. Furthermore, similar proportions of pts achieved BASDAI50 and SF-36 responses within each patient population regardless of the BL CRP cutoff evaluated.

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Response to Treatment With Ixekizumab in Patients With Active Non-Radiographic Axial Spondyloarthritis Based on HLA-B27 Status and Disease Duration

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Objectives: This analysis evaluated the efficacy of ixekizumab at week 16 in patients with non-radiographic axial spondyloarthritis (nr-axSpA) with or without baseline HLA-B27 positivity and disease duration using a 5-year cutoff.

Methods: COAST-X (NCT02757352) was a phase 3, randomized, double-blind, placebo-controlled study in patients with active nr-axSpA who received 80 mg ixekizumab every 4 weeks (IXE Q4W, N = 96) or every 2 weeks (IXE Q2W, N = 102), or placebo (PBO, N = 105) up to 52 weeks. Post hoc analysis at week 16 included two subpopulations of patients based on baseline HLA-B27 status (positive or negative) or disease duration (< 5 or ≥ 5 years). Here we report Assessment of Spondyloarthritis International Society 40% (ASAS40) and Bath Ankylosing Spondylitis Disease Activity Index 50% (BASDAI50) responses at week 16. Missing data were imputed using non-responder imputation. Treatment comparison was performed using Fisher's exact test.

Results: Of patients treated with IXE Q4W, IXE Q2W, and PBO through week 16, 74.0% (n = 71), 71.6% (n = 73), and 73.3% (n = 77) respectively were HLA-B27+, and 25.0% (n = 24), 27.5% (n = 28), and 25.7% (n = 27) respectively were HLA-B27-. Of patients treated with IXE Q4W, IXE Q2W, and PBO through week 16, 42.7% (n = 41), 40.2% (n = 41), 37.1% (n = 39) respectively had disease duration < 5 years and 57.3% (n = 55), 59.8% (n = 61), 62.9% (n = 66) had disease duration ≥ 5 years. ASAS40 and BASDAI50 response rates were higher with IXE Q4W and IXE Q2W vs. PBO at week 16 regardless of HLA-B27 status or disease duration < 5 or ≥ 5 years. Patients who were HLA-B27+ showed a significantly higher ASAS40 (IXE Q4W, 38%, $P = .047$; IXE Q2W, 44%, $P = .005$ vs PBO, 22%) and BASDAI50 response (IXE Q4W, 32%, $P = .020$; IXE Q2W, 37%, $P = .003$ vs PBO, 16%) at week 16. Patients with disease duration < 5 years showed a significantly higher ASAS40 (IXE Q4W, 42%, $P = .029$; IXE Q2W, 42%, $P = .029$ vs PBO, 18%) and BASDAI50 response (IXE Q4W, 39%, $P = .001$; IXE Q2W, $P = .003$ vs PBO, 8%) at week 16, and patients with disease duration ≥ 5 years showed a significantly higher ASAS40 response for IXE Q2W (39%, $P = .019$ vs PBO, 20%) at week 16.

Conclusion: Patients treated with ixekizumab saw improvement in signs and symptoms of nr-axSpA as assessed by ASAS40 and BASDAI50 responses regardless of HLA-B27 status (positive or negative) or disease duration (< 5 or ≥ 5 years). However, the responses with IXE Q4W and IXE Q2W were significant over placebo for the HLA-B27+ patients and those with < 5 years of disease.

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Effect of Upadacitinib on Reducing Pain in Patients With Active Ankylosing Spondylitis and Inadequate Response to Nonsteroidal Anti-inflammatory Drugs

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Objectives: To evaluate the efficacy of upadacitinib (UPA) on multiple pain assessments through 64 weeks in the randomized phase 2/3 SELECT-AXIS 1 study.

Methods: SELECT-AXIS 1 (NCT03178487) enrolled adults with active AS, who had an inadequate response, intolerance or contraindications to ≥ 2 NSAIDs, were biologic DMARD naive and met the modified New-York Criteria. Patients were randomized 1:1 to UPA 15 mg once daily (QD, $n = 93$) or PBO ($n = 94$) for 14 weeks (Period 1), followed by open-label UPA 15 mg QD 90-week extension (Period 2). Pain endpoints included the proportion of patients achieving $\geq 30\%/\geq 50\%/\geq 70\%$ reduction in Patient's Global Assessment (PGA) of pain on a 0-10 numeric rating scale (NRS) and the minimal clinically important difference (MCID, defined as ≥ 1 point reduction or $\geq 15\%$ reduction from baseline) in PGA of pain. In addition, mean change from baseline in PGA of pain, BASDAI Q2 (neck/back/hip pain) and 3 (peripheral pain/swelling), and patient's assessment of total back pain and nocturnal back pain NRS scores (NRS 0-10) were assessed.

Results: A significantly higher proportion of patients receiving UPA vs PBO achieved reductions in all PGA of pain assessments as early as week 2 that was sustained at all time points in Period 1; the only exception was $\geq 70\%$ reduction in PGA of pain that was significant at week 4 and sustained thereafter. For $\geq 30\%/\geq 50\%/\geq 70\%$ reduction, the response rate increased over time with UPA; the difference for UPA vs PBO also continued to increase over time for $\geq 50\%$ and $\geq 70\%$ reduction endpoints. For MCID, an increase from baseline to week 2 was observed and plateaued thereafter. The mean change from baseline in PGA of pain, BASDAI Q2, total back pain, and nocturnal back pain NRS scores were significantly greater for UPA vs PBO at all time points in Period 1; BASDAI Q3 was significant at week 8 and 14. The effect of UPA on pain reduction was sustained through week 64. PBO patients who switched to open-label UPA at week 14 generally reached the same level of pain reduction as those initially randomized to UPA.

Conclusion: In the SELECT-AXIS 1 study, a greater proportion of patients treated with UPA achieved rapid, significant, and clinically meaningful reductions in pain vs PBO through 14 weeks across multiple pain assessments. The reductions in pain were sustained over time, and patients who switched from PBO to UPA reached the same level of improvement as the continuous UPA group.

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Efficacy and Safety of Upadacitinib in Patients With Active Ankylosing Spondylitis: 1-Year Results From a Randomized, Double-Blind, Placebo-Controlled Study With Open-Label Extension

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Objectives: To report efficacy and safety of upadacitinib (UPA) in patients with active ankylosing spondylitis (AS) who had an inadequate response to NSAIDs through 1 year in the SELECT-AXIS 1 study.

Methods: SELECT-AXIS 1 (NCT03178487) included a randomized, placebo-controlled, 14-week period followed by 90-week open-label extension; reported here are data up to week 64. The study enrolled adult patients with active AS (defined as BASDAI ≥ 4 and patient assessment of back pain ≥ 4 [numeric rating scale, 0-10] at screening and baseline) who had an inadequate response to ≥ 2 NSAIDs or intolerance to or contraindication for NSAIDs and were biologic DMARD naive. At baseline, patients were randomized 1:1 to UPA 15 mg once daily (QD) or placebo (PBO); at week 14, patients continued in the open-label extension and received UPA 15 mg QD. Efficacy assessments included the percentage of patients with ASAS 20/40 response, ASAS partial remission, BASDAI50, and ASDAS responses over time and as change from baseline in ASDAS and BASFI. Treatment-emergent adverse events (TEAEs) were monitored throughout the study and reported as events per 100 patient-years (PY) up to January 31, 2020.

Results: Of 187 patients, 178 (each $n = 89$ for UPA and PBO arms) completed week 14 on study drug and entered the open-label extension; 160 patients completed week 64. Efficacy was maintained or continued to improve throughout the study in the continuous UPA group: 72% (63%-81%) of patients achieved ASAS40 at week 64 in the non-responder imputation (NRI) analysis. Patients who switched from PBO to UPA at week 14 showed a similar speed of onset and magnitude of response compared with patients who were initially randomized to UPA: 70% (61%-80%) of patients in the NRI analysis achieved ASAS40 at week 64. Similar results were observed for other efficacy endpoints. Among all 182 patients receiving UPA (237.6 PY), 618 AEs (260.1/100 PY) were reported. AEs leading to discontinuation (15 events [6.3/100 PY]) and serious AEs (14 events [5.9/100 PY]) were low. No serious infections, active tuberculosis, venous thromboembolic events, gastrointestinal perforation, major adverse cardiovascular events, renal dysfunction, or deaths were reported.

Conclusion: UPA 15 mg QD showed sustained and consistent efficacy over 1 year. Patients who switched from placebo to UPA at week 14 showed a similar efficacy response compared with those who received continuous UPA. No new safety findings were observed compared with safety data from the UPA clinical development program in other indications.

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A Retrospective Study on the Effectiveness of Ixekizumab After Treatment With Secukinumab for Patients With Active Psoriatic Arthritis

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Objectives: Psoriatic arthritis (PsA) is a chronic inflammatory disease associated with skin and nail psoriasis that can cause peripheral arthritis, spondylitis, enthesitis, and dactylitis. Interleukin (IL) 17A is a cytokine that has been identified in the pathogenesis of PsA and two molecules secukinumab and ixekizumab which block IL17A have been shown in clinical trials to be effective for the treatment of this condition. To date one randomized controlled trial has demonstrated efficacy when switching patients with axial spondyloarthritis who have an inadequate response to a TNF inhibitor to an IL17A inhibitor. There have been no studies reporting the efficacy of ixekizumab in patients with active psoriatic arthritis and axial spondyloarthritis and a prior inadequate response to secukinumab. Consequently, clinicians may be hesitant to try a second IL17A inhibitor and instead choose a therapy with an alternative mode of action. This study aims to assess the effectiveness of ixekizumab for treating psoriatic arthritis among patients with psoriatic arthritis treated with secukinumab and who have had an inadequate clinical response.

Methods: We conducted a chart review of adult patients with psoriatic arthritis treated at one clinical center. We identified all patients with active inflammatory arthritis who were switched from secukinumab to ixekizumab. Baseline demographics such as disease duration, age, gender, number of previous DMARDs, and previous time on secukinumab were collected.

We collected clinical outcome data such as tender and swollen joint count, enthesitis based on SPARCC score, dactylitis, psoriasis severity, CRP, and BASDAI if axial involvement was present.

Results: Eight of 10 patients were included in the analysis. Most patients were female, average age 62 years old, and had been on secukinumab for an average of 79 weeks. Twelve weeks following switch to ixekizumab, 6/8 had improvement in tender joint count, 6/8 improved in swollen joint count, 2/2 had resolution of enthesitis, 4/4 had resolution of dactylitis, 5/6 had improvement in psoriasis severity, 1 patient had absolute improvement of 2.3 in BASDAI, and 7/8 had improvement in CRP level.

Conclusion: Patients with active psoriatic arthritis despite treatment with secukinumab may still have a clinical response following treatment with another anti-IL17 agent. Larger studies will be required to confirm this finding and studies which emphasize dactylitis and enthesitis outcomes will be needed as most patients did not have activity in these domains.

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The Added Value of Whole Spine MRI in Ankylosing Spondylitis Vs Psoriatic Arthritis for Disease Activity Assessment

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Objectives: We aimed to compare the spinal and sacroiliac joint (SIJ) magnetic resonance imaging (MRI) finding of patients with ankylosing spondylitis (AS) vs psoriatic arthritis (PsA) and understand the added value of spine MRI in addition to SIJ MRI in the real-life setting.

Methods: Axial MRI scans (whole spine and SIJ) requested by rheumatologists at the Ottawa Hospital between January-2012 and January-2018 were screened retrospectively, and patients who had known diagnosis of AS or PsA were included in the study. SIJ and spine MRIs were read by two experienced radiologists separately, blinded to each other, patients' diagnosis and clinical features. Active (bone marrow edema) and structural (erosion, fatty lesions, bone proliferation, ankylosis, sclerosis) changes were recorded. Reports were compared to identify any discrepancies in 2 subgroups and analysis was done after readers reached the consensus. Since bone marrow edema does not always indicate active inflammation when seen with concomitant degenerative changes, radiologists were also asked to determine a confidence level for inflammation suggestive of SpA.

Results: Among 644 whole spine and sacroiliac joint MRIs, 90 patients known to have a diagnosis of AS (n = 55) or PsA (n = 35) were included in the analyses. Both active and structural changes in AS and PsA patients were found in similar frequencies in the spine. Regarding particular regions of the spine, AS patients had numerically more active [n = 11 (20%) and n = 3 (9%), respectively, P = 0.233] and structural changes [n = 26 (47%) and n = 13 (37%), respectively, P = 0.388] in the cervical spine than PsA, although statistically not significant. The two groups had a similar rate of active and structural changes of the thoracic spine, lumbar spine and SIJs. The percentage of people with only active change of the spine with normal SIJ were 13/55 (24%) in AS and 8/35 (23%) in PsA. Among 72 patients whose confidence active inflammation score was available by consensus, only 1 patient's spine MRI was scored as active while SIJ was negative.

Conclusion: Our results showed that AS patients may have more cervical active changes than PsA on MRI. Additionally, the contribution of spinal MRI to the SIJ MRI to assess disease activity is limited for both diseases; but may identify a subset of patients with spinal inflammation in the absence of SIJ inflammation. Our results suggest screening of the spine to be limited to patients with normal SIJ MRI.

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Epicardial Fat as Cardiovascular Risk Factor in Inflammatory Arthritis

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Objectives: Cardiovascular disease (CVD) is the leading cause of death in inflammatory arthritis. Epicardial fat volume (EFV) has emerged as one of the novel markers of CVD. The objective of the study was to examine the association of EFV with disease activity and other cardiovascular surrogate markers in rheumatoid arthritis (RA) and spondyloarthritis (SpA) patients. **Methods:** RA (n = 114) and SpA patients (n = 128), including 28 ankylosing spondylitis and 100 psoriatic arthritis patients, were recruited. EFV was assessed from cardiac computed tomography scan data obtained for coronary artery calcium scoring (CACS). Additionally, carotid intima-media thickness and carotid plaque area data obtained by carotid ultrasound were used to study the correlation between EFV and atherosclerosis. We compared EFV between RA and SpA patients and assessed the association between EFV and arthritis disease activity indices as well as other inflammatory and atherosclerotic markers in these arthritis populations using multivariate regression models adjusted for age and sex as well as, Framingham risk.

Results: RA patients were older than SpA patients (62.3 ± 10.7 vs. 56.3 ± 9.6 years, $P < 0.0001$). Compared to RA patients, SpA group had higher proportion of males (48% vs. 13%, $P < 0.0001$), Caucasians (85% vs. 63%, $P = 0.002$) and metabolic syndrome (47% vs. 31%, $P = 0.01$) with higher mean BMI (30.6 ± 7.2 vs. 28.7 ± 7.1 kg/m², $P = 0.03$) and waist circumference (100.4 ± 16.8 vs. 93.7 ± 16.6 cm, $P = 0.002$) respectively. SpA patients had significantly higher mean EFV (104.2 ± 46.7 vs. 86.7 ± 47.9 ml, $P = 0.004$) than RA patients, which remained statistically significant in multivariate models (β 18.3, 95% confidence interval [CI] 5.5-31.1, $P = 0.005$ adjusted for age and sex; β 17.4, 95% CI 5.8-28.9, $P = 0.003$ adjusted for Framingham risk score (FRS)). While high sensitivity C-reactive protein was significantly associated with elevated EFV in the whole study population in multivariate models (β 0.97, 95%CI 0.39-1.56, $P = 0.001$ adjusted for age, sex and disease category; β 0.82, 95%CI 0.24-1.39, $P = 0.006$ adjusted for FRS and disease category), no similar association was observed between individual arthritis-clinical disease activity indices and EFV. Among atherosclerotic markers, only CACS was associated with increase in EFV in the whole study population in the multivariate model adjusted for FRS and arthritis disease category (β 0.02, 95% CI 0.01-0.05, $P = 0.045$).

Conclusion: The higher EFV in patients with SpA and its association with inflammatory markers and CACS highlight the increased CV risk in this patient population. Obesity and its related metabolic abnormalities may underlie this association.

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A Rare Case of Cystic Neutrophilic Granulomatous Mastitis With Erythema Nodosum and Polyarthritis

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Background: Cystic neutrophilic granulomatous mastitis (CNGM) is a rare subtype of a benign inflammatory breast disease. We report the first case of a patient with biopsy-proven CNGM, erythema nodosum (EN), and polyarthritis.

Case: A 38-year-old, previously healthy female, with a family history of ankylosing spondylitis and rheumatoid arthritis, developed a tender left breast mass in July 2020. She was given a course of antibiotics, without improvement. Breast imaging and biopsy demonstrated mild, chronic inflammation, without atypia.

In August 2020, the patient developed symmetrical polyarthritis, bilateral

lower extremity nodules, night sweats, fatigue, and fevers > 38°C. She was admitted and infectious work up including tuberculosis, COVID-19, ASOT, syphilis, HIV, Hepatitis B, and C was negative. ANCA, ANA, ENA, anti-CCP, rheumatoid factor, cryoglobulin, ACE level, IgG subclass, and SPEP were unremarkable. CRP peaked at 240 and HLA-B27 was positive. Skin nodule biopsies were compatible with EN.

Repeat core needle biopsy of her breast mass showed granulomatous inflammation with giant cells, neutrophils, and cyst formation. Two pathologists concluded histology was consistent with CNGM. Gram stain for *Corynebacterium*, acid-fast bacilli, fungus, and bacterium were negative. The patient was treated with Prednisone 0.5mg/kg for 7 days with a tapering course and maintained on low dose methotrexate. She had rapid clinical improvement with prednisone and at 2 months follow up, she has had resolution of breast pain, systemic symptoms, and progressive size reduction of her breast mass.

Conclusion: Histological features of CNGM were first described in 2002. However, there is no established diagnostic criteria. This condition is highly associated with *corynebacterium*, isolated in around 58% of cases. Patients often present with a unilateral breast mass and local symptoms of pain, nipple discharge, erythema and abscess. Systemic features are very rare.

We suggest that in patients with a presumed diagnosis of CNGM and systemic features, the initial step in management should be an attempt to isolate *corynebacterial*. Comprehensive workup should be done to rule out other entities on the differential diagnosis, including malignancy, infection, foreign bodies, vasculitis, rheumatoid nodule, sarcoidosis, and IgG4-related disease.

Initial treatment with antibiotics effective towards *corynebacterium* and Non-steroidal anti-inflammatory drugs (NSAIDs) are reasonable. However, if patients fail to respond and develop progressively debilitating symptoms, a trial of corticosteroids may be beneficial. We caution against surgical options as the initial therapy given higher rate complications.

Conclusion: Here, we describe the first case of CNGM associated with polyarthritis and EN in the English literature.

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#ArthritisThenNow: Reflecting on Treatment Changes in Inflammatory Arthritis

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Objectives: Over the last twenty years, treatments for inflammatory arthritis have changed dramatically. The first biologic response modifiers were approved by Health Canada in 2001[i] and resulted in significant improvements to quality of life for patients, including increased participation in activities of daily living, pursuing life goals such as schooling, parenting and work, and overall improved health outcomes. The Canadian Arthritis Patient Alliance led a campaign, #ArthritisThenNow, to increase awareness of how different life is today for people living with inflammatory arthritis as a result of these changes and convey this significant shift to policy makers, the public and the patient community. [i] Canada. Health Canada. Drug Product Database, Product Monograph for Etanercept (Enbrel), accessed September 10, 2020.

Methods: A one-hour Twitter Chat was held on September 26, 2020 on #ArthritisThenNow from 12:00 to 13:00 EDT. The chat was organized by CAPA and co-hosted by Michael Kuluva, a well-known fashion designer and patient advocate, and Lene Anderson, an arthritis blogger and writer (www.theseatedview.com). The chat questions were developed in advance and blog posts were shared on CAPA's website. Each host promoted the Twitter Chat through their websites, newsletters and their digital communities.

Results: Thirty-eight people participated in the chat and over 450 tweets were shared by people living with arthritis, patient organizations and the general public. There were 4.25 million Twitter impressions (this represents the number of times a tweet appeared to users in either their timeline or search results). A social media analytic tool, Symplur, was used to measure audience engagement using the hashtag #ArthritisThenNow. In addition, pertinent Tweets before, during, and after the chat were obtained.

Conclusion: The #ArthritisThenNow campaign was successful in increasing awareness of the fundamental changes in arthritis diagnosis and treatment over the last twenty years. CAPA is continuing this campaign to ensure policy makers, the patient community and the general public recognize the evolution in treatment and related outcomes. These treatment changes have improved several outcomes important to patients, improved workforce participation[i] and reduced rates of disability and inpatient hospital costs[ii]. [i] ter Wee MM, Lems WF, Usan H, Gulpen A, Boonen A. The effect of biological agents on work participation in rheumatoid arthritis patients: a systematic review. *Ann Rheum Dis.* 2012;71(2):161-171. doi:10.1136/ard.2011.154583 [ii] Hsieh PH, Wu O, Geue C, McIntosh E, McInnes IB, Siebert S. Economic burden of rheumatoid arthritis: a systematic review of literature in biologic era. *Ann Rheum Dis.* 2020;79(6):771-777. doi:10.1136/annrheumdis-2019-216243

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Factors Associated With Depression and Anxiety in People Living With Rheumatic Disease: Findings from an International Survey Administered During the COVID-19 Pandemic

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Objectives: Individuals with rheumatic diseases are disproportionately affected with depression and anxiety. Given the repercussions of the COVID-19 pandemic for this immunocompromised patient population it is important to understand its impact on their mental health. Our objective was to survey people living with rheumatic diseases to characterize the burden of depression and anxiety during the COVID-19 pandemic as well as identify associated factors.

Methods: We conducted a cross-sectional international online survey from 04/23/2020 - 10/06/2020 among individuals with self-identified rheumatic disease(s). Depression and anxiety were assessed using the 9-item Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder 7-item (GAD-7), respectively, and a score ≥ 10 indicated presence of either. Independent variables included demographic characteristics, disease severity and duration, social isolation (6-item Lubben Social Network Scale [LSNS-6]), loneliness (3-item UCLA Loneliness Scale [UCLA-3]), and health behaviours (e.g., alcohol, physical activity, sleep). We used multiple linear regression to evaluate associations between independent variables and depression or anxiety.

Results: 687 participants (91.2% female; 45.2 ± 14.0 years) completed the survey with the majority diagnosed with rheumatoid arthritis ($n = 490$, 71.3%) or systemic autoimmune rheumatic diseases ($n = 168$, 24.5%). Depression was indicated in 264 (43.0%) participants, anxiety in 210 (33.9%), and comorbid depression and anxiety among 163 (27.2%). Overall, 188 (29.8%) participants were characterized as being socially isolated (LSNS-6 score < 12) and the mean LSNS-6 score was $14.7 (\pm 5.6)$. A total of 320 (51.1%) participants experienced loneliness (UCLA-3 score ≥ 6) and the mean UCLA-3 score was $5.6 (\pm 1.9)$. Factors independently associated with depression included age ($\beta = -0.05$, $P = 0.012$), moderate or severe disease severity ($\beta = 2.50/\beta = 3.90$, $P < 0.0001$), worries about expenses ($\beta = 1.40$, $P = 0.006$), social isolation ($\beta = 2.70$, $P < 0.0001$), loneliness ($\beta = 3.19$, $P < 0.0001$), increased alcohol consumption ($\beta = 1.52$, $P =$

0.022), and decreased sleep ($\beta = 2.22$, $P < 0.0001$). All of these factors were also associated with the presence of anxiety. Finally, 60.3% of participants with depression and/or anxiety received treatment for their mental health during the COVID-19 pandemic.

Conclusion: Our survey results demonstrate a substantial burden of depression and anxiety for people living with rheumatic diseases during the COVID-19 pandemic. Clinical awareness of the detrimental impact of social isolation, loneliness, and changes in health behaviours on depression and anxiety are important for monitoring and supporting the mental health of individuals with rheumatic diseases.

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Rates of Disease Flares and Adverse Pregnancy Outcomes Among Pregnant Women Treated With Tumour Necrosis Factor Inhibitors (TNFi) for Inflammatory Arthritis

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Objectives: Women with inflammatory arthritis (IA) have an increased risk for disease flares and adverse outcomes in pregnancy, but the contributory impact of therapy versus other risk factors is unclear. This study sought to advance knowledge surrounding the impact of TNFi use in pregnancy by comparing rates of disease flares and adverse pregnancy outcomes among pregnant women with IA treated with TNFi or non-biologic agents (nBA).

Methods: Pregnancies among women with IA were identified from a single Rheumatology practice in Edmonton, Canada. Medical records were reviewed from documented visits during pregnancy and post-partum. Disease flares and adverse pregnancy outcomes were compared between pregnancies in women treated with TNFi or nBA. Adverse pregnancy outcomes were defined as miscarriage, pre-term labour, intra-uterine growth restriction, pre-eclampsia, Cesarean section, small/large for gestational age infant, and newborn admission to neonatal intensive care. Disease flares were defined as an escalation in treatment or corticosteroid use in pregnancy or post-partum.

Results: Among 17 pregnancies, 29.4% ($n = 5$) were treated with TNFi and 70.6% ($n = 12$) were treated with nBA. The mean age at delivery was similar between groups ($31.2 \text{ yrs} \pm 3.4$ vs. $31.4 \pm 3.70 \text{ yrs}$). The most common diagnosis was rheumatoid arthritis (58.8%, $n = 10$). Certolizumab pegol was the most common medication used by TNFi treated women (60%, $n = 3$). Disease flares were more common in nBA treated women compared to TNFi treated women (66.7%, $n = 8$ vs. 20%, $n = 1$). A higher proportion of TNFi treated women experienced at least one adverse pregnancy outcome compared to nBA treated women (100%, $n = 5$ vs. 50%, $n = 6$). In-depth chart review of TNFi treated women revealed 3 pregnancies complicated by uncontrolled disease and confounding obstetrical risk factors (including miscarriage, trisomy 21, ectopic pregnancy, in-vitro fertilization, prednisone use, and/or gestational hypertension). Among 2 pregnancies, disease was well controlled, but one woman underwent C-section delivery for failure to thrive, and one woman delivered a post-term infant with macrosomia.

Conclusion: Pregnant women with IA treated with TNFi experienced fewer disease flares but more adverse pregnancy outcomes compared to those treated with nBA. Women treated with TNFi also had confounding refractory disease and obstetrical risk factors which possibly contributed to an increased risk for adverse pregnancy outcomes, reinforcing the need for collaboration between rheumatologists and obstetricians for optimal care. Further research should control for obstetrical risk factors in pregnant women with IA to elucidate the independent impact of TNFi treatment on risk for adverse pregnancy outcomes.

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Disease Modifying Anti-rheumatic Drugs (DMARDs) and Biologic Therapy Use During Pregnancy: A Single-center Mixed Methods Study

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Objectives: Rheumatic diseases including rheumatoid arthritis (RA),

seronegative inflammatory arthritis (SpA) and systemic lupus erythematosus (SLE) commonly affect women of child-bearing age. Both these diseases and their treatments have been shown to impact fetal and maternal outcomes. Although there is growing evidence outlining safety of many anti-rheumatic drugs (ARDs) in pregnancy, many patients discontinue treatments in pregnancy 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 at St. Michael's Hospital in Toronto, Canada, from January 2013 until November 2019. A 12-item questionnaire was administered to women attending this clinic. Data was analyzed using descriptive statistics.

Results: Thirty-eight women and forty-five pregnancies were identified, with RA ($N = 12$, 32%), SLE ($N = 18$, 27%) and SpA ($n = 8$, 16%) representing the majority. Twenty-nine patients (60%) were exposed to disease modifying anti-rheumatic drugs (DMARDs) and seven patients (16%) to biologics during pregnancy. Of those who experienced perinatal medication changes, the highest proportion (57%) occurred pre-partum, with fewer changes in each subsequent trimester. Patients who received pre-pregnancy counselling were more likely to have pre-pregnancy medication adjustments and were more likely to utilize a DMARD or biologic during pregnancy. The survey was completed by 19 respondents. Fourteen women (74%) reported that they would consider ARD use in pregnancy, with the highest proportion endorsing comfort with DMARDs ($N = 16$, 84%; hydroxychloroquine 8 (42%), azathioprine 7 (37%), sulfasalazine 3 (16%)), compared to steroids ($N = 3$, 16%), non-steroidal anti-inflammatory drugs ($N = 6$, 32%) and biologics ($N = 2$, 11%). Fifteen participants (79%) believed their questions were adequately answered by health care providers with the majority (79%) describing their rheumatologist as their primary information source. Most patients believed that information received from healthcare providers was helpful ($N = 15$, 79%) and felt that they were provided adequate resources to inform decisions about medications in pregnancy ($N = 11$, 58%).

Conclusion: While the majority of women with rheumatic diseases in our cohort continued on ARD therapy during pregnancy, most survey respondents reported discomfort with their use, despite evidence supporting their safety in recent literature. This discrepancy between patient perspectives and available evidence is important to consider when counseling patients on ARD use in pregnancy. Survey respondents relied on their rheumatologist as their primary information source, highlighting the important role rheumatologists can play in informing patient perspectives surrounding ARD use in pregnancy.

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A Transcontinental Comparison of Patient Characteristics and Minimal Disease Activity in Psoriatic Arthritis

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Objectives: Psoriatic Arthritis (PsA) is a heterogeneous disease with both environmental, genetic factors playing a role in this diversity. The aim of this study is to compare the patient profiles and outcomes in PsA patients in 3 countries from 3 different continents.

Methods: PsA patients from 3 countries (Turkey, $n = 184$; Canada, $n = 200$; Italy, $n = 177$) from the Psoriatic Arthritis- International Database (PsArt-ID) were compared for patient demographics, disease features, treatment approaches as well as minimal disease activity (MDA) rates. Odds

ratios were calculated to determine the impact of the country of residence on the MDA achievement.

Results: Patient profiles were different such as patients from Italy were older [median (Q1-Q3): 59 (51-65)] than patients from Turkey [48 (37-58)] and Canada [55 (44-65)] and Italian patients had more frequent comorbidities and were more frequently smokers. For disease phenotypes, patients from Italy had axial disease less frequently (12%) than others (Turkey 23%, Canada 52%). Similarly, disease activity in patients from Italy were higher for the joints and skin activity than patients from Turkey and Canada [Joints: median (Q1-Q3) swollen joint count (SJC)-Italy: 2 (1-2.7), Turkey: 0 (0-1), Canada: 0 (0-1); median (Q1-Q3) tender joint count (TJC)-Italy: 4 (2-6), Turkey: 1 (0-4) Canada: 1 (0-4); Skin: median (Q1-Q3) body surface area (BSA)- Italy: 2 (1-4), Turkey: 1 (0-1), Canada: 1 (0-3)]. Reflecting these, MDA was achieved less often in patients from Italy (Turkey = 38 (27%), Canada = 90 (47), Italy = 26 (21%). Lowest rate of biologic use was observed in Italy [25/147 (18.4%), Turkey: 46/176 (26.1%), Canada: 58/171 (33.9%)]. Logistic regression analysis between country pairs showed that MDA was achieved 3.33 times more in Canada than Italy and 2.39 more than Turkey [OR (CI): Turkey vs Italy = 1.391 (0.786-2.460), $P = 0.257$; Canada vs Turkey = 2.392 (1.498-3.818), $P < 0.001$; Canada vs Italy = 3.326 (1.983-5.577); $P < 0.001$].

Conclusion: PsA patient characteristics differ across countries which may be leading to differences in treatments and MDA rates. The differences can be a combination of genetic or geographical differences as well as the demographics of the general population in that area. Therefore, the unmet needs of PsA patients may vary globally.

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Practical Strength Training Prescription Parameters for People With Rheumatoid Arthritis: A Scoping Review With Recommendations for Future Research

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Objectives: Strength training is an effective disease management strategy for people with rheumatoid arthritis (RA). While guidelines supporting the use of strength training in the management of RA exist, strategies to address the numerous RA-specific barriers to strength training (e.g., fatigue, pain, flares, etc.) are needed to help improve low rates of strength training participation. The objectives of this scoping review were to 1) summarize current strength training prescription parameters for RA and how they address RA-specific barriers to participation and 2) identify areas for future research.

Methods: Recommendations by Levac et al. (2010) and PRISMA-ScR were followed in the conduct and reporting of this review, respectively. Using an integrated knowledge translation approach, patient/healthcare provider partners were engaged in research question development, data extraction, and review and interpretation of the findings. Medline, Embase, and CINAHL databases, and gray literature were systematically searched. Inclusion criteria were: i) recommendations, guidelines and review articles, ii) articles describing strength training prescription parameters, and iii) people with RA as the target population. Data were extracted using an iteratively developed data charting form. Data were mapped to strength training participation barriers identified in a previous qualitative study of people with RA. Quality of guidelines were appraised using the AGREE II. Data screening and extraction were performed in duplicate by two reviewers.

Results: A total of 27 articles met the inclusion criteria. Strategies for managing pain, stiffness, fear of activity, providing flexible exercise

prescriptions, identifying individual strength training limits, and identifying RA-specific resources were addressed at least once across the included studies. RA-specific barriers to strength training remaining to be addressed in the available guidelines, recommendations, and reviews included memory, sleep, mental health, fatigue, medication side effects, and acceptance of capabilities when performing strength training. The lowest average AGREE II domain score (19%) across guidelines was given for applicability. We identified priorities for future research including how: 1) strength training can be manipulated (e.g., dose, type, delivery) to increase participation, 2) RA symptoms and assessment strategies can guide appropriate prescription, and 3) to develop and execute optimal recovery strategies.

Conclusion: Greater details within current strategies for targeting RA-specific barriers when prescribing strength training are needed and several more barriers remain unexplored. This review highlights recommendations for the development of future guidelines and research to move strength training prescriptions into practice.

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Airway Compromise from Cricoarytenoid Joint Swelling Secondary to Rheumatoid Arthritis

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder predominantly affecting small joints. The cervical spine is involved in 30-50% of RA patients, with C1-C2 being the most commonly affected level. We present a patient with cricoarytenoid joint swelling causing airway obstruction thought to be due to RA.

Case: A 63-year-old male with RA was admitted with a 3-week history of dyspnea. He was diagnosed with RA in 2017 with high-titre anti-CCP and RF, and negative ANA and ANCA. He was initially managed with hydroxychloroquine and methotrexate (MTX) SC. Despite increased doses of MTX, he had recurrent flares with max CRP 41 requiring IM triamcinolone for joint pain control. After over a year on this dual regimen, he was switched to leflunomide, but continued to have joint swelling, right hand paresthesias, and neck pain with normal cervical X-rays except for mild narrowing of the C6-7. His CRP at this time was 65. Adalimumab was added with no improvement in his symptoms after 8 months. Finally, leflunomide with tocilizumab regimen was started 9 months prior to his current presentation, and the patient was able to achieve a low disease score.

In August 2020, he presented with stridor with an upper airway obstruction as demonstrated by vocal cord paralysis, posterior glottic stenosis, and cricoarytenoid fixation by ENT assessment. He was subsequently intubated and transferred to the ICU. His peripheral joints were inactive, and his CRP (albeit on tocilizumab) and WBC were normal. MRI cervical spine demonstrated diminished T1 and mixed T2 weighted signal in the C5-6 vertebral bodies accompanied by disc space narrowing and irregularity of the adjacent endplates, as well as diffuse thickening and enhancement of the supraglottic and glottic soft tissues. Investigations into other causes of airway compromise were unrevealing. To maintain and secure his airway, the patient underwent a tracheostomy, which noted purulence in the oropharynx, and immobile cricoarytenoid joints on palpation with overlying soft tissue edema resulting in a narrow airway. His hospital stay was complicated by MSSA pneumonia with paratracheal cellulitis treated with a course of cefazolin. The patient was discharged in stable condition on leflunomide with plans to reassess effectiveness of tocilizumab as an outpatient.

Conclusion: Airway obstruction secondary to cervical spine RA is uncommon but can occur in the setting of severe, chronic, and poorly controlled disease.

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Fibromyalgia in Patients With Breast Implants: Improvement in Symptoms and Mitochondrial Integrity After Explanation

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Objectives: For many Canadians, fibromyalgia is a chronic but debilitating disease characterized by severe fatigue, diffuse pain and other symptoms such as cognitive impairment and autonomic dysregulation. Patients with breast implants may present with similar symptoms fulfilling the criteria for fibromyalgia. At the molecular level, patients with fibromyalgia may develop dysregulated metabolic function(s) associated with increased cell-free mitochondrial DNA (mtDNA). In this study, we sought to determine if explanation results in the improvement of fibromyalgia symptoms and/or the normalization of cell free mitochondrial DNA (mtDNA).

Methods: Patients with breast implants referred to our Rheumatology Clinic were evaluated for fibromyalgia symptoms using the modified 2010 ACR criteria for fibromyalgia. mtDNA integrity was determined as the ratio of the necrotic/apoptotic mtDNA fragments in patient serum. Univariate and multivariate statistical analyses were conducted using STATA 16.

Results: In analysis of 36 breast implant patients, we found that patient reported symptoms of fibromyalgia (Widespread Pain Index, 11.6:6.33, $P < 0.001$; System Severity Scale, 10.1:6.6, $P < 0.001$) were significantly improved from pre-explanation values. Analysis of cell free mtDNA integrity showed that breast implant patients who had not had their implants removed ($n = 9$), had significantly reduced mtDNA integrity when compared to patients who had been explanted ($n = 9$) (1.02:1.32, < 0.001), as well as healthy controls ($n = 5$) (1.02:1.30, $P = 0.01$). Pre-explant patients' mtDNA integrity was found to be similar to fibromyalgia controls ($n = 6$) (1.02:0.98, $P = 0.65$).

Conclusion: Patients with breast implants may develop fibromyalgia clinically indistinguishable from other patients with fibromyalgia. Importantly, in these patients, symptoms are reversible with silicone removal. Furthermore, we show that breast implant related fibromyalgia results in abnormal mtDNA integrity, as previously demonstrated in idiopathic fibromyalgia. Remarkably, following explantation patients do not only experience symptomatic improvement but also demonstrate recovery of mtDNA integrity to near normal levels. Understanding these mechanisms requires much deeper exploration; however, improvement of this biomarker following explantation of breast implants is a notable finding. Funding: Dutch Kidney Foundation (17PhD01) Arthritis Society (19-0558)

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Use of Subcutaneous Immunoglobulin in Connective Tissue Disease: A Literature Review

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Objectives: Intravenous Immunoglobulin (IVIg) is used as an alternative or adjunct therapy for refractory rheumatic disease. Treatment with IVIg requires frequent visits and is limited by patients' access to hospital, appointment availability, and risk of infection from close contacts in hospital. Studies with immunodeficiency patients have demonstrated that home-based subcutaneous immunoglobulin (SCIg) therapies are cost-effective with similar outcomes and less adverse events compared to IVIg. The use of SCIg has been reported in rheumatic disease but there are no randomized trials and so efficacy is not known. The objective of this systematic review was to summarize published data on the effectiveness and safety of SCIg for the treatment of Connective Tissue Disease (CTD).

Methods: We searched the literature using Medline, EMBASE, and the Cochrane Central Register of Controlled Trials, for clinical studies pertaining to use of SCIg in adults with a diagnosis of CTD. Case reports were excluded given the expected amount of bias. Two independent reviewers screened studies and extracted data on effectiveness defined by disease remission, and safety outcomes defined by all-cause mortality and treatment-related toxicities. Patient characteristics, diagnosis and treatment outcomes were summarized descriptively. Methodological quality was assessed using the NIH Quality Assessment Tool.

Results: We identified 606 articles in the initial search and included 4 studies for analysis with a total of 69 patients from Europe and a mean NIH Quality Assessment score of 7.5/9. All were case series related to myositis; no reports on other CTD met criteria for inclusion. All patients had been on prior corticosteroids and immunosuppressants, and 43/69 (62%) had been treated with IVIg. All studies reported improvement or stability in muscle, skin, and dysphagia symptoms in addition to improved functional scores and reduced corticosteroid use. One study noted symptom progression in 6/11 (55%) patients with cardiac involvement and 1/8 (13%) patients with respiratory involvement. Three deaths were reported, none related to SCIg use. SCIg was well tolerated. 13/42 (31%) patients reported injection site reactions; otherwise there were 2 cases of diarrhea, 3 cases of headache, 4 cases of myalgia, and 3 cases of fatigue. There were no cases of serious infections.

Conclusion: Our review demonstrates that SCIg is well tolerated and effective in the treatment of myositis, resulting in maintenance of disease remission in both patients transitioned from IVIg treatment and those initially treated with SCIg. Larger studies are needed to characterize the clinical utility of SCIg in myositis and other CTDs.

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Clinical Features of Patients With Interstitial Lung Disease and Anti-Ro52 Antibody.

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Objectives: Autoantibody testing is customarily completed in patients with interstitial lung disease (ILD) to assess for possible underlying connective tissue disease (CTD). The anti-Ro52 antibody is commonly obtained as part of the extractable nuclear antigen antibodies (ENA) panel in this context. However, the clinical significance of positive anti-Ro52 antibodies in these patients remain unclear. This study describes a Canadian cohort of patients with ILD and positive anti-Ro52 antibodies and aims to identify common clinical, laboratory, and radiologic features in this population.

Methods: We performed a retrospective chart review of all patients seen at the ILD clinic of a tertiary care centre since its inception until September 2020. All adult patients who were anti-Ro52 positive with a diagnosis of ILD by American Thoracic Society criteria were included. Signs and symptoms associated with CTD, serologic markers, high resolution CT (HRCT) findings and pulmonary function test (PFT) results were recorded using a standardized data extraction form. Proportion of patients with progression of ILD at 1-year follow-up was also recorded. This was defined as a decrease in forced vital capacity (FVC) greater than 10% of predicted or a decrease in diffusing capacity of carbon monoxide (DLCO) of greater than 15% predicted.

Results: A total of 22 patients were included in this study. The mean age was 70.3 years \pm 11.6 and 59% were female. ANA was positive in 72.7% of patients and 13.6% of patients were positive for both anti-Ro52 and anti-Ro60. Mean MRC dyspnea score on initial assessment was 2.45 \pm 1. 40.9% of patients had arthritis, 22.7% had photosensitive rash, 36.4% had Raynaud's phenomenon, 22.7% had xerophthalmia and 27.2% had xerostomia. HRCT was completed in 21/22 patients. Of patients who underwent HRCT, scan patterns were most consistent with usual interstitial pneumonia (UIP) in 57.1%, non-specific interstitial pneumonia (NSIP) in 28.6% and other in 14.3% of patients. Progression of disease based on worsening PFT was found in 13.6% of patients at 1-year follow-up. 3 patients had a pre-existing diagnosis of CTD. After assessment by a rheumatologist, 9 additional patients were diagnosed with CTD.

Conclusion: We describe, to our knowledge, the first Canadian cohort of patients with ILD and anti-Ro52 positivity. This cohort can now be compared to patients with ILD who are negative for anti-Ro52, or patients who carry other autoantibodies in the ENA panel to further clarify the role of autoantibody testing in ILD.

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Paraneoplastic Vasculitis Secondary to Renal Cell Carcinoma

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Background: A 50-year-old man presented with features of systemic vasculitis and was later diagnosed with Renal Cell Carcinoma (RCC), highlighting the importance of considering paraneoplastic phenomena as an underlying cause of systemic vasculitis.

Case: A 50-year-old male with asthma and allergic rhinitis presented to hospital with binocular diplopia, diffuse joint swelling, and rash. He reported two months of progressive daily headaches, drenching night sweats and a swollen nose that had failed two courses of antibiotics for presumed sinusitis. On examination: HR 109, BP 151/74, and T 38.8°C. He had pronounced right peri-orbital swelling and conjunctival injection, a chronic annular tongue lesion, and swelling/erythema of the nasal bone and upper cartilage. There was bilateral synovitis in the PIPs, wrists, elbows, feet, ankles, and knees and palpable purpura in lower limbs and buttocks.

Investigations revealed normocytic anemia (Hb 115 g/L) and neutrophilic leukocytosis (WBC $20.2 \times 10^9/L$, neutrophils $17.3 \times 10^9/L$). Renal function was maintained however urine studies revealed hematuria and non-nephrotic proteinuria (2.48 g/day). Inflammatory markers were elevated (ESR 122 mm/hr, CRP > 190 mg/L). Infectious work-up was negative. Autoimmune serologies revealed RF 123 kIU/L, anti-CCP 250 u, ANA 1:80 speckled, a mildly positive anti-RO52/TRIM21 of 45 cu, and negative anti-dsDNA, complements, APLA, immunoglobulins, and ANCA/PR-3. Imaging revealed pre-septal thickening of the right orbit, neck and abdominal lymphadenopathy, bilateral pulmonary ground-glass opacities, a 17 mm nodule in the left kidney, and a suspected left scapular metastatic lesion. Biopsy of skin revealed leukocytoclastic vasculitis (LCV) and of scapular lesion revealed Clear Cell RCC. Paraneoplastic systemic vasculitis secondary to RCC was suspected. He was started on Prednisone 60mg PO daily and Hydroxychloroquine 400mg PO daily and received radiotherapy to his renal and scapular lesions with symptomatic improvement. 7 months later, he has been weaned off prednisone with no recurrence of symptoms. He awaits definitive management of his RCC.

Conclusion: RCC is associated with several paraneoplastic syndromes. Conversely, paraneoplastic vasculitis secondary to solid tumours is rare. Our patient demonstrated a collection of somewhat atypical features; dramatic periorbital and nasal swelling, extensive polyarthritis, prominent palpable purpura, and negative ANCA. Systemic vasculitis, particularly when atypical or resistant to immunosuppression, should prompt investigation of an underlying trigger such as malignancy. Treatment of the malignancy leads to resolution of paraneoplastic vasculitis, while recurrence of the vasculitis can signal recurrence of malignancy. Our case highlights the importance of exploring the precipitant of a systemic vasculitis.

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Rheumatic Complications of Cancer Immunotherapy: Answering the Call and Meeting the Educational Needs of Canadian Rheumatologists

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Objectives: Background: Immune checkpoint inhibitors (ICI) have revolutionized the treatment of many advanced stage malignancies. Their use has been limited by a host of off-target immune-related adverse events (irAE) including those of a rheumatic nature (Rh-irAE). Rheumatologists have been increasingly called upon to assist with management of de novo Rh-irAE and advise on the use of ICI in patients with pre-existing rheumatic disease (PRD). This is a rapidly evolving area of medicine with limited clinical data. The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO) is a network of rheumatologists with interest and expertise in the management Rh-irAE. A needs assessment of Canadian Rheumatologists

conducted by CanRIO in 2019 highlighted important knowledge gaps in this emerging field and provided the rationale for the development of educational initiatives.[1] Objectives: CanRIO developed and presented a small group case-based educational session at the 2020 Canadian Rheumatology Association Annual Scientific Meeting, addressing the 4 most common Rh-irAE and the management of PRD. The primary objective was to educate rheumatologists on these topics but also to evaluate the effectiveness of interactive case-based learning modules.

Methods: To evaluate the pre- and post-session level of knowledge on the topics presented and as a marker of knowledge acquisition, a voluntary pre- and post-session questionnaire was distributed to participants. The questionnaire included 10 questions covering inflammatory arthritis, myositis, vasculitis, sarcoidosis and PRD and was distributed to participants both prior to and following the one-hour educational session. Questionnaires were scored 0-10. Pre- and post-questionnaires were not individually linked.

Results: Results: Pre- and post-workshop questionnaires were completed by 25 participants. Overall, there was an increase in scores from an average of 3.7/10 pre- to 6.7/10 post-session. There was no significant difference between pre- and post-session scores when questions were analyzed based on topic.

Conclusion: CanRIO identified significant knowledge gaps in the emerging field of Rh-irAE. A small group case-based educational session resulted in knowledge acquisition. This session, including the case-based format and pre- and post-questionnaires, will form the basis of interactive online educational modules that are currently being developed through the support of a Canadian Initiatives for Outcomes in Rheumatology cAre (CIORA) grant. Future research will focus on long-term knowledge acquisition with questionnaires sent to participants 3-6 months following module completion. References: [1.] Maltez N, Abdullah A, Fifi-Mah A, Hudson M, Jamal S. Checking in with immune checkpoint inhibitors: Results of a needs assessment survey of Canadian rheumatologists. J Cancer Sci Therap 2019;2(1):12.

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Response During the Pandemic: Are Delivering Accredited Webinars Feasible?

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Objectives: Despite the limited online provision of Continuing Professional Development (CPD) in some areas of healthcare, immediate opportunities for collaboration happened following the call of the global pandemic. While clinical considerations for patient care, managing patients and the need to provide accurate information was important; it was not clear how this education would be delivered.

Methods: The Canadian Rheumatology Association leadership early on identified concerns related to managing patients with rheumatic diseases during the pandemic as a high priority, with appropriate education of membership. This fostered collaboration and led to a need's assessment. Clear Terms of Reference of the Planning Committee with a separate CPD Accreditation Committee were formed, with guidelines for evaluation and feedback, at each step of the CPD cycle.

Results: The first webinars were delivered on 2020-03-25, with a total of seven webinars by 2020-09-08. These engaged local Canadian faculty in adult and pediatric rheumatology, as well as colleagues from Milan, Italy and New York, USA. Topics included telerheumatology, journey of the rheumatology patient during the pandemic, insights from Italy, everything you need to know about being a rheumatologist during the pandemic, COVID-related hyperinflammation in the pediatrics, SARS CoV-2 testing, transitioning to in person care, and getting through 2020 together. Synchronous participant numbers ranged from 51 to 133 out of approximately 600 members (8.5% - 22.2%). Asynchronous participant numbers ranged from 42 to 165 (7.0% - 27.5%). Total participant numbers ranged

from 93 to 298 (15.5% - 49.7%). Feedback was positive and added to the need's assessment for future webinars. Additional learning will be shared as these evaluations are reviewed.

Conclusion: Rapid development of web based accredited CPD delivery is possible in a framework of a supportive and collaborative environment, to an engaged target audience.

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Recent Use, Missed Doses and Discontinuation of Infliximab in New-users: Comparisons of Biosimilar and Originator Exposures

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Objectives: To describe new users of infliximab in the US, comparing biosimilar and bio-originator, in terms of missed doses and discontinuation.

Methods: We used from data MarketScan® Commercial Claims and Encounters and the Medicare Supplemental and Coordination of Benefits databases (January 1st, 2017 to December 31st, 2018). We studied adult individuals (age > 18 years), who were infliximab-naïve (new users). The date of first infliximab claim was defined as the index date. We assessed i) first missed dose and, ii) occurrence of complete discontinuation. Missed dose was defined as any gap between infusions beyond recommended intervals (0, 2, and 6 weeks during the induction phase and 8 weeks in the maintenance phase). If there was no record of an infliximab infusion at the expected date of the next injection (plus a grace period of 7 days), a discontinuation event was assigned.

Results: In the new-user cohort there were 5,596 new users of infliximab, including 301 biosimilar users. Among patients initiating treatment with infliximab biosimilar, 30.9% missed at least one scheduled infusion during the induction phase, similar to the percent (28.6%) among the originator infliximab users. After multivariable adjustment for age, sex, date of treatment initiation, medication use (other biologic medications, synthetic DMARDs, and corticosteroids), and underlying diseases, we were unable to detect if first missing dose in the induction phase differed between the two groups (adjusted hazard ratio, aHR = 1.14; 95% CI = 0.92-1.41). For patients completing the induction phase (n = 3,282), 33.1% of biosimilar users missed at least one infusion within one year during the maintenance phase, which was not statistically different from the originator users (40.1%). The adjusted analysis showed no clear difference for first missed dose between groups (aHR = 0.94, 95% CI = 0.71;1.24). Complete discontinuation in the maintenance phase (a gap more than 90 days beyond the expected infusion date without restarting therapy), was similar in the biosimilar group (13.1%) and originator group (15.5%). In adjusted analysis, we were unable to show significant difference among groups for complete discontinuation (aHR = 1.00, 95% CI = 0.63;1.59).

Conclusion: Biosimilar infliximab use in the United States continues to be low over 2017-2018. In new users, we were unable to detect differences between biosimilar and bio-originator, in terms of missed doses and discontinuation.

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Spontaneous Pneumomediastinum due to Anti-Melanoma Differentiation-Associated Protein 5 requiring a Bilateral Lung Transplant

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Background: Clinical amyopathic dermatomyositis (CADM) is a rare subset of dermatomyositis associated with respiratory complications. Rapidly progressive interstitial lung disease (RPILD) is commonly cited with spontaneous pneumomediastinum (SPM) being a rare complication. Melanoma differentiation-associated gene 5 (MDA5) antibody is used for clinical diagnosis and is a poor prognosticator in CADM. We report the first MDA5 case with SPM which was successfully treated with a double lung transplant.

Case: A 48-year-old diabetic male presented in May 2019 with a cough, low-grade fevers, erythroderma over the ears and radial aspect of his fingers (without mechanic hands), 10-pound weight loss, and arthralgias. Imaging demonstrated ILD and bronchoscopy was unremarkable. Serology was positive for anti-scl70, Jo1, Ro52, MDA5, and anti-NT5c1A antibodies. Initial treatment comprised of high dose prednisone, mycophenolate, and hydroxychloroquine. He was discharged with a diagnosis of possible anti-synthetase syndrome initially with ILD given the anti-Jo1 positivity. The weakly positive MDA5 was of unclear significance initially. A year later, in June 2020, he presented with progressive shortness of breath and continued widespread macular erythematous rashes over his face, with erythematous ulcerations over the fingertips. A CT scan confirmed extensive subcutaneous emphysema within the upper chest, neck, and extensive contiguous pneumomediastinum. Methylprednisolone pulse and IV antibiotics were started, hydroxychloroquine was continued, and mycophenolate was held. His oxygen demands climbed to 55% FiO₂ on Optiflow. One dose of rituximab was given but he still deteriorated, requiring intubation with VV-ECMO. Two days later, he received a double lung transplant. Since then, he is doing well and is on immunosuppressives (tacrolimus, mycophenolate, prednisone) for post lung transplant therapy.

Conclusion: To our knowledge this is the first published case of MDA5-SPM requiring a double lung transplant. There are case reports of lung transplant rescue therapy in MDA5-RPILD; however, no such literature for MDA5-SPM exists. Interestingly, SPM can occur both independent and paradoxically of ILD. Predictors of poor outcomes in SPM include cutaneous vasculopathy, elevated ferritin, Ro-52, and MDA5, all present in our case. Early aggressive immunosuppressive therapy and ECMO has been the mainstay treatment of MDA5-associated SPM, albeit fatality still remains significantly higher in SPM compared to RPILD-CADM. We propose that similarly to RPILD, lung transplantation should be considered early in MDA5-SPM.

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Crossing Generations and a Shared Blood Supply: New Onset Polyarthritis in Pregnancy and a Neonatal Vasculitis Syndrome

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Background: Some chronic autoimmune diseases may show an improvement in the patient's symptoms during pregnancy. Transmission of auto-antibodies across the placenta has been associated with neonatal cutaneous vasculitis and lupus syndromes. Herein, we report a case of a new-onset maternal seronegative inflammatory arthritis associated with transient systemic vasculitis in a neonate.

Case: A 28-year-old woman developed new onset symmetrical polyarthritis at 6 weeks gestation. It was presumed this was reactive arthritis secondary to a dental infection. She began having severe joint pain in her knees and ankles which progressed to her elbows, shoulders, wrists, MCPs and PIPs. Infectious work up and autoantibodies were negative. She was treated with high dose prednisone for the remainder of her pregnancy.

Within the first 24 hours of life, the preterm son was noted to have blue discoloration to all four extremities. A workup for sepsis and thrombosis were negative. Despite antibiotics, fresh frozen plasma and anticoagulation, the discoloration remained, particularly in the left index finger. This was associated with fever and maximum CRP of 148. Erythema of the hands

and feet prompted consideration of neonatal Kawasaki disease, and two doses of IVIG were given with short-term improvement. Echocardiogram and head ultrasound were normal. He continued to have fever and elevated CRP which responded to high dose steroid administration. MRA of body and heart showed tortuosity of arteries of upper and lower extremities with gadolinium uptake, suggestive of a vasculitis. Investigations including ANA, ENA, APLA, ANCA, ASMA, immunoglobulins, C3/C4 were normal or negative. Genetic panel for hereditary autoinflammatory diseases was negative as was whole exome sequencing performed on the trio (infant/parents). The baby was weaned off steroids by 5 months of age. A small distal autoamputation of the left index finger occurred.

The mother was weaned off prednisone and treated with hydroxychloroquine for 8 months post-partum and remains in remission. A repeat MRI done at 1 year old showed mild residual tortuosities of the arteries in the forearms. The remainder of the medium and large vessels were within normal limits with no gadolinium enhancement to suggest active disease. The child is now 4 years old with normal growth and development.

Conclusion: This is a unique case of new-onset seronegative presumed reactive arthritis in a mother with the rare development of a transient medium vessel vasculitis in an infant. The etiopathogenesis is speculative.

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An Imbalance Between Regulatory and Inflammatory T Cell Subsets Distinguishes Systemic Autoimmune Rheumatic Disease Patients from Asymptomatic ANA+ Individuals

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Objectives: The anti-nuclear antibody (ANA)-associated systemic autoimmune rheumatic diseases (SARDs) are characterized by a prolonged preclinical phase in which ANAs are produced without symptoms. ANAs are also seen in healthy, non-symptomatic individuals (ANA+NS), the majority of whom will not progress to SARD. Currently, the immunologic features that discriminate progressors from non-progressors are incompletely understood. Previous work has suggested that T regulatory (Treg) cell function may be disturbed in SARD. To determine whether alterations in these cell populations could contribute to SARD progression we investigated the balance between regulatory and inflammatory T cells in patient populations representative of various stages in SARD development.

Methods: ANA+ (IF \geq 1:160) participants were recruited through the clinic and classified as ANA+NS, ANA+ with \geq 1 SARD classification criteria but lacking a SARD diagnosis (UCTD), or early SARD. All SARD patients were within 2 years of diagnosis and not taking DMARDs (hydroxychloroquine allowed) or prednisone. ANA- healthy controls were recruited from on-site staff. PBMCs were isolated and stained with fluorescence-labeled antibodies to identify immune cell populations via flow

cytometry. Respective plasma aliquots were retrieved to measure TGF- β 1 levels (pg/ml) through ELISA. Statistical comparisons were made using the Kruskal-Wallis test.

Results: ANA+NS and UCTD patients had significant increases in the proportion of extrafollicular Tregs (CD3+CD4+CXCR5-PD1hiFOXP3+HELIOs+) and Type 1 (CD3+CD4+CD45RA-LAG3+) regulatory (Tr1) cells, relative to ANA-HC, whereas the levels of these cells were similar to ANA-HC in SARD patients. The same trends were observed for TGF- β 1 levels. In ANA+NS individuals there was a moderate correlation between TGF- β 1 levels and the proportion of Tr1 cells ($r = 0.43$, $P = 0.009$), a population previously shown to secrete this regulatory cytokine. To examine inflammatory T cell subsets, CD3+CD4+CD45RA-PD1hi activated memory T peripheral (CXCR5-, Tph) and follicular (CXCR5+, Tfh) helper cells were gated and the proportion of Th1 (CXCR3+CCR6-), Th2 (CXCR3-CCR6-) and Th17 (CXCR3-CCR6+) cells in each subset were determined. Increased proportions of Tph2 cells were seen in all ANA+ patient subsets, compared to ANA-HC, but were most pronounced for SARD patients. Although similar trends were seen for Tph17 cells, the increase was only significant in SARD patients. The same but less significant trends were seen for Tfh cells.

Conclusion: Our findings suggest that expanded proportions of extrafollicular Treg and Tr1 cells may act to regulate the autoimmune response in asymptomatic ANA+ individuals and that in SARD patients this becomes attenuated resulting in an imbalance between regulatory and inflammatory T cell subsets which promotes disease development.

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Risk Factors of Antimalarial-induced Retinopathy in Systemic Lupus Erythematosus and Other Autoimmune Conditions

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Objectives: Hydroxychloroquine (HCQ) and chloroquine (CQ) are antimalarial (AM) medications prescribed for a variety of autoimmune conditions, especially systemic lupus erythematosus (SLE). Many patients will remain on these medications for years, and possibly lifelong. HCQ and CQ are associated with irreversible vision loss secondary to retinal toxicity. The prevalence of AM-induced retinopathy varies between studies and few studies have compared prevalence rates between rheumatologic conditions. The purpose of this study was to describe the pattern and risk factors for AM-associated retinopathy.

Methods: A chart review was conducted at a university urban Canadian centre for patients with AM use greater than three months and documented retinopathy screening. Each patient was classified as SLE, based on ACR criteria, or non-SLE, including cutaneous lupus. AM-induced retinopathy was classified as possible or definite, which was determined based on characteristic visual field loss, abnormal retinal imaging and eye specialists' opinion. Univariate and multivariate regression analyses were performed to determine risk factors for retinopathy. Sensitivity analyses included stratification of analysis by method of screening and by HCQ versus CQ.

Results: A total of 641 patients were included in the final analysis, with SLE ($N = 267$) as the most common diagnosis, followed by rheumatoid arthritis ($N = 206$); 95% of patients prescribed AM therapy for the first time at our institution had an eye exam within the first 5 years. Definite AM-induced retinal toxicity was observed in 12 patients, 11 of whom had SLE. The earliest diagnosis of toxicity occurred after 5.4 years of AM therapy. The prevalence of toxicity between five to ten years of therapy was 2.92%, with the prevalence beyond 10 years similar at 2.68%. In univariate analysis, a diagnosis of SLE ($P = 0.008$, OR = 16.03, CI: [2.06-124.89]), the daily weight-based dose of HCQ ($P = 0.034$, OR = 1.55, CI: [1.03-2.31]), cumulative CQ dose ($P = 0.014$, OR = 4.75, CI: [1.37-16.50]), and daily CQ weight-based dose ($P = 0.0001$, OR = 1.90, CI: [1.39-2.60]) were significantly associated with toxicity. In multivariate analysis, diagnosis of SLE ($P = 0.018$, OR = 13.04, CI: [1.55-109.66]) and daily CQ weight-based

dose ($P = 0.005$, $OR = 2.00$, $CI: [1.24-3.25]$) were significant after adjusting for standard covariates. Patients on an average HCQ dose less than the recommended maximum of 5mg/kg/day still developed retinopathy.

Conclusion: The risk of AM-induced retinopathy increases after five years of therapy. There may be higher rates of toxicity in SLE patients due to longer duration of treatment, higher weight-based dosages, and more CQ use in this population, and SLE may be an independent risk factor.

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Autoantibody Profile of Systemic Lupus Erythematosus Patients With Cognitive Impairment

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Objectives: Cognitive impairment (CogImp) has been reported in 17-90% of SLE patients although the exact mechanism of pathogenesis remains unclear. Autoantibodies such as anti-ribosomal-P, anti-phospholipids and anti-N-methyl-D-aspartate receptor 2 (NMDAR2) antibodies have been associated with CogImp, suggesting a potential antibody-mediated mechanism leading to neuronal impairment. The purpose of this study was to utilize an extensive autoantibody profile of over 25 SLE-related antigens to determine if autoantibodies are associated with CogImp in SLE.

Methods: Between 2016-2019, consecutive adult SLE patients (followed at a single lupus centre) were administered the ACR Neuropsychological Battery (NB) at baseline and classified as non-CogImp (control) or having CogImp using two definitions: 1) Group A (CogA) when two or more domains had a z score < -1.5 standard deviation (SD), 2) Group B (CogB) had one or more domains with z score < -2.0 SD. Demographic and clinical information at baseline were used. The autoantibody tests were performed at a central laboratory (MitogenDx, Calgary, AB) including the SLE-profile (C1q, dense fine speckled 70, Ku, nucleosome, ribosomal-P, Ro52/TRIM21, RNP, Sm, SSA/Ro60, SSB/La) by FIDIS Connective Profile-13, (TheraDiag, Paris) in an addressable laser bead immunoassay (ALBIA) or by enzyme linked immunosorbent assay (ELISA: Inova Diagnostics, San Diego, CA), anti-dsDNA by chemiluminescent assay (BioFlash: Inova Diagnostics), anti-phospholipid antibodies (anti-cardiolipin IgG, domain 1 beta-2 glycoprotein (B2GP1), Phosphatidylserine/Prothrombin Complex (PS/PT) IgM/IgG) (Inova Diagnostics), and other autoantibodies associated with neurological diseases (Glyceraldehyde-3-Phosphate Dehydrogenase, Glial fibrillary acidic protein, interferon-gamma, melanoma-associated antigen 4 and 10, NMDAR2) by ALBIA. Lupus anticoagulant was performed at the home site laboratory. Univariable analyses were performed to determine whether baseline clinical and demographic factors and SLE antibodies were associated with CogA vs. non-CogA and CogB vs. Non-CogB.

Results: There were 136 SLE patients; 10.29% were male and 61.76% were White. 67 (49.26%) had CogA and 110 (80.88%) had CogB. There were no differences in baseline characteristics between patients with CogImp vs. non-CogImp by either definition of CogImp except CogA patients were less likely to be White compared to non-CogA patients ($OR\ 0.39$ [95%CI 0.19, 0.80]). CogA patients were less likely to have a positive anti-PS/PT IgM antibody ($OR\ 0.31$ [95%CI 0.13, 0.75]) compared to non-CogA patients. CogB patients were less likely to have anti-DFS70 antibodies ($OR\ 0.08$ [95%CI 0.00, 1.12]) compared to non-CogB patients.

Conclusion: SLE patients without CogImp were less likely to have anti-PS/PT IgM and anti-DFS70 antibodies. No association between autoantibodies previously reported with CogImp in SLE such as anti-ribosomal-P and NMDAR2 were found.

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"Nutrition Information Resources Used by People With Scleroderma and Perceived Advantages and Disadvantages: A Nominal Group Technique Study"

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Objectives: The evidence base for nutritional and dietary strategies for people with systemic sclerosis (scleroderma, SSc) is limited, despite gastrointestinal manifestations being some of the most commonly experienced complications of the disease. Dietary guidelines for symptom management for SSc have therefore not been established in clinical practice, which may result in individuals seeking information from other sources. However, no studies have looked at where people with SSc seek nutritional and dietary information and their experiences with different information resources. The objectives of the present study were to identify the resources from which people with SSc seek nutritional and dietary information and advice and perceived advantages and disadvantages of different information resources.

Methods: We conducted nominal group technique (NGT) sessions with people with SSc who reported resources they have used to obtain information and advice on nutrition and diet and perceived advantages and disadvantages of accessing and using each resource. Participants indicated whether they had tried each resource and rated each for perceived helpfulness, and rated advantages and disadvantages for importance (0-10 scale). Items elicited across sessions were merged to eliminate overlap. A final list of items was reviewed by study investigators, including a SSc patient advisory team.

Results: We conducted four 90-120-minute NGT sessions (3 English-language, 1 French-language; 15 total participants), and identified 33 nutrition information resources, 147 perceived resource-specific advantages, and 118 perceived resource-specific disadvantages. Resources were categorized into five categories, including "Health care providers" ($N = 10$, e.g. registered dietitian, gastroenterologist, rheumatologist), "Websites and other media platforms" ($N = 8$, e.g. scleroderma patient organization website, Facebook group with autoimmune disease patients, website by functional medicine doctor), "Events" ($N = 6$, e.g. support groups, conference by a nutritionist, congress on scleroderma), "Print materials" ($N = 5$, e.g. academic journals, books/magazines by medical professionals, scleroderma patient organization magazine), and "Alternative and complementary practitioners" ($N = 4$, e.g. homeopath, holistic nutritionist, naturopath). Common themes for advantages and disadvantages were identified, including quality and specificity of information, and accessibility of resources in terms of cost, location and comprehensibility of information.

Conclusion: People with scleroderma seek nutritional and dietary information from a wide range of different resources. Many rely on information provided by medical professionals for credible information, which may be provided through books, articles and websites, if individual consultation is not easily accessible. In-person events may be an important and overlooked source of health information, while informal interpersonal sources (e.g., family, friends) are not commonly used resources for people with SSc.

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Granulomatosis With Polyangiitis Presenting as Severe Refractory Raynaud's Phenomenon

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Background: Granulomatosis with polyangiitis (GPA), a clinical condition formerly known by its eponymous name, Wegener's granulomatosis was first described in a case report in the late 19th century by Friedrich Wegener. Based on the review of 16 case reports, Lau et al suspected the prevalence of digital ischemia and gangrene as a presenting symptom in GPA to be approximately < 1%. Underlying pathophysiology of digital ischemia is thought to be related to the active vasculitis of the small and medium size vessels. As of now there is no general consensus on treatment of GPA with digital ischemia. We report an infrequent presentation of GPA as refractory Raynaud's with severe digital ischemia treated with bosentan, sildenafil and nifedipine.

Case: A 51-year-old diabetic patient presented with a two-week history of progressive pain, swelling, dynamic skin and color changes involving bilateral fingertips. Review of systems was positive for purpuric rash on lower extremities and polyarthralgia. On examination, he was afebrile with heart rate 78/min, blood pressure 119/79 mm hg, respiratory rate 18/min and Spo2 98% on room air. His fingers were swollen, tender and all fingertips showed cyanosis in both hands without ulceration. There was palpable purpura on both legs extending up to upper thigh. Positive laboratory studies include ESR 68mm/h, CRP 13.5mg/dl, urine RBC16cells/hpf, urine Protein 70mg/dl, D dimer 8.07 ug/ml, Rheumatoid factor > 256IU/ml, Serum Proteinase 3 IgG- 298 AU/ml, ANCA IgG by IFA < 1:20. He tested negative for ANA, SSB Ab IgG, SSA 52 Ab IgG, SSA 60 IgG, Smith Ab IgG and Smith/RNP Ab IgG, C3, C4 complements, cold agglutinins, cryoglobulin qualitative screen, HIV, Hepatitis B&C and Tb quantiferon.

Conclusion: The prompt diagnosis and treatment are important in long term reduction of morbidity and mortality. For GPA he was initiated on Methylprednisolone and Rituximab. Therapeutic regimen for Raynauds included aspirin, nifedipine, topical nitroglycerin and sildenafil. However due to his underlying symptoms of active Raynaud's, patient also underwent digital nerve block of three ischemic digits along with escalation of therapy with Bosentan and Epoprostenol. Despite timely therapy patients finger ischemia worsened, and he developed dry gangrene in three fingers. After 12 days of remission induction treatment his symptoms of purpura and digital cyanosis improved in the remaining fingers. Patient underwent interval amputation of three digits. He was sent home on remission maintenance therapy with methotrexate for GPA and nifedipine, sildenafil along with bosentan for Raynauds.

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Chronic Fatigue Syndrome (CFS), Cognitive Failure and Anxiety in ANCA-associated Vasculitis

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Objectives: Chronic fatigue is a major burden of disease in patients with ANCA-Associated Vasculitis (AAV) which results in a decreased quality of life. The prevalence of fatigue in AAV is, however, unknown. The aim of our study is to evaluate the presence of chronic fatigue in patients with a diagnosis of AAV i.e., granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis or microscopic polyangiitis, and to identify potential clinical and biopsychosocial determinants.

Methods: 59 participants included in our study completed the validated DePaul Symptom Questionnaire (DSQ). Patients were labelled with "Myalgic Encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS)" when they fulfilled the Canadian Consensus Criteria for ME/CFS. Disease

activity was scored using 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). Statistical analysis was carried out using Fischer's exact test.

Results: We found that 32/59 (54%) of AAV patients fulfilled the case definition for ME/CFS. There was no relationship between the presence of ME/CFS and BVAS ($P = 0.5$), VDI ($P = 0.78$), sleep disorders ($P = 0.8$), depression ($P = 0.09$) or C-reactive protein ($P = 0.2399$) in our study population. However, a substantial statistically significant correlation was present in patients with AAV suffering from ME/CFS, cognitive failure ($P = 0.004$) and/or anxiety ($P = < 0.001$).

Conclusion: Chronic fatigue affects AAV patient's mental wellbeing. From our analysis we conclude that chronic fatigue, cognitive failure and/or anxiety co-occur independently of vasculitis disease activity. We postulate that therapies aimed at improving anxiety may be utilized as adjunct agents for patients with AAV suffering from fatigue. Funding: Dutch Kidney Foundation (17PhD01) Arthritis Society (19-0558).

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A Rare and Fatal Case of Intracranial Giant Cell Arteritis

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Background: Giant cell arteritis (GCA) is a granulomatous medium-to-large vessel vasculitis that causes luminal narrowing, occlusion, and downstream tissue ischemia. GCA preferentially affects branches of the extra-cranial carotid arteries, while intracranial involvement is rare and has a high mortality rate. Cerebral manifestations of GCA necessitate initiation of high-dose intravenous corticosteroids for 3-5 days and subsequent transition to oral therapy. Cyclophosphamide or methotrexate may be added in refractory cases and have been associated with improved outcomes. In this report, we present a severe case of intracranial GCA with consequent multifocal cerebral infarcts leading to death despite immunosuppressive therapy.

Case: A 66-year-old woman with a history of dyslipidemia and thalassemia trait presented with acute confusion, nausea, and vomiting following a three-week history of temporal, frontal and parietal headache, scalp tenderness, jaw claudication, and transient left-sided vision loss. Examination revealed bilateral temporal artery tenderness. C-reactive protein was elevated at 127 mg/L and ANCA were negative. Computed Tomography Angiogram (CTA) revealed diffuse segmental wall thickening of the carotid and cerebral arteries. GCA was diagnosed and high dose intravenous steroids and ASA 81 mg daily were initiated. On day two, the patient developed right facial droop and weakness. CT/CTA showed acute left cerebellar and temporal lobe infarcts, with interval narrowing of the mid-basilar artery, left pre-foraminal and right intradural vertebral arteries. Clopidogrel 75 mg daily was added. On day three, her level of consciousness (LOC) decreased, necessitating endotracheal intubation with a CTA showing new intracranial infarcts. On day five she stabilized, returned to the ward, and was transitioned to oral prednisone. On day seven, she again developed decreased LOC requiring re-intubation. Repeat imaging again demonstrated new intracranial infarcts. Cyclophosphamide 750mg/m² was initiated for refractory GCA. Unfortunately, on day eight, she passed away. Post-mortem neuropathological examination revealed co-existence of GCA, atherosclerosis and vasa vasorum.

Conclusion: This case demonstrates GCA involving many intracranial arteries, leading to multifocal infarction and rapid decompensation despite timely treatment. A prominent histologic feature of this case was the

co-existence of GCA, atherosclerosis, and vasa vasorumitis in sampled arteries. Inflammation in the vasa vasorum is hypothesized to lead to destruction of smooth muscle cells and fibrosis, key events in both GCA and atherosclerosis. Further study is required on the potential role of vasa vasorumitis in the pathogenesis of these diseases. Furthermore, small cohort studies have shown that cyclophosphamide reduces mortality in refractory intracranial GCA, however further investigation is necessary to guide management on this devastating disease.

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Effect of Physiological Concentrations of Astaxanthin, Deer Antler and their Combinations on Inflammatory Mediators in Cartilage Explants

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Objectives: Osteoarthritis (OA) is a debilitating disease affecting over 240 million people worldwide. Pain and inflammation are two major symptoms of OA. Available drugs offer pain relief and target inflammation but present many side effects. Nutraceuticals with less or no side effects are well sought after as alternative OA treatment. Astaxanthin and deer antler are two relatively new nutraceuticals touted as natural therapeutic agents for OA. They, however, are not well studied and their mechanisms of action remain unclear. This study aims at investigating the effect of physiologically relevant concentrations of astaxanthin, deer antler and their combinations on nitric oxide (NO) and prostaglandin E2 (PGE2), known pain and inflammatory mediators of OA using interleukin-1 beta (IL-1 β) induced cartilage explant model.

Methods: Two 6mm bovine cartilage explants were cultured per well in a 48-well culture plate and maintained in DMEM:F12 media for 48 hours before treatment started. All treatments received 10% fetal bovine serum (FBS). There were ten treatments; 1. FBS control, 2. 20ng/ml IL-1 β , 3. IL-1 β + 5ug/ml astaxanthin, 4. IL-1 β + 15ug/ml astaxanthin, 5. IL-1 β + 30ug/ml astaxanthin, 6. IL-1 β + 2mg/ml deer antler, 7. IL-1 β + 5mg/ml deer antler, 8. IL-1 β + 10mg/ml deer antler, 9. IL-1 β + 5ug/ml astaxanthin + 2mg/ml deer antler and 10. IL-1 β + 30ug/ml astaxanthin + 10mg/ml deer antler. Conditioned media were collected at 0, 24, 48 and 72 hours, stored at 4°C, and used for NO and PGE2 biochemical analyses.

Results: IL-1 β -induced release of NO was significantly decreased by 5 and 30ug/ml astaxanthin as well as the 5ug/ml astaxanthin + 2mg/ml deer antler combination at all time points. The suppression with 5 and 30ug/ml astaxanthin at 48 and 72 hours were to the level of FBS control. Deer antler alone, at all concentrations, did not suppress NO release. All concentrations of astaxanthin numerically abrogated IL-1 β -stimulated PGE2 release at 48 hours. Significant reduction of PGE2 to levels comparable to FBS control was observed at 72 hours with all three concentrations of astaxanthin as well as all concentrations of deer antler, and both combinations of astaxanthin and deer antler.

Conclusion: Astaxanthin suppressed both NO and PGE2 release while deer antler reduced levels of PGE2 in in vitro cartilage culture. This supports the purported anti-inflammatory ability of astaxanthin and deer antler, and their potential as OA treatment.

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Rheum Service: Improving Virtual Care During COVID-19

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Objectives: During COVID-19, rheumatology outpatients need timely access to care while social distancing. Video consults have potential to improve virtual assessments, however, some patients and providers are apprehensive about using this technology. Our objective was to provide delightful and effective video consults for 90% of new patients by July 1, 2020.

Methods: We redesigned video appointments to create a seamless virtual experience. PDSA Series 1 identified improvement opportunities with a process map, fishbone, and driver diagram. PDSA Series 2 tested and implemented change ideas: digital appointment confirmations, reminders,

and forms; video consults with limited pre-call testing; digital reports, requisitions, and messaging. PDSA Series 3 refined changes by decreasing reminders, increasing pre-call tests, and adding backup video platforms. Outcome measures were: 1) % consults by video, 2) % requesting more video appointments. Process measures were: 1) pre-call tests completed, 2) technical difficulties. Our balance measure was % virtual diagnoses modified after in-person visits. We collected data over ten weeks and emailed anonymized patient surveys one week after video consults. We analyzed data with run charts and descriptive statistics.

Results: We scheduled 135 new consults: 120 (89%) video, 14 (10%) phone, and 1 (1%) office. Twenty-one patients (16%) did not own a video-enabled device. Pre-visit, 12 patients (10%) participated in pre-call testing. Video consults were initiated for 97% of scheduled patients; of these, 6% suffered technical difficulties, requiring a switch to phone or another video platform. Surveys were completed after 40% (48/120) of video visits: 68% of patients wanted another video appointment; 28% were 'not sure'; 4% declined. Virtual diagnoses stayed the same for 84% (32/38) of patients with follow-up in-person assessments.

Conclusion: While video consults proved effective for most patients, sociodemographic and technological barriers prevented others from participating. Next steps include improving access to video-enabled devices and providing more pre-visit training to reduce these barriers.

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Characterization of the Rheumatologist-Extended Role Practitioner Model of Care in an Inpatient Tertiary Care Network

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Objectives: Although treatment advancements have shifted rheumatology practice from inpatient to outpatient settings over time, patients continue to require hospitalization due to underlying diseases, sequela or comorbidities. To address the gap of increasing prevalence of rheumatic diseases and too few rheumatologists, the first Canadian rheumatologist (MD)-extended role practitioner (ERP) model of care (MOC) for inpatients was introduced at Trillium Health Partners (THP).

Methods: A retrospective review was completed of all referred patients to the rheumatology consultation services at THP (Mississauga Hospital and Credit Valley Hospital sites). Patients were referred and first assessed by the on-site ERP, reviewed and later seen by the on-call rheumatologist. Patient demographics, admission and rheumatologic diagnoses, interventions, follow-up and additional referrals generated from MD-ERP assessments were extracted from THP monthly reports and Meditech electronic health records system for descriptive analyses.

Results: Between January 2015-December 2019, 2361 patients were seen by the ERP-MD team with 59% female and median age of 72 (IQR 57-82). The majority were referred from hospitalist/internal medicine/surgical wards (94%), intensive care (3%) and otherwise from medically cleared units (i.e., psychiatry, rehab). Most were new patients (69%) defined as having no previous rheumatologist prior to admission. A third of consulted patients had a musculoskeletal (MSK) diagnosis as their reason for hospitalization which included possible rheumatologic or orthopedic etiologies. The most common rheumatologic diagnoses were OA/MSK-related (26%), crystal disease (27%) followed by systemic autoimmune rheumatic diseases (15%), inflammatory arthritis (13%), vasculitis (11%), infection (3%). The most common concurrent diagnoses were OA/MSK-related (n = 169) and crystal disease (n = 73). Nearly all (98%) consults required interventions which included bloodwork (69%), medication (56%), imaging (47%) and/or intra-articular injection (28%). Additional referrals to other services (other specialties, radiology, surgery, allied health) were arranged (14%), and outpatient follow-up required (42%), particularly for those with systemic autoimmune rheumatic diseases, inflammatory arthritis or vasculitis.

Conclusion: Due to the volume of inpatient consultation services required at THP, ERPs are integral in expediting inpatient assessments as rheumatologists balance busy outpatient practices. Many patients were hospitalized for non-MSK etiologies but were impacted by OA/MSK-related and/or crystal disease during their admission which could affect discharge planning. Most patients also did not have prior rheumatology involvement until their admission. This study highlights the importance of inpatient rheumatology care to address multi-morbidities and provide relevant recommendations through a collaborative MOC.

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How Many *Pneumocystis jirovecii* Pneumonia Cases, in CHUS Hospital from 2008 to 2018, Resulted of Omission of Antibioprophylaxis in Patients With Rheumatic Diseases?

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Objectives: *Pneumocystis jirovecii* pneumonia (PCP) prophylaxis is recommended for patients with rheumatic diseases treated with a corticosteroid dose equivalent to Prednisone 20 mg per day for one month and with a second immunosuppressant agent. Our primary objective is to determine how many PCP cases resulted from omission of an indicated PCP prophylaxis in the course of the treatment of a rheumatic disease. Secondary objectives are to describe the rheumatic diseases and treatments involved in these cases.

Methods: A retrospective review of hospitalized adults with PCP and a rheumatic disease at CIUSSS-Estrie-CHUS from 2008 to 2018 was performed. Cases affected with concomitant human immunodeficiency virus, transplant recipient and patients treated with chemotherapy for cancer were excluded.

Results: 21 cases were included. In the month before the PCP diagnosis, 6 received corticosteroids equivalent to more than Prednisone 20 mg per day, with a mean dose of 38 mg per day. 3 had concomitant treatment with methotrexate, which was an indication for PCP prophylaxis, and didn't receive it without any justification. For these 3 cases, 2 had rheumatoid arthritis, and 1 had giant cell arteritis. 2 had concomitant lymphopenia, 1 chronic kidney disease and 1 multiple myeloma. The mean age was 80 years. 2 went to the intensive care unit with endotracheal intubation. The mean hospital stay was 16 days.

Conclusion: We recommend an increased awareness from clinicians caring for patients with rheumatic disease to prescribe PCP prophylaxis when indicated. This could have prevented roughly 1 case every 3 years for this deadly complication in our center.

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Patient Satisfaction With Outpatient Rheumatology Phone-Visits During the COVID-19 Pandemic

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Objectives: The COVID19 pandemic required an abrupt transition from in-person clinic visits to virtual means, without consideration for its safety or agreement among patients. We sought to evaluate patient satisfaction with virtual care in the first 3 months of the pandemic, and factors that may be associated with dissatisfaction.

Methods: This was a quality improvement survey study conducted by the rheumatology division at The Ottawa Hospital. Surveys were mailed to all patients who had a phone visit between March 15th and June 19th, 2020. Patients' satisfaction with various aspects of the virtual care visit was collected on a 5-point scale and analyzed according to demographic variables using chi-square and regression analyses.

Results: Of 2423 surveys mailed, we received 742 responses (31%). Seventy percent of patients were > 60 years old and 72% were female; rheumatoid arthritis (41%) and spondyloarthritis (27%) were the most common diseases. Among all visits 4% were new consultations. Eight percent of patients stated they spoke with a resident and their rheumatologist, 17% spoke with a resident only, and the remaining 75% spoke directly to their staff rheumatologist. Seventeen percent needed an in-person visit following the virtual visit. Eighty-nine percent of patients were satisfied overall with the phone visit. Despite the high overall satisfaction rate, only 55% stated they would prefer to have virtual visits after the COVID19 period. Statistically significant less satisfaction was seen in patients who spoke to a resident compared to their rheumatologist ($P < 0.001$), or who stated they were not called on time ($P < 0.001$). Statistically significant less satisfaction and preference for an in-person visit was observed in patients who had difficulty using a telephone ($P < 0.001$), needed assistance of a second person at clinic visits ($P < 0.01$), or whose visit was a new consultation (versus routine follow-up, $P = 0.01$). Underlying diagnosis or age category did not affect satisfaction. In multivariate analysis, speaking directly to their rheumatologist ($P = 0.001$), being phoned on time ($P = 0.005$), and capability using a telephone ($P = 0.007$) were associated with satisfaction.

Conclusion: Patient satisfaction with virtual clinic visits was very high, and patients preferred virtual visits to clinic visits during COVID19. Lower satisfaction was correlated with difficulty using a telephone, needing a second person at visits, new consultations, not speaking directly with their staff rheumatologist, and being called late. These results have highlighted opportunities for improving conduct of virtual care as well as an approach to triaging in-person visits during the pandemic.

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Real-world Clinical Profiles of Adults With Hypophosphatasia (HPP) from the Global HPP Registry

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Objectives: Hypophosphatasia (HPP) is a rare, inherited, metabolic disease caused by low activity of tissue non-specific alkaline phosphatase (ALP). HPP in adults has multiple musculoskeletal and systemic manifestations, which can lead to misdiagnosis and substantial delays in diagnosis.

Methods: Data from 270 adults with confirmed HPP diagnosis (≥ 18 year of age, low ALP and/or ALPL mutation) in the Global HPP Registry were analyzed. Most were women (75.2%) with a median age at enrollment into the Registry of 50 years and a median ALP activity of 25 U/L (normal range: 40-150 U/L).

Results: Based on medical history, pain (74.8%), mostly described as chronic bone pain or generalized body pain, was the leading symptom reported. Dental manifestations, such as early loss of primary teeth, were reported in 60.4% of adults. Skeletal manifestations, such as recurrent and poorly healing fractures or pseudofractures, were observed in 47.8% of adults. Substantial proportion also reported fatigue (35.2%) and muscle weakness (26.3%). Of the quality-of-life data available, median (range) of SF-36v2 Physical Component Score was 42.4 (17.9, 63.3; $n = 203$; population norm = 50) and pain interference on the BPI-SF was 3.5 (0, 9.5; $n = 196$; 0 = does not interfere; 10 = completely interferes). Most adults with available data ($n = 212$) reported some disability on the HAQ-DI (66%). Of 270 adults, 77 were treated with enzyme replacement therapy (asfotase α) while 193 had never received treatment. Demographics and baseline ALP activity were similar between ever and never treated adults. Treated patients had a higher occurrence of pain, dental issues, recurrent and

poorly healing fractures or pseudofractures, fatigue, and muscle weakness compared with untreated patients. Generally, treated adults reported poorer quality of life before treatment initiation compared with untreated adults, though data were limited in treated adults. Of the patients treated, 61.0% had pediatric-onset HPP which likely reflects the indication for asfotase alfa in most countries; 29.9% had unknown onset. 57.5% of untreated adults had adult-onset HPP, 24.3% had pediatric-onset, and 18.1% has unknown onset.

Conclusion: Pain, dental issues, fatigue, recurrent and poorly healing fractures or pseudofractures, and muscle weakness were the most frequently reported symptoms in both adults with pediatric- or adult-onset HPP. These results establish real-world clinical profiles of adults with HPP, both untreated and before treatment started. Similarities in clinical profiles between adults with pediatric-onset and adult-onset HPP suggest that the age at onset itself is of limited clinical utility; current clinical status and the degree of disability are likely more meaningful in making treatment decisions.

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Survey of Medical Cannabis Use in Lupus and Scleroderma

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Objectives: Despite the lack of research regarding medical cannabis, marijuana and its by-products have gained popularity. A 2019 Statistics Canada report revealed that approximately 16% of Canadians used marijuana in the last year. A Canadian study also revealed that 80% of rheumatologist participants were questioned by their patients weekly regarding medical marijuana. In a similar study, 75% of participants were not comfortable prescribing medical marijuana. Despite being a common and debilitating feature in rheumatic diseases, there is little attention given to studying medical options to manage pain. The effects, both positive and negative, of medical marijuana in patients who have lupus or scleroderma, is still unclear. We surveyed patients diagnosed with lupus or scleroderma to evaluate their beliefs, concerns and personal experience with medical cannabis.

Methods: Patients with diagnosed lupus or scleroderma were recruited from the Ottawa Hospital Division of Rheumatology. Consent was implied with the completion of the survey, and answers remained anonymous. Inclusion criteria: age > 18, diagnosis of systemic lupus or scleroderma and able to complete the survey in English or French. Data analysis of the results of the survey is qualitative.

Results: On preliminary results, 24% of participants are actively using medical cannabis, primarily in the form of CBD oil or inhaled. Those taking medical cannabis reported no significant side effects. Of those not using cannabis, 53% considered using it, and 78% would like a further discussion with their rheumatologist regarding medical cannabis. Among our participants, the most common reasons for medical cannabis use were sleep, anxiety, and pain. The majority (66%) were aware that there could be side effects, which was often the reason for wanting more information. Alternative medications used for pain management were acetaminophen (65%), steroids (55%) and NSAIDs (55%). The factors critical to the discussion were trust in their treating physician, having a non-judgmental discussion, the degree of uncontrolled pain/symptoms and the need for alternatives, and receiving reliable information.

Conclusion: Our survey results suggest that some patients have already tried medical cannabis. Most have an interest in using cannabis to help with symptoms not relieved by standard therapies to date. We need to be better prepared to guide our patients concerning medical cannabis. These results will highlight common indications for medical cannabis use in this patient population. This study will help broaden our understanding of medical cannabis, its impact on our patients and guide us in elaborating new strategies when discussing medical cannabis.

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Characteristics of Adult Patients With Rheumatic Diseases During the COVID-19 Pandemic: Data from an International Patient Survey

Jonathan Hausmann (Boston Children's Hospital/Beth Israel Deaconess

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Objectives: Patients with rheumatic diseases are at increased risk of infection due to immune dysregulation and the use of immunosuppression. It is unknown whether they are also at increased risk of SARS-CoV-2 infection or of COVID-19-related complications. Using real-world data from the COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey, we describe the demographic and clinical characteristics of adult respondents.

Methods: We distributed a patient-reported outcomes survey for adults with rheumatic diseases, regardless of COVID-19 status, to all six WHO regions and available in nine languages. The survey was disseminated through patient support organizations and on social media. Participants answered questions regarding their demographics, rheumatic disease diagnoses, medications, whether they had suspected or confirmed diagnoses of COVID-19. We evaluate participant demographics and describe the clinical characteristics of COVID-19 infection collected from April 3-May 8, 2020.

Results: A total of 9,393 adults completed the survey. Respondents represented all six WHO regions; most were female (90.0%), and the mean age was 46.1 years (SD 12.8). Common diagnoses included systemic lupus erythematosus (SLE) (38.9%), rheumatoid arthritis (38.6%), and Sjogren's syndrome (13.7%). Majority of patients were taking conventional synthetic DMARDs (70.9%), while 34.7% and 30.8% were on steroids and biologic DMARDs, respectively. Comorbidities included pain syndromes (23.2%), hypertension (22.8%), and pulmonary diseases (21.4%). Of participants surveyed, 519 (5.5%) reported suspected or confirmed COVID-19 diagnoses. Frequently reported symptoms included malaise/fatigue (87.1%), cough (78.6%), and headache (78.0%). Only 65 COVID-19 patients (12.5%) required hospitalization.

Conclusion: These results demonstrate the feasibility of conducting an international patient-reported outcomes survey to address the impact of the COVID-19 pandemic among people with rheumatic diseases. It was a successful collaboration between patients, researchers, rheumatologists, and patient organizations. Only 5.5% of survey respondents had suspected or confirmed COVID-19 and only 12.5% of them required hospitalization, even though most were on immunosuppressive drugs. Future analyses will explore the relationships between disease states and diagnosis of COVID-19.

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Modeling the Effects of Covid-19 Protective Behaviors and Healthcare Delivery on the Health of Patients With Rheumatic Disease

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Objectives: COVID-19 caused global disruptions in chronic illness management and the extent of its impact on the rheumatology community and the changes in health service delivery remains unknown. We present a model capturing the effects of the pandemic on the physical and mental health of adult rheumatic disease patients.

Methods: The COVID-19 Global Rheumatology Alliance Patient Experience Survey was disseminated online to patients with rheumatic diseases. Patients reported age, gender, region, employment status, ethnicity, smoking status, rheumatic disease control, methods of communication with rheumatologist, medications, possible exposure to COVID-19, COVID-19 diagnosis, COVID-19-related hospitalization, mental/physical health, and

protective measures taken for COVID-19. Patient responses were entered into two simple multiple linear regression models to determine the associations between access to rheumatologists, COVID-19, and protective behaviours on mental and physical health.

Results: From 8,511 complete responses and after adjusting for current/changes in employment status, current rheumatic disease activity, region, ethnicity, age, disease activity, smoking status, medications, and gender; variability in patient physical and mental health were explained by the independent predictors entered into the model with a large and moderate effect size, respectively ($R^2_{adj} = 0.40$, $F = 162.3535$, 8511 , $P < 0.001$; $R^2_{adj} = 0.26$, $F = 88.2235$, 8511 , $P < 0.001$). Relative to those who did not need to communicate, patients unable to communicate with their rheumatologist were associated with lower physical and mental health. Patients who only visited the office and those who specified using 2 or more methods of communicating with their rheumatologist were associated with lower physical health. Patients reporting at least one incident of potential exposure to COVID-19 were associated with lower mental health. Patients reporting symptoms of, were hospitalized with, or tested positive for COVID-19 were associated with greater mental health and lower physical health. Relative to patients only indicating self-isolation, patients who only practiced social distancing or reported 2 or more protective behaviours were associated with greater physical health.

Conclusion: By modeling the effects of COVID-19 behaviors and health-care delivery, we demonstrated that having COVID-19 caused worse physical health, however, contracting, or surviving COVID-19 paradoxically led to improved mental health. This could be a result of patients perceiving a reduced mortality risk despite having physical health consequences. We have also captured a group of patients reporting lower mental and physical health and are unable to communicate with their rheumatologist. Clinicians should aim to identify communication barriers, offering multiple modes of contact.

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Impact of the COVID-19 Pandemic on Racial and Ethnic Minority Groups Diagnosed With Rheumatic Diseases

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Objectives: The COVID-19 pandemic has exacerbated structural and systematic barriers in access to healthcare for racial and ethnic minorities. The impact of these increased barriers on patients with rheumatic disease has not been studied. We describe the clinical characteristics and COVID-19 disease burden among racial and ethnic minority participants in an international survey of patients with rheumatic disease.

Methods: The COVID-19 Global Rheumatology Alliance Patient Experience Survey is an international, self-reported survey for adults and parents of children with rheumatic disease, with or without COVID-19 infection. The survey was distributed online by patient support organizations and social media platforms. Responses of participants living in Canada, the United States, and Europe were analyzed to compare outcomes between minority and non-minority groups. Descriptive statistics were used to describe patient characteristics and COVID-19 related outcomes.

Results: We report data on 6,581 respondents to the Patient Experience Survey in North America and Europe. There were 5,703 (86.7%) respondents who identified as White, and 878 (13.3%) belonged to all other racial or ethnic groups. Respondents from ethnic minority groups were mostly

female (92.3%) with a mean age of 44.0 (SD 12.4). The most common rheumatic diseases include systemic lupus erythematosus (47.8%) and rheumatoid arthritis (37.2%). A total of 455 (6.9%) participants reported a diagnosis of COVID-19; of these, 66 (14.5%) self-identified as a racial or ethnic minority including 12 (2.6%) who were Black. Among ethnic minorities, 24 patients diagnosed themselves based on symptoms and 42 were diagnosed by a physician according to symptoms or a lab result. Of patients who were hospitalized with COVID-19, 33 (73.3%) were White and 12 (26.7%) belonged to other ethnic groups.

Conclusion: This international survey reports data related to the impact of COVID-19 on racial and ethnic minorities with rheumatic disease. There were differences in high-risk comorbidities, yet no difference in incidence of COVID-19 and severity of disease among various racial and ethnic groups compared to White participants. Racial and ethnic minorities were under-represented in our survey, likely a consequence of systemic barriers. This study reinforces the importance of collecting race-related data, particularly where there are concerns of inequities influencing health outcomes, and the need to implement targeted recruitment strategies to enhance representation of minority groups in research.

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Antimalarial Drug Shortages During the COVID-19 Pandemic: Results From the Global Rheumatology Alliance Patient Experience Survey

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Objectives: The early COVID-19 outbreak saw the repurposing of hydroxy-chloroquine and chloroquine to prevent and treat SARS-CoV-2 infection, causing concern about potential shortages. This study aimed to assess (1) the prevalence and impact of drug shortages during the COVID-19 pandemic, and (2) whether the use of antimalarials in rheumatic disease patients lowered their risk of COVID-19 infection.

Methods: The COVID-19 Global Rheumatology Alliance Patient Experience Survey was distributed online through patient support organizations and social media. Patients with rheumatic diseases (or their caregivers) anonymously reported their rheumatic disease diagnosis, medications, COVID-19 status, and disease outcomes. Impact of drug shortages was evaluated for the effect on patient disease activity, mental health, and physical health states by comparing mean values with two-sided independent t-tests.

Results: Of 9,393 respondents (mean age 46.1 (SD 12.8) years, 90.0% female), 3,872 (41.2%) were taking antimalarials. Of these, 230 (6.2%) reported pharmacy supply shortages and were unable to continue taking antimalarials. 21.4% of patients in South-East Asia and 26.7% in Africa reported an inadequate antimalarials supply in pharmacies, in contrast to 6.8% of patients in the Americas and 2.1% in Europe. Patients who were unable to access medications due to pharmacy shortages compared to those who did not, experienced higher levels of rheumatic disease activity ($5.1 > 4.3$, $t(244) = 4.44$, $P < 0.001$) and poorer mental ($5.8 < 6.3$, $t(252) = 3.82$, $P < 0.001$) and physical health ($5.6 < 6.4$, $t(254) = 5.97$, $P < 0.001$). COVID-19 infection rates were similar among patients taking antimalarials compared to those not on these drugs (6.7% vs. 4.7%). A total of 28 patients (10.8%) with COVID-19 who were taking antimalarials were hospitalized.

Of 519 COVID-19-diagnosed patients, 68 (13.1%) reported receiving antimalarial prescriptions for their COVID-19 infection treatment.

Conclusion: Patients in Africa and South-East Asia reported greater difficulty obtaining antimalarials for their rheumatic disease in contrast to patients in the Americas and Europe. These antimalarial drug shortages were associated with poorer mental and physical health outcomes than those able to obtain their medications. Antimalarials did not protect rheumatic disease patients from COVID-19 nor related hospitalization. The unintended harmful consequences of repurposing antimalarials, without adequate evidence for benefit, highlights the importance of maintaining scientific rigor even in the context of a pandemic. Regional disparities of medication access should be addressed to ensure everyone, particularly those living in developing countries, receive fair and equitable access to these essential medications.

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COVID-19 Hospitalizations, ICU Admission, and Death among Ontario Residents With Immune Mediated Inflammatory Diseases

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Objectives: To investigate the risk of COVID-19-related hospitalizations and their outcomes in patients with immune mediated inflammatory diseases (IMIDs) compared with matched non-IMIDs comparators from the general population in Ontario.

Methods: A population-based, matched cohort study was conducted in adult Ontario residents using administrative health data. Ten cohorts of the following IMIDs were assembled: rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, systemic autoimmune rheumatic diseases (SARDs, including systemic lupus, scleroderma, Sjogren's, dermatomyositis/polymyositis, undifferentiated connective tissue disease), multiple sclerosis (MS), iritis, inflammatory bowel disease, polymyalgia rheumatica, and vasculitis (including giant cell arteritis and other types of vasculitides). Each patient was matched with 5 non-IMIDs comparators based on age, sex, area of residence and living in long-term care (LTC). Patients who were admitted to hospital from January 1st to April 30th, 2020 and had ICD-10 COVID-19 diagnostic codes (U07.2 or U07.1) were identified. Among those with COVID-19-related hospitalizations, we determined those with admissions to intensive care unit (ICU) or in-hospital death. The proportion of patients with COVID-19 hospitalizations and ICU admission/death were compared between patients with and without IMIDs.

Results: In total, 505,302 IMIDs patients and 2,525,958 non-IMIDs comparators were assessed. The mean age of all patients hospitalized with COVID-19 was 72.1 ± 14.4 years (49.8% females). Of the IMIDs patients, 257 (0.05%) were hospitalized for COVID-19 and 78 (0.02%) were admitted to ICU or died. Of subjects without IMIDs, 895 (0.04%) were hospitalized for COVID-19 and 311 (0.01%) were admitted to ICU or died. Death during hospitalization occurred in 55 of 257 (21.4%) of IMIDs patients with IMIDs, versus 208 of 895 (23.2%) of non-IMIDs comparators. Age- and sex-standardized rate of COVID-19 hospitalizations was higher in IMIDs (3.6 per 100,000, 95% confidence interval 3.1, 4.1) versus non-IMIDs patients (2.4 per 100,000, 95% CI 2.2, 2.6). The highest standardized rates of COVID-19 hospitalizations were in vasculitis

(10.7/100,000), MS (6.7/100,000) and SARDs (5.8/100,000), however, the confidence intervals overlapped with other IMIDs. The standardized rate of ICU admission/death in IMIDs patients was 1.1/100,000 (95% CI 0.8, 1.4) versus 0.83/100,000 (95% CI 0.73, 0.93) in those without IMIDs. ICU admission/death was highest in vasculitis (3.6/100,000). Among those with COVID-19 hospitalization, IMIDs patients were less likely to live in LTC and more likely to have multi-morbidities, cardiovascular and kidney diseases than non-IMIDs comparators.

Conclusion: Patients with IMIDs were at higher risk of being hospitalized with COVID-19, and the risk may be especially high in vasculitis, SARDs and MS. Best Abstract On Research By Young Faculty.

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Outcomes After Hydroxychloroquine Reduction or Discontinuation in a Multinational Inception Cohort of Systemic Lupus

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Objectives: Hydroxychloroquine (HCQ) is a cornerstone treatment for several autoimmune diseases including Systemic Lupus Erythematosus (SLE). Recently, concerns regarding HCQ shortages for SLE patients and HCQ-induced conduction abnormalities arose due to its use as a potential COVID-19 treatment. Although some patients may remain well after reducing or stopping therapy, others will have potentially life-threatening complications related to SLE flares. We evaluated if HCQ reduction or discontinuation is associated with increased risk of poor outcomes.

Methods: We analyzed prospective data from the Systemic Lupus International Collaborating Clinics (SLICC) cohort, which includes SLE patients from 33 sites in Europe, Asia, and North America, enrolled within 15 months of diagnosis and followed annually, from 1999 to 2019. In patients receiving HCQ, we identified two sub-cohorts, one who reduced HCQ and one who stopped HCQ. We did not require patients to be in disease remission at the time of HCQ reduction/discontinuation for these analyses. Time zero for these sub-cohorts was the date of the first HCQ reduction/discontinuation. For comparison, we identified a third group of patients remaining on HCQ. A poor outcome was defined as either subsequent need for SLE therapy augmentation (steroids or other immunosuppressives), increase of ≥ 4 points in the SLE Disease Activity Index-2000 (SLEDAI-2K) or hospitalization for SLE. We estimated adjusted hazard

ratios (HRs) and 95% confidence intervals (CIs) for poor outcomes among the three HCQ exposure groups. Models were adjusted for demographics and baseline clinical characteristics.

Results: A total of 1460 patients were included (89% female, 52% Caucasian). The crude poor outcome rate was significantly lower in the HCQ maintenance group (31.6 events per 100 person-years, 95%CI 29.0, 34.5; N = 1649 person-years) than in the reduction (43.0, 95%CI 39.3, 47.1; N = 1087 person-years) and in the discontinuation (43.0, 95%CI 38.3, 48.2; N = 677 person-years) groups. Patients reducing or discontinuing HCQ had higher adjusted HRs for poor outcomes versus those maintaining HCQ (HR 1.35, 95%CI 1.19, 1.53; HR 1.36, 95%CI 1.17, 1.56, respectively). Other factors independently associated with poor outcomes included active SLE and use of prednisone or immunosuppressive drugs, all measured at time zero.

Conclusion: Patients reducing or discontinuing HCQ are at greater risk of having a poor outcome versus those maintaining the drug. These analyses do not account for reasons HCQ was reduced/discontinued (40% had SLEDAI-2K > 4 at baseline). Regardless, baseline disease activity, prednisone and immunosuppressive drugs were associated with the risk of poor outcomes in SLE patients reducing, discontinuing, or maintain HCQ.

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MicroRNA146a Gene Polymorphism in Patients With Rheumatoid Arthritis and Its Association With Disease Activity and Extra-Articular Manifestations

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Objectives: To assess the association between the microRNA146a (miR146a) rs2910164 Single Nucleotide Polymorphism (SNP) and rheumatoid arthritis (RA) disease activity and extra-articular manifestations.

Methods: Fifty patients with RA disease (N = 50) were recruited, examined for the relevant SNP using Real time PCR. The distribution of the genotypes was studied in relation to patients' clinical data. Disease activity was measured using disease activity score (DAS) 28.

Results: The CC genotype was significantly associated with higher swollen joint count (P = 0.0397). The same genotype was also associated with a longer duration of morning stiffness, higher tender joint count, physician global assessment and DAS 28 score, however the P value did not reach the level of statistical significance. The CC genotype was also significantly associated with the presence of sicca symptoms (P = 0.0104), while the GC genotype seemed to have a protective effect against the development of such symptoms. There was no significant association with other extra-articular manifestations, namely rheumatoid nodules (RN), interstitial lung disease (ILD) and vasculitis.

Conclusion: The CC genotype of the miR146a rs2910164 SNP is probably associated with a more severe form of rheumatoid arthritis disease and is associated with the development of sicca symptoms.

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Optimizing Rheumatology Practice through an Interprofessional Model of Care

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Objectives: According to a recent Canadian Rheumatology Association (CRA) survey, the deficit in clinical rheumatologists is 283 nationally. Furthermore, 1/3 of surveyed clinicians plan to retire within the next 5-10 years. To counter this workforce deficit, and protect the health of

professionals involved, it is imperative to simultaneously increase specialists training while improving existing practices. This report looks at an inter-professional nursing model of care, to demonstrate how improved patient care, time efficiencies, and economic sustainability are achievable.

Methods: Implementation began in 2014 at the private rheumatology clinic of Dr. Michelle Teo in British Columbia, Canada, and relies on the recruitment of extended-role practitioners (ERP) to reduce rheumatologist consultation time (per patient). The model revolves around three principles: streamlining the consultation process, preemptive preparation of follow-up appointments (including telehealth), and team-based approach to administrative tasks. The rheumatologist responsibilities are focused on three interventions: diagnosis, treatment and problem-solving. During the analyzed period (2013-2017), Dr. Teo's weekly practice time remained constant (averaging 27 hours/week), while she gradually recruited and integrated 3 ERPs into her model of care. Variables captured were working hours and the number of appointments for new and existing patients. Consultation duration (per specialty) and costs were calculated.

Results: The implementation of an interprofessional nursing model of care led to a steady increase in the number of appointments at the clinic. Driven by optimal task delegation, a reduction in rheumatologist average consultation time, from 29 minutes in 2013 to 12 minutes in 2017 was counter-balanced by an increase in ERP consultation time. Consultation time per patient nearly doubled, rising from 29 to 50 minutes. The increase in efficiency allowed just over 2000 additional patients to have their first consultation at the clinic between 2014 and 2017. In spite of additional cost of ERP support, a positive balance sheet was maintained due to the increased consultation capacity for new/existing patients. For every \$1 invested, an additional \$1.3 was generated.

Conclusion: In conclusion, an interprofessional nursing model of care represents a feasible solution to the alarming forecast anticipated by the CRA regarding rheumatology workforce deficits. It represents a win-win-win scenario for patients, healthcare providers and the public system. ERP recruitment and increased efficiency delivered growth and sustainability, while providing patients with earlier access, maintaining a high standard quality of care and increasing clinical support outside of scheduled appointments, a newly revealed asset in pandemic times.

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Prevention of Chronic Diseases Due to Inflammation in Inflammatory Arthritis: Results of a Delphi Process to Select Care Recommendations for an Electronic Medical Record (EMR) Intervention

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Objectives: Inflammatory arthritis (IA) predisposes patients to several chronic conditions including cardiovascular diseases (CVD), diabetes (DM), osteoporosis (OP) and infections, likely due to systemic effects of inflammation. Studies have found that patients with IA often receive suboptimal care for screening and managing these conditions. This is the first phase of a study which will develop, and pilot test automated EMR reminders for

family physicians. The reminders will prompt family physicians to screen for and address risk factors for these conditions. We conducted a Delphi process to select care recommendations to be addressed by the EMR reminders.

Methods: We conducted a review of current BC, Canadian and international guidelines for screening and addressing risk factors for CVD, DM, OP and infection. A list of 22 care recommendations, including their level of evidence and risks/benefits of implementation, was reviewed by a panel of six family physicians, three rheumatologists and three IA patients, in a three-round online modified Delphi process. Panelists rated each care recommendation, using 9-point scales, on 1) their clinical importance, 2) their likelihood of improving outcomes, and 3) implementation feasibility. Results were discussed in an online forum. Panelists then rated slightly revised care recommendations, modified based on feedback from the discussion. Care recommendations were retained if the median rating was ≥ 7 with no disagreement as defined by the RAND/UCLA Method handbook.

Results: A list of 15 care recommendations was selected by the Delphi process for EMR integration, including recommendations that address CVD risk assessment (1), hypertension screening (1), DM screening (2), fracture risk assessment (1), BMD testing (1), osteoporosis prevention (1) and treatment (1) with bisphosphonates, preventing infections through immunization (2), minimizing steroids (1) and hepatitis screening (1), screening for hydroxychloroquine retinal toxicity (1), and counselling for lifestyle modifications (2). We excluded 7 recommendations which addressed lipid testing (1), BMD testing in steroid users (1), immunizations (2), weight management (1), and DMARD laboratory test monitoring (2). Recommendations were excluded on the basis of importance (1) or feasibility (6).

Conclusion: The results of the Delphi process will inform the development of reminders, integrated in EMRs, that will support family physicians in their efforts to engage IA patients in addressing risk factors for chronic diseases related to inflammation. We hope to improve the prevention of these diseases, which represent an important cause of morbidity and mortality for people with inflammatory arthritis. Supported by a CIORA grant.

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Rheumatoid Arthritis Care Gap Time Between Prescription and Start Date: A Local Practice Audit

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Objectives: Previous studies had showed that a delay in initiating disease modifying agents, delay in getting patients into remission will lead to irreversible damage and disability in Rheumatoid Arthritis patients. In order to improve patient's clinical outcome, we have conducted a local practice audit to review the time gap between prescription and start dates for Rheumatoid Arthritis (RA) patients on JAK-inhibitors and non-Anti-TNF biologic agents. Limited literature has been written on this topic, whereby most focus on the delay in diagnosis and prescription of treatment rather than the care gap between prescription and the start date of the drug.

Methods: PubMed, Ovid MEDLINE and EMBASE databases were searched to provide background information. Inclusion criteria where patients with RA prescribed the drugs of interest. Using medical charts, prescription and start dates were collected. Median, mean, and range were calculated using a 95% confidence interval. The care gap is defined by the difference in days between prescription and start date of the drug. The drugs examined include: JAK-1 inhibitors, anti-CD2 monoclonal antibodies, Interleukin-6 inhibitors, TNF-alpha inhibitors, T-cell agents, DMARDs, and corticosteroids.

Results: A total of 306 patients on a total of 16 different drugs were examined. The care gaps are listed below from fastest to longest between prescription and start date.

Drug	n	Median	Range	Mean	CI Interval
Hydroxychloroquine	26	0	0,54	2.3	-1.7,6.3
Methotrexate	30	0	0,82	5.4	-1.3,12.1
Sulfasalazine	15	0	0,112	11.5	-3.7,26.7
Leflunomide	69	0	0,1855	29.3	-23.0,81.7
Upadacitinib	8	14.5	0,30	13.4	5.4,21.3
Baricitinib	9	23.0	0,231	50.4	5.7,95.1
Etanercept	21	27.0	0,147	38.0	20.8,55.2
Tofacitinib	81	38.0	0,615	76.3	52.9,99.8
Certolizumab	27	32.0	2,205	52.1	33.5,70.8
Adalimumab	32	32.5	3,442	53.9	26.4,81.4
Golimumab	46	33.0	8,491	46.0	25.7,66.2
Abatacept	131	35.0	0,455	55.5	44.5,66.5
Tocilizumab	123	40.0	0,401	54.1	44.7,64.1
Sarilumab	9	48.0	14,94	48.9	33.6,113.0
Infliximab	58	48.0	0,473	70.6	50.0,91.2
Rituximab	61	64.0	0,406	93.1	74.5,111.8

Conclusion: Significant delays exist; however the sample is small, contributing to the large ranges. The drugs come in different methods of delivery: oral medications tend to have a shorter care gap whereas injectable forms require more time to be approved. Delays could possibly be contributed to waiting for insurance approvals, financial issues, or non-compliant patients. The reasons for this care gap should be investigated further in order to reduce the delays in practice.

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Insight Into Intraindividual Variability Across Neuropsychological Tests and Its Association With Cognitive Dysfunction in Patients With Systemic Lupus Erythematosus

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Objectives: Dispersion is defined as the variability in an individual's performance across multiple tasks at a single assessment visit. This measure has been studied in a number of neurodegenerative and neurodevelopmental disorders, in which increased dispersion was generally found to be associated with cognitive dysfunction (CD). We aim to compute a dispersion score using the tests of the American College of Rheumatology Neuropsychological battery (ACR-NB) and to determine the association between this dispersion score and the risk of CD in SLE patients.

Methods: This retrospective longitudinal study included patients who attended the Lupus Clinic from January 2016 to October 2019. A total of 301 adult SLE patients were administered the ACR-NB at their initial visit, 6 months, and 12 months. CD was defined as a z-score of ≤ -1.5 on ≥ 2 domains or $z \leq -2$ on ≥ 1 domain. The 19 tests of the ACR-NB were used to compute a type of dispersion score, the intraindividual standard deviation

(ISD). To obtain the ISD, the standard deviation of the age- and sex-adjusted z-scores was calculated for each visit, resulting in a maximum of 3 scores per patient. To estimate the association between ISD and patient's cognitive status (CD and non-CD), we used multi-level logistic regression, adjusting for clinically important covariates.

Results: CD was observed in 106 patients (35.2%) at baseline, 52 patients (27.8%) at 6 months, and 53 patients (28.0%) at 12 months. Among all observations across 3 visits, the mean age- and sex- adjusted ISD was 1.40 ± 0.55 . Prior to adjustment for covariates, the mean ISD for the non-CD group was 1.10 ± 0.31 compared with 1.50 ± 0.70 for the CD group. After adjusting for ethnicity, education, employment, socioeconomic status, and anxiety/depression, there was a statistically significant association between ISD and cognitive status (odds ratio [OR] for one unit increase in ISD: 13.56, 95% confidence interval [CI]: 4.80-38.31; OR for 1/10th unit increase in ISD: 1.30, 95% CI: 1.17-1.44). Findings were robust to multiple sensitivity analyses.

Conclusion: Dispersion scores such as ISD have been explored as a pragmatic and sensitive marker of cognitive function in different patient populations. We showed that among adult SLE patients, increased ISD across the cognitive tests of the ACR-NB was associated with an increased likelihood of having CD, adjusting for important covariates. Additional research is warranted to evaluate the promise of dispersion scores in clinical practice.

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Rheumatic Immune Related Adverse Events Associated With Cancer Immunotherapy: A Single-Centre Retrospective Chart Review of the Toronto Experience

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Objectives: Immune checkpoint inhibitors (ICIs) are a family of therapeutic agents used in cancer immunotherapy to enhance the anti-tumor immune response. Toxicities secondary to these medications, termed immune-related adverse events (irAEs), are common, with a wide variety of manifestations described including those resembling common rheumatologic diseases. Further insight is needed into characterizing rheumatic irAEs (rh-irAEs) and determining their management. In this retrospective chart review, we aim to describe the clinical presentation and management of rh-irAEs in patients presenting to our large academic center.

Methods: A single-center, retrospective chart review was performed to identify patients presenting with rh-irAEs between October 1, 2019 and April 24, 2020 at Mount Sinai Hospital in Toronto. Standardized data related to demographics, oncologic history, presenting symptoms, and management of rh-irAEs were extracted by chart review. Data were pooled and analyzed descriptively.

Results: A total of 24 patients without pre-existing autoimmune disease who developed 27 rh-irAEs were identified. 66.7% of patients were male, with a mean age of 64.2 years, and an average of 5 medical co-morbidities in addition to their primary malignancy. The most common indication for ICI therapy was melanoma ($n = 13$, 54.2%), followed by genitourinary malignancies ($n = 4$, 16.7%), and lung cancer ($n = 4$, 16.7%). 62.5% of patients had stage 4 disease. ICI included: nivolumab ($n = 9$, 37.5%), pembrolizumab ($n = 4$, 16.7%), durvalumab ($n = 2$, 8.3%), combination therapy ($n = 7$, 29.2%), or an unknown ICI received through a clinical trial ($n = 2$, 8.3%). Rh-irAEs identified included: seronegative, symmetric polyarthritis ($n = 9$, 33.3%), oligoarthritis ($n = 6$, 22.2%), polymyalgia rheumatica ($n = 2$, 7.4%), sarcoidosis ($n = 2$, 7.4%), vasculitis ($n = 2$, 7.4%), myositis ($n = 3$, 11.1%), sicca symptoms ($n = 1$, 3.7%), acute monoarthritis ($n = 1$, 3.7%), and seronegative spondyloarthritis ($n = 1$, 3.7%). On average, patients received 7.3 months of ICI therapy prior to the onset of a rh-irAE. ICI was discontinued in 62.5% of patients and held temporarily in 41.7% of patients. Patients were managed with non-steroidal anti-inflammatories (NSAIDs; $n = 8$, 33.3%), intra-articular corticosteroid injections ($n = 9$, 37.5%), hydroxychloroquine ($n = 9$, 37.5%), mycophenolate mofetil ($n = 2$, 8.3%), sulfasalazine ($n = 5$, 20.8%), and anti-tumor necrosis alpha agents

($n = 1$, 4.2%). In addition, 70.8% of patients also received oral prednisone ($n = 17$), with doses ranging from 10mg daily to 1000mg daily (median dose 25mg daily). At the time of study completion, 64.7% ($n = 11$) of patients were still requiring oral prednisone therapy.

Conclusion: Seronegative, symmetric polyarthritis was the most common Rh-irAE identified at our center. The most common management of Rh-irAEs included oral prednisone therapy in combination with hydroxychloroquine, intra-articular corticosteroid injections, and/or NSAIDs.

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A Comparison of Two Classification Systems for Juvenile Idiopathic Arthritis (the International League of Associations for Rheumatology (ILAR) and the Newly Proposed Pediatric Rheumatology International Trials Organization (PRINTO) Criteria) With Classification Systems for Adult Arthritides: Results From the Research in Arthritis in Canadian Children, Emphasizing Outcomes (ReACCh-Out) Cohort.

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Objectives: PRINTO recently proposed a revision of the ILAR criteria to define conditions unique to children and align subtype diagnoses with adult arthritides. We classified patients in the ReACCh-Out cohort according to ILAR and PRINTO (provisional) criteria in order to evaluate their agreement and compare their alignments with adult arthritides.

Methods: New-onset JIA patients seen in Canadian centers between January 2005-December 2010 were considered. Patients were computationally classified under PRINTO, ILAR, and four adult arthritis criteria (rheumatoid arthritis [RA], psoriatic arthritis [PsA], adult-onset Still's disease [AOSD], and spondyloarthritis [SpA]). Relationships between resulting groupings were visualized using Circos and alignment was assessed by interpreting the standardized residuals (z) of chi-square tests.

Results: 1,228 newly diagnosed JIA patients with ≥ 1 follow-up visit were included. By PRINTO criteria, 63% did not meet criteria for any subtype and therefore were classified as other JIA. 20% were early-onset ANA-positive (EOANA+), 13% as enthesitis/spondylitis-related (E/SpR), 3.1% as systemic (sJIA), 0.81% as RF-positive (RF+), and 0.2% as unclassified JIA. By ILAR criteria, 44% had oligoarthritis, 18% RF-negative polyarthritis, 18% enthesitis-related arthritis (ERA), 12% undifferentiated, 2.9% systemic, and 0.49% RF+ polyarthritis. The PRINTO and ILAR classifications contained significantly different groups (chi-square = 2,540, $P < 0.001$). All patients categorized as ILAR sJIA and RF+ polyarthritis was categorized as PRINTO sJIA and RF+ JIA, respectively. 62% of ILAR ERA were categorized as PRINTO E/SpR JIA. However, the majority of the following ILAR subtypes mapped to PRINTO other JIA: oligoarthritis, 71%; RF-negative polyarthritis, 79%; psoriatic arthritis, 89%; and undifferentiated arthritis, 55%. Only 32% of ($n = 389$) patients satisfied adult criteria. Significant associations ($z \geq 2.5$) for ILAR categories were as follows: 81% with sJIA categorized as AOSD; 97% with psoriatic arthritis and 19% with undifferentiated arthritis as PsA; 53% with RF-negative polyarthritis and 100% with RF+ polyarthritis as RA; and 28% with psoriatic arthritis, 36% with ERA, and 21% with undifferentiated arthritis as SpA. Associations for PRINTO categories were as follows: 79% with sJIA categorized as AOSD, 100% with RF+ JIA as RA, and 48% with E/SpR JIA as SpA. PRINTO EOANA+ JIA was not associated with any adult arthritis.

Conclusion: More than half our JIA cohort was unclassifiable by PRINTO criteria and we recommend the development of additional subtypes. Our findings suggest that most childhood arthritis is unique with no relationship to adult arthritis. The EOANA+ PRINTO subtype is unique to childhood but may constitute only a small proportion of JIA patients.

Disease Course of Juvenile Localized Scleroderma

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Objectives: Juvenile localized scleroderma (jLS) is a rare autoimmune disease that may result in tissue damage and functional disability. Methotrexate (MTX) is considered first-line therapy. There is a paucity of information on disease course during MTX treatment and after MTX discontinuation. The aim of our study was to determine the proportion of remission on MTX treatment, the proportion and time to flare after MTX discontinuation, as well as to determine the potential predictors of disease relapse.

Methods: This retrospective study included data from patients with jLS (any subtype) followed at a specialized multi-disciplinary pediatric rheumatology-dermatology clinic at the Alberta Children Hospital in Calgary, Canada between September 2014 and June 2019. Clinical data included demographic patient characteristics, standardized disease activity measures and treatment. Remission was defined as change from 'active' to 'inactive' disease state within 6 months, whereas flare was defined as a change from 'inactive' to 'active' state at any time. Descriptive statistics were used to report the cohort characteristics and proportions achieving disease remission or flare. The mean time to flare and rate of relapse was measured. Possible predictors of disease flare were evaluated using univariable and multivariable mixed-model logistic regressions.

Results: Twenty-four patients with jLS were included. The median age was 12.1 years (interquartile range [IQR] = 10.6-14.3), 70.8% were female, and 75% had linear jLS subtype. Ninety-three percent of patients achieved remission on MTX treatment. There were nine flare events occurring in 29% of our patients; three occurred during MTX treatment and six occurred after MTX discontinuation. The proportion of patients who flared after MTX discontinuation was 30%. The average duration of MTX treatment was 279 days, with no significant difference in duration between those who flared or did not (241 vs 284 days; $P = 0.76$). The average time to flare after MTX discontinuation was 599.5 days. Univariable analysis identified male sex with borderline significance as a predictor of flare (OR 1.99, 95% CI: -0.03-5.16, $P = 0.07$) - this finding held in multivariable modeling (est 3.06 [-0.19 -6.31], $P = 0.07$). No significant difference was seen based on age, ANA, or jLS subtype.

Conclusion: Most patients with jLS achieve remission on MTX, but a small proportion may flare during MTX treatment and after MTX discontinuation, particularly within the first two years. Further studies are required to establish optimal duration of systemic treatment. Our results suggest that jLS patients should be monitored closely for flare after MTX discontinuation, particularly males.

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Cardiac Biomarkers are Associated With the Development of Cardiovascular Events in Patients With Psoriatic Arthritis and Psoriasis

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Objectives: N-terminal pro-brain-type natriuretic peptide (NT-proBNP)

and troponin I (TnI) are established cardiac biomarkers that predict cardiovascular events (CVEs) and mortality in apparently healthy individuals and at-risk populations. While patients with psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), have an increased risk of developing CVEs, the use of these cardiac biomarkers to predict CV risk has not been investigated in this population. We aimed to evaluate the association between these cardiac biomarkers and incident CVEs and assess their predictive value beyond the Framingham Risk Score (FRS).

Methods: A longitudinal cohort study was conducted in patients with PsD without prior history of CVEs. NT-proBNP and TnI concentrations were measured using automated clinical assays in the first available serum sample. The study outcome included any of the following CVEs occurring within the first 10 years of biomarker assessment: angina, myocardial infarction, congestive heart failure, transient ischemic attack, cerebrovascular accident, revascularization procedures and CV death. Associations with incident CVEs were analyzed separately for each biomarker using Cox proportional hazards regression models first adjusted for age and sex, and subsequently for the FRS. The added value of cardiac biomarkers to improve predictive performance beyond the FRS was assessed using the area under the receiver operator characteristic curve (AUC), net reclassification index (NRI) and integrated discrimination index (IDI).

Results: A total of 1000 patients with PsD were assessed between 2005 and 2019 (mean age 49 ± 12.8 years, 44.6% female). During a mean follow-up of 7.1 years, 72 (7.2%) patients developed incident CVEs. Both TnI (Hazard Ratio (HR) 3.63, 95% Confidence Interval (CI) 1.47, 8.95) and NT-proBNP (HR 1.78; 95% CI 1.16, 2.74) predicted CVEs independently of the FRS. The association was stronger in males than females. Including all cardiac biomarkers and the FRS in a single model, both TnI (HR 3.25, 95% CI 1.34, 7.88) and NT-proBNP (HR 1.68, 95% CI 1.12, 2.54) retained statistical significance. When comparing the predictive performance of the base model (FRS alone, AUC 74.3) to the expanded models, there was no significant improvement in any of the predictive indices with the addition of TnI, NT-proBNP, or both TnI and NT-proBNP.

Conclusion: In patients with PsD, elevated NT-proBNP and TnI predict incident CVEs independent of the FRS. We did not observe a significant improvement in the performance of the predictive model when combining these cardiac biomarkers with the FRS.

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Targeted Metabolomic Profiling and Prediction of Cardiovascular Events: A Prospective Study of Patients With Psoriatic Arthritis and Psoriasis

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Objectives: Psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), are associated with increased cardiovascular (CV) risk. Metabolites comprise biomarkers that may add predictive value over traditional CV risk factors. We aimed to identify metabolites associated with CV events (CVEs) and to determine whether they could improve CV risk prediction beyond traditional risk factors.

Methods: Patients from a longitudinal PsD cohort without a prior history of CVEs were included. In the first available serum sample, a targeted nuclear magnetic resonance (NMR) metabolomics platform was used to quantify 64 metabolite measures comprised of lipoprotein subclasses, fatty acids, glycolysis precursors, ketone bodies and amino acids. The study outcome

included any of the following CVEs occurring within the first 10 years of biomarker assessment: angina, myocardial infarction, congestive heart failure, transient ischemic attack, cerebrovascular accident, revascularization procedures and CV death. The associations of each metabolite with incident CVEs were analyzed separately using Cox proportional hazards regression models adjusted for age and sex, and age, sex and traditional CV risk factors. Variable selection was then performed using the proportional sub-distribution hazards regression model adjusted for age and sex via penalization with boosting. The added predictive value of the selected metabolites to improve risk prediction beyond traditional risk factors was assessed using the area under the receiver operator characteristic curve (AUC).

Results: A total of 977 patients with PsD, followed between 2005 and 2019, were analyzed (mean age 49.1 ± 12.6 years, 45.1% female). During a mean follow-up of 7.1 years, 70 (7.2%) patients developed incident CVEs. In Cox regression models adjusted for CV risk factors, alanine, tyrosine, degree of unsaturation, high-density lipoprotein (HDL) cholesterol, and medium and large HDL particles were significantly associated with decreased CV risk. Glycoprotein acetyls, apolipoprotein B, remnant cholesterol, very low-density lipoprotein (VLDL) cholesterol, and very small VLDL particles were associated with an increased CV risk. Thirteen metabolites were selected based on the penalization and boosting algorithm. The age- and sex-adjusted expanded model (base model + 13 metabolites) significantly improved prediction of CVEs beyond the base model (only age and sex) with an AUC of 79.9 vs. 72.6, respectively ($P = 0.019$).

Conclusion: Using NMR metabolomics profiling, we identified a variety of metabolites associated with a lower and higher risk of developing CVEs in patients with PsD. Further study of their underlying association with CVEs is needed to clarify the clinical utility of these biomarkers to guide CV risk assessment in this population.

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Safety of Low Dose Methotrexate (MTX) in Human Immunodeficiency Virus (HIV) Infection

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Objectives: Increased awareness of the efficacy of MTX in rheumatic disease is leading to more MTX use in patients from HIV endemic areas. Current management guidelines for rheumatic disease do not address HIV in the context of MTX use. We aimed to systematically review the published literature on safety of using MTX < 30 mg per week in HIV.

Methods: We searched CINAHL, Embase, Global, MEDLINE and World of Science databases (Jan 1990 to May 2018) for terms including 'methotrexate' and 'human immunodeficiency virus'. Titles, abstracts or full manuscripts were screened independently by 2 reviewers to identify studies reporting HIV in patients taking MTX. Study quality was assessed using the McGill Mixed Methods Appraisal Tool (MMAT). Data was extracted on MTX and HIV adverse events (MTX toxicity, HIV viral load, CD4 count).

Results: Forty-two of 2714 identified reports met criteria and provided adequate information. (1 clinical trial, 2 cohorts, 1 cross-sectional study, 38 case reports/case series). Most reports (81%) originated from USA or Europe. Most studies fulfilled 50-100% of MMAT criteria. The trial (USA) assessing MTX on atherosclerotic disease in HIV showed more adverse events with MTX versus placebo (12.8% vs 5.6%, $P < 0.05$) including infection, transient CD4/CD8 drop, pulmonary toxicity, and death. In a South African cohort of 43 RA on MTX who acquired HIV, RA improved despite only 5 individuals continuing MTX. In a USA cohort of 13 HIV patients with myositis, one received MTX (with other immunosuppression) without MTX adverse effects but died due to AIDS. In a cross-sectional

study (France) of 43 HIV patients with autoimmune disease one patient on MTX (and other immunosuppression) developed cytopenia compared to 5/33 patients not on MTX. The 38 case reports/series described 54 individuals with HIV receiving MTX. Twenty-seven (describing 42 subjects) reported MTX adverse events in 29 subjects (hematologic 13, renal/hepatic 1, opportunistic infections 10, other events 2). Thirty-five (describing 46 subjects) reported HIV adverse events 23 subjects (Kaposi's sarcoma 4, CD4 decrease 16, HIV viral titer increase 4). Five deaths were reported (infection 2, infection and wasting 1, HIV related 2).

Conclusion: There remains limited data on the safety of low dose MTX in HIV. Surveillance for HIV is warranted for individuals on MTX who are at risk for acquiring HIV. Caution and careful monitoring for MTX toxicity, opportunistic infections and HIV state is suggested if MTX is used in the setting of HIV particularly if combined with other immunosuppression.

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Motor Control Adaptations in Response to Fatigue in Patients With ANCA-associated Vasculitis

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Objectives: Physical fatigue is the largest burden of disease in patients with ANCA-associated vasculitis (AAV). Importantly, muscle strength and muscle fatigue are reduced in these patients. This pilot study aims to better understand the underlying mechanisms of fatigue associated with AAV and determine if there are potential motor control adaptations that occur in response to fatigue which may impact our approach to the delivery of effective non-pharmacological therapies targeting improvements in function.

Methods: Maximal knee extension force output as well as time to muscle fatigue was assessed in six male AAV patients and 3 healthy male controls. A force gauge (ergoFET) was used to capture knee extension force data and convert the signal for storage and analysis on a local computer. Maximal knee extension over a 5 second Maximal Voluntary Contraction (MVC) as well as time to fatigue for maintaining alternating cycles of 10 second sustained maximal knee extension contraction/relaxation to evaluate muscle strength and muscle fatigue, respectively were measured. Muscle fatigue was defined as the inability to maintain 50% of their previously recorded MVC.

Results: Male AAV patients had significantly less MVC force outputs (mean = 371 N) compared to healthy controls (mean = 505 N). Conversely, time to fatigue for maintaining alternating cycles of 10 second sustained maximal knee extension contraction/relaxation was longer in AAV patients (mean = 6:47 minutes) compared to healthy controls (mean = 3:55 minutes).

Conclusion: Patients with AAV had a significantly lower MVC force output but were able to sustain a longer time to muscle fatigue compared to healthy controls. The study suggests possible central muscle recruitment strategies that adapt in response to AAV-associated fatigue. AAV patients may develop motor unit recruitment strategies that reduced their total maximal force output but allowed sustained muscle activity at a lower threshold of their physiological maximum. This may have implications for the types of exercises and physical activities that clinicians recommend for AAV patients and may serve as an important educational piece for why AAV patients struggle with certain functional activities more than others.

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"Application of the Eurofever/PRINTO Clinical Classification Criteria for Auto-inflammatory Recurrent Fevers in a Canadian Cohort."

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Objectives: New clinical classification criteria for five of the auto-inflammatory recurrent fever disorders were published in 2019 by a European

consensus group, Eurofever/PRINTO (Gattorno et al, Ann Rheum Dis 2019;78:1025). As these criteria were developed based on data from European patients, we sought to apply these new clinical criteria to a Canadian cohort of pediatric patients diagnosed with recurrent fever disorders.

Methods: Children enrolled in the CanFever registry at BC Children's Hospital, Vancouver, BC, between September 2015 - September 2020, who received a clinical diagnosis from a Pediatric Rheumatologist of one of the following: TRAPS (Tumor Necrosis Factor-Associated Periodic Syndrome; n = 6), FMF (Familial Mediterranean Fever; n = 10), PFAPA (Periodic Fever, Aphthous stomatitis, Pharyngitis, Adenitis; n = 37), MKD (Mevalonate Kinase Deficiency; n = 3), CAPS (Cryopyrin-Associated Periodic Syndromes; n = 1) or unclassified fever syndrome (n = 53), were included. Clinical data was extracted from the registry to allow the application of the new proposed classification criteria. The Eurofever/PRINTO classification criteria were applied to all participants, to examine the correlation between clinical-determined diagnosis and disease classification.

Results: A total of 110 patients were evaluated; median age 5.6 years (range: 9 months - 16.2 years) and 50% female (n = 55). There was variable correlation between clinician-determined diagnosis and PRINTO classification, ranging from low (17%) to moderate (62%) agreement. Of the 37 PFAPA patients, 37% (n = 14) did not meet classification criteria for PFAPA, with 1 meeting criteria for FMF, 4 meeting criteria for MKD, and 9 not meeting any classification criteria; in addition, 7 PFAPA patients met classification criteria for both PFAPA and MKD. Of the 53 unclassified patients, 12 met classification criteria for FMF, 4 for PFAPA, and 4 for MKD; 70% remained unclassified by the PRINTO system. Of the 6 TRAPS patients, 83% did not meet classification criteria for TRAPS, with 1 meeting criteria for MKD. One clinically diagnosed CAPS patient met classification criteria for MKD.

Conclusion: In this cohort, the Eurofever/PRINTO clinical classification criteria do not perform as well as initially described. This may be due to variation in clinical diagnostic practice, differences in ethnic composition of the populations, or inclusion of non-specific criteria. This study also highlights the importance of not equating classification criteria with diagnostic criteria. These findings are limited by the small number of patients within our cohort, and further studies are warranted.

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Observations on Biomarkers in Very Early Rheumatoid Arthritis Over 20 Years, from Baseline Presentation to Five-Year Outcomes

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Objectives: To analyze the impact of biomarkers over 20 years on baseline variables, treatments, comorbidities and outcomes over the first 5 years of follow up of consecutive adults with recent-onset immune-mediated polyarthritis recruited since July 1998 (Early Undifferentiated Polyarthritis (EUPA) cohort).

Methods: Variables and Outcomes were collected over 5 years in patients fulfilling RA criteria, grouped according to date of inclusion (Period 1: 1998-2004; Period 2: 2005-2010; Period 3: 2011-2018). Comparisons of baseline characteristics, treatment, and outcomes over 5 years between the 3 Periods were previously presented (ACR 2018, 2019). Erosive damage was scored according to Sharp/van der Heijde; erosive status defined as ≥ 5 Erosion units. We now present observed associations between baseline prognostic biomarkers (ACPA, RF, anti-Sa, and erosive status) with concomitant and subsequent disease activity levels, radiographic scores, comorbidities and impact of treatment. False discovery rate correction was used to adjust p-values for multiple comparisons.

Results: 753 patients were included: 247, 263 and 243 in Periods 1, 2 and 3, respectively. At baseline, no biomarkers were associated with demographics or disease activity. Erosive disease was more prevalent in ACPA+ (19.9% vs

13.9%, $P = 0.0417$). All comorbidities were significantly more present in ACPA negatives (RR 1.55 to 1.99). Prevalence of cardiovascular (CV; 44.8, 55.0, 60.0%; $P = 0.036$) and cancer (4.1, 7.1, 13.1%; $P = 0.02$) comorbidities increased over time in ACPA negatives while stable in ACPA+ (CV: 33.0, 30.8, 40.7, NS; cancer: 3.0, 4.4, 6.2, NS). RF positivity decreased by period (47.8, 36.9, 36.7%, $P = 0.03$), but ACPA+ remained stable (40.8, 35, 35.4%, NS). Over 5 years of follow up, there was no link between any biomarker and subsequent disease activity. Positive antibodies at baseline predicted development of more erosive status (RR 1.37 to 1.52, all $P < 0.001$). 70.3% ACPA negatives reached DAS28 remission vs 65.2% ACPA+. CV comorbidities increased significantly more over time in ACPA+ vs negatives (RR = 1.18, $P = 0.03$). Erosion scores increased significantly more in ACPA+ treated with DMARDs only vs a biologic (Δ Erosions: 2.58 vs 1.83, $P = 0.02$). Erosive status decreased significantly in periods 2 vs 1: RR = 0.65, $P = 0.002$; 3 vs 1: RR = 0.42, $P = 0.002$; 3 vs 2: RR = 0.64, $P = 0.007$, in ACPA+ and negatives.

Conclusion: In this cohort, we observed a constant drift towards baseline RF-negative arthritis. While seronegative patients had more comorbidities at baseline, positive antibodies were associated with more cardiovascular comorbidities' accrual. Autoantibody positive (especially ACPA) developed more erosive status and had better erosion outcomes with biologic treatments.

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Disease Activity Trajectories for Early and Established Rheumatoid Arthritis: Results From The Ontario Best Practices Research Initiative (OBRI)

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

Objectives: Description of disease activity status in patients with rheumatoid arthritis (RA) at fixed points in time modelled as continuous (e.g. number of swollen joints counts), dichotomous variable (e.g. remission or low disease status using composite measures) do not reflect the patient's disease course in chronic and relapsing RA. We proposed to describe the longitudinal disease activity trajectories for patients with early and established RA over two years' follow-up in routine clinical care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) with available DAS28-ESR over two years of follow-up were included. Using a latent growth curve modelling (LGCM), subgroups of patients following distinct pattern of DAS28-ESR change over time were identified. Model selection was based on Bayesian information criterion (BIC).

Results: A total of 1273 patients were included, 454 (36%) with early RA and 819 (64%) with established RA. At baseline, patients with early RA were significantly younger (57.3 vs. 59.1 years) and with higher DAS28-ESR (4.6 vs. 4.3) and were less likely to have an erosion (25.0% vs. 59.7%), to be RF-positive (70.3% vs. 76.8%), and to use biologic DMARDs (7.0% vs. 29.2%). In patients with early RA, three subgroups of patients were identified by LGCM with a better fit (BIC: -3070.84). Almost 88% patients with moderate disease activity reached remission (group 1: 48.4%) or low disease status (group 2: 39.3%) at year 2, while 12% of patients with high disease profile remained in a moderate state (group 3). In patients with established RA, seven subgroups of patients were identified by LGCM with a better fit (BIC: -5378.13). After 2 years' follow-up, 37.5% of patients in remission or low disease state at baseline remained or reached to remission (group 1 and 2, respectively). Only 17.3% of patients with high disease activity at baseline reached remission (group 5). 16.5% patients with high disease activity at baseline remained in high disease status at year 2 (group 4 and 6). Two other group of patients (group 3 and 7) with moderate or high disease activity at baseline remained in a moderate state after two years.

Conclusion: These findings suggest the potential effects of receiving early treatment and health care. The impact of sociodemographic, clinical and medication profile on disease course will be examined as future work for this study.

Sociodemographic, Disease, and Medication Profile of RA Patients under 65 years Compared With 65 Years or Older at Registry Enrollment: Results From The Ontario Best Practices Research Initiative (OBRI)

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

Objectives: Age is an important factor that can affect disease course, physical function and treat to target strategy for patients with rheumatoid arthritis (RA). We aimed to describe sociodemographic, disease and medication profile of patients with RA in the Ontario Best Practices Research Initiative (OBRI) by their assigned age group at time of their enrollment.

Methods: RA patients enrolled in the OBRI between 1st Jan 2008 and 31st Dec 2019 were included. Patients were allocated into two age groups, under 65 years and 65 years or older. Descriptive analysis was used to compare sociodemographic characteristics, disease activity, patient report outcomes (PROs), comorbidity, and antirheumatic medication profile. We calculated the standardized difference as the difference in means or proportions divided by the standard error. A significant difference between the two groups was defined as an absolute value ≥ 0.10 .

Results: A total of 3,734 patients were included; 2562 (68.5%) were under 65 years old and 1172 (31.5%) were 65 years or older. Sociodemographic profile: Patients under 65 years were significantly more likely to be female (79.7 vs. 73.5%), non-Caucasian (14.4 vs. 7.4%), current smokers (18.8 vs. 9.3%) and have post-secondary education (62.6 vs. 44.6%), and more likely to have private health insurance (75 vs. 49%) and report English as their spoken language (7.0 vs. 9.8%). Disease activity and PROs profile: Patients under 65 years were significantly more likely to be antiCCP positive (63.0 vs. 57.5%), report higher PtGA (mean: 4.8 vs. 4.5), higher global pain (mean 4.8 vs. 4.4), higher fatigue score (mean 5.0 vs. 4.6), and lower HAQ-DI (mean 1.1 vs. 1.2). In terms of comorbidity, patients under 65 years had significantly lower proportions of hypertension, cardiovascular disease, diabetes mellitus, lung disease, gastrointestinal disease and malignancy. However, interestingly this group of patients had a higher proportion of depression (17.8% vs. 13.3%). Antirheumatic medication profile: At enrollment, patients under 65 years were significantly more likely to have used prior bDMARDs (31.4 vs. 26.1%) and were more likely to be starting a new bDMARD (17.1 vs. 12.8%), or csDMARDs (38.6 vs. 35.6%).

Conclusion: In this real-world descriptive study, we found that disease activity measures were similar in patients under 65 years compared to those 65 years or older. However, sociodemographic, PROs, comorbidity, and antirheumatic medication profiles were different between two groups. These differences should be taken into account for any clinical decision toward outcome improvement in patients.

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Discontinuation Rate of Tofacitinib Is Similar When Compared to TNF Inhibitors in Rheumatoid Arthritis Patients: Results From the Ontario Best Practices Research Initiative (OBRI)

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); other OBRI investigators

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 TNFi compared to TOFA, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (adalimumab, certolizumab, etanercept, golimumab, and infliximab)

between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Time to discontinuation were assessed using adjusted Kaplan-Meier (KM) survival and Cox regression models. To deal with confounding by indication, we estimated propensity scores for selected covariates with a standard difference greater than 0.1. We then adjusted models by applying stratification and inverse probability of treatment weight (IPTW) methods to compare discontinuation of TNFi versus TOFA. Multiple imputation ($N = 20$) was used to deal with missing data for covariates at treatment initiation.

Results: A total of 721 patients initiated TNFi ($n = 417$) or TOFA ($n = 304$) with mean (SD) disease duration of 8.9 (9.0) and 13.6 (9.6) years, respectively. In the TNFi group 82% were female and mean age (SD) at treatment initiation was 57.0 (13) years. In the TOFA group, 85% were female and mean (SD) age at treatment initiation was 60.7 (11) years. The TNFi group was less likely to have prior biologic use (22%) compared with the TOFA group (66%). At treatment initiation, the mean (SD) 28-swollen joint counts were significantly lower in the TNFi group [4.8 (4.0)] compared to the TOFA group [5.7 (4.4)]. Physical function measured by HAQ-DI was also significantly lower in TNFi compared to the TOFA group (1.1 vs. 1.3). Over a mean of 20.3-month follow-up, discontinuation was reported in 134 (32.1%) and 108 (35.5%) of all TNFi and TOFA patients, respectively. After adjusting for propensity score across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 0.80, 95% CI: 0.60-1.05; $P = 0.11$). The results were similar for two propensity adjustment methods.

Conclusion: In this real-world data study, we found that TNFi and TOFA retention is similar in patients with RA. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

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Differential Influence of CDAI Components Based on Disease State in Rheumatoid Arthritis Patients:

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Objectives: Treat-to-target recommendations for rheumatoid arthritis (RA) dictate that remission or low disease activity should be aimed. Although numerous composite indices are available, the clinical disease activity index (CDAI) is commonly used in routine clinical care due to its simplicity and non-reliance on acute phase reactants. The purpose of this analysis was to evaluate the CDAI properties both cross-sectionally and longitudinally in a cohort of RA patients followed in Canadian routine care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI), with available follow-up for ≥ 6 months and data on CDAI, disease activity score based on 28 joints (DAS28), health assessment questionnaire (HAQ), and ACR/EULAR Boolean remission were included. For both the CDAI score and its change from baseline to 6 months, construct validity was assessed with principal component analysis, internal consistency with the Cronbach's alpha coefficient (α), correlational validity with the Spearman's rho coefficient, agreement in disease state classification with percent concordant pairs and the kappa statistic. Stratified analysis by presence of CDAI low disease activity (LDA) or remission was performed.

Results: 1,582 patients met the inclusion criteria. Principal component analysis showed that CDAI could be reduced to a single component when CDAI is > 10 with SJC28 accounting for most variance in score and patient global assessment (PtGA) the least; whereas, when CDAI is ≤ 10 , two distinct components were identified, the first comprising PtGA and physician global assessment (PhGA) and the second SJC28 and TJC28. In terms of internal consistency, high levels were observed for both CDAI at baseline ($\alpha = 0.83$) and its change from baseline to 6 months ($\alpha = 0.81$);

however, the consistency between CDAI components was very low when CDAI is ≤ 10 ($\alpha = 0.23$). Overall, a strong positive correlation was observed between CDAI and DAS28 ($\rho = 0.86$) and their changes ($\rho = 0.87$) while its correlation with HAQ was weak. When stratifying by CDAI levels, the correlation of CDAI with DAS28 was moderate when CDAI is ≤ 10 and very weak when CDAI is ≤ 2.8 . Similarly, agreement in the classification of LDA between CDAI and DAS28 or HAQ was fair to moderate, and agreement in classification of remission was poor to fair.

Conclusion: CDAI and DAS28 correlate well when disease activity is moderate or high and poorly in LDA or remission. PtGA had a stronger influence on CDAI at LDA or remission state compared to moderate or high disease state. Careful interpretation of PtGA is necessary particularly in patients who are identified as CDAI non-remitters.

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Sex Differences in the Efficacy and Safety of Tofacitinib in Patients With Rheumatoid Arthritis: A Post Hoc Analysis of Phase 3 and Long-Term Extension Trials

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Objectives: Differences in efficacy favouring males vs females with rheumatoid arthritis (RA) have been reported with csDMARDs and TNF inhibitors; JAK inhibitor results are less clear. This post hoc analysis assessed the impact of sex on efficacy, safety and persistence in tofacitinib RA clinical trials.

Methods: Efficacy and safety analyses included data pooled from Phase 3 RCTs of patients with RA and inadequate response to methotrexate (NCT00847613; NCT00853385) or ≥ 1 DMARD (NCT00856544) receiving tofacitinib 5 or 10 mg BID, adalimumab 40 mg Q2W or placebo, all + csDMARDs. Persistence analyses included patients receiving tofacitinib 5 or 10 mg BID \pm csDMARDs using data pooled from LTE trials (NCT00661661; NCT00413699). Efficacy outcomes to M12 included: ACR20/50/70 responses, changes (Δ) from baseline in DAS28-4(ESR), CDAI, HAQ-DI, and FACIT-F, and DAS28-4(ESR) remission (< 2.6). Safety was evaluated to M24 for tofacitinib and adalimumab. Kaplan-Meier persistence analyses assessed time to discontinuation.

Results: 2265 patients were included from Phase 3 RCTs. Demographics/baseline characteristics were comparable across sexes and treatments. Tofacitinib or adalimumab vs placebo generally led to significantly higher ACR20/50/70 responses in both sexes through M6. To M12, ACR20/50/70 responses were broadly comparable across active treatments and between sexes, with significantly higher rates observed for males at some timepoints. Across treatments, Δ DAS28-4(ESR) and DAS28-4(ESR) remission rates were significantly greater for males vs females at most timepoints through M12. Δ CDAI, Δ HAQ-DI, and Δ FACIT-F significantly favoured males vs females receiving tofacitinib 5 mg BID at most timepoints, while Δ HAQ-DI and Δ FACIT-F tended to favour females receiving tofacitinib 10 mg BID. Rates of adverse events (AEs), serious AEs, severe AEs and discontinuations due to AEs were slightly higher in females vs males with tofacitinib 5 mg BID; this was generally reversed with tofacitinib 10 mg BID and adalimumab. AEs of special interest, including deaths, serious infections, herpes zoster (non-serious and serious), malignancies, MACE and venous thromboembolism, were comparable between sexes with active treatments, although low event numbers limited interpretation. Time to all-cause discontinuation and discontinuation due to AEs/lack of efficacy with tofacitinib 5 mg BID was similar between sexes. Numerical differences favouring females vs males were observed for time to all-cause discontinuation and discontinuation due to AEs with tofacitinib 10 mg BID.

Conclusion: Efficacy outcomes with tofacitinib and adalimumab were

generally higher in males and comparable in females vs previously published response rates for advanced therapies. Safety findings did not reveal a consistent pattern between sexes. Tofacitinib persistence was generally similar between sexes.

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Metrics and Definitions Used in the Assessment of Cognitive Impairment in Systemic Lupus Erythematosus: A Systematic Review

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Objectives: To systematically review the literature on: (1) the measurement tools used to assess cognitive impairment (CI) in systemic lupus erythematosus (SLE), (2) studies using neuropsychological batteries (NB) and compare the tests within them to the American College of Rheumatology (ACR) NB, and (3) the definitions of CI from studies that used a NB.

Methods: This review included studies that evaluated CI in SLE patients using an objective neuropsychological metric for screening/diagnosis. The literature search was conducted in Ovid Medline, Embase, and PsycINFO for articles on CI in adult SLE patients. For our first objective we categorized cognitive measurement tools into four categories: NB, screening, incomplete/mixed batteries, computerized batteries. The NB category constituted a well described NB, where studies used the terms "battery" or a variant and consisted of ≥ 4 tests covering > 2 cognitive domains. The screening category consisted of studies that used one or more screening tools (e.g., MoCA, MMSE, etc.). The incomplete/mixed category consisted of studies that did not meet the definition for our screening, NB, or computerized category. The computerized category consisted of studies that used only a computerized battery. For our second objective we reviewed studies that used a NB, and compared those tests to the tests from the ACR-NB. For our third objective, we reviewed definitions of CI based on studies that used a NB when sufficient information was available.

Results: Of 8727 references, 118 were selected for detailed review and 93 were included in the final analysis. Objective 1: the most commonly used measurement tool for assessing CI in SLE was a NB (67% of studies), although the use of screening tests and computerized batteries have both increased in the last decade. Objective 2: only two of 57 studies that used a NB used the ACR-NB exactly as published regarding content. All other studies used varying proportions of ACR-NB tests and other neuropsychological tests. Objective 3: Definitions for CI varied and consisted of T- or Z-scores that ranged from 1 standard deviation (SD) to 3 SD below the mean, compared to normative data or controls. The number of cognitive domains or tests to determine impairment also varied widely.

Conclusion: The assessment and definition of CI in SLE is heterogeneous. A consensus meeting to address existing inconsistencies should be considered to harmonize the field of CI in SLE.

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Evaluation of Comorbidities and Damage in Canadian Patients With Systemic Lupus Erythematosus

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Objectives: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with a wide array of clinical manifestations, treated with corticosteroids and long term immunosuppressants to reduce the disease activity and damage. Our objectives were to examine a Canadian cohort of SLE patients in comparison to the general Canadian population to examine potential risk factors for comorbidities and disease damage in SLE patients. We hypothesize that SLE patients accumulate more damage and comorbidities with greater disease activity and corticosteroid exposure over time compared to the general population.

Methods: We explored the Canadian Network for Improved Outcomes in SLE (CaNIOS) registry, a multi-centred cohort of Canadian SLE patients, to identify prevalence of damage using the SLICC SLE Damage Index (SDI) and comorbidity using the Charlson Comorbidity Index (CCI). We also performed an age-matched data analysis to compare the comorbidities prevalence between the CaNIOS registry and the general Canadian population (Canadian Community Health Survey). Exploratory analysis was done using descriptive statistics. Univariable analysis was performed to identify potential predictors of comorbidities and damage in the CaNIOS SLE population at baseline. Variables that were significant at the univariable level were included in a Generalized Linear Model (GLM).

Results: 603 SLE patients from the CaNIOS registry were included, mean age 50.9 years (SD = 14.6), average disease duration 14.2 years (SD = 11.9), 91% being female. Mean SLE disease activity score (SLEDAI) was 3.1 (SD 3.5) and mean ACR classification criteria 5.3 (1.5). Mean CCI was 1.33 (SD = 0.69), and mean SDI was 1.34 (SD = 2.04). The most common comorbidities in CaNIOS patients were cerebrovascular disease (6.5%), followed by solid tumours (5.8%). Compared to their age-matched general population counterparts, SLE patients had higher rates of cancer (7.8% vs 2%) and cerebrovascular disease (6.5% vs 1.8%) ($P < 0.0001$). Multivariable GLM showed age to be a significant predictor for increased comorbidities ($P < 0.05$). Baseline risk factors associated with increased damage (SDI) were age, longer disease duration, higher ACR scores, current smoking and prednisone use within the last year ($P < 0.05$). Female gender ($P < 0.0160$), a recent onset of disease (< 12 months) ($P < 0.0001$) and intravenous steroid use ($P < 0.0286$) were found to be associated with less disease damage.

Conclusion: Canadian lupus patients have a greater burden of certain comorbidities compared to the general population. Identifying the risk factors associated with these comorbidities and disease damage is a very important step in treating those patients.

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Association Between Gastroprotective Agents and Risk of Incident Interstitial Lung Disease in Systemic Sclerosis

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Objectives: Although interstitial lung disease (ILD) occurs in half of systemic sclerosis (SSc) patients and represents a leading cause of mortality, there are currently no preventative strategies. We evaluated if gastroprotective agents were associated with a lower incident risk of SSc-ILD.

Methods: An SSc cohort without clinically apparent ILD at baseline was constructed from the Canadian Scleroderma Research Group. The primary exposure was any use of gastroprotective agents (including proton pump inhibitors or histamine-2 receptor antagonists). Treatment with promotility agents was assessed as a secondary exposure. Time to new diagnosis of ILD was compared between exposed and unexposed person-time, using a multivariate marginal structural Cox model incorporating inverse probability of treatment weights to address potential time-varying confounding by indication. The probability of treatment exposure was estimated using logistic regression models, conditional on age at baseline, sex, race, current smoking history, disease duration at baseline, disease subtype (limited or diffuse), presence of autoantibodies (ACA, ATA and ARNAP), time-varying presence of gastroesophageal disease, time-varying use of corticosteroids, NSAIDs, immunosuppressive drugs and promotility drugs, and history of gastroprotective agent exposure until that visit.

Results: In total, 798 subjects met inclusion criteria. At cohort entry, median disease duration was 7.6 (IQR 3.9-15.6) years. Patients contributed a median 4.4 (IQR 2.6-7.2) years of follow-up. During this time, 158 new ILD cases were diagnosed, for a crude incidence of 4.4 (95% CI 3.8-5.1) events per 100 person-years. Most (2085, 73.4%) person-visits were exposed to gastroprotective agents, 579 (20.4%) were exposed to promotility agents, and 554 (19.5%) were exposed to both agents. The marginal structural weighted hazard ratio (HR) for incident ILD related to gastroprotective agents was 0.86 (95% CI 0.52-1.41). When exposure was defined as treatment with promotility agents, the weighted adjusted HR was 0.79 (95% CI: 0.35-1.77).

Conclusion: In this large SSc cohort with a median SSc duration of 7.6 years, the incident risk of clinically apparent ILD was not altered by exposure to gastroprotective agents. This finding does not support the use of gastroprotective agents to prevent ILD in SSc patients.

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The Accumulation of Organ Damage in Systemic Sclerosis Disease Subsets

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Objectives: The natural history of systemic sclerosis (SSc) includes progressive and irreversible damage to multiple organs. Patient subsets may be characterized by the extent of cutaneous involvement, the presence of SSc-specific antibodies or the combination of the two methods. How to best combine serological and phenotypic data to accurately risk stratify SSc patients remains an ongoing challenge. To quantify the accumulation of irreversible organ damage, an international collaboration developed the Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI). In this study, we aimed to determine which sub setting method best predicted the accrual of damage over time.

Methods: A prospective cohort of SSc patients from in the Canadian Scleroderma Research Group (CSRG) and Australian Scleroderma Cohort Study (ASCS) registries was used. Patients who had initial disease duration of less than two years and underwent a minimum of 2 standardized follow-up assessments were included. Patients were evaluated with the SCTC-DI and trajectories were compared for various sub setting methods.

Results: A total of 409 patients, 176 with diffuse cutaneous disease (dcSSc) and 233 with limited disease (lcSSc), were identified and included in this analysis. Follow-up duration varied between 2 to 9 years. Patients with dcSSc had a higher baseline SCTC-DI Score than those with lcSSc (5.1 vs. 3.5). Furthermore, patients with dcSSc disease had higher mean-annual increase in STCC-DI (0.87 vs. 0.42). Differences between those with ACA, ATA, and ARNAP were also observed (Mean-annual increase: 0.41 vs. 0.76 vs. 0.78). However, when patients were first subset as dcSSc, the SCTC-DI trajectories were similar for those with ATA, ANRAP, or other serological profiles (Mean-annual increase: 0.86 vs 0.80 vs 0.98).

Conclusion: The SCTC-DI can be used to measure the accumulation of organ damage in SSc and demonstrates unique trajectories for different disease subsets. Cutaneous sub setting was superior to antibody sub setting or a combination of antibody and cutaneous assessment in predicting damage accrual trajectories. In comparison to those with lcSSc, patients with dcSSc have an increased burden of organ damage present within the first two years of diagnosis and have accelerated accumulation of damage thereafter. These findings may help inform risk stratification for SSc patients.

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Characterization of Visual Manifestations and Identification of Risk Factors for Permanent Vision Loss in Patients With Giant Cell Arteritis

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Objectives: Permanent vision loss (PVL) is a feared complication and a leading cause of morbidity in Giant Cell Arteritis (GCA). Multiple risk factors for ocular involvement have been identified with variable consistency, including older age, male sex, presence of cardio-vascular risk factors, transient ischemic symptoms, jaw claudication and thrombocytosis. The objective of this study is to describe visual manifestations and identify risk factors that predict ocular involvement in patients with GCA.

Methods: The retrospective database, CAPHECO-GCA (Characteristics, Phenotype, Evolution and Complications of patients with GCA at Hopital du Sacre-Coeur de Montreal) was used to collect data between January 1st, 2000 and December 31st, 2019. Descriptive statistics comparing patients with and without visual symptoms and PVL were performed.

Results: A total of 100 patients with GCA were included. Of these, 53 had visual symptoms. Visual symptoms included blurred vision (30% of patients), diplopia (16% of patients), amaurosis fugax (14% of patients) and blindness (19% of patients). Out of the 19 patients with blindness, 16 did not recuperate and had PVL. Patients with PVL were older (79.2 ± 6.7 vs 74.2 ± 7.6 years; $P = 0.008$), more likely to have coronary artery disease (31% vs 10%; $P = 0.018$) and peripheral artery disease (19% vs 5%; $P = 0.044$) than patients without PVL. However, patients with PVL were less likely to have other cranial symptoms (81% vs 96%; $P = 0.019$), mainly headaches (64% vs 92%; $P = 0.003$). A total of 58 patients underwent ophthalmologic examination: 10 had anterior ischemic optic neuropathy, 3 had central retinal artery occlusion, 1 had branch retinal artery occlusion and 3 had cranial nerve palsy. Risk factors associated with an abnormal ophthalmologic examination were the same as for PVL, but patients were also more likely to have diabetes (29% vs 7%; $P = 0.026$) and less likely to have constitutional symptoms (53% vs 80%; $P = 0.033$). Presence of visual symptoms was associated with a lower mean C-reactive protein level (73.7 ± 59.3 vs 104.3 ± 80.3 mg/L; $P = 0.035$). There was no statistically significant difference for sex, prior eye disease, delay to presentation, polymyalgia rheumatica, abnormal temporal artery on physical examination, extra-cranial large vessel vasculitis and platelet count.

Conclusion: Patients with GCA and PVL and/or abnormal ophthalmologic examination were older and more likely to have baseline diabetes,

coronary artery disease and peripheral artery disease. A predisposing vascular vulnerability might therefore increase the risk of ocular involvement in GCA.

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What Rheumatology Content Should We Be Teaching in Medical School? Learning Outcomes from a National Delphi

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Objectives: Rheumatic and musculoskeletal disorders are increasingly prevalent and represent significant morbidity in patients and a burden on the healthcare system. However, medical students lack confidence and competence to appropriately evaluate and manage these disorders. A major barrier is the lack of agreement between rheumatologists on how much and what to teach in medical school and a lack of standardization of rheumatology learning outcomes. The objective of this project is to develop learning outcomes for Canadian undergraduate rheumatology curricula.

Methods: A comprehensive list of musculoskeletal learning outcomes was created using the Medical Council of Canada objectives for qualification for medical practice in Canada and the global recommendations for a musculoskeletal undergraduate curriculum generated by experts in rheumatology, orthopedics and rehabilitation medicine. Experts in undergraduate rheumatology education, postgraduate family medicine program directors and trainees from all Canadian medical schools were invited to participate in a face-to-face discussion to refine this list. Fifteen rheumatology education experts, representing eleven medical schools, are currently participating in a Delphi and have completed Round 1. They anonymously scored each learning outcome on a 9-point Likert scale according to how critical each outcome is to a Canadian undergraduate rheumatology curriculum (1-3 not critical; 4-6 important, but not critical; 7-9 critical). Learning outcomes will be included if at least 70% of participants ranked the outcome as "critical" with no more than 15% "not critical" rankings. Learning outcomes will be excluded if at least 70% of participants ranked the outcome as "not critical" with no more than 15% "critical" rankings. Round 1 allowed for new item generation. Learning outcomes that did not reach consensus, as well as newly suggested learning outcomes, will be re-scored in two subsequent rounds.

Results: Of the 115 learning outcomes reviewed in round 1, 45 met consensus criteria and were included in the final list. Items not reaching consensus ($n = 70$) and new items ($n = 11$) will be re-scored in two subsequent rounds. Participant comments generated the following themes: the increased need for learning outcomes to address non-medical expert roles and the non-specific terminology used in learning outcomes may make it difficult to interpret and apply in real-life practice. Final results to be reported.

Conclusion: Through a systematic process, a common set of learning outcomes will be developed for Canadian undergraduate rheumatology curricula. This will inform undergraduate planning committees and hopefully improve the knowledge, skills and attitudes of our graduating medical students, ultimately improving patient care.

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Rheumatologists' Attitudes Toward Palliative Care and Medical Assistance in Dying

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Objectives: Despite advances in the treatment of systemic rheumatic diseases, a population remains - including those with vasculitis, myositis and systemic sclerosis - who suffer from life-limiting disease. These patients have little access to palliative care, and there is a paucity of data on this potential

care gap. This study aims to define the referral practices of Canadian rheumatologists to palliative care and to explore rheumatologists' attitudes toward palliative care and medical assistance in dying (MAiD).

Methods: All rheumatologist members of the Canadian Rheumatology Association were invited to complete an online questionnaire using Survey Gizmo. Responses were received anonymously, aggregated and analyzed using descriptive statistics.

Results: 37 (19%) of rheumatologists completed the survey. 22 (60%) self-identified as academic physicians. The majority were general rheumatologists ($n = 30$, 83%), caring for adult patients ($n = 33$, 89%). 68% reported exposure to palliative care during medical training, covering pain management ($n = 23$, 77%), end-of-life planning ($n = 19$, 63%) or communication skills ($n = 21$, 70%). Rheumatologists categorized up to 50% of their inpatients and 10% of their outpatients as having advanced rheumatologic disease with significant functional limitation or poor prognosis. 44% ($n = 16$) reported access to palliative care services for their patients, and 36% ($n = 13$) were aware of local palliative home care services. 54% ($n = 19$) had never referred a patient to palliative care. For those who had, they did so most often for uncontrolled symptoms and prognosis less than 1 year ($n = 22$, 66%), or for terminally ill inpatients requiring assistance with discharge planning ($n = 24$, 60%). 14% ($n = 5$) reported feeling "very comfortable" identifying patients with life-limiting rheumatic conditions who might benefit from a palliative approach to care, and 22% ($n = 5$) were "very comfortable" discussing this approach with their patients. While 33% ($n = 12$) of rheumatologists had been approached by a patient requesting MAiD, many rated their knowledge of eligibility criteria ($n = 17$, 47%) and of the assessment and approval process ($n = 19$, 53%) as "poor".

Conclusion: This study is the first to describe self-reported referral practices of rheumatologists to palliative care services, and to identify attitudes of these physicians towards palliative care consultation. The results expose gaps in knowledge of, and comfort with, palliative care services for patients with life-limiting rheumatic diseases, as well as barriers to accessing these services for patients with non-cancer illnesses. Further work is needed to engage rheumatologists about the role that palliative care teams can play in providing higher quality care to patients with advanced systemic rheumatic illnesses toward the end of life.

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Improved Self-efficacy and Knowledge in Pediatric Rheumatology: A Pilot Teaching Curriculum

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Objectives: Self-efficacy and knowledge in core pediatric rheumatology (PR) topics are generally low among pediatric residents. The objective of this study was to improve self-efficacy and knowledge in PR among general pediatric residents through a pilot standardized teaching curriculum. Specifically, we aimed to increase the mean self-efficacy score from an estimated baseline of ≤ 5 pre-rotation to ≥ 7 post-rotation (on a 10-point Likert scale), and the mean knowledge score from an estimated baseline of $\leq 60\%$ pre-rotation to $\geq 80\%$ post-rotation.

Methods: Interactive presentations on 4 core PR topics (Juvenile Idiopathic Arthritis, Systemic Lupus Erythematosus, Kawasaki Disease, and Macrophage Activation Syndrome) were developed and delivered by PR fellows to general pediatric residents during their rotations. Self-efficacy (16 questions on a 10-point Likert scale) and knowledge (12 multiple choice questions) were assessed using questionnaires pre- and post-rotation. Questions were mapped to objectives of training in PR and general pediatrics, where possible. Mean scores for self-efficacy and knowledge were determined. Differences between pre- and post-rotation scores were assessed by Wilcoxon signed-rank test. Statistical significance was defined by a p -value of ≤ 0.05 . Qualitative feedback was collected using open-ended questions.

Results: Thirty-two residents were provided the teaching curriculum

during their PR rotations from January 2019 to June 2020. Mean self-efficacy score was 4.5 and mean knowledge score was 58.9% pre-rotation ($n = 31$). Among residents who completed both the pre- and post-rotation questionnaires ($n = 21$), 100% improved their individual mean self-efficacy scores. 76% improved and 24% had no change in their individual mean knowledge scores. Overall mean self-efficacy score increased from 4.2 pre-rotation to 7.4 post-rotation ($P < 0.00001$), and mean knowledge score increased from 57.9% pre-rotation to 77.0% post-rotation ($P < 0.05$). Qualitatively, residents felt the teaching was effective, topics chosen were relevant, and the teaching curriculum should be implemented formally into their PR rotations.

Conclusion: Introduction of this pilot teaching curriculum in core PR topics improved self-efficacy and knowledge among general pediatric residents from the beginning to the end of their PR rotations. Several knowledge questions were challenging, which may explain why the 80% post-rotation target was not achieved. Qualitative feedback from residents was highly positive. The data supports integration of this pilot standardized teaching curriculum into the general pediatrics PR rotation. Future directions include revision of knowledge questions, development of presentations on additional PR topics, and administrative facilitation for scheduling and delivery of the curriculum.

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Understanding and Improving Patient Education of Cardiovascular Disease in Psoriatic Arthritis: How Well Are We Doing?

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Objectives: It has been well established that rheumatoid arthritis is associated with increased cardiovascular disease (CVD). To this end, researchers have improved screening for CVD risk management, as evidenced through international guidelines and practice statements. Like rheumatoid arthritis, psoriatic arthritis (PsA) is being increasingly shown to have similar, if not equal, cardiovascular burden. Unlike rheumatoid arthritis, rheumatologists do not seem to be having these comparable, important conversations with patients with PsA. Therefore, the purpose of this project was to explore how well patients are educated by rheumatologists about cardiovascular risk in PsA.

Methods: A retrospective chart review was performed of patients assessed from July 2018 through March 2020 at an academic rheumatology outpatient clinic. Demographics, comorbidities, treatment, and cardiovascular counseling recommendations were extracted. Counseling specifically referred to discussions about: blood pressure control; cholesterol control; diabetes control; weight management; dietary modifications; smoking cessation; interplay between non-steroidal anti-inflammatory drugs (NSAIDs) and CVD; interplay between glucocorticoids and CVD; and the association between increased CVD and PsA. Descriptive statistics were used to summarize results.

Results: A total of 50 charts were reviewed, encompassing 158 clinic visits. The mean patient age was 62.3 years (range 28 - 89), of which 70% were female. Mean duration of diagnosis was 121 months (range 3 months to 50 years), with 88% of patients meeting CASPAR criteria for PsA diagnosis. Regarding medication: 58% were currently on versus 24% had previously been on NSAIDs; and 6% were currently on versus 48% were previously on glucocorticoids. Regarding relevant cardiovascular demographics: mean BMI was 32.25 kg/m² (range 22.2 - 43.7 kg/m²); 12% of patients were currently smoking, with 40% former smokers; 56% of patients had hypertension; 46% dyslipidemia; 14% diabetes mellitus; 22% coronary artery disease (MI, previous angioplasty, angina, or heart failure); and 8% cerebral vascular disease. Across the entire 158 visits, zero mentions were made regarding counseling recommendations on CVD or the relationship between increased cardiovascular risk and PsA.

Conclusion: In this population sample of patients with PsA, CVD risk factors were highly prevalent; sadly, counselling on CVD was not documented once. This provides an important opportunity to improve this aspect of patient care in PsA. Future goals of this project include directly

evaluating patient knowledge of CVD, and ultimately utilizing this data to create a novel physician tool to use in clinical encounters to enhance overall CVD care in patients with PsA.

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Do Comorbidities Limit Improvement in Pain and Physical Function After Total Knee Arthroplasty in Patients With Knee Osteoarthritis? The BEST Knee Prospective Cohort Study

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Objectives: Total knee arthroplasty (TKA), a treatment for moderate-to-severe osteoarthritis (OA), has become one of the most common surgical procedures in Western countries, yet current understanding of outcomes after TKA for individuals with knee OA who have comorbidities remains unclear. In the context of the rising prevalence of comorbidity in individuals with OA, we sought to assess the relationship between comorbidities and amount of improvement in pain and physical function, as well as achieving an acceptable symptom state, in recipients of TKA for knee OA.

Methods: Patients with knee OA were assessed one month prior and 12 months after TKA at two centres in Alberta, Canada. Standardized questionnaires assessed patient-reported sociodemographic, social support, smoking status, comorbidities (12 assessed), pain (WOMAC pain subscale), physical function (KOOS physical function short-form), and acceptable symptom state (PASS). A subset of patients underwent six-minute walk test (6MWT), an objective measure of physical function. Multivariable general estimating equation modelling assessed the relationship between specific comorbid conditions, a priori hypothesized to impact pain and function, and total number of conditions, reflecting comorbidity burden, with change in pain, physical function, and 6MWT walking distance at 12 months after TKA, and reporting a PASS at 12 months, after controlling for potential confounders and clustering of patients by treating surgeon.

Results: 1051 participants were included; 278 for the 6MWT subset. Mean age was 67 years (SD 8.8), 59% were female, and 85% reported at least one comorbidity. Individuals with higher number of comorbidities had worse pre-TKA scores for pain, physical function, and walking distance. At 12-month follow-up, mean changes in pain, function and walking distance, as well as reporting a PASS, were similar for those with and without comorbidities. In regression analysis, no specific comorbidities, nor total number of comorbidities, were associated with less improvement in pain, physical function, or 6MWT distance at 12 months after TKA. Patients with diabetes (OR 0.64, 95% CI 0.44 to 0.94) and higher number of lower extremity troublesome joints (per joint OR 0.85, 95% CI 0.76 to 0.96) had lower odds of reporting a PASS.

Conclusion: For individuals with knee OA, comorbid conditions do not limit improvement in pain, physical function, and walking ability after TKA, and most conditions do not decrease the likelihood of reporting an acceptable symptom state. These results importantly provide more data for clinicians to draw upon when discussing TKA with the increasing number of patients with OA and comorbidities.

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Impact of the COVID-19 Pandemic Among Children With Rheumatic Diseases from Around the Globe

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Objectives: Children with rheumatic diseases face unknown risks in the setting of the COVID-19 pandemic. These children are often immunosuppressed due to their underlying disease or the medications used to

treat them. It is unknown whether children with rheumatic diseases are at increased risk of SARS CoV-2 infection or of developing serious disease complications should they become infected. We report on the pediatric data from the COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey.

Methods: The C19-GRA launched an international Patient Experience Survey for adults and parents of children with rheumatic disease. The survey was distributed online through patient support organizations and on social media. Parents entered data on behalf of their children, including their child's rheumatic disease diagnosis, medications, disease activity (as measured by a visual analog scale from 0-10, where 0 = very good and 10 = very poor), whether or not they developed COVID-19, and COVID-19 disease outcomes. Parents also completed the PROMIS Parent Proxy Scale v1.0 - Global Health 7. We report on data for children less than 18 years of age from April 3-May 8, 2020.

Results: Of 427 children included in the analysis, most resided in the Americas (64.9%) and were white (73.3%), female (63.0%), and between the ages of 5-14 (64.9%). The majority (40.7%) had juvenile idiopathic arthritis, and most were taking conventional synthetic DMARDs (54.6%) and/or biologic DMARDs (51.8%). The median disease activity score was 3 (IQR 1-6). The median T-score of the PROMIS Global Health measure was 43.9. Within this group, 5 children (1.2%) were reported as having a COVID-19 diagnosis, determined either by their parents (60.0%) or by a physician (40.0%). At the time of COVID-19 diagnosis, only 1 child was taking an immunosuppressive drug (methotrexate), and none of the survey participants with COVID-19 required hospitalization.

Conclusion: Our international survey of children with rheumatic diseases revealed only a handful of children developed COVID-19, all of whom had benign outcomes. Similar to otherwise healthy children, those with rheumatic disease do not seem to be at greater risk of developing COVID-19 or of COVID-19-related complications, even while taking immunosuppression. Limitations of this study include a convenience sample of parents engaged in social media, which may not be representative of the pediatric rheumatology population. Data were self-reported and could not be verified. Future studies should assess the long-term effect of the COVID-19 pandemic in children with rheumatic disease.

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Does Sex Affect Seropositivity in Rheumatoid Arthritis? A Systematic Review and Meta-Analysis

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Objectives: Approximately 75% of rheumatoid arthritis (RA) patients test seropositive for the autoantibodies rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA). Typically, seropositive RA patients experience more aggressive disease than seronegative patients. Women also have worse RA disease outcomes. Could increase seropositivity in women contribute to worse prognosis? The purpose of this systematic review and meta-analysis was to investigate whether autoantibodies are more often found in women than men with RA.

Methods: Databases were searched and studies exploring RA were included if they reported proportion of seropositive RA patients by sex and had a sample size of ≥ 100 subjects. Studies were included in the meta-analysis if relevant covariates were reported. Meta-analyses and meta-regression were conducted using the random effects model for RF positivity and ACPA positivity, separately. Covariates regressed were smoking, age, body mass index, functional score and disease activity score.

Results: One-hundred and twenty-four studies reported seropositivity by sex. Twenty of these studies reported covariates of interest while stratifying by sex. These 20 studies were included in the meta-analysis. Of these 20 studies, 90% were conducted in Western countries, the mean age ranged from 47-65 years and 48-79% of subjects were female. Results indicated that women were less likely than men to be positive for RF (logOR of -0.16[95%CI:-0.31, -0.02] $P = 0.03$). ACPA seropositivity was not

different by sex (logOR of -0.13[95%CI: -0.31, 0.05] $P = 0.64$). There was significant heterogeneity between studies. Meta-regression determined that age ($P < 0.0001$) and smoking ($P = 0.03$) significantly affected the relationship between sex and seropositivity.

Conclusion: In conclusion, despite women having more severe disease and seropositivity predicting worse outcomes, we could not identify a clear relationship between sex and seropositivity.

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Screening, Monitoring, and Treatment of Juvenile Idiopathic Arthritis-Associated Uveitis in the Canadian Context: Adolopment of the American College of Rheumatology/Arthritis Foundation Guidelines

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Objectives: In 2019, the ACR/AF published guidelines for the screening, monitoring and treatment of JIA-associated uveitis. JIA-associated uveitis has significant morbidity; thus, it is important to have Canadian guidelines for rheumatologists and ophthalmologists. The ACR/AF guidelines used GRADE methodology; therefore, we used the adolopment method to consider Canadian contextual differences, including differences in patients' preferences, cost/resource considerations, and feasibility of implementation. This work represents the first CRA guideline to apply this method which combines adoption, adaptation and, as needed, de novo development of recommendations.

Methods: A working group was assembled, an updated systematic literature review performed (Oct 13, 2017 - Feb 6, 2020) and summary tables were produced. Each member reviewed two ACR/AF recommendations, working in pairs to develop evidence to decision tables (EtD). Recommendations and EtDs were circulated, and a detailed survey distributed to assess agreement and issues requiring group discussion. A virtual meeting was held in August 2020 where EtDs with candidate recommendations were presented, discussed and voted upon to produce the final set of recommendations. Each recommendation was considered using a table of equity filters developed by the Quality care committee of the CRA that included indigenous, rural/remote, refugee and low socioeconomic status.

Results: The working group comprised 20 physician volunteers from across Canada (14 pediatric rheumatologists, 6 ophthalmologists with expertise in pediatric uveitis) along with 2 advisors from the CRA Guidelines Committee and Cochrane MSK group and 2 parent/patient representatives. All 19 ACR/AF recommendations for JIA-associated uveitis care encompassing screening (4) glucocorticoid use (4) DMARD and biologic use (4), education (2) and tapering of therapy (2) were reviewed. Following the survey, a virtual meeting was held to review the process, the health equity considerations, and discuss in depth 6 of the 19 recommendations that required significant revision. In addition to 15/20 working group members, patient/parent representatives and facilitators attended the meeting to discuss Canadian specific (and potentially controversial) topics including the frequency of ophthalmic screening and by whom performed, initial use of biologics, use of subcutaneous versus oral methotrexate, and role of alternative biologic and non-biologic therapies for patients failing methotrexate and anti-TNF therapies. Equity issues related to access to advanced therapeutics across provinces and territories were highlighted.

Conclusion: We applied a novel epidemiologic method to efficiently evaluate and modify the ACR/AF guidelines for JIA-associated uveitis to be applicable in the Canadian context with a lens for cost, equity and access.

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Late Cardiovascular Outcomes in Children With Kawasaki Disease: A Population-based Cohort Study

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Objectives: Kawasaki disease (KD) is a common childhood vasculitis associated with coronary artery aneurysms (CAA). The incidence of KD has significantly increased in Ontario over the past two decades. However, the risk of long-term cardiovascular events in children without large CAA remains unknown. Our objectives were to determine the risk and timing of long-term cardiovascular events and death among KD survivors.

Methods: We identified all children (0-18yr) surviving hospitalization with a KD diagnosis in Ontario between 1995-2018, through validated algorithms using population health administrative databases. We excluded children previously diagnosed with KD and non-residents. KD cases were matched to 100 non-exposed controls by age, sex and index year. Follow-up continued until death or March 2019. We determined incidence rates (per 1000 person-years (py)) and adjusted hazard ratios (aHR) for cardiovascular events, major adverse cardiac events (MACE; cardiovascular death, myocardial infarction or stroke composite) and all-cause mortality, comparing KD and non-exposed cohorts during the following time periods: 0-1yr, 1-5yr, 5-10yr and > 10yr.

Results: Among 4,597 KD survivors, 746 (16.2%) experienced cardiovascular events, 79 (1.7%) MACE and 9 (0.2%) died during median 11-year follow-up. The most frequent cardiovascular events among KD survivors were ischemic heart disease (231 children, 4.6 events/1000py), arrhythmias (229, 4.5/1000py), hypertension (159, 3.1/1000py) and peripheral vascular disease (107, 2.1/1000py). Following diagnosis, KD survivors were at increased risk of cardiovascular events between 0-1yr (aHR 11.65, 95%CI 10.34-13.13), 1-5yr (aHR 3.35, 95%CI 2.89-3.89), 5-10yr (aHR 1.87, 95%CI 1.53-2.28) and > 10yr (aHR 1.39, 95%CI 1.18-1.63). They were at increased risk of MACE between 0-1yr (aHR 3.27, 95%CI 2.25-4.76) and 5-10yr (aHR 2.13, 95%CI 1.30-3.50). KD survivors experienced cardiovascular events and MACE sooner than non-exposed children (Kaplan-Meier method, log-rank $P < 0.0001$). KD survivors were at increased risks of myocardial infarction (aHR 2.85, 95% CI 1.67-4.87) and percutaneous coronary intervention or coronary artery bypass grafting (aHR 11.02, 95% CI: 5.74-21.17) throughout follow-up. KD survivors were at lower risk of mortality throughout follow-up (aHR 0.36, 95%CI 0.19-0.70). KD survivors without coronary artery aneurysms were also at increased risk of cardiovascular events at all time periods and MACE between 0-1yr and 5-10yr, compared to non-exposed children.

Conclusion: Children diagnosed with KD are at increased risk of cardiovascular events for more than 10 years after index hospitalization. Despite the higher incidence of cardiovascular disease, they have a lower risk of long-term mortality. Our findings highlight the need for cardiovascular disease surveillance and risk reduction strategies among KD survivors.

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Long-term Hearing and Neurodevelopmental Outcomes Following Kawasaki Disease: A Population-based Cohort Study

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Objectives: Kawasaki disease (KD) incidence is increasing in Ontario. Cardiovascular sequelae following KD are well-described. However, there are limited data on non-cardiovascular outcomes. Our objective was to determine the risk of hearing loss, anxiety, developmental disorders, intellectual disabilities and attention-deficit/hyperactivity disorder (ADHD) among KD survivors vs. non-exposed children.

Methods: We included all Ontario children (≤ 18 yr) surviving

hospitalization with a KD diagnosis between 1995-2018, using population-based health administrative databases. We excluded children with prior KD diagnoses and non-residents. KD cases were matched with 100 non-exposed children by age, sex and year. Follow-up continued until death or March 2019. We calculated the prevalence, incidence rate (IR, per 1000 person-years (py)) and adjusted hazard ratios (aHR, 95%CI) of outcomes between 0-1yr, 1-5yr, 5-10yr and > 10yr follow-up.

Results: Among 4,597 KD survivors, 364 (7.9%, IR 7.5/1000py) were diagnosed with hearing loss, 1,213 (26.4%, IR 27.7/1000py) anxiety disorders, 398 (8.7%, IR 8.2/1000py) developmental disorders, 51 (1.1%, IR 1.0/1000py) intellectual disability and 21 (0.5%, IR 0.3/1000py) ADHD, during median 11-year follow-up. Compared to 459,700 non-exposed children, KD survivors were not at increased risk of hearing loss, after adjustment for potential confounders. KD survivors were at increased risk of anxiety disorders between 0-1yr (aHR 1.75, 95%CI 1.46-2.10), 1-5yr (aHR 1.13, 95%CI 1.01-1.28), 5-10yr (aHR 1.14, 95%CI 1.03-1.28) and > 10yr (aHR 1.11, 95%CI 1.02-1.22); developmental disorders between 0-1yr (aHR 1.49, 95%CI 1.28-1.74) and 1-5yr (aHR 1.19, 95%CI 1.02-1.40); intellectual disabilities > 10yr (aHR 2.36, 95%CI 1.36-4.10); and ADHD > 10yr (aHR 2.01, 95%CI 1.14-3.57). KD survivors were diagnosed with developmental disorders and anxiety sooner, compared with non-exposed children (Kaplan-Meier method, log-rank $P < 0.0001$ for each).

Conclusion: KD survivors are at increased risk of adverse neurodevelopmental outcomes, which may impair their academic and social functioning. This may justify enhanced developmental and audiological surveillance of KD survivors.

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Conduction Disorders/Dysrhythmias and Hydroxychloroquine in Rheumatoid Arthritis

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Objectives: To determine whether HCQ exposure (versus methotrexate, MTX) is associated with increased conduction disorders/dysrhythmias in rheumatoid arthritis (RA) in the pre-COVID-19 era.

Methods: Using MarketScan Commercial and Medicare Supplemental databases (Jan 2011-Dec 2018), we identified adult RA new users of HCQ or MTX. Time-zero was set as the date of first prescription. Conduction disorder or dysrhythmia episodes recorded as the main diagnosis of hospitalization were measured: i) within 30 days of time-zero (short-term effect); or ii) any time after time-zero. Individuals with previous diagnoses of conduction disorder/dysrhythmia were excluded from the analysis. Patients were followed until first event or censored (for loss of health plan coverage, discontinuation/switching of initial HCQ/MTX, or end of study). Cox regression was used to compare outcomes for HCQ versus MTX exposure. Models were adjusted for age, sex, calendar year at time-zero, health plan type (commercial or Medicare), comorbidities, previous ER visits/hospitalizations, and relevant medications one year before time-zero (corticosteroids, biologics, and DMARDs other than HCQ/MTX: sulfasalazine, leflunomide, cyclophosphamide) or 30 days before time-zero (antimicrobials).

Results: The RA patients included 70,995 new users HCQ and 95,230 new users of MTX. Subjects were mostly women (77%), averaging 53.3 (standard deviation 13.2) years old. Within the 30-days after time-zero, 151 patients experienced conduction disorder/dysrhythmias, with an event rate of 1.01/100 p-y (95% confidence interval, CI = 0.78-1.31) among HCQ users vs 1.24/100 p-y (95% CI = 1.01-1.52) for MTX users. We did not detect a clear difference in the 30-day risk for HCQ versus MTX (adjusted hazard ratio, HR = 0.84, 95% CI = 0.60-1.17). We identified 1,020 events occurring any time after time-zero, with an event rate of 1.04/100 p-y (95% CI = 0.94-1.15) among HCQ users vs 1.08/100 p-y (95% CI = 1.00-1.16)

for MTX users. We were also unable to detect a clear difference in HR for HCQ versus MTX (adjusted hazard ratio, HR 0.99, 95% CI = 0.87-1.13). Older age, Medicare plan type, and past ER visits/hospitalizations were associated with a higher risk of conduction disorders/dysrhythmia at both 30 days and in the longer-term. For corticosteroids, DMARDs, biologics and comorbidities, there were variations in HR estimates for short-term versus longer-term effects, potentially due to multicollinearity.

Conclusion: In this RA population, HCQ was not clearly associated with higher conduction disorders/dysrhythmia risk versus MTX. Greatest risk was seen in patients with older age, health plan type, and previous ER visits/hospitalization.

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Prevalence of Primary Biliary Cirrhosis in Systemic Sclerosis and Sjögren's Syndrome Over Time: A Systematic Review

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Objectives: Primary biliary cirrhosis (PBC) is known to be associated with rheumatological conditions such as Sjögren's syndrome (SS) and systemic sclerosis (SSc). The objectives were to determine the prevalence of: 1) PBC in patients with SS and SSc (and the subsets of limited cutaneous SSc (lcSSc) and diffuse cutaneous SSc (dcSSc)), 2) SSc and SS in patients with PBC, and 3) to analyze changes in frequency over time. SSc occurs in 3/10,000 and PBC in 4-40/10,000 but these rare autoimmune diseases are known to coexist together. We speculated that there could be more cases diagnosed due to increasing availability of standardized antibody tests such as ANA, centromere antibodies, ENA and mitochondrial antibodies.

Methods: A systematic review of the literature was performed using Medline, EMBASE, CINAHL, and the Cochrane Library databases up till June 16, 2020. Only full text articles in the English language with at least 40 patients were included. Cohorts, case series, cross-sectional studies, correspondences and registries with reported prevalence rates of both PBC in patients with SS and SSc as well as SSc and SS in patients with PBC were included. Data on frequency of co-existent diseases was studied by year of publication to determine if prevalence changed over time using linear regression. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist to assess the quality of the studies.

Results: Of 2876 citations identified, 67 were included in the analysis ($n = 33$ for PBC, 15 for SSc 18 for SS and 1 for SSc/SS). STROBE checklist scores ranged from 7-21. The prevalence of PBC was 5% in patients with SSc. Within the subsets, the prevalence of PBC in lcSSc was 8% and in dcSSc was 1%. In patients with SS, the prevalence of PBC was 4%. The prevalence of SSc overall in those with PBC was 5% and, within the subsets was 6% in lcSSc and 0% in dcSSc. The prevalence of SS in PBC was 18%. There was also no significant association between year of publication and prevalence. There was a lack of standardized definitions so misclassification may have occurred.

Conclusion: PBC is increased in SSc but mostly in the lcSSc subset. SS in PBC is common at nearly 1 in 5. Over the years, there was no change in the prevalence of PBC in SSc indicating stability over time.

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Damage Trajectories in Systemic Sclerosis Using Group-Based Trajectory Modeling

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Objectives: Systemic sclerosis (SSc) is a rare systemic autoimmune disease associated with a high mortality and characterized by the accrual of organ damage over time. The Scleroderma Clinical Trials Consortium Damage

Index (SCTC-DI) is a recently validated tool to measure this damage [1]. Identifying predictors of future damage is of utmost importance for prognostication and guiding research. This study aimed to identify if there are distinct trajectories of damage accrual from early in the disease and to determine which variables are associated with different trajectories, which could help guide when to initiate aggressive therapy early.

Methods: Using a prospective cohort design, incident adult cases of SSc (disease onset < 2 years) were identified in the Australian Scleroderma Interest Group (ASIG) and the Canadian Scleroderma Research Group (CSRG) prospective databases. Patients from these databases are enrolled consecutively and followed with yearly standardized assessments. Patients who met the ACR-EULAR Scleroderma classification criteria with at least two cohort visits and two SCTC-DI values were included. Due to missing data, six elements of the SCTC-DI were removed from the scoring (small joint contractures, pericardial effusion, GAVE, calcinosis, right ventricular dysfunction, myocardial disease). Group-based trajectory modelling (GBTM) was used to identify clusters of patients with similar DI trajectories. Their baseline characteristics were then compared for statistical significance using a one way-analysis of variance (ANOVA) and Kruskal-Wallis Test for continuous variables and chi-square test and Fisher's exact test for categorical variables.

Results: 409 patients were included in this study. Four trajectories of damage accrual were identified, with increasing damage over time. The average of posterior probabilities of group membership assigned to each group was 0.92, suggesting our trajectory model fits very well. The groups were distinct at baseline, with patients who had the fastest damage accrual also having a higher baseline SCTC-DI. Clinical factors that were more prevalent in the worst damage trajectories were male gender, current or previous smoking history, diffuse disease, tendon friction rubs, renal impairment, anti-RNA polymerase positivity and higher baseline inflammatory markers. Anti-centromere antibody positivity was more prevalent in the lower disease damage groups.

Conclusion: We have identified four distinct trajectories of disease damage in a combined incident cohort of patients with SSc. Several clinical and serological characteristics were more prevalent in those with worse damage trajectories. These findings may be helpful in recognizing patients in whom early aggressive treatment is necessary. Best Abstract By A Rheumatology Resident.

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Hemophagocytic Lymphohistiocytosis (HLH) Gene Variants in Childhood-onset SLE (cSLE) With Macrophage Activation Syndrome (MAS)

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Objectives: Macrophage activation syndrome (MAS), is a life-threatening complication of SLE. MAS is also referred to as secondary hemophagocytic lymphohistiocytosis (HLH) due to its clinical similarity to primary HLH, an autosomal recessive disorder. We compared the number of HLH-associated exonic (protein-coding) variants in childhood-onset SLE (cSLE) patients with and without MAS.

Methods: The retrospective cohort included patients diagnosed and followed for SLE in the Lupus Clinic at SickKids, Toronto from 1987-2018. All

participants met ACR, and/or SLICC SLE classification criteria. MAS diagnosis was based on expert physician diagnosis. Demographic, clinical and laboratory features were extracted from the lupus database and ancestry was genetically inferred using multiethnic genotyping array data. The non-MAS cSLE comparator group, comprised of patients suspected monogenic SLE (young age of SLE diagnosis, consanguineous parents or SLE affected first-degree relatives), underwent paired-end whole genome sequencing (WGS) by Illumina HiSeq X platform (read depth 37-40X). Most (n = 15) of the MAS cSLE group underwent whole exome sequencing (WES) by Illumina HiSeq 2500 platform (read depth 70-118X) and the remaining (n = 4) underwent WGS similar to the comparator group. We compared the number of non-synonymous (missense, stop gain/loss, frameshifts or nonsense) variants from 16 HLH-associated genes (MAF < 0.05), between patients with and without MAS. Allele frequencies were compared between patients MAS and without MAS using two-tailed Fischer's exact tests. Allele frequencies were also compared with the general population (gnomAD and TopMed) using Chi-squared tests (P < 0.005).

Results: The cohort included 81 patients, 19 with MAS. There was no difference in the number of HLH variants (exonic or non-synonymous) between MAS and non-MAS patients. We identified 53 non-synonymous HLH variants, 11 variants in 7 of 19 MAS patients and 42 variants in 30 of 62 non-MAS patients (P = 0.78). The HLH variant frequencies were not significantly different between the MAS or non-MAS cSLE populations, when compared to their ancestrally matched general population.

Conclusion: We did not observe a difference in the frequency of non-synonymous HLH genetic variants in cSLE patients with MAS compared to those without MAS. This is the first study to test the HLH-variant burden in relation to MAS, among patients with cSLE. Future studies of expanded sample size are required to validate our findings.

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Optimizing Non-pharmacologic Management of Gout: A Quality Improvement Project

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Objectives: Gout is a common inflammatory joint disease associated with metabolic syndrome, chronic kidney disease, and cardiovascular mortality. The 2016 EULAR and 2020 ACR guidelines provide recommendations on the long-term management of gout. Several non-pharmacologic strategies are recommended, including patient education, weight loss, exercise, reduction in alcohol, and dietary modification (Richette 2017, Fitzgerald 2020). However, studies have demonstrated many patients are not adherent to their therapy, and observational data suggests targeted interventions around patient education and lifestyle recommendations may improve hyperuricemia (Rees 2013). Our objective was to improve the documentation of counselling regarding the non-pharmacologic management of gout to 80% of each non-pharmacologic factor by summer 2021.

Methods: A retrospective clinical audit of 20 gout patients followed at Women's College Hospital was conducted. Initial rates of documentation around non-pharmacologic gout management strategies were identified. Following this, a standardized communication template was created in the electronic medical record. Several PDSA cycles were performed to refine the communication further after incorporating physician feedback. Ongoing PDSA cycles are planned to continue improving the quality of the template or including alternative strategies to meet our target documentation rate. A re-audit is scheduled for November 2020.

Results: Baseline data from our initial audit prior to any intervention demonstrated: 55% of patients never had dietary recommendations or dietitian referral performed and documented in the chart; 50% of the patients were documented to consume alcohol, however only 10% of these were clearly counselled on alcohol reduction; 70% of patients were considered not active and were not advised regarding increasing exercise. The first PDSA cycle involved feedback from staff rheumatologists on the content

development of the standardized communication. Subsequent PDSA cycles involving the authors and several trainees noted issues with layout and length of template. Changes based on feedback from these PDSA cycles noted improved ease of use and readability while maintaining comprehensiveness. Subsequent PDSA cycles are planned with all users in rheumatology with a re-audit planned in Nov 2020 with results to follow.

Conclusion: This QI project is aimed at enhancing quality and frequency of counselling relating to non-pharmacologic factors in gout management. This allows for better adherence to the latest gout guideline recommendations. Thus far, PDSA cycles have been effective to generate a standardized gout communication to effectively complete the patient visit including addressing these non-pharmacologic factors. Future work will include ongoing PDSA cycles and re-audit.

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Comparative Efficacy of Upadacitinib and Other Janus Kinase (JAK) Inhibitors in Patients With Moderate-to-Severe Rheumatoid Arthritis (RA): A Network Meta-analysis (NMA)

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Objectives: To date, three JAK inhibitors have been approved and one is under regulatory review. However, there are no head-to-head trials comparing their efficacy. We therefore conducted a NMA to evaluate the comparative efficacy of upadacitinib [UPA], tofacitinib [TOF], baricitinib [BAR] and filgotinib [FIL] in csDMARD-experienced patients with moderate-to-severe RA.

Methods: Phase III RA trials of all JAK inhibitors as monotherapy or in combination with csDMARD among patients with csDMARD-experienced RA were identified from various databases. ACR 20/50/70 responses and remission rates based on DAS28-CRP < 2.6 at 12 and 24 weeks were estimated using Bayesian ordinal NMA with posterior medians and 95% credible intervals (CrI) reported. The surface under the cumulative ranking curve (SUCRA) was estimated for the overall ranking of each treatment.

Results: All JAK inhibitors demonstrated significantly better efficacy than csDMARD in both ACR response and DAS28-CRP remission and no JAKi was statistically better than the others. For combination therapy, UPA 15 mg had the highest 12-week ACR50 response (median [95% CrI]: 45.1% [34.9%, 56.1%]), followed by TOF 5 mg (40.2% [29.9%, 51.4%]), FIL 200 mg (38.7% [26.6%, 52.0%]), BAR 2 mg (38.7% [26.3%, 52.2%]), BAR 4 mg (38.3% [28.6%, 48.7%]) and FIL 100 mg (29.7% [19.3%, 42.2%]). The SUCRA values among combination therapy ranged from 0.209 (the lowest) for FIL 100 mg to 0.907 (the highest) for UPA 15 mg. The efficacy trend was similar for ACR20/70. In terms of DAS28-CRP remission, UPA 15 mg had the highest numerical clinical remission rate at week 12 (32.3% [19.4%, 49.1%]), followed by TOF 5 mg (26.6% [14.6%, 42.3%]), BAR 4 mg (25.2% [13.7%, 39.6%]), FIL 200mg (24.4% [11.6%, 42.2%]), BAR 2 mg (22.3% [10.0%, 39.4%]), and FIL 100mg (16.3% [6.9%, 31.6%]), with SUCRA ranged from 0.220 for FIL 100 mg to 0.935 for UPA 15 mg. Efficacy ranks were largely similar at week 24, with UPA 15 mg having the highest ACR50 and DAS28-CRP remission rates. In terms of monotherapy, UPA 15 mg monotherapy had a numerically higher ACR50 response (40.1% [26.6%, 54.9%]) compared to TOF 5 mg monotherapy (31.8% [19.2%, 47.0%]) at week 12.

Conclusion: All JAK inhibitors consistently showed significantly better efficacy compared to csDMARDs with some numerical differences versus each other in moderate-to-severe RA patients. UPA 15 mg had numerically higher rates of ACR response and DAS28-CRP remission compared with TOF, BAR, and FIL for combination therapy and monotherapy.

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Potential Savings for Canadian Public Drug Insurance Plans Related to Biosimilar Adalimumab

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Institute of the McGill University Health Centre, Montreal); Gilles Boire (Université de Sherbrooke, Sherbrooke); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal); Laura Targownik (University of Manitoba, Winnipeg); Waqqas Afif (McGill University, Montreal); Peter Lakatos (McGill University, Montreal); Carter Thorne (Southlake Regional Health Centre, Newmarket); Sasha Bernatsky (McGill University Health Centre, Montreal)

Objectives: The high cost of biologics has created a demand for biosimilars as a cost-saving alternative, but the Canadian market for biologics is still dominated by bio-originators, including adalimumab. We estimated potential savings that provincial public drug insurance plans might realize from listing of biosimilar adalimumab (e.g., Hadlima®, approved by Health Canada in 2018 but not yet marketed) over the five-year horizon 2020-2024.

Methods: Data on adalimumab dispensation between January 1, 2014 and December 31, 2016 was available from provincial public drug insurance plans/programs in Canada (except Québec). We reviewed the public drug plan/program formularies and determined average annual costs (drug cost plus associated professional fee and markup, if applicable) to public drug plan/programs for a standard full-year regimen on adalimumab. We calculated compound annual growth rates for the quantity of adalimumab dispensed and its average annual cost over 2014-2016. We then forecasted potential savings related to biosimilar uptake for the 2020-2024 period, based on different scenarios. The three scenarios were: (a) 100%; (b) 50%; (c) 25% uptake of biosimilar adalimumab in treatment-naïve patients. Further sensitivity analyses performed for each of the three scenarios included: (1) a range of price discounts from 15%-35%; and (2) a range of switching of treatment-experienced patients from 33%-100%.

Results: In the worst-case scenario (25% uptake in treatment-naïve patients; 33% switch in treatment-experienced patients; 15% price discount), we estimated that \$241.7M of savings would accrue to the public drug plans/programs over 2020-2024. In the best-case scenario (100%; 100%; 35%), we estimated that \$889.7M of savings would accrue to the public drug plans/programs over the same period. Taking a modest stance (50%; 67%; 25%), we estimate the public drug plans/programs may save \$552.1M over five years.

Conclusion: Our research demonstrates significant potential cost savings related to future biosimilar adalimumab use in Canada, particularly with high uptake in both treatment-naïve and treatment-experienced patients. These conditions will require legislative intent, coordination between clinicians and sponsors of public drug plans/programs, and education for patients informing the safety and efficacy of biosimilars. A potential limitation is that we did not consider the emergence of competitor drugs for the indications of adalimumab, and how this might impact prescribing. Best Abstract By An Undergraduate Student.

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Investigating SLE Patients' Access to Health Information Pre and During the COVID-19 Pandemic

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Objectives: We conducted an online survey of Canadians with SLE to assess how patients access and trust health information pre and during COVID-19.

Methods: Patients fulfilling the ACR or Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for SLE from four Canadian cohorts (Alberta, Manitoba, Ontario, Maritime provinces) completed an online survey (June-September 2020) regarding sources of health information accessed in the 12 months preceding (pre-March 11, 2020) and during the COVID-19 pandemic (post-March 11, 2020). Descriptive statistics were used to calculate percentage accessing each information source, preferred sources, and associated level of trust. McNemar

tests were used to compare frequencies preceding/during the pandemic.

Results: 346 of 777 patients completed the survey (44.5% response rate); 41.0% from Alberta, 24.3% from Manitoba, 22.8% from Ontario, 11.9% from the Maritimes, 91.9% female, 69.6% Caucasian, mean age at diagnosis 33.5 (SD 13.5) years, mean disease duration 17.6 (SD 12.3) years, 77.6% with postsecondary education, and 45.6% with a household income exceeding \$100,000. Patients accessed news (42.8% pre vs 55.8% during, difference 13.0%, 95%CI 7.4%, 18.6%) and social media (28.9% pre vs 34.1% during, difference 5.2%, 95%CI 0.4%, 10.0%) more frequently during the pandemic, while access to family physicians (66.2% pre vs 50.9% during, difference -15.3%, 95%CI -21.1%, -9.6%) and SLE specialists (74.0% pre vs 54.1% during, difference -19.9%, 95%CI -25.1%, -14.8%) decreased post-March 11. Lupus specialists (1st) and family physicians (2nd) were ranked most preferred sources pre- and post-March 11 and considered the most trustworthy sources (78.9% rated family physicians as somewhat/very trustworthy during the pandemic, 95%CI 74.2%, 83.1%; SLE specialists: 85.6%, 95%CI 81.4%, 89.1%). News (4th pre vs 3rd during) and social media (8th pre vs 6th during) were ranked more highly as preferred sources post-March 11 but were considered less trustworthy than physicians (39.0% rated online news media as trustworthy during the pandemic, 95%CI 33.8%, 44.4%; 11.3% for Facebook, 95%CI 8.1%, 15.1%). With the exception of peers (24.6% pre vs 30.1% during, difference 5.5%, 95%CI 1.5%, 9.4%), trust in most sources decreased during the pandemic.

Conclusion: Although SLE specialists and family physicians are ranked as most preferred and trustworthy sources, their frequency of access decreased during the pandemic. Frequency of access to news and social media, less trusted sources, increased during the pandemic. We are expanding to international centers to further investigate the sociodemographic/geographic factors influencing access to health information. This research will improve information dissemination and enhance public health responses during the pandemic and beyond.

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The Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO): The Development of a National Collaboration for Research, Advocacy, Education and Optimizing Patient Care in an Emerging and Complex Domain

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Objectives: Immune Checkpoint Inhibitors (ICI) have revolutionized cancer therapy. However, a variety of immune-related adverse events (irAE), including rheumatic irAEs (Rh-irAE) often occur during treatment. There is limited data on the optimal management and long-term outcomes of patients who develop de-novo Rh-irAE, both in terms of their rheumatic disease and their tumor response. Furthermore, there is limited data on the use of ICI to treat cancer in patients with pre-existing rheumatic disease as these patients were largely excluded from clinical trials. Objectives: (1) To create a national collaboration of clinicians and researchers across

Canada interested in rheumatic complication of immuno-oncology for optimization of care, advocacy and education. (2) To develop a standardized, comprehensive, prospective cohort of clinical and biological data on patients developing Rh-irAE including those with pre-existing rheumatic disease and with de-novo Rh-irAE.

Methods: A small group of rheumatologists interested in adverse events of cancer immunotherapy came together to form a national network of clinicians, basic scientists, immunologists and epidemiologists interested in research, advocacy and education. Rheumatology division heads at all the academic sites across Canada were contacted to identify regional champions and ultimately formed the Canadian Research Group of Rheumatology in Immuno-Oncology (CanRIO). CanRIO investigators subsequently collaborated to develop a prospective research cohort study with harmonized inclusion criteria and data collection parameters of longitudinal clinical and biological data.

Results: (1) The CanRIO network was established in December 2018 and includes 19 members at 12 sites across Canada. In less than 2 years, CanRIO investigators have published 2 review articles, a national needs assessment, highlighting the need for clinical guidelines for Canadian rheumatologists, and the largest retrospective case series of Rh-irAE in the world. (2) The CanRIO prospective clinical cohort was established in November 2019 with harmonized inclusion criteria, electronic database, case report forms, and standard operating procedures for bio-data collection. Patient recruitment began in January 2020 and as of October 2020, 10 sites have obtained ethics approval and 18 patients have been recruited.

Conclusion: The CanRIO network is an example of the power of collaboration in the Canadian rheumatology community. CanRIO investigators are becoming experts in the rapidly evolving field of immuno-oncology and with the establishment of a prospective, national cohort, will be international leaders in describing the clinical, epidemiological, and physio-pathological aspects related to Rh-irAE secondary to immunotherapy for cancer.

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Perceived Barriers and Facilitators of Using Synchronous Telerehabilitation of Physical and Occupational Therapy in Musculoskeletal Disorders: A Scoping Review

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Objectives: Rehabilitation interventions, such as physical therapy and occupational therapy, play a crucial role in limiting disability and improving health-related quality of life in people with musculoskeletal disorders. People with rare musculoskeletal diseases, including systemic sclerosis (SSc; scleroderma), however, often have difficulty accessing appropriate services. E-health interventions delivered via videoconferencing with a healthcare professional are increasingly common to overcome barriers to delivering face-to-face physical and occupational therapy interventions and could be used to improve services in rare diseases. However, knowledge is needed on possible facilitators and barriers of successful use of telerehabilitation. Thus, the objective of this scoping review was to identify barriers and facilitators of using synchronous telerehabilitation to deliver physical and occupational therapy interventions for musculoskeletal disorders, to inform the development of a telerehabilitation intervention for SSc.

Methods: MEDLINE, EMBASE, CINAHL, PsycInfo, Cochrane Library, and Proquest Dissertations and Theses databases were searched from inception until May 27, 2020. Publications that described perceived barriers and facilitators of synchronous telerehabilitation in patients with musculoskeletal disorders were eligible. Two investigators independently evaluated

titles/abstracts and full-text publications for eligibility and extracted data from included publications. Barriers and facilitators were categorized using the Consolidated Framework for Implementation Research.

Results: The database searches yielded 1728 unique citations. Of these, 1464 articles were excluded after the title and abstract review, leaving 264 publications for full-text review to further assess their eligibility. Of these, 23 publications were included in the scoping review. 59 facilitators and 41 facilitators to using telerehabilitation were identified from the included publications. All included studies reported on facilitators and 20 (87%) studies reported on barriers. Facilitators that were most commonly reported included convenience and accessibility of services (Patient Needs & Resources), audio and visual quality (Design Quality & Packaging), and financial savings (Cost). Most commonly reported barriers included technological issues (Design Quality & Packaging), privacy concerns (Knowledge & Beliefs About the Intervention), impersonal connection and difficulty establishing rapport between patients and healthcare professionals (Networks & Communications).

Conclusion: Videoconferencing can be an effective tool to deliver physical or occupational therapy interventions for musculoskeletal diseases. Factors including quality and user-friendliness may facilitate the delivery of physical or occupational therapy interventions for musculoskeletal diseases using telerehabilitation. Strategies to address key barriers should be considered when developing and implementing such interventions. The knowledge obtained from this study will inform the development and evaluation of a telerehabilitation program for patients with SSC.

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Effectiveness after Transition to SB4 (Brenzys, Etanercept Biosimilar) Versus Continuation of Etanercept (ETN) Originator (Enbrel) Among Rheumatoid Arthritis (RA) Patients in Low Disease Activity: A Prospective Multinational Multicenter Observational Study (COMPANION-B)

Janet Pope (University of Western Ontario, London); Stephen Hall (Cabrini Medical Centre, Cabrini Private Hospital, Malvern); Claire Bombardier (University of Toronto, Toronto); Edward Keystone (University of Toronto, Toronto); Boulos Haraoui (Institut de Rhumatologie de Montréal, Montreal); Graeme Jones (University of Tasmania, Hobart); Latha Naik (University of Saskatchewan, Saskatoon); Carol Etzel (Corrona, LLC, Waltham); Dena Ramey (Merck & Co., Inc., Kenilworth); Ricardo Infante (Merck & Co., Inc., Carolina); David Wu (Merck & Co., Inc., Kenilworth)

Objectives: As biosimilar transition policies are implemented in Canada, real-world evidence from clinical practice can provide reassurance that transitioning from originator biologics to biosimilars is a safe and effective way of reducing healthcare costs. COMPANION-B was the first prospective real-world observational study designed to provide evidence on the effectiveness of SB4 (Brenzys, etanercept (ETN) biosimilar), compared to ETN originator (Enbrel, ETN-O) in stable rheumatoid arthritis (RA) patients in Canada and Australia. Descriptive analyses were performed to compare disease worsening over 12 months in RA patients with low disease activity /in remission who elected to transition to SB4 vs. those who continued ETN-O.

Methods: 14 Canadian (CAN) and 5 Australian (AUS) sites participated. Patients were ≥ 18 years old, treated with ETN-O for at least 6 months, with DAS28-ESR < 3.2 at enrollment. Use of stable background disease modifying antirheumatic drugs was permitted. Data were collected from routine clinic visits.

Results: Demographic characteristics were generally comparable between groups and countries; however, on average, CAN subjects were older (CAN mean age (SD): 61.8 (12.38), AUS: 55.1 (14.16)). Baseline DAS-28-ESR was similar for SB4 and ETN-O, as was mean (SD) duration of RA: 17.2 (10.4) and 18.6 (10.8) years for the ETN-O and SB4 groups, respectively, and approximately half of both groups used concomitant methotrexate. The study was completed by 83.5% of ETN-O patients and 75.9% of SB4 patients. Over 80% of both groups received ≥ 36 weeks of study treatment. Of the 152 patients included in the descriptive efficacy analysis, 125 (82%) were from CAN. 101 patients (90 CAN) elected to continue ETN-O and

51 patients (35 CAN) transitioned to SB4. RA disease activity at Month 12 was similar between groups; the proportion of disease worsening was 17.6% (95% CI [8.4%, 30.9%]) for SB4 and 22.8% (95% CI [15.5%, 32.2%]) for ETN-O. Occurrence of adverse events was low and similar between groups.

Conclusion: In this prospective real-world observational study, the biosimilar SB4 demonstrated similar efficacy and safety over 12 months compared to ETN-O in RA patients with stable disease. There was no evidence of a nocebo effect given no difference in worsening between groups, potentially indicative of patient-physician therapeutic alignment and trust. As economic pressures increase on our healthcare system and biosimilar transition policies are implemented in Canada, this study provides important reassurance to physicians, patients and policy makers that transitioning patients from originator ETN to its less costly biosimilar SB4 is safe and effective.

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A Collaborative Nurse-Led Model of Care for Stable Patients With Rheumatoid Arthritis Compared to Rheumatologist-Led Care: A Retrospective Cohort Study Evaluating Effectiveness and Appropriateness of Care

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Objectives: We assessed effectiveness and appropriateness of care for stable patients with rheumatoid arthritis (RA) followed within a nurse-led care (NLC) model compared to the traditional rheumatologist-led care (RLC) model.

Methods: A retrospective chart review was conducted at 2 teaching hospitals in Calgary, Alberta for patients followed in 2 models of care, NLC and RLC. Demographic and clinical characteristics were extracted. Consecutive patients with RA were included in the NLC group. For the RLC group, stable patients were identified using the following criteria: i) no more than 1 rheumatology visit every 6 months in 2013, ii) no changes in medications in 2013, and iii) being in remission or low disease activity at baseline appointment (2014) as defined by Disease Activity Score-28 (DAS28) ≤ 3.2 or a physician note indicating that the patient was stable. Care effectiveness was defined as percentages of: i) patients with a DAS28 ≤ 3.2 at 1-year follow-up and ii) visits where patients had a DAS28 > 3.2 with a change made at that visit. Care appropriateness was defined by percentages of patients with chart documentation about: i) comorbidity screening; ii) education on flare management, and iii) vaccinations screening at least once between baseline and 1-year follow-up. Percentages (numerator (N)/denominator (D)), means (standard deviation (SD)) or medians (interquartile range (IQR)) were used to summarize data.

Results: A total of 124 patients were included in each group. At baseline, patients were comparable in their clinical characteristics: i) median (IQR) disease duration - NLC: 5.88 (2.56-9.82) years and RLC: 6.12 (3.79-14.54) years, $P = 0.56$, and ii) mean (SD) DAS28 - NLC: 1.76 (0.69) and RLC: 1.89 (0.65), $P = 0.21$. Patients were more likely to be treated with conventional disease modifying anti-rheumatic drugs (DMARDs) only in the NLC group and biologic DMARDs in the RLC group, $P < 0.01$. NLC was non-inferior to RLC in terms of its effectiveness with NLC: 96% (N/D: 110/114) and RLC: 92% (N/D: 67/73) patients having a DAS28 ≤ 3.2 at 1-year follow-up. In active disease, patients' treatment was adjusted in NLC: 60% (N/D: 3/5) and RLC: 50% (N/D: 6/12) of visits. Patients in the NLC group were more likely to have chart documentation about i) screening for cardiovascular diseases (NLC: 90% (N/D: 112/124) and RLC: 2% (N/D: 3/124)) and osteoporosis (NLC: 92% (N/D: 88/96) and RLC: 19% (N/D: 19/101)), ii) education on flare management (NLC: 98% (N/D: 121/124) and RLC: 2% (N/D: 3/124)), and iii) vaccinations screening (NLC: 99% (N/D: 123/124) and RLC: 8% (N/D: 10/124)).

Conclusion: For stable patients with RA, NLC was non-inferior to RLC and there was evidence of higher documentation of comorbidities screening, education about flares management, and vaccinations screening in the NLC group.

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Immunization Rates Among Rheumatoid Arthritis Patients in a Canadian Outpatient Clinic

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Objectives: To assess immunization frequencies among patients with rheumatoid arthritis on JAK inhibitors and non-Anti-TNF biologic agents in an outpatient clinical setting

Methods: We conducted an investigators initiated retrospective chart review of electronic health records of patients at an urban rheumatology clinic between July 2010 and July 2020. All the data were prospectively collected. Our study sample consisted of all active and inactive patients diagnosed with rheumatoid arthritis who were previously or are being currently treated with medications from the following classes: JAK inhibitors (tofacitinib, upadacitinib, and baricitinib), Anti-CD20 (rituximab), Anti-IL-6 (tocilizumab and sarilumab), and CTLA4-Ig (abatacept). Anti-TNF patients were not included in this study due to our lack of resources to conduct a larger scale study. We collected data regarding influenza vaccination within 12 months of their last clinic visit, and vaccination status for herpes zoster and pneumococcus, in line with Canadian immunization guidelines for patients who have immune mediated disorders or immunosuppression. Descriptive statistics were calculated and summarized.

Results: 306 Active and Inactive Rheumatoid Arthritis patients were identified. The proportions of patients on JAK inhibitors, Anti-CD20, Anti-IL-6 and CTLA4-Ig were 35.5%, 28.7%, 56.0%, and 53.1%, respectively. In total, 45.6% of patients had received at least one dose of the herpes zoster vaccine, whereas 16.9% and 41.7% of patients were immunized against the influenza virus and pneumococcus, respectively. The rates of immunization varied significantly between different drug classes as follows: (1) JAK inhibitors: herpes zoster 82.6%, influenza 12.8%, pneumococcal 49.5%; (2) Anti-CD20: herpes zoster 43.2%, influenza 11.4%, pneumococcal 55.7%; (3) Anti-IL-6: herpes zoster 41.3%, influenza 12.8%, pneumococcal 41.3%; (4) CTLA4-Ig: herpes zoster 41.7%, influenza 18.4%, pneumococcal 42.3%.

Conclusion: Immunization coverage was suboptimal across all recommended vaccine types and medication subgroups. However, there was a slight increase, compared to data collected in 2019, in herpes zoster immunization among patients on JAK inhibitors, which was the patient population that was exclusively studied in the previous audit. This increase may have resulted from recent implementation of collaboration of the clinic's nursing and administrative staff with local pharmacists, one of the practice strategies that were identified previously to improve immunization rates at the clinic. Increasing the scale and scope of these efforts, in addition to investigations to identify factors mediating vaccine uptake and quality improvement studies to assess the impact of these community-based strategies, is required to address suboptimal vaccination coverage in this vulnerable population.

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Factors Associated With Fears due to COVID-19: A Scleroderma Patient-centered Intervention Network (SPIN) COVID-19 Cohort Study

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Objectives: Individuals who are vulnerable to COVID-19 due to pre-existing medical conditions likely experience high levels of fear, which could lead to acute and ongoing anxiety. There is great concern about mental health implications of COVID-19, and massive amounts of evidence have been published. However, no studies have examined factors associated with fear in any group of people vulnerable during COVID-19 due to pre-existing medical conditions. The objective of the present study was to investigate factors associated with fear of consequences of COVID-19 among people living with a pre-existing medical condition, the autoimmune disease systemic sclerosis (SSc; scleroderma), including country, comparing results from Canada, France, the United Kingdom, and the United States.

Methods: Pre-COVID-19 data from the Scleroderma Patient-centered Intervention Network (SPIN) Cohort were linked to COVID-19 data collected from April 9, 2020 to April 27, 2020. The validated 10-item COVID-19 Fears Questionnaire for Chronic Medical Conditions, which was the only instrument specifically designed for populations with pre-existing medical conditions, was applied among people with SSc. Multivariable linear regression was used to assess factors, including sociodemographic characteristics, medical characteristics, and COVID-19 variables, associated with continuous scores of fears due to COVID-19, controlling for pre-COVID-19 anxiety symptoms.

Results: Compared to France (N = 156), COVID-19 Fear scores among participants from the United Kingdom (N = 50) were 0.12 (95% CI 0.03 to 0.21) standard deviations higher; scores for Canada (N = 97) and the United States (N = 128) were higher, but not statistically significant. Greater interference of breathing problems was associated with higher fears due to COVID-19 (Standardized regression coefficient = 0.12, 95% CI 0.01 to 0.23). Participants with higher financial resources adequacy scores had lower COVID-19 Fear scores (Standardized coefficient = -0.18, 95% CI -0.28 to -0.09).

Conclusion: This was the first study to investigate factors associated with fears related to COVID-19 among participants with a chronic disease using a validated measure. Fears due to COVID-19 among people with SSc were greatest among participants from the United Kingdom, followed by Canada, the United States, and France. Fears due to COVID-19 were associated with clinical and functional vulnerabilities in this chronically ill population. This suggests that interventions may benefit from addressing specific clinical issues that apply to specific populations. Financial resources, health policies and political influences may also be important. The needs of people living with chronic illness during a pandemic may differ depending on the social and political context in which they live.

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The Link Between Joints and Entheses in Psoriatic Arthritis: An Ultrasound Study Supporting the Synovio-entheseal Complex Theory

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Objectives: The aim of this study is to explore the link between the severity of the joint and entheses involvement in psoriatic arthritis (PsA) using musculoskeletal ultrasound (US). The demonstration of a link between these two anatomical structures using a more objective tool that is not dependent on pain assessment can support the synovio-entheseal complex theory.

Methods: PsA patients from 2 centers (Canada and Italy, $n = 126$) in the Psoriatic Arthritis- International Database (PsArt-ID) included the study. Clinical activity indices including both the physical examination findings and blood test results in addition to the patient-reported outcome measures and physician global assessment were collected. On the same day of the clinical assessment, patients underwent an US assessment of 46 joints and 12 large entheses. The correlation between joint and enthesitis scores on the US was analyzed in addition to the clinical indices versus the US.

Results: Fifty-six of the 126 patients (44.4%) were male, and the mean (SD) age was 54.8 (14.6) years. The mean PsA duration was 7.6 (8.3) years. Greyscale (GS) synovitis score for the joints was moderately correlated with the total enthesitis score ($r = 0.410$, $P < 0.001$). The Global Outcome Measure in Rheumatology in Clinical Trials-European League Against Rheumatism Synovitis Score (GLOESS) score was also found in correlation with the total enthesitis score ($r = 0.400$, $P < 0.001$). The link between the US and clinical examination findings only showed a poor correlation between swollen joint counts (SJC) and joint-US scores ($r = 0.298$, $P = 0.001$ for GLOESS). Assessment of the entheses on US showed a poor-moderate correlation between the entheseal damage scores and tender joint counts (TJC) ($r = 0.217$, $P = 0.018$) and SJC ($r = 0.326$, $P = 0.001$). In terms of the clinical examination and activity parameters, none of the clinical parameters and acute phase reactants were correlated to Leeds Enthesitis Index.

Conclusion: Our study showed a link between the severity of the sonographic findings in the joints and the entheses in PsA patients which also supports the synovio-entheseal complex theory. Imaging using US to assess enthesitis in trials would improve our understanding on the role of enthesitis in disease pathogenesis.

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Ultrasound Versus Temporal Artery Biopsy in The Diagnosis of Giant Cell Arteritis

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Objectives: Historically, the diagnosis of giant cell arteritis (GCA) has been made on clinical grounds and confirmed with temporal artery biopsy (TAB). There has been a shift in recent years, and the 2018 EULAR guidelines recommends ultrasound (US) and magnetic resonance imaging as first-line investigations for suspected cranial GCA. In North America, US for GCA has been slow to catch on, in part due to an absence of Canadian data. This is the first Canadian study to compare the diagnostic accuracy of US and TAB.

Methods: Patients aged 50 and older with a clinical suspicion of GCA and at least one of the following were included: c-reactive protein (CRP) over 5 mg/L, new-onset headache, jaw claudication, fever, pain and/or stiffness in the hips and/or shoulders, temporal artery tenderness, or recent visual

impairment. Patients were excluded if they had a previous diagnosis of GCA, were taking over 10 mg of glucocorticoids for more than 4 weeks prior to US, had TAB performed prior to US or were unable to provide informed consent. Participants were prospectively enrolled from a single centre in Vancouver, British Columbia. Data including age, sex, co-morbidities, signs and symptoms suggestive of GCA, glucocorticoid use, disease modifying anti-rheumatic drug use, inflammatory markers, CTA and MRI was collected. US images were captured using a Canon Aplio i800 with a 33 MHz probe to assess the cranial arteries (temporal with frontal and parietal branches, facial, occipital) and a 11 MHz vascular probe for the large vessels (carotid, vertebral, subclavian, axillary). Images were collected by an unblinded ultra-sonographer (MB) and reviewed by a blinded, expert ultra-sonographer (APD).

Results: We present preliminary data from our study. 73 patients have been recruited. 43 were female and 30 were male. Average age was 74 (range 57-96). The most common presenting symptoms were headache (70%) and scalp tenderness (41%). Average CRP was 51 mg/L (range 0.3-284). Participants received an average of 8.1 days of glucocorticoid therapy prior to US (range 1-27 days). US was positive for vasculitic changes in 52 (71%), whereas TAB was positive in 26 (36%). The sensitivity and specificity for US and TAB will be calculated, using clinical diagnosis at 6 months as a diagnostic standard.

Conclusion: US has been recommended as a first line investigation for suspected GCA. The present study will report the accuracy of US compared to TAB in the Canadian population.

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Rapid Onset of Immune-Related Adverse Events After Transition from Combination Pembrolizumab/Cytotoxic Chemotherapy to Pembrolizumab Monotherapy.

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Objectives: Pembrolizumab is an immune-checkpoint inhibitor (ICI) that inhibits PD-1 to restore T cell-mediated antitumor immune activity and therefore enhances the body's immune response to cancer cells. Due to the nature of this therapy, immune-related adverse events (irAE) can occur, manifesting in nearly every organ system. Recent studies have also shown that there is a synergistic effect when pembrolizumab is used concurrently with cytotoxic chemotherapy for cancer treatment. We report two cases of irAEs that occurred shortly after patients transitioned from a combined pembrolizumab/chemotherapy regimen to pembrolizumab monotherapy.

Methods: We report two cases identified in the Rheumatology in Immunology clinic at the University of Alberta who were on pembrolizumab plus another chemotherapy agent, subsequently transitioned to pembrolizumab monotherapy and shortly after developed an irAE. Clinical data was extracted by retrospective chart review. Individual patient consent was obtained.

Results: Case 1: A 58-year-old female with metastatic non-small cell lung adenocarcinoma who presented with new inflammatory polyarthritis following transition from pemetrexed/pembrolizumab to treatment with single-agent pembrolizumab. She was initially started on cisplatin/pemetrexed/pembrolizumab ten months prior to this transition, and the cisplatin component was discontinued six months prior. Within one month of pemetrexed cessation, but continued pembrolizumab use, she developed severe tenderness and swelling to her bilateral knees, ankles, elbows, wrists and proximal interphalangeal joints. She was initiated on a course of prednisone and hydroxychloroquine. Case 2: A 50-year-old male with locally advanced squamous cell carcinoma of the right tonsil who took part in a clinical trial comparing chemoradiation with pembrolizumab vs. chemoradiation with placebo. He was presumed to be in the pembrolizumab arm when he presented with new hyperthyroidism six weeks after transitioning from presumed cisplatin/pembrolizumab to presumed pembrolizumab monotherapy. He developed intractable nausea and vomiting and was found to have a TSH level of 0.03, positive thyroid stimulating hormone receptor antibodies and a pertechnetate thyroid scan consistent with Graves

disease. He was initially managed with methimazole alone, but due to lack of response received a course of prednisone with disease remission. When he reinitiated the presumed pembrolizumab his disease recurred, once again requiring prednisone followed by methimazole.

Conclusion: These cases demonstrate irAEs that occurred very quickly after transitioning from combined pembrolizumab and chemotherapy regimens to pembrolizumab monotherapy suggesting that chemotherapy may suppress immune-related adverse events in patients on pembrolizumab. Physicians should be alert to rapid development of irAEs when transitioning from combination chemotherapy/ICI therapy to ICI monotherapy.

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A Triad of Myositis, Myasthenia Gravis, and Myocarditis in Patients Receiving Immune Checkpoint Inhibitor Therapy for Advanced Cancer: A Case Series

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Objectives: Immune checkpoint inhibitors (ICIs) have revolutionized the treatment of advanced malignancies. Clinical outcomes are impressive with complete remission in some patients. However, these drugs can also result in immune related adverse events (irAEs), affecting nearly every organ system. We report two cases of a life-threatening triad of rheumatic diseases--myositis, myasthenia gravis, and myocarditis--following ICI therapy.

Methods: We identified patients at Mount Sinai Hospital in Toronto, Canada who were diagnosed with concomitant myositis, myasthenia gravis, and myocarditis associated with ICI therapy. Clinical data was extracted by retrospective chart review.

Results: Case 1: A 75-year-old man with metastatic urothelial carcinoma presented with pain and weakness in the neck flexor muscles following three weeks of cabozantinib along with combination immunotherapy with ipilimumab and nivolumab. There was objective weakness on physical exam and elevation in his CK. Troponin and CK-MB were elevated, without evidence of myocardial dysfunction on cardiac imaging. Rheumatology and Oncology were consulted. Immunotherapy was stopped and the patient was treated with methylprednisone 1g daily for three days, followed by prednisone 1mg/kg/day. As prednisone was tapered, he developed a left eyelid ptosis with associated double vision and nystagmus. EMG and nerve conduction studies supported a diagnosis of necrotizing myopathy and detected a neuromuscular junction defect consistent with early myasthenia gravis. The patient's disease stabilized with high-dose glucocorticoid therapy. He was eventually managed with a prednisone taper, mycophenolate mofetil and monthly intravenous immunoglobulin.

Case 2: A 77-year-old man with recurrent stage III melanoma presented to the ER with proximal and truncal muscle weakness, bulbar symptoms with fatigability, chest pain and dyspnea following a single dose of nivolumab. Elevated troponin and echocardiogram findings were supportive of possible myocarditis, later confirmed on cardiac MRI. EMG and nerve conduction studies supported neuromuscular junction dysfunction concerning for myasthenia gravis. After cessation of ICI therapy and five days of IV 1g of solumedrol, as directed by Rheumatology, Neurology, Cardiology and Medical Oncology, there was significant clinical improvement. He was continued on prednisone 1mg/kg with a slow taper, and started on mycophenolate mofetil, with eventual recovery.

Conclusion: Concomitant myositis, myasthenia gravis, and myocarditis is a rare, but serious, triad of immune-related adverse events associated with ICI therapy. Early recognition, expert consultation with a multi-disciplinary team, and aggressive management with cessation of ICI therapy and initiation of immunosuppression are key principles of management, which led to good outcomes in these two case examples.

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Transitioning from Pediatric to Adult Care: How to Address Socio-professional Integration of Young People With Juvenile Idiopathic Arthritis?

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Objectives: The aim of this scoping review was to describe interventions facilitating socio-professional integration within a context of transition from pediatric to adult care for young people with juvenile idiopathic arthritis (JIA).

Methods: Electronic databases Medline, PsychInfo, CINALH and Embase were systematically searched for articles published between January 2000 to December 2019. Articles were retained for review if they described interventions treating or having a potential effect on the socio-professional integration (e.g., work, school, interpersonal relationships and independent living) of young people and adults living with JIA aged between 8 and 40 years. Studies with qualitative, quantitative or mixed method design were included in the review in addition to reports, research protocols and guidelines. The Template for Intervention Description and Replication (TIDieR) was used to extract data from the proposed interventions and their potential effects were classified according to the International Classification of Functioning, Disability and Health (ICF).

Results: One thousand and thirty-four articles were identified through electronic and reference search. After titles and abstracts verification, 41 articles were read in their entirety and 18 articles were included in the scoping review. The 13 interventions found to potentially facilitate socio-professional integration were grouped into 3 distinct types: self-management, transition from pediatric to adult care, and occupational performance and participation. The majority (n = 12) addressed one or more aspects of socio-professional integration in their content but was not the primary target. The effects of the interventions were potentially positive on a variety of body functions and structures, personal and environmental factors and youth's health-related quality of life. On socio-professional integration, school absenteeism, presence in physical education classes, career advice received by adolescents and adolescent's work experience were favorably reported.

Conclusion: Findings demonstrate that socio-professional integration is often not the main intervention goal in transition care in JIA. Our research emphasizes the importance of setting up an intervention adapted to the needs of young people with JIA and their families by involving health professionals with the necessary expertise to favour successful socio-professional integration and involvement as productive members of society.

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Improvements in Transition Readiness in Adolescents With Juvenile Idiopathic Arthritis and Systemic Lupus Erythematosus

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Objectives: The transition from pediatric to adult rheumatology involves a significant change in expectations as patients move from a family-oriented, multidisciplinary pediatric care model to the adult care model, which requires active engagement and independence. This transition in care is associated with poor outcomes, such as increased morbidity, mortality and loss to follow-up. Comprehensive transition programs recognize the variability in transition preparedness among similarly aged individuals and allow for individualized interventions to enhance self-management skills among this vulnerable group of patients. The objective of our study was to assess how goal setting affects changes in transition readiness over time among adolescents with juvenile idiopathic arthritis (JIA) and juvenile systemic lupus erythematosus (jSLE).

Methods: Individuals with JIA and jSLE (age 14-19) were recruited from pediatric transition and young adult rheumatology clinics at a single academic institution. The TRANSITION-Q is a validated, self-administered questionnaire which includes 14 questions assessing healthcare

self-management skills. Respondents answer “never”, “sometimes” or “always” and a weighted total score is determined (maximum 100). Higher scores reflect greater transition readiness. Participants completed the TRANSITION-Q at the time of consent and at each subsequent clinic visit. Upon completion of the TRANSITION-Q, participants and multidisciplinary care members established goals in areas identified as needing improvement based on the participants’ responses. Patient characteristics at baseline and TRANSITION-Q scores at each clinic visit were summarized using descriptive statistics.

Results: Among 38 respondents who had ≥ 2 clinic visits, 13 were male and 25 were female (mean (SD) age 16.4 (1.2) years); $n = 31$ JIA (82%), $n = 7$ SLE (18%). The mean (SD) duration between the baseline and first follow-up visit was 7.1 (4.4) months. Sixteen were seen 3 times (mean (SD) time from first to second follow-up 4.8 (2.7) months) and 3 were seen 4 times (mean (SD) time from second to third follow-up 5.6 (5.1) months). Mean (SD) TRANSITION-Q scores increased throughout the study period: 59.8 (14.9), 66.5 (11.3), 71.9 (9.5), and 78.0 (6.9).

Conclusion: The TRANSITION-Q is a validated tool that was used to track transition readiness and to identify areas for improvement in self-management skills among adolescents preparing for transition from pediatric to adult rheumatology care. TRANSITION-Q scores consistently increased over time suggesting that goal setting may be beneficial in improving self-management skills. This tool can be feasibly implemented into clinical care to track longitudinal changes in transition readiness in adolescents and young adults.

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“Functional Impact Screening in Children With Juvenile Idiopathic Arthritis: Results from the CAPRI JIA Registry”

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Objectives: To explore the use of two functional screening questions as a rapid screening tool to assess functional impact of Juvenile Idiopathic Arthritis (JIA) in routine clinical practice.

Methods: Data was extracted from the CAPRI registry for patients newly diagnosed with JIA between Feb 2017 to Dec 2018. Data included clinic visits up to May 2019 (216 patients, 856 visits). The two questions “does your child usually need help from you or another person because of arthritis” (‘help’) and “is it hard for your child to run and play because of arthritis” (‘hard’) were scored on a 21-point horizontal numerical scale from 0-10. Answers were compared to CHAQ disability index at enrollment, and to patient and parent perceived change from previous visit (much worse, worse, same, better, much better), to examine reliability, responsiveness, and criterion validity. Means, distribution of answers and Spearman correlation coefficients were calculated.

Results: Mean score for ‘hard’ was 2.4, ‘help’ was 1.6, and CHAQ 0.431. Reliability: When parents reported no change, mean score change was -0.16 (95%CI: -0.5, 0.1) for ‘hard’, -0.3 (-0.5, -0.03) for ‘help’. When patients reported no change, mean change was -0.4 (-0.9, 0.04) for ‘hard’, -0.15 (-0.5, 0.2) for ‘help’. Responsiveness: In 134 visits when parents reported much better, mean change was -1.8 (-2.3, -1.4) for ‘hard’, -1.4 (-1.8, -0.9) for ‘help’. In 118 visits when patients reported much better, mean change was -1.4 (-2.0, -0.9) for ‘hard’, -0.9 (-1.3, -0.4) for ‘help’. Conversely, in 5 visits when parents reported much worse, mean change was 3.9 (-2.0, 9.8) for ‘hard’, 3.8 (-1.2, 8.8) for ‘help’. In 9 visits where patients reported much worse, mean change was 1.3 (-0.8, 5.4) for ‘hard’, 2.5 (-0.01, 5.0) for ‘help’. Criterion validity: Spearman correlation with CHAQ at enrollment was 0.65 for

‘hard’; 0.64 for ‘help’. Correlations were higher for female patients for both questions (0.67 vs 0.55, 0.66 vs 0.62, respectively), and for children ≤ 8 y in the ‘help’ question (0.73 vs 0.57). Ceiling effect: At enrollment, CHAQ scores were 0 in 35% of visits, 31% for ‘hard’, 46% for ‘help’.

Conclusion: These two functional screening questions demonstrate good reliability and reasonable responsiveness to change in functional status in JIA. They show moderate correlation with CHAQ, and the ceiling effect was less prominent for the ‘hard to run/play’ question. They may be combined as a brief functional screen that could be easily applied at each clinic visit.

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The Rheum4U Precision Health Registry Platform: Enabling Quality Care for Patients With Inflammatory Arthritis During the COVID-19 Pandemic in Two Outpatient Rheumatology Clinics

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Objectives: Rheum4U Precision Health Registry Platform (Rheum4U) is a web-based, outpatient rheumatology data platform that enables prospective longitudinal data collection and integration for patients with inflammatory arthritis at two high-volume Calgary rheumatology clinics. The COVID-19 pandemic has highlighted the importance of providing safe and effective care for vulnerable rheumatology patients through remote consults.

Methods: Rheum4U is a prospective cohort of 1120 participants captured since August 2016, in which participants report patient-reported outcome measures (PROMs), measures of disease activity, and medication use. Healthcare providers capture assessment data and changes to medications, while disease activity scores (CDAI, DAS28CRP) are automatically calculated. We compare the use of Rheum4U, patient-reported outcomes measures, and disease activity scores before and after the COVID-19 pandemic.

Results: Between March and September 2020 (during the pandemic), 755 visits by 592 unique patients were captured in Rheum4U, a 5% ($n = 793$) decrease in visits and an 8% ($n = 645$) decrease in unique patients compared to the same time last year (pre-pandemic). Baseline visits during the pandemic decreased by 61% ($n = 61$) compared to the pre-pandemic period ($n = 157$). Patients rated their overall health using EQ5D-5L (during pandemic: $n = 404$; pre-pandemic: $n = 524$). No change was observed in the visual analogue scale rating between the two periods (pre-pandemic: mean = 73%, SD = 20.7; during pandemic: mean = 72%, SD = 21.4). A CDAI score was available in 91% ($n = 685$) of visits, constituting a decrease of 7% compared to the pre-pandemic period ($n = 778$). During the pandemic, 63% ($n = 434$) of visits were in remission (CDAI ≤ 2.8); 34% ($n = 234$) had low/moderate activity (CDAI > 2.8 to ≤ 22); and 2% ($n = 17$) had high activity (> 22). Pre-pandemic, 42% ($n = 327$) of visits were in remission; 52% ($n = 403$) had low/moderate activity; and 6% ($n = 48$) had high activity. The percent of visits with an available DAS28CRP score during the pandemic was 30% ($n = 226$), a 42% decrease compared to pre-pandemic period ($n = 573$). There was no change in DAS28CRP scores during the pandemic and pre-pandemic (cases in remission (DAS28CRP < 2.6): during pandemic 69% ($n = 155$), pre-pandemic 69% ($n = 394$); low/moderate activity (DAS28CRP ≥ 2.6 to ≤ 5.1): during pandemic 30% ($n = 68$), pre-pandemic 29% ($n = 165$); high activity (DAS28CRP > 5.1): during pandemic 1% ($n = 3$), pre-pandemic 2% ($n = 14$)).

Conclusion: Outpatient rheumatology care was significantly impacted by the COVID-19 pandemic, limiting in-person clinic appointments to urgent cases and making new paths of data capture for co-production of care critically important. Rheum4U is an innovative platform that supports the collection of PROMs and facilitates effective monitoring of disease for both in-person and virtual consults.

Pediatric Patients With a Dual Diagnosis of Inflammatory Bowel Disease and Chronic Recurrent Multifocal Osteomyelitis: A Single-Centre Case Series

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Objectives: Review of the literature reveals scant case reports describing the prevalence of chronic recurrent multifocal osteomyelitis (CRMO) amongst patients with a diagnosis of inflammatory bowel disease (IBD), with approximately 20 pediatric patients reported. Within our pediatric centre, several patients in recent years were noted to have this overlap. The objective of our case series was to identify and describe the characteristics and courses of pediatric patients with a diagnosis of both CRMO and IBD.

Methods: McMaster Children's Hospital patient database was used to identify patients under 18 years old with a diagnosis of IBD or CRMO from January 1st, 2010 to June 30th, 2020. The lists were compared to identify patients with a dual diagnosis of IBD and CRMO. A retrospective chart review was performed for timelines of diagnosis, patient characteristics, and treatment courses. A descriptive analysis of the data was performed.

Results: Of the 600 patients with IBD and 47 with CRMO, 7 patients (2 male, 5 female) were found to have a dual diagnosis of CRMO and IBD. Contrary to previous reports, most patients (6/7) had a diagnosis of IBD first, and subsequently were diagnosed with CRMO. One patient had a diagnosis of CRMO, and upon screening investigations, had an elevated fecal calprotectin and later received a diagnosis of IBD. Of those with IBD who developed CRMO, all presented with bony pain and had findings in keeping with CRMO on initial diagnostic MRI. Bony lesions were localized to the femoral metaphysis (3/7; 2 proximal, 1 distal), proximal tibia (2/7), clavicle (2/7) and mandible (1/7). At the time of CRMO diagnosis, their IBD treatment regimens included sulfasalazine (1/6), infliximab (3/6), adalimumab (1/6) or nothing (1/6). Initial management for their CRMO was methotrexate (2/6), naproxen (2/6), celecoxib (1/6) or nothing (1/6).

Conclusion: We identified 1% of pediatric patients with IBD at our centre also had CRMO. Although the etiology of the link remains unknown, most patients had an initial diagnosis of IBD and were later diagnosed with CRMO. There does not seem to be an association to a specific type (Crohn's, Ulcerative Colitis or IBD undefined), age, or treatment of IBD. In patients with IBD who have prolonged episodes of bony pain it may be important to consider MRI imaging. If patients with a diagnosis of CRMO develop chronic abdominal pain, diarrhea, or bloody stools not otherwise explained, gastroenterology consultation and further workup for IBD should be considered.

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Transgender Patients in The Rheumatology Setting

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Objectives: Minimal medical research exists regarding transgender patients, particularly within the field of rheumatology. A few case reports note that male to female transitions with exogenous estrogen may precede presentation of autoimmune disease. There are currently no published data reporting transgender demographics and disease presentation in the rheumatologic setting.

Methods: We conducted a retrospective chart review of transgender patients who presented to our academic and community clinics, and inpatient rheumatology service. We collected information on patients' medical history and rheumatologic diagnoses, transition status, presenting symptoms and treatment regimens.

Results: From 25 rheumatologists contacted, 12 transgender patients were identified. Patients' ages ranged from 22-66 years old and had the

following diagnoses: PsA, seronegative SpA, PM with SSc overlap, SSc, PMR, FM, leucocytoclastic vasculitis, periodic fever syndrome and osteopenia. Nine (75%) patients were transgender males, 8 of whom were treated with intramuscular testosterone and 2 had hysterectomies with bilateral salpingoopherectomies. Only 3/9 transgender male patients had a documented start time of testosterone therapy. Seven patients had either been on testosterone at diagnosis or were on it for at least 1 year before being diagnosed with their rheumatologic conditions. Of 3 transgender females, 2 were exposed to estrogen therapy prior to presentation. One patient had a one-time exposure to exogenous estrogen and significant silica exposure for > 20 years as her major risk factor for developing SSc. Five (42%) patients had uncontrolled disease or relapse of their disease requiring adjustment of their treatment regimens. The most common co-morbidities were depression and anxiety (n = 7, 58% patients). A family history of autoimmune disease was documented in 5 (42%) patients.

Conclusion: The majority of our patients were transgender males which corroborates prior research indicating most rheumatologic diseases have a higher prevalence for biologic females. However, of the diseases with female prevalence in our study (PM, PMR, SSc, osteopenia and FM), almost half the patients diagnosed were biologically male (3/7). Larger studies are needed to assess whether hormone transitions, either via gonadectomy and/or with exogenous hormones, can affect the incidence of these diseases in transgender patients. In addition, we recommend rheumatologists carefully document when medical transitions occur relative to their rheumatologic diagnosis in order to better understand the impact of the transition on new diagnoses, or changes in disease state. Additionally, given the high prevalence of depression and anxiety, we recommend assessing the mental health of transgender patients at each follow-up and direct them to supports as needed.

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Safety of Low Dose Methotrexate (MTX) and Tuberculosis (TB)

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Objectives: Increased awareness of the importance of MTX in rheumatic disease is leading to more MTX use in patients from TB-endemic areas. Current management guidelines for rheumatic disease address TB in the context of biologics but not MTX use. We aimed to systematically review the published literature on TB rates with MTX < 30 mg per week.

Methods: We searched CINAHL, Embase, Global, MEDLINE and World of Science databases (Jan 1990 to May 2018) for terms including 'methotrexate' and 'tuberculosis'. Titles, abstracts or full manuscripts of 4707 identified reports were screened independently by 2 reviewers for studies reporting TB in patients taking MTX. Study quality was assessed using the McGill Mixed Methods Appraisal Tool (MMAT). Data was extracted on TB incidence (new TB diagnosis vs reactivation of latent TB), and outcomes (pulmonary, dissemination, death) and safety of isoniazid (INH). Descriptive summaries are presented on studies providing outcomes in patients taking MTX < 30 mg per week.

Results: Thirty-one of 4707 identified studies met inclusion criteria and provided sufficient information (8 cohort, 7 case-control, 1 clinical trial, 15 case reports/case series). Only 27% of articles reported data from low to moderate human development index countries. Studies were of moderate quality. Seven case control studies were heterogeneous, but most demonstrated a modest increased risk of TB with MTX. Five cohort studies reported TB incidence rates in rheumatic disease (treated with MTX ± biologics) ranging from 102-367.9/100,000 patient-years. These rates were generally higher than comparator general population rates. Two cohort studies of MTX in RA (without biologic) reported cumulative TB

incidence in Moldova (12 TB cases in 44 RA patients, 27%) and in China (9/114, 7.9%). Other cohort studies generated rates of overt infection (143/100,000 patient years in Spain, higher if co-prescribed with corticosteroids and other immunosuppressants in South Africa), and latent TB rates detection (16/922 RA screened, 1.7%, in Canada). When reported, rates of extra-pulmonary TB were higher than comparator general population rates. One clinical trial (China), 2 cohorts (Japan, USA) and 2 case series (Belgium, USA) evaluated safety of INH and MTX. Isoniazid-related hepatotoxicity and neutropenia were generally more common when taken with MTX but were usually reversible.

Conclusion: Despite a paucity of high-quality data, this review confirms that TB screening and clinical surveillance are needed in patients from TB-endemic areas who are prescribed MTX, particularly with co-administration of corticosteroids or other immunosuppressants. Isoniazid, if monitored, appears safe.

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Instruments to Assess Patient Complexity in Rheumatology: A Scoping Review

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Objectives: Patient complexity refers to the cumulative and interacting impact of clinical, psychosocial and environmental factors. Factors impacting complexity may include medical and psychiatric conditions, health literacy, and socioeconomic factors. Patients with rheumatic diseases often have multiple comorbidities. High rates of mood disorders are also associated with many rheumatic conditions. Furthermore, persons with rheumatic diseases may experience impacts of their disease on their daily function and employment leading to high psychosocial complexity. The objective of the study was to conduct a scoping review of complexity measures/tools used in rheumatology that could be used to help in planning and coordinating care.

Methods: A protocol was developed, and preliminary searches informed a search of MEDLINE, EMBASE, and CINAHL from database inception to December 14, 2019. References lists were hand searched and authors of existing complexity tools were contacted. English articles describing the development or use of complexity measures/tools in patients with adult rheumatologic diagnoses were included regardless of study design. Included articles were evaluated for risk of bias where applicable.

Results: The search yielded 407 articles, 37 underwent full text review and 2 were identified during a hand search with 9 included articles. Only 2 complexity tools used in populations of adult patients with rheumatic disease were identified: the SLENQ and the INTERMED. The SLENQ is a 97-item patient needs questionnaire developed for patients with systemic lupus (n = 1 study describing tool development) and applied in 5 cross-sectional studies. Factors associated with high patient needs were identified including frequent flares, lower education levels, and unemployment/disability. Three studies (a practice article, randomized clinical trial (RCT) and a cross-sectional study) applied the INTERMED, a clinical interview to ascertain complexity and support coordinated care, in patients with rheumatologic diagnoses. In rheumatoid arthritis (RA) populations higher INTERMED scores have been associated with higher healthcare utilization not otherwise explained by RA disease activity.

Conclusion: Many patients with rheumatic diseases have high complexity as measured by validated tools. Previous reports demonstrate that coordinated care improves patient health outcomes. While complexity tools/measures have been used to assist in coordinating care to improve outcomes in other healthcare conditions, there is limited information on the use of existing patient complexity measures/tools in patients with rheumatic diseases and further study is warranted. Such tools could be applied to coordinate and direct multidisciplinary care and improve patient experience and outcomes.

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Patient Preferences for Hydroxychloroquine in Systemic Lupus (SLE): Preliminary Analyses

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Objectives: Hydroxychloroquine (HCQ) is used in the majority of SLE patients. Although HCQ has been shown to reduce serious flares, concerns exist regarding side effects from long-term use. Not much is known about patient preferences regarding decisions to continue, lower, or stop the drug over the course of SLE. It is important for treating physicians to understand patient preferences and what factors shape patients' decisions. To address these knowledge gaps, we evaluated patient preferences for HCQ therapy and qualitatively assessed themes underlying these preferences.

Methods: Telephone interviews were conducted with SLE patients from the Montreal Lupus Clinic Registry. Patients were recruited consecutively during clinical assessments. The interviews were conducted in English (N = 17) and French (N = 7) using a standardized script. The interview recordings were transcribed, and French transcripts were translated to English. Two reviewers conducted a thematic analysis by individually generating codebooks, and then synthesized their findings and reconciled discrepancies.

Results: A thematic analysis of 24 interviews was conducted. The majority (N = 21, 88%) of subjects were female and the average age was 56.1(12.9) years. Most subjects (N = 19, 79%) were Caucasian, with the remainder being Black (N = 2, 8%), Asian (N = 1, 4%) or other (N = 2, 8%). Three themes were identified. Theme one focused on the parties involved in decision-making regarding HCQ: the patient, the physician, and other health professionals including pharmacists. For many interviewees (17/24), the doctor's opinion was the primary factor affecting patient decisions. Theme two focused on actions across time; one-third (8/24) had reduced HCQ at some point in time, a similar number (7/24) had stopped HCQ for a period, and a minority (3/24) considered lowering HCQ but never did. Theme three focused on how patient preferences and decisions were linked to overall health (i.e., management of multiple drugs, comorbidities), HCQ-related factors (side effects experienced by 5/24, while the majority experienced positive effects) and SLE-related factors (manageability of symptom, fear of jeopardizing stable SLE).

Conclusion: We present preliminary evidence of patient preferences and themes related to patient choices regarding HCQ. While common themes were identified, a large range of factors may affect patient decisions. The final results of our study will inform discrete choice experiments to help further develop personalized approaches to HCQ SLE treatment.

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Cannabis and Cannabinoid Use in Patients With Systemic Lupus Erythematosus

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Objectives: The role of cannabis and cannabinoids in systemic lupus (SLE) is unknown. We performed a literature review regarding use and effects of cannabis and cannabinoids in SLE, as well as a scan of registered clinical trials.

Methods: We searched six databases (CINAHL, Cochrane, EMBASE, MEDLINE, Scopus, Web of Science), without calendar-year or language limits, using the keywords cannabi*/marijuana and rheumat*/lupus/SLE, and all corresponding subject headings. We included human (all ages) and non-human studies, of all study designs. References from included papers were also scanned, as well as ClinicalTrials.gov.

Results: Searching the six databases produced 5799 records. Titles and

abstracts were reviewed and of these, 98 papers were judged potentially relevant for full text review. Of the 98, most were excluded after full text review because they did not focus on SLE (e.g. heterogeneous rheumatic disease cohorts) leaving ten (five clinical and five non-clinical) studies for our review. The clinical studies included three case reports, one cohort, and one cross-sectional study. The non-clinical studies included three in-vitro and two murine SLE model studies. The cohort study (N = 276) reported cannabis use among 30.4% of SLE patients; users were more likely to report younger age, unemployment or disability, tobacco use, opioid use, non-adherence to medical therapy, and neuropsychiatric SLE. A significant increase in end-stage renal disease over a 5-year period was noted in cannabis users. The cross-sectional study reported that 7.8% of SLE patients used cannabis. Neither study detailed reasons for use nor measures of efficacy. Three case reports described adverse events in SLE cannabis users: neuroretinal dysfunction; giant bullous emphysema; and rapid deterioration of neuropsychiatric SLE. In the three in-vitro assays, cannabinoids were found to selectively reduce CD8+ T-cell responses as well as IL-6 levels, but cannabidiol (CBD) was found to increase Th17 cell differentiation in CD4+ T-cells derived from SLE patients. In one SLE murine model study, topical endocannabinoid administration prevented cutaneous lesions. In another, CBD accelerated the progression of glomerular disease. The ClinicalTrials.gov search found one ongoing trial of JBT-101, a synthetic endocannabinoid receptor type-2 agonist in SLE; results are not currently published.

Conclusion: There exist few studies of cannabis and cannabinoid use in SLE. The proportion of SLE patients who regularly use cannabis may be significant. The cases reporting potential harm warrant further study.

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Hearing Loss in SLE Patients Taking Hydroxychloroquine: A Literature Review of Reported Cases

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Objectives: Hydroxychloroquine (HCQ) is an antimalarial commonly used in the treatment of systemic lupus erythematosus (SLE). Rheumatology concerns about potential complications of HCQ have mostly focused on retinal and cardiac effects. However, reports of hearing loss in survivors of COVID-19 treated with HCQ have raised questions about ototoxicity, since antimalarials can potentially harm cochlear and vestibular hair cells. We performed a review of case reports of hearing loss in SLE patients taking HCQ.

Methods: A literature search was performed on PubMed and Embase from their inception to September 2020 using the strategy “(SLE OR lupus) AND hydroxychloroquine AND (ototoxicity OR hearing loss) AND (case report OR case series)”. There was no language limitation. Publications were included if they described cases of hearing loss in SLE patients receiving HCQ. We also searched references of identified case reports and series. We extracted information on the age, sex, HCQ dose and duration, and pattern of hearing loss for these cases.

Results: The literature search generated 25 publications exclusively in English and French language, of which 7 were duplicates. We excluded 12 articles: 4 were unrelated to SLE, 6 unrelated to HCQ treatment, and 2 unrelated to hearing loss. We identified 3 case reports and 1 case series published between 1998 and 2018 that described 12 SLE patients who developed hearing loss during HCQ treatment. Of these, 8 were female. The mean age at hearing loss was 38.5 years old, ranging from 11 to 69 years old. HCQ doses at time of hearing loss ranged from 100mg to 600mg daily. Duration of HCQ treatment was mostly between 1 week and 5 years (mean 2.4 years), with one case occurring 18 years after starting treatment. Hearing loss was unilateral in 4 patients and bilateral in the remainder. Seven patients did not recover following discontinuation of HCQ. One case reported a positive re-challenge with HCQ 16 years following the first HCQ discontinuation due to hearing loss.

Conclusion: We reviewed twelve reports of hearing loss in SLE patients taking HCQ, mostly occurring within 5 years of HCQ treatment. These case reports ascribed HCQ as a putative cause of the hearing loss, although at least one small study suggested that SLE patients on and off HCQ had similar auditory performance (Roverano, 2006). Since hearing loss may also occur in SLE patients unexposed to HCQ (Polanski, 2020), further studies of HCQ and hearing loss in SLE would be helpful.

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Gordonia Species Central Line-associated Bloodstream Infection in a Patient With Connective Tissue Disease-associated Pulmonary Arterial Hypertension

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Background: The genus *Gordonia* is a group of soil- and rubber-degrading, gram-positive, nocardioform actinomycetes related to the genera *Rhodococcus*, *Mycobacterium*, and *Nocardia*. *Gordonia* spp. are occasional opportunistic human pathogens. Herein we describe a case of *Gordonia* central line-associated bloodstream infection in a patient with connective tissue disease-associated pulmonary hypertension.

Case: A 35-year-old woman with systemic lupus erythematosus and systemic sclerosis overlap syndrome, pulmonary arterial hypertension on intravenous vasodilator therapy, antiphospholipid syndrome, and immune thrombocytopenia presented to hospital with a one-day history of fever, subacute fatigue, and generalized weakness. She had discontinued hydroxychloroquine six months prior. On examination, she was febrile, tachycardic, and tachypneic, with peripheral volume overload. She was pancytopenic, with elevated dsDNA and hypocomplementemia. High resolution computed tomography demonstrated scattered solid pulmonary nodules with ground-glass halos suspicious for atypical infection versus septic emboli. The spleen measured 19 cm on ultrasound. Transthoracic echocardiography suggested worsening of pulmonary hypertension, but no vegetation was seen. Bone marrow biopsy was not suggestive of a lymphoproliferative disorder. Rheumatology was consulted as to whether her presentation was consistent with a connective tissue disease flare. Cultures from the Hickman line subsequently grew gram-positive bacilli initially reported as a contaminant but ultimately confirmed by the provincial reference laboratory to be a *Gordonia* sp. The catheter was exchanged, and she completed six weeks of antibiotics. Hydroxychloroquine was restarted. Follow-up imaging demonstrated resolution of the pulmonary nodules, reduction in the splenic size, and echocardiographic parameters returned to baseline. The pancytopenia improved. Ultimately, her presentation was attributed to *Gordonia* line sepsis leading to decompensated pulmonary hypertension and congestive hypersplenism with stable background connective tissue disease.

Conclusion: Since 1992, 33 cases of *Gordonia* spp. bacteremia have been reported in the literature, including 28 cases of central line-associated bloodstream infection. Most arose in patients with underlying hematologic malignancy. To our knowledge, this case is one of only two reported in a patient with connective tissue disease.

Infections due to *Gordonia* spp. are likely underrecognized, as they are difficult to identify using conventional microbiologic techniques and may be mistaken for *Corynebacteria*, *Nocardia*, or *Rhodococcus* spp., or contaminants. Some *Gordonia* spp. form biofilms, which may explain their association with indwelling catheter infections warranting prolonged antibiotic treatment or catheter removal. It is therefore important to be aware of this emerging pathogen as patients immunosuppressed in the context of systemic rheumatic disease, and those with connective-tissue disease-associated pulmonary arterial hypertension may be at increased risk.

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A Rare Case of Disseminated Histoplasmosis-related Aortitis in an Immunocompetent Middle-Aged Male: Thinking Beyond Giant Cell Arteritis
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Objective: In Canada, the fungus *Histoplasma capsulatum* is endemic to regions bordering the St-Lawrence River and the Great Lakes. Histoplasmosis may result in a range of clinical manifestations, some of which mimic systemic autoimmune disease. There are limited reports of histoplasmosis causing aortitis, and none involving an immunocompetent host. We report the case of an immunocompetent male with disseminated histoplasmosis-related aortitis.

Methods: Case report and review of literature.

Results: A 53-year-old male with coronary artery disease, hypertension, and atrial fibrillation presented to hospital with a several-month history of progressive shortness of breath, non-productive cough and intermittent fevers. Notably, he had been exposed to bat guano in his attic several months prior. CT chest with contrast demonstrated a 2-cm right lower lobe mass with associated hilar and mediastinal adenopathy. Diffuse thickening of the aorta, particularly surrounding the origin of the right common carotid artery was appreciated. A subsequent PET-FDG scan demonstrated uptake in the aortic root and ascending aorta. Lung cancer was suspected and a transbronchial needle biopsy of the right hilar node was performed. It demonstrated necrotic tissue without evidence of malignancy. Fungal, mycobacterial and bacterial cultures were negative. He was discharged with outpatient follow-up. He re-presented to hospital 6-weeks later with worsening dyspnea and constitutional symptoms. CT chest without contrast demonstrated persistence of the aortic thickening and enlargement of the lymphadenopathy. He had a marked leukocytosis and a significantly elevated CRP. An extensive infectious workup was negative including histoplasma serologies. A systemic autoimmune disease-causing large vessel vasculitis was suspected; however, autoantibody testing was negative as were bilateral temporal artery biopsies, and serum IgG4 levels were within normal limits. Despite empiric broad spectrum antibiotics and supportive care, he continued to decline with increasing oxygen requirements. A large pericardial effusion causing cardiac tamponade necessitating urgent pericardiocentesis was identified. He subsequently underwent left lower lobe wedge resection of the lung and pericardial window. Histopathology from the lung tissue demonstrated necrotizing granulomas with fungal organisms compatible with histoplasma species. Gradual clinical and radiologic improvement was noted after four-weeks of anti-fungal therapy including resolution of the aortitis.

Conclusion: Histoplasmosis is a rare cause of aortitis in the immunocompetent host and may not be identified by fungal serology. In endemic regions, a high index of suspicion must be maintained in atypical presentations of inflammatory disorders to avoid the harmful initiation of immunosuppressing medications.

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Sex Differences in Inflammatory Myopathies: A Cross Sectional Study

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Objectives: Autoimmune inflammatory myopathies (AIM) are rare and heterogeneous systemic diseases. Little is known about sex differences in AIM and how they influence clinical presentation and patient-reported outcomes (PROs). Our objective was to compare sex differences in AIM in a multi-center cohort of patients using a contemporary clinico-serological sub setting approach.

Methods: Patients from the Canadian Inflammatory Myopathy Study (CIMS) are incident cases of AIM aged 18 years or older. At baseline, patients were subsetting as dermatomyositis (DM), overlap myositis (OM), immune mediated necrotizing myopathy (IMNM), polymyositis (PM) or inclusion body myositis (IBM) using the classification system proposed by Mariampillai et al. (JAMA Neurol 2018). Disease severity at onset was

rated by the recruiting physician as mild, moderate or severe, function was measured by the Health Assessment Questionnaire (HAQ), and physical health-related quality of life (HRQoL) was measured by the Medical Outcomes Study Short Form 36 (SF-36) physical component summary score (PCS). We compared disease severity and PROs at baseline between women and men for the whole cohort and stratified by AIM subsets.

Results: This study included 178 patients (122 women and 56 men). The mean age of the cohort was 56.1 ± 14.2 years, with no sex differences. Time between onset of symptoms and diagnosis tended to be longer in men than women (2.4 ± 3.4 vs. 1.1 ± 1.6 years, $P = 0.13$). Although severe disease was more common in women compared to men (21.2 % vs. 14%), this did not reach statistical significance. Women had more functional impairment than men (HAQ 1.2 ± 0.9 vs. 0.8 ± 0.9 , $P = 0.04$). Impairment in physical HRQoL was also greater in women compared to men (PCS score 33.5 ± 11.2 vs. 38.2 ± 12.2 , $P = 0.04$). When stratifying subjects by disease subsets, more women than men had DM (46/59, 78%), OM (60/89, 67%) and IMNM (5/5, 100%), but not PM&IBM (10/20, 50%). Also, OM was the only subset in which women had more functional (HAQ 1.3 ± 0.7 vs. 0.5 ± 0.6 , $P < 0.001$) and physical HRQoL (PCS 31.1 ± 9.7 vs. 42.5 ± 10.5 , $P < 0.001$) impairment compared to men.

Conclusion: In this AIM cohort, more women had severe disease than men, and women had significantly more functional and HRQoL impairment than men. These differences were most marked in the OM subset. These novel findings are useful for hypothesis-generation. They suggest biologic differences in the disease and in the health care trajectories of women and men with early AIM. Further research will be required to test these hypotheses.

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Identification of Biomarkers for Psoriatic Arthritis Through Proteomic Analysis of Synovial Fluid

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Objectives: Arthritis has an immense and growing burden on society due to their negative impact on work productivity, quality of life and mortality. Common forms of arthritis include osteoarthritis (OA), rheumatoid arthritis (RA) and psoriatic arthritis (PsA). Currently, diagnostic biomarkers for PsA are lacking. With the hypothesis that there are differences in the expression of proteins in the synovial fluid (SF) of patients with OA, RA and PsA, we aimed to identify markers for PsA by proteomic analysis of SF obtained from knee joints. Our objectives were to identify proteins and pathways differentially expressed between 1. the inflammatory arthritides, PsA and RA, and OA. 2. PsA and OA, and PsA and RA.

Methods: Mass spectrometry was used to identify the SF proteome obtained from 10 OA, 10 PsA, and 10 RA patients. Next, we used student's t-test for differential expression analysis (p -value < 0.05 ; fold change > 1.5) to identify potential protein biomarkers of PsA. Finally, we performed pathway enrichment analysis to obtain biological insights on differentially expressed proteins.

Results: Aim 1: We observed 4 proteins present and 45 proteins missing only in OA compared with PsA and RA. As for proteins that were present in all conditions, we observed 56 and 66 differentially expressed proteins in OA compared to PsA and RA, respectively, including DEFA3 and VIM. Enriched pathways were involved in inflammation, cell damage, and the immune response including NF- κ B, Toll-Like Receptors, and IL-1. Aim 2: There were no proteins present only in PsA or RA, suggesting similarity in SF composition between these two conditions. This was further supported by the comparison of protein expression levels which revealed only 22 differentially expressed proteins in PsA versus RA. Although we observed statistically significant differences in the SF composition between the inflammatory arthritides, these changes were more subtle than the

differences detected from OA seen in Aim 1. We found only 4 differentially expressed proteins in common between our comparison of PsA with OA and RA, including IGLV7-46. Interestingly, despite detection of immune system pathways in PsA versus RA, at the top of the enriched pathways list were pathways associated with cell metabolism including glycolysis which has been previously detected to be differentially expressed between PsA and RA.

Conclusion: We have identified differential proteins and pathways between PsA, OA, and RA. The SF profiles of PsA and RA are similar but distinct from that seen in OA.

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Treatment of Osteoporosis Related to Adult Hypophosphatasia

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Background: Hypophosphatasia (HPP) is a rare, inherited disorder characterized by a deficiency of serum and bone alkaline phosphatase (ALP), leading to defective bone and teeth mineralization. With more than 400 ALPA gene mutations, clinical presentations range from a perinatal lethal form to a mild late adult-onset form. Patients with adult-onset HPP often present with osteoporosis, but there is limited evidence supporting specific drug therapies. It is not clear if bisphosphonates are effective for HPP-related osteoporosis, and there are concerns of a greater than expected risk of atypical femoral fractures in this population.

Case: A 63-year-old Caucasian woman with osteoporosis presented with an atypical femoral fracture, believed to be related to long-term alendronate therapy. Her history was significant for genu varum, multiple caries, bimalleolar fracture, multiple broken toes, stress fractures and nephrolithiasis. Alendronate was stopped and three years later, she tripped and fractured her left distal radius, ulna and pelvis. A workup for secondary osteoporosis led to a diagnosis of hypophosphatasia (ALP 25). She was treated with teriparatide for two years, leading to an increase in her femoral neck bone mineral density from a T-score of -3.1 to -2.5. One month following discontinuation of teriparatide, she suffered another fragility fracture of her left proximal humerus, and she was started on denosumab for long-term osteoporosis management. Currently she has been taking denosumab for 1 year with no new fractures. We are currently exploring funding options to obtain asfotase alfa, a human recombinant TNSALP for the treatment of HPP.

Conclusion: In patients with HPP-related osteoporosis, case reports have described increased bone formation and decreased bone pain with anabolic treatment modalities (teriparatide or romosozumab). As in our patient, these therapies are only approved in Canada for 1-2 years, after which, an alternative therapy must be started to prevent loss of new bone formation. In this case, after treatment with teriparatide, the patient was treated with denosumab after weighing the risk of another atypical fracture with the benefit of preventing future fragility fractures. We are unaware of case reports that could help guide prescribing decisions in HPP patients following anabolic treatment modalities.

There is little evidence to guide the choice of long-term osteoporosis therapy following a course of anabolic treatment in patients with HPP-related osteoporosis. In our case, we have used denosumab following a course of teriparatide. Ongoing research and monitoring are required to assess long-term safety and efficacy.

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Genetics of Age at Diagnosis in Systemic Lupus Erythematosus

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Objectives: Genome wide association studies (GWAS) have identified > 90 SNPs associated with systemic lupus erythematosus (SLE) risk. There may be additional loci impacting the age of diagnosis. The purpose of this study is to identify genetic variants for age of SLE diagnosis.

Methods: Our cohort included patients with childhood-onset SLE (cSLE) diagnosed < 18 years of age, and adult-onset SLE (aSLE), who met ACR and/or SLICC classification criteria for SLE. Patients were followed at tertiary care centers. We censored patients with age at diagnosis ≥ 70 y. Patients were genotyped on the Illumina Multiethnic Array (MEGA), ungenotyped SNPs were imputed using the Haplotype Reference Consortium (HRC) reference. We restricted to SNPs with a minor allele frequency (MAF) ≥ 0.01 and imputation quality ≥ 0.8 . Ancestry was genetically inferred from principal components (PCs) and ADMIXTURE calculated in reference to 1000 Genome Project (1KGP). Non-HLA, additive SLE weighted genetic risk scores (GRSs) were computed using published SLE GWAS log-odds ratio weights. Single-variant genome-wide linear regression of age of SLE diagnosis was performed with GENESIS. Multivariate models were adjusted for sex, aSLE/cSLE status, indicator for center, 5 PCs and SLE non-HLA GRS. We also completed a genome-wide test of cSLE risk (vs. aSLE) using a logistic regression model adjusted for the same covariates.

Results: Our cohort included 1093 patients, 88% female. 36% were of European ancestry, 23% East Asian and 18% Admixed. The median age at diagnosis was 17.1y (IQR 13.6, 30.8). We included 8.9M SNPs in GWAS. The most significant SNP associated with age at SLE diagnosis in the linear model was on chr11, rs138239231 (Beta 10.0y, SE 1.85y, $P = 5.73 \times 10^{-8}$, MAF 0.01) upstream of DHCR7 and NADSYN1. The second locus on chr14 (rs144180822: Beta 5.7y, SE 1.15y, $P = 7.15 \times 10^{-7}$, MAF 0.03) is intronic to NUBPL. In the logistic model, the most significant SNPs were on chr1, rs12024309 upstream to SMG7-AS1 (OR 0.5, [95% CI: 0.4, 0.7], $P = 1.16 \times 10^{-6}$, MAF 0.39); chr4, rs10001705 upstream to HS3ST1 (OR 3, [95% CI: 1.9, 4.6], $P = 1.31 \times 10^{-6}$, MAF 0.11); on chr17, rs116981214, intronic to MRPL45P2 (OR 4.7, [95% CI: 2.5, 8.7], $P = 1.46 \times 10^{-6}$, MAF 0.05). None of these loci reached genome-wide significance ($P < 5 \times 10^{-8}$).

Conclusion: In our multiethnic cSLE and aSLE cohort, GWAS did not identify a genome-wide significant SNP association with the age at diagnosis or cSLE risk. We identified 2 loci near genome-wide significance for age at SLE diagnosis, and 3 near genome-wide significance for cSLE risk. We plan to expand our analyses including more patients. Best Abstract on SLE Research By A Trainee - Ian Watson Award.

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TEN out of ten, a Dermatologic Emergency With Sulfasalazine Treatment for Enthesitis Related Arthritis.

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Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life-threatening mucocutaneous reactions with high mortality and morbidity. This case report describes a patient with SJS/TEN reaction to sulfasalazine and the subsequent management.

Case: A 12-year-old female with enthesitis related arthritis subtype of juvenile idiopathic arthritis was started on sulfasalazine and restarted on meloxicam for the management of active enthesitis and mildly symptomatic bilateral sacroiliitis. Ten days after starting sulfasalazine, she presented to the emergency department with facial flushing, generalized morbilliform rash, and mild conjunctival redness. Within 12 hours, she developed fevers, severe oral and genitourinary mucositis, rapidly evolving generalized blistering of the face and body, and positive Nikolsky's sign. Due to suspicion of evolving SJS/TEN, sulfasalazine and meloxicam were discontinued. She was admitted with a presumptive diagnosis of TEN (> 30% body surface area involvement) and multidisciplinary consultations by Dermatology, Rheumatology, General Pediatrics, Plastic Surgery, Ophthalmology, and Gynecology. Histopathology of skin rash was consistent with TEN showing pauci-immune vacuolar interface dermatitis with extensive keratinocyte necrosis and secondary dermal epidermal separation. Immunosuppressive therapy was started immediately with etanercept and a 2-week course of cyclosporine. Supportive care consisted of hydromorphone patient-controlled analgesia, wound care, ocular lubricating ointment, vaginal and vulvar topical steroids and Premarin, urinary catheterization, and nasogastric tube for medications, nutritional and fluid support. Over her 2-week admission, there was gradual mucocutaneous healing, reduced pain, and advancement to oral feeds. She was discharged home after significant clinical improvement and continues to have close follow-up for monitoring for potential long-term complications such as scarring and strictures.

Conclusion: Although rare, prompt recognition and management of SJS/TEN is critical to improve outcomes and prevent complications. Suspected causative medications must be identified and discontinued immediately. Common medications associated with SJS/TEN include sulfonamides such as sulfasalazine, specific COX-2 inhibitors, anti-epileptics, and allopurinol. Although theoretically possible, association of SJS/TEN with oxim class medications have not been established. Current evidence supports the use of anti-TNF inhibitors and cyclosporine, both of which were given in this case with favourable response. Counselling for sulfasalazine, a commonly used disease modifying antirheumatic drug, should include SJS/TEN with an emphasis on prompt seeking of medical assessment to facilitate early recognition and treatment. Due to the risk of recurrence, the causative medication and structurally similar medications should be avoided.

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Scleroderma Renal Crisis Presenting in Pediatric Mixed Connective Tissue Disease

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Background: Mixed connective tissue disease (MCTD) is rare in pediatrics with a reported frequency of 0.1-0.5%. Of adult patients diagnosed with MCTD, scleroderma renal crisis (SRC) is a potential but rare complication associated with serious morbidity and mortality. Herein, we report a case of SRC presenting in a pediatric MCTD patient.

Case: A 17-year-old female with type 1 diabetes mellitus and Raynaud's phenomenon presented with 10 days of headache and bilateral diplopia. Ophthalmology assessment ruled out diabetic retinopathy but found blood pressures of 200/110 on retinal angiogram. She was admitted to the pediatric intensive care unit for hypertensive emergency. Review of systems and physical exam was negative other than a one-year history of mild

Raynaud's syndrome. Investigations showed an elevated creatinine of 145, normal urinalysis, normal renal ultrasound, and normal bloodwork except for positive anti-nuclear antibody. ENA profile was positive for anti-Smith and high titre anti-RNP but negative for all other autoantibodies. A diagnosis of evolving MCTD was suspected, based on the history of Raynaud's and high titre anti-RNP. Initial antihypertensives included nicardipine infusion, amlodipine, prazosin, labetalol, and p.r.n. nifedipine. On repeat ophthalmology assessment, findings suspicious for active lupus retinitis led to initiation of prednisone. Renal biopsy showed arterial hypercellularity, luminal narrowing and sparing of glomerular capillaries, which were findings strongly suggesting SRC. Enalapril was started and a rapid prednisone taper was initiated. Blood pressure management improved, and she was discharged from the hospital with stable blood pressures on enalapril, amlodipine, and prazosin.

Conclusion: Although there have been reports of SRC presenting in adult MCTD, this is the first description of SRC in pediatric MCTD to our knowledge. In this case, onset of SRC occurred prior to the initiation of steroids and improved on combination treatment with enalapril, amlodipine, and prazosin. Current mainstay of SRC management includes prompt recognition and timely initiation of ACE inhibitor which highlights the importance of considering SRC despite its rarity in the pediatric population.

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Variations in Pediatric Rheumatology Workforce and Care Processes Across Canada

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Objectives: The objectives of this cross-sectional study were to examine the variations in pediatric rheumatology practice across Canada with respect to workforce, triage and referral practices, and delivery of clinical rheumatology services.

Methods: All Canadian academic and community-based pediatric rheumatologists and academic-based pediatric allied health professionals (AHPs) were invited to participate in an electronic survey. Rheumatologists were identified through the CRA Pediatrics committee. Eligible AHPs were identified by consulting the divisional director at each academic centre with pediatric rheumatology presence. A designee from each academic centre provided workforce data including number of providers, and the total and breakdown of full-time equivalents (FTE). Remaining respondents were asked about ambulatory care practices. We derived median clinical pediatric rheumatology FTE (cFTE: FTE dedicated to clinical care) available per 75,000 and 150,000 pediatric population using 2019 census data.

Results: The overall response rate was 54% (79/145). Seventy-three percent (56/77) of pediatric rheumatologists responded, and 34% (23/68) of AHPs responded. All 15 (100%) academic centre designees provided additional workforce data. The majority of rheumatologists (91%) practiced in academic centres. The median number of rheumatologists per centre was 3 (IQR:3) and median cFTE per centre was 1.85 (IQR:1.5). The median percentage of clinical time allocated to a rheumatology practice for community rheumatologists was 23%(IQR:27.5). When using the current recommended workforce benchmark, the median cFTE per 75,000 was 0.19 (IQR:0.32) with a national deficit of 80 cFTEs. With an estimated pediatric rheumatology-specific benchmark of 1:150,000, the median cFTE per 150,000 was 0.40 (IQR:0.54) with a national deficit of 48 cFTEs. All academic centres engaged in a multi-disciplinary practice with a median of 4 different AHPs, although the median FTE for the majority

of AHPs was considerably less than 1; the median FTE for nurses was 1.0 (IQR:0.9), physiotherapists was 0.6 (IQR:0.7), occupational therapists was 0.3 (IQR:0.5), and social workers was 0.3 (IQR:0.2). Most centers (87%) utilized a centralized triage process. Six (40%) centres were capable of calculating wait times and 4 (27%) centres used wait time as a performance measure. Most clinicians integrated quality improvement practices, such as pre-visit planning (68%), post-visit planning (69%), and periodic health outcome monitoring (68%).

Conclusion: Our study highlights the shortages of both Canadian pediatric rheumatologists and AHPs. Most rheumatologists work in multidisciplinary teams, but AHP support is likely inadequate at most centers. More work is needed to determine appropriate workforce benchmarks for number of pediatric rheumatologists and allied health FTE to support the pediatric rheumatology population.

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Choosing Wisely: The Canadian Rheumatology Association Pediatric Committee's List of Items Physicians and Patients Should Question

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Objectives: The "Choosing Wisely" (CW) campaign helps clinicians and patients engage in conversations about unnecessary tests and treatments and make smart and effective care choices. We aimed to develop a list of tests or treatments frequently used in pediatric rheumatology which may be unnecessary based on existing evidence.

Methods: A CW working group composed of 16 pediatric rheumatologists, 1 allied health practitioner, 1 parent, and 1 patient used the Delphi method to generate, rank, and refine the ranking of a list of tests, procedures and treatments used in the care of pediatric rheumatology patients that may be unnecessary, nonspecific or harmful. The items with the highest content agreement and perceived impact were presented in a survey to all Canadian Rheumatology Association (CRA) physician and trainee members who practice pediatric rheumatology. Respondents were asked to consider their agreement with the item, its impact, and ranking of the items. Composite scores (agreement, impact, rank) were tabulated for each item, and the five with highest scores were put forward for literature review. Additional items were also selected for literature review, based on consensus from the CW methodology subcommittee.

Results: In the initial Delphi procedure, 80 unique items were generated by the CW working group. After 3 rounds of Delphi, the list was narrowed down to 13 items. The CW survey was sent to 81 CRA physician and trainee members and was completed by 41 (51%) participants (an additional 8 partially completed). Participants were 56% (n = 27) female, 47% (n = 23) were between 36-49 years of age, and 18% (n = 9) have been in practice for 25 years or longer. Geographic distribution included: 50% (n = 24) in Ontario, 21% (n = 10) in British Columbia, 19% (n = 9) in Prairie provinces, 10% (n = 5) in Quebec and Atlantic provinces. The items with the highest composite scores from the CRA survey were: antinuclear antibody testing, drug toxicity monitoring, HLAB27 testing, rheumatoid

factor/anti-CCP testing, and g serology. Three additional items were also felt to be important by consensus of the CW methodology subcommittee (spine MRI, numerous or repeated intra-articular steroid injections, routine proton pump inhibitor prescribing). Thus, these eight highest priority items were advanced for literature review.

Conclusion: We have identified areas for potential quality improvement in the care of children and youth being evaluated and treated for rheumatic disease. The content and wording of the final CW list will be refined based on literature review. Best Abstract On Quality Care Initiatives In Rheumatology.

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Combination Therapy With Tofacitinib and IL-17A or IL-23 Inhibition for the Treatment of Refractory Psoriatic Arthritis

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Objectives: Psoriatic arthritis (PsA) is a heterogenous disease, which makes treatment challenging as different manifestations of the disease respond favourably to different treatment modalities. We describe four patients with resistant PsA and psoriasis with incomplete clinical response to IL-17A or IL-23 inhibition who then received concomitant tofacitinib.

Methods: Retrospective data was collected from a single rheumatology practice and information regarding patient demographics, disease characteristics, previous and concomitant medications, adverse events and serious adverse events was collected. All patients fulfilled the CASPAR classification criteria. Three patients were female, and one was male. Average age was 50 (range 34-69). Patients had highly resistant disease, failing an average of 2.5 (range 1-4) conventional synthetic disease modifying anti-rheumatic drugs (DMARD) and 4 (range 2-6) biologic DMARDs (bDMARDs). Baseline average swollen joint count was 7 (range 3-9) and average tender joint count was 8.5 (range 5-11). One patient was treated with tofacitinib and risankizumab, one with tofacitinib and guselkumab and two with tofacitinib and ixekizumab. After the addition of tofacitinib, average swollen joint count improved from 7 to 1 (range 0-3) and tender joint count from 8.5 to 1.25 (range 0-3). After an average 8 months of follow up (range 5-12 months), there were no adverse or serious adverse events.

Results: Combination therapy with DMARDs has been standard therapy for rheumatoid arthritis for over 20 years. There are no prospective studies examining the efficacy and safety of combination targeted synthetic DMARD (tsDMARD) therapy for PsA and no reports of combination therapy with tofacitinib and IL-17A or IL-23 inhibition for PsA. The only published report on the combination of tofacitinib with a biologic in PsA was by Barroso et al. who described a 51-year-old female who failed therapy with seven DMARDs. She was next treated with tofacitinib and tocilizumab. Therapy was discontinued after 28 months due to fever, leukopenia and lack of therapeutic effect.

Conclusion: There remain safety concerns around using combination therapy with bDMARDs. However, use with a tsDMARD such as tofacitinib may confer a more favourable safety profile due to different mechanisms of action. Tofacitinib does not effectively inhibit the IL-17A or IL-23 pathway, which may explain the additive effect seen when tofacitinib is used in combination with IL-17A or IL-23 inhibitors. Further research is warranted to clarify the efficacy and safety of tofacitinib in combination with a bDMARD for the treatment of resistant PsA.

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Managing Psoriatic Arthritis in Canadian Practice With Apremilast: Results From the Real-World Study APPRAISE

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Objectives: Apremilast, an oral phosphodiesterase-4 inhibitor that modulates immune response, is approved for the treatment of patients with active psoriatic arthritis (PsA) and moderate to severe plaque psoriasis. We analyzed baseline characteristics, 4-month effectiveness outcomes, and patient perceptions while receiving apremilast in a real-world setting.

Methods: APPRAISE (NCT03608657) is an ongoing observational study of adult patients with active PsA prescribed apremilast per routine care. Patients are assessed from treatment initiation to 12 months, with follow-up visits every 4 months. Baseline patient demographics were assessed descriptively. Outcomes at 4 months were analyzed by paired Student's t-test or McNemar's test.

Results: Between July 2018 and March 2020, 101 patients were enrolled; 84 patients reached the 4-month visit; 5 patients had not reached Visit 2 and 12 patients discontinued the study. Mean (SD) age was 52.1 (11.6) years and 57 (56.4%) were women. Mean (SD) duration of PsA at baseline was 5.5 (8.0) years. PsA subtypes included mainly oligoarticular (41.2%) and polyarticular (35.1%). Plaque-type psoriasis was most common (62.2%), with 70.3% of patients having < 3% body surface area involvement. Common comorbidities reported at baseline include cardio-metabolic conditions (49.0%), and anxiety and depression (24.0%). Prior therapies include: conventional DMARDs (92.1%) and biologics (16.8%); 37.6% of patients initiated apremilast in combination with methotrexate. Small joints of the hands and/or feet were the most commonly affected. At 4 months, mean (SD) swollen joint count (SJC) (0-66) and tender joint count (TJC) (0-68) significantly decreased from 5.4 (5.5) and 7.5 (6.7) at baseline to 2.2 (2.8) and 4.5 (6.7) (both $P \leq 0.001$), respectively. Proportions of patients with dactylitis and enthesitis decreased from 17.5% and 33.7% at baseline to 8.6% and 25.0%, respectively. Most patients (73.3%) had moderate or high disease activity at baseline, as measured by the Clinical Disease Activity Index for PsA (CDAPSA), 62.7% of patients achieved remission or low disease activity at 4 months. Significant improvements were observed from baseline to 4 months in both Physician and Patient Global Assessments, pain scores and patient-reported outcomes.

Conclusion: Canadian patients with PsA, treated with apremilast were within 5 years of diagnosis, often had oligoarticular PsA, and were usually biologic-naïve. At 4 months, remission or low disease activity was achieved in two-thirds of patients, SJC and TJC significantly improved, as did dactylitis or enthesitis. Physician and Patient Global Assessments of PsA, along with pain scores, showed statistically significant improvement with apremilast treatment.

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Safety Profiles of Ixekizumab versus Adalimumab: 52-Week Results from a Head-to-Head Comparison in Patients With Active Psoriatic Arthritis

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Objectives: Ixekizumab (IXE) was shown to be superior to adalimumab (ADA) in achievement of simultaneous improvement of joint and skin disease (American college of Rheumatology [ACR]50 and Psoriasis Area and Severity Index [PASI]100) in patients with active psoriatic arthritis (PsA) and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).[1] The objective of this study is to compare the safety and tolerability profile of IXE vs ADA in patients with PsA up to 52 weeks of treatment.

Methods: SPIRIT-H2H (NCT03151551) was an open-label,

head-to-head, blinded assessor study in patients with active PsA (≥ 3 tender joint count + ≥ 3 swollen joint count) and plaque psoriasis (body surface area $\geq 3\%$) who were inadequate responders to csDMARD therapy but naïve to biologic DMARDs. Patients were randomized (1:1) to approved dosing of IXE or ADA. Safety events were assessed at each patient visit up to Week 52. Frequencies of adverse events (AEs) were based on the number of patients in the safety population (patients who received ≥ 1 dose of study drug). Cases of inflammatory bowel disease (IBD) and cerebro-cardiovascular events were adjudicated by external committees. Kaplan-Meier analysis of time to onset of serious adverse events (SAEs) was performed.

Results: Of the 283 patients randomized to each treatment, 87% (246/283) of patients who received IXE and 84% (237/283) of patients who received ADA, completed 52 weeks of treatment. The frequency of treatment-emergent AEs (TEAEs) was similar between the groups (74% IXE vs 69% ADA); however, fewer severe TEAEs were reported in the IXE group (3.2% IXE vs 7.1% ADA). SAEs were significantly more frequent in the ADA vs IXE group (12% vs 4.2%; $P < 0.001$), and the time to develop a patient's first SAE was significantly shorter for ADA vs IXE ($P < 0.001$). Discontinuations due to AEs were numerically more frequent in the ADA vs IXE group (7.4% vs 4.2%; $P = 0.15$). IXE-treated patients reported more injection-site reactions (ISR) than ADA-treated patients (11% vs. 3.5%; $P = 0.002$). Study withdrawals due to ISR were comparable (0.7% IXE vs 1.1% ADA), and one injection-site reaction on ADA was severe. There were two IBD cases reported for IXE; one case was confirmed as IBD.

Conclusion: Safety results were consistent with previous trials with IXE and ADA. Compared with IXE, patients with PsA treated with ADA had significantly more serious AEs. Reference: [1.] Mease PJ, et al. Ann Rheum Dis. 2020;79(1):123-31.

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Efficacy of Ixekizumab Versus Adalimumab in Psoriatic Arthritis (PsA) Patients With and Without Moderate-to-Severe Psoriasis: 52-Week Results from a Multicentre, Randomised Open-Label Study

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Objectives: The efficacy of ixekizumab (IXE), a selective interleukin-17A inhibitor, was compared to adalimumab (ADA) in patients (pts) with psoriatic arthritis (PsA) and concomitant psoriasis (PsO) in the SPIRIT-H2H (NCT03151551) study. Here we report results at weeks (wks) 24 and 52 from a subgroup analysis based on baseline PsO severity.

Methods: SPIRIT-H2H was a 52-wk, multicenter, randomized, open-label, assessor-blinded, parallel-group study of biologic DMARD-naïve pts ($N = 566$) with PsA and active PsO ($\geq 3\%$ body surface area involvement). Pts were randomized (stratified by concomitant use of conventional synthetic DMARDs and PsO severity) to IXE or ADA. Pts received on label dosing according to the severity of PsO. We report efficacy outcomes at wks 24 and 52 for the subgroup analysis of patients with/without moderate-to-severe PsO at baseline. Logistic regression models were performed with treatment, baseline PsO severity and treatment-by-baseline PsO severity interaction as independent variables. Missing data were imputed using non-responder imputation.

Results: At baseline, 49/283 (17.3%) IXE-treated pts and 51/282 (18.1%) ADA-treated pts had moderate-to-severe PsO. One ADA pt had missing PsO severity at baseline and was not included in the analysis. A greater proportion of IXE-treated pts achieved the combined endpoint of ACR50+PASI100 (with moderate-to-severe PsO, IXE/ADA, wks 24 and 52: 40.8%/17.6% and 38.8%/17.6%, both $p \leq 0.05$; without moderate-to-severe PsO: 35.0%/30.3% and 39.3%/28.1% [$p \leq 0.05$], respectively),

and PASI100 (with moderate-to-severe PsO, IXE/ADA, wks 24 and 52: 59.2%/27.5% [$p \leq 0.05$] and 59.2%/25.5% [$p \leq 0.001$]; without moderate-to-severe PsO: 60.3%/51.1% [$p \leq 0.05$] and 65.4%/45.0% [$p \leq 0.001$], respectively) compared to ADA at wks 24 and 52, regardless of baseline PsO severity. Similar efficacy was observed on the joints for IXE and ADA across both pt subgroups. Higher proportions of IXE-treated pts achieved minimal disease activity (MDA) and Disease Activity in Psoriatic Arthritis (DAPSA) remission regardless of PsO severity (MDA and DAPSA remission [wk 24], with moderate-to-severe PsO, IXE/ADA: 57.1%/39.2% and 38.8%/21.6%; without moderate-to-severe PsO: 45.7%/34.6% [$p \leq 0.05$] and 23.9%/17.3%, respectively), and for very low disease activity (VLDA) in pts with moderate-to-severe PsO (VLDA [wk 24], IXE/ADA: 32.7%/9.8% [$p \leq 0.01$]). Similar trend was observed for these outcomes at wk 52.

Conclusion: In pts with active PsA, a significantly higher proportion of IXE-treated pts achieved the combined ACR50+PASI100 endpoint, and PASI100 at wk 52 compared to ADA, regardless of baseline PsO severity. High response rates in MDA and DAPSA remission were observed with IXE than with ADA. These results were consistent with the overall SPIRIT-H2H population.

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Improvement in Patient-Reported Outcomes in Patients With Psoriatic Arthritis With Inadequate Response to Non-Biologic DMARDs Treated With Upadacitinib Versus Placebo or Adalimumab: Results From a Phase 3 Study

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Objectives: To present an analysis of patient-reported outcomes (PROs) data from the SELECT-PsA 1 study assessing upadacitinib (UPA) in active PsA.

Methods: SELECT-PsA 1 (NCT03104400) is a Phase 3, randomized, placebo- (PBO) and active-controlled trial in patients with active PsA and inadequate responses to ≥ 1 non-biologic DMARD. Eligible patients were randomized to receive UPA 15 mg once daily (QD), UPA 30 mg QD, adalimumab (ADA) 40 mg every other week, or PBO for 24 weeks. PROs included: Patient Global Assessment of Disease Activity (PtGA), Patient's Assessment of Pain, HAQ-DI, FACIT-Fatigue, SF-36, EQ-5D, Self-Assessment of Psoriasis Symptoms (SAPS), Work Productivity and Activity Impairment, BASDAI, and morning stiffness (items 5 and 6 from the BASDAI). BASDAI was assessed in patients with presence of psoriatic spondylitis at baseline. Percentages of patients reporting improvements \geq minimal clinically important differences (MCID) from baseline through Week 24 were compared between treatment groups.

Results: Data from 1704 patients (UPA 15 mg: 429; UPA 30 mg: 423; PBO: 423; ADA: 429) were analyzed. At Week 12, both doses of UPA resulted in significant improvements from baseline vs PBO across all PROs. At Week 12, UPA 15 mg and 30 mg resulted in significant improvements from baseline vs ADA in HAQ-DI, SAPS, and SF-36 physical component summary and UPA 30 mg vs ADA in 4 SF-36 domains. Compared with PBO, significantly more patients treated with UPA 15 mg and 30 mg reported improvements \geq MCID in PtGA, pain, and HAQ-DI as early as Week 2 (first post-baseline visit) that were maintained through Week 24. At Week 12, the proportions of patients reporting improvements \geq MCID

were significantly greater with both doses of UPA vs PBO across all PROs except SF-36 mental component summary (UPA 30 mg) with NNTs ranging from 3.0-11.4 for all PROs. The proportions of UPA-treated (both doses) patients reporting improvements \geq MCID at Week 12 were similar to ADA-treated patients across most PROs and significantly higher than ADA-treated patients in HAQ-DI; improvements were maintained through Week 24.

Conclusion: Treatment with UPA 15 mg or UPA 30 mg resulted in clinically meaningful improvements in PROs vs PBO at 12 weeks in biologic DMARD-naïve patients with active PsA, which were maintained or further improved at Week 24. Overall, improvements were similar between UPA 15 mg and UPA 30 mg and improvements with both doses of UPA were similar or greater than those reported with ADA.

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Impact of Upadacitinib on Reducing Pain in Patients With Active Psoriatic Arthritis: Results From Two Phase 3 Trials in Patients With Inadequate Response to Non-biologic or Biologic DMARDs

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Objectives: To compare the efficacy of upadacitinib (UPA) vs placebo (PBO) and adalimumab (ADA) on pain using different assessments through 24 weeks in patients with active psoriatic arthritis (PsA) in the SELECT PsA 1 and 2 studies.

Methods: The SELECT-PsA program enrolled adult patients with active PsA with prior inadequate response (IR) or intolerance to ≥ 1 non-biologic DMARD (SELECT-PsA 1; NCT03104400) or prior IR or intolerance to ≥ 1 biologic DMARD (SELECT-PsA 2; NCT03104374). Patients were randomized to UPA 15 mg or UPA 30 mg once daily (QD) or PBO (both studies), and ADA 40 mg every other week (EOW; SELECT-PsA 1 only). Pain was assessed as proportion of patients achieving $\geq 30\%$, $\geq 50\%$, or $\geq 70\%$ reduction from baseline in Patient's global assessment (PGA) of pain numeric rating scale (NRS) score (0-10), proportion of patients achieving minimal clinically important difference (MCID) in pain (defined as ≥ 1 point reduction or 15% reduction from baseline on a 0-10 NRS) and change from baseline in pain NRS (0-10) at all time points. In addition, change from baseline in BASDAI questions 2 (spinal pain) and 3 (joint pain/swelling) and SF-36 questions 7 (bodily pain) and 8 (pain interference) at weeks 12 and 24 were assessed.

Results: In both studies, a significantly higher proportion of patients receiving UPA 15 mg QD and UPA 30 mg QD vs PBO achieved improvements in most pain endpoints as early as week 2, and improvements were generally either sustained or increased through week 24 (nominal $P < 0.05$). A significant improvement with UPA vs PBO was also observed for change from baseline in PGA of pain NRS scores over time, as well as in BASDAI spinal pain and joint pain/swelling and SF-36 bodily pain and pain interference at weeks 12 and 24. In SELECT-PsA 1 significantly higher proportions of patients receiving UPA 30 mg QD vs ADA 40 mg EOW achieved improvements in most pain assessments as early as week 2 which were sustained through week 24; improvements in several assessments were also significantly greater with UPA 15 mg QD vs ADA 40 mg EOW at week 24 (nominal $P < 0.05$).

Conclusion: In patients with active PsA who had inadequate response to non-biologic or biologic DMARDs, a greater proportion of patients treated with UPA vs PBO achieved rapid, significant, and clinically meaningful reductions in pain across multiple pain assessments. The reductions in pain were sustained over 24 weeks.

Outcomes of Virtual Rheumatoid Arthritis Care - A Systematic Review
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Objectives: To conduct a systematic review comparing the efficacy of virtual care and conventional care in rheumatoid arthritis (RA) based on disease activity management and patient experience.

Methods: A systematic search of MEDLINE, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials was performed from database inception to 03/19/2020, based on a search strategy developed in consultation with a medical librarian. Observational and randomized controlled trials (RCTs) describing the use of RA virtual care supplanting conventional visits and reporting on disease activity and/or patient experience were included. A narrative synthesis of results pertaining to the main outcomes was conducted, additional outcomes highlighting other potential benefits of virtual care were also examined. Risk of bias of included studies was assessed.

Results: 352 studies were identified through the search, and 6 were selected for final inclusion: 3 were RCTs and 3 were observational studies. Overall, the data from selected studies indicated that disease activity and patient experience were comparable between the virtual and conventional care models. In addition, one RCT found no difference in observed outcomes between virtual care delivered by a rheumatologist and by a rheumatology nurse. The RCTs selected included both patient populations with stable disease, as well as those with shorter disease duration and higher activity. Additional benefits of virtual care included improving treatment adherence, maintaining functional status, and improving quality of life. The observational studies included patient populations from urban centres and rural settings. One observational study demonstrated that over half of the patients who received virtual care still expressed preference for in-person care, despite finding no difference in the quality of care. Quality assessment of the included studies found that overall risk of bias was indeterminate in the RCTs due to challenges with blinding due to the nature of the intervention, but high in the observational studies. Observational study quality was limited by incomplete data reporting, lack of sample size justification, and lack of sufficient timeframe to assess objectives.

Conclusion: Virtual care appears to be an acceptable alternative to conventional care in RA, maintaining comparable patient outcomes and experience of care. However, studies evaluating the efficacy of virtual care in RA are scarce and more research is needed to further support the feasibility of this method of care. Additional research into effective implementation strategies and long-term health system and patient outcomes of virtual care are also needed.

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Biosimilar Candidate ABP 798: Additional Analyses from the Comparative Clinical Study

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Objectives: ABP 798 is being developed as a biosimilar to Rituxan® (rituximab) reference product (RP), a CD20-directed cytolytic antibody. Evidence from analytical assessments demonstrate that ABP 798 is similar to the RP. Results from the comparative clinical study in patients with RA have demonstrated similar pharmacokinetics, efficacy and safety. Here we report results for the ACR individual components, detailed pharmacodynamics (PD) and additional safety findings.

Methods: This was a randomized, double-blind, active-controlled study conducted in adult subjects with moderate-to-severe RA who had an inadequate response or intolerance to other DMARDs. Subjects were randomized (1:1:1) to receive 2 IV infusions of 1000 mg, 2 weeks apart as first dose of either ABP 798, rituximab sourced from the EU (rituximab EU),

or rituximab sourced from the US (rituximab US). At Week 24, subjects in ABP 798 and rituximab EU arms received the second dose of the same treatment, while those in the rituximab US arm transitioned to receive ABP 798 for their second dose. Details of the study design have been previously reported.

Results: A total of 311 subjects were randomized (ABP 798 = 104; rituximab EU = 104; rituximab US = 103); all subjects were treated with at least one infusion of investigational product. Baseline characteristics were well balanced between groups and clinical equivalence between ABP 798, and rituximab RP was established. The ACR20 response rate at week 24 was 70.7% for ABP 798 group and 65.5% for pooled RP group (risk difference = 0.0517; 90% CI: -0.0389, 0.1423), supporting the conclusion of clinical similarity between the treatment groups. Results for individual ACR components were comparable over the study duration; for example, at baseline swollen joint counts were: ABP 798 = 19.253; rituximab EU = 18.388; rituximab US = 18.960; at week 24: ABP 798 = 6.204; rituximab EU = 6.058; rituximab US = 5.901 and at week 48: ABP 798 = 4.462; rituximab EU = 3.159; rituximab US = 4.602. The PD endpoint of CD19+ B-cell depletion at study day 3 were similar between ABP 798 and rituximab RP treatment arms. The overall safety of ABP 798 and rituximab RP was comparable and adverse events profiles by age (< 65 and ≥ 65 years) were similar. Incidence rates of developing binding ADAs were consistent across the treatment groups (ABP 798/ABP 798 = 14.4%; rituximab EU/EU = 13.8%; rituximab US/ABP 798 = 20.6%).

Conclusion: These data further support that ABP 798 is similar to rituximab RP in PD, efficacy and safety.

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Adherence to System-level Performance Measures for Rheumatoid Arthritis Care in Ontario

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Objectives: To assess adherence to system-level performance measures (PMs) measuring access and treatment in rheumatoid arthritis (RA) in a population-based inception cohort within the Ontario RA administrative Database (ORAD).

Methods: Patients are included if they have 1 hospitalization or ≥ 3 physician RA claims over 2 years with at least 1 by a rheumatologist, internist or orthopedic surgeon (case definition sensitivity 78%, specificity 100%, PPV 78%). Patients were diagnosed between 2002 to 2014 (to permit at least 5 years of follow-up to 2019). Over the first 5 years following cohort entry, we assessed whether PMs were met including: being seen by a rheumatologist within 1 year of the first RA code, and whether patients had an annual rheumatology visit. Medication data were available for individuals > 65 years of age, in whom two additional PMs were assessed: DMARD dispensation within 14 days of the first rheumatologist visit, and DMARD dispensation on an annual basis. We assessed differences in PMs across calendar periods (diagnosis 2002-2009 vs. 2010-2014), by age at disease onset (< or ≥ 66 years), and whether a rheumatologist was the initial specialist establishing the diagnosis (vs internists or orthopedic surgeons).

Results: The cohort included 72,303 RA cases (33% ≥ 66 years old). The majority (83%) were seen by a rheumatologist within 1 year of their first RA

diagnosis code. Patients with disease onset between 18 and 65 years of age were more frequently seen by a rheumatologist within the first year (73%) compared to those with disease onset ≥ 66 years (85%). Approximately 15% of patients met cohort inclusion criteria through physician claims made by internists or orthopedic surgeons and $< 30\%$ of these were seen by a rheumatologist within 1 year of first RA code. Adherence to the annual rheumatology follow-up PM declined in consecutive years, from 77% in the first year to 49% in the fifth year of follow-up. Adherence to annual follow-up was higher for cases diagnosed in the more recent calendar period, among those diagnosed between 18 and 65 years of age and among those with a rheumatologist as the initial specialist. Among those covered by provincial drug coverage (age ≥ 66 years), 34% filled a DMARD prescription within 14 days of their first rheumatologist visit (63% within one year).

Conclusion: System-level improvement initiatives should focus on maintaining ongoing access to rheumatology specialty care. PMs indicating lower and less timely DMARD use in seniors require additional investigation to target improvements.

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Comparing Academic and Community Practices in the Management of Rheumatoid Arthritis: Data from the OBRI Registry

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Objectives: Rheumatologists vary in their management of rheumatoid arthritis (RA). The treat-to-target paradigm requires responsive treatment escalation to obtain low disease activity and prevent morbidity. Advanced Therapy (bDMARD or tsDMARD) initiation requires rheumatologists' time and effort. Given resources differences between settings, we aimed to determine if time to Advanced Therapy (AT) initiation, or switch, in patients with moderate-high disease activity differed between community and academic practices in Ontario.

Methods: We included adult patients enrolled in the Ontario Best Practices Research Initiative (OBRI) registry between 2008-2019 with at least 2 visits and 6 months of follow-up with moderate-high disease activity. Population A included those with at least 2 months of combined csDMARD therapy (either Methotrexate and Leflunomide; or Methotrexate, Sulfasalazine and Plaquenil) who ultimately started AT. Population B included those on any AT who ultimately switched AT. We used independent adjusted cox proportional hazards models to compare academic and community settings in time from first recorded moderate-high disease activity to initiation, or switch in AT. We completed exploratory analyses to assess disease activity at the 3 visits prior to therapy change, and time-to-therapy change between those started on bDMARDs and tsDMARDs.

Results: Baseline characteristics were similar between community and academic settings in both population A ($n = 135$) and B ($n = 453$). Swollen joint count was 1 higher and RA duration was slightly longer in the academic setting. There was no difference between community and academic settings in time to initiation or switch in AT before and after adjustment. In both settings, there was a significant delay in starting AT: on average 241 days following first moderate-severe disease activity while on combination csDMARDs. Across three visits leading to therapy change, disease activity and swollen joint count were high (mean CDAI: 24; mean SJC: 6.3). These were lower numerically for new tsDMARD starts (mean CDAI: 5.9; mean SJC: 1.8).

Conclusion: Conclusions are limited due to the study's small sample size and observational nature. We found no difference in prescriber response to moderate-high disease activity between community and academic settings. Ontario Rheumatologists are allowing for significant delays during which disease is uncontrolled prior to initiating AT, however we could not account for therapeutic dose adjustment. We propose that paperwork burden may be

contributing, thus we will next compare time to initiation between AT with and without Limited Use codes.

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Who Is Receiving Influenza Vaccinations Prior to and After a Diagnosis of RA? Results from the Canadian Early Arthritis Cohort (CATCH)

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Objectives: Annual influenza vaccinations are recommended for individuals with rheumatoid arthritis. We examined influenza vaccination rates in the years prior to and following diagnosis of RA, and sociodemographic characteristics and beliefs associated with flu vaccination among participants in the Canadian Early Arthritis Cohort (CATCH).

Methods: The sample was drawn from baseline visit of adults enrolled in the Canadian Early Arthritis Cohort (CATCH) between December 2014 and 2019. All participants met ACR1987 or 2010 ACR/EULAR criteria, had at least 1 year of follow-up data, and had completed a survey asking about vaccination status and the Beliefs about Medicines Questionnaire. Characteristics of vaccinated and non-vaccinated groups were compared using t-tests and chi-square. Multivariable logistic regression was used to identify characteristics associated with flu vaccination around diagnosis and 1 year later.

Results: Participants ($N = 362$) were mostly white (79%) women (64%) with a mean (SD) age of 56 (14) years, and symptom duration of 5 (3) months. 36% reported receiving a flu vaccination in the year prior to diagnosis, increasing to 46% in the year post diagnosis. At baseline, as compared to those not vaccinated, patients who were vaccinated in the previous year were significantly older, less likely to smoke, had more comorbidities, and had a higher mean necessity-concerns score ($p < .03$). However, groups did not differ by sex, education, BMI category, region (Western Canada vs. ON or QC), CDAI, private insurance status or RA medication necessity beliefs. In multivariable analyses, predictors of vaccination in the year prior to RA diagnosis were age ≥ 55 (OR [95% CI] = 3.0 [1.7, 5.0], not smoking (OR [95% CI] = 2.1 [1.0, 4.4]), and having comorbidities (OR [95% CI] = 1.2 [1.0, 1.4]). Multivariable predictors of vaccination at 12 months were vaccination in the year prior diagnosis (OR [95% CI] 12.0 [5.2, 27.8]) and not smoking (OR [95% CI] 5.6 [1.7, 18.4]).

Conclusion: Slightly more than a third of newly diagnosed adults with RA had reported receiving an influenza vaccination in the previous year. Individuals who were not vaccinated prior to RA diagnosis and smokers were also at high risk of not receiving an influenza vaccination in the first year of RA. Smoking may be an important marker of individuals less likely to be vaccinated both before and after RA diagnosis. Conversations about vaccination history and attitudes as part of the diagnostic workup may offer an opportunity to increase vaccine acceptance and uptake.

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Long-Term Treatment in a Patient With Cryptococcal Meningitis and Rheumatoid Arthritis

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Case: A 69-year-old woman was admitted to hospital with confusion, headaches, and vomiting for two weeks. Medical history was significant for seronegative rheumatoid arthritis well-controlled with Infliximab, Prednisone 5 mg daily as needed, and Leflunomide 20 mg daily. Previously failed

management strategies included Etanercept, Tofacitinib, Methotrexate, and Hydroxychloroquine. Other medical history includes superficial venous thrombosis and surgically cured ovarian cancer. Physical examination was non-contributory, specifically, there were no focal neurological findings. Magnetic Resonance Imaging (MRI) suggested meningitis or autoimmune encephalitis. Antibiotics and Acyclovir were given until investigations for viral, bacterial, and fungal infections were negative and she improved clinically. Cerebrospinal fluid (CSF) analysis showed elevated protein at 1.33 g/L, decreased glucose at 1.3 mmol/L, and elevated leukocyte count of $160 \times 10^6/L$ with lymphocyte predominance. Cerebral spinal fluid analysis was negative for mycobacterium and viruses. Syphilis PCR was negative. Cryptococcal antigen was negative in the serum and CSF. Based on these investigations, she was diagnosed with aseptic meningitis. After discharge, her CSF fungal culture was reported to be positive for *Cryptococcus neoformans*; therefore, her final diagnosis was Cryptococcal Meningitis. The Infectious Disease team suggested stopping Leflunomide and managing the infection with long-term antifungals. In addition, her Infliximab dose was decreased in frequency from every 6 weeks to every 8 weeks. Two months later, her Infliximab was changed to Abatacept. Management of her rheumatoid arthritis at this time included Abatacept and Prednisone 5 mg daily as needed. The cryptococcal infection was managed as an outpatient with 6 weeks of induction therapy of 5-Flucytosine, followed by 6 months of Fluconazole 200 mg daily. Follow-up MRI of the brain showed an area suspicious for parenchymal abscess, which is currently being followed with serial imaging.

Discussion: The role tumor necrosis factor (TNF) alpha has in protecting against cryptococcal infection is well understood [1]. *Cryptococcus* infection with concurrent TNF alpha inhibitors has been reported previously [2-6]. One case of disseminated cryptococcal infection suspected to be caused by infliximab therapy was fatal [7]. However, culture-proven cryptococcal meningitis has only been reported twice [8, 9], direct CSF examination was used to diagnose in one case [10], and treatment included discontinuation of infliximab [8, 10].

To the best of our knowledge, we are the first to report ongoing management with concurrent immunosuppressive and chronic antifungal therapies. Our report also highlights the potentially serious complications of iatrogenic immunosuppression, and the difficulty of managing infections while preventing autoimmune disease flares.

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Real-World Estimates of Early Rheumatoid Arthritis Patients at Increased Risk for Severe COVID-19 to Inform Emerging Vaccination Strategies: Results from the Canadian Early Arthritis Cohort (CATCH)

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Objectives: Worldwide anticipation for the 2021 vaccine against SARS-CoV-2 is high. Supply of a successful vaccine will initially be insufficient for all Canadians. Our objective was to identify risk factors for severe COVID-19 in rheumatoid arthritis patients; and estimate the prevalence of these risk factors in a large multi-centre cohort of real-world early RA (ERA) patients treated in routine practice settings.

Methods: We carried out a scoping review of systematic reviews and meta-analyses of adults with severe COVID-19 complications published between Dec 2019–Aug 2020 in PubMed, Medline, and EMBASE databases. We categorized identified risk factors from the literature as major risk factor versus minor risk factor for severe COVID-19 based on consistency

of reporting across studies and strength of associations as indicated by pooled odds ratios or risk ratios from meta-analysis. Data on frequency of identified risk factors from the review were estimated from ERA patients actively enrolled in the Canadian Early Arthritis Cohort (CATCH) study, between Jan 2007–Feb 2020. Descriptive statistics were used to estimate prevalence and cumulative counts of risk factors for severe COVID-19 infection for each CATCH participant at their most recent study visit closest to March 2020.

Results: Of 1345 articles, 41 studies met the inclusion criteria. Identified major risk factors associated with severe COVID-19 were age (> 65 yrs old), male sex, hypertension, coronary artery disease (CAD), COPD, cerebrovascular disease, diabetes, chronic renal disease. Identified minor risk factors associated with severe COVID-19 were smoking, elevated BMI, malignancy, chronic liver disease, and ethnic minorities. A rheumatoid arthritis specific risk factor identified was high prednisone use > 10 mg/day. Data from 1,967 patients actively enrolled in CATCH were analyzed. Sample mean (SD) age was 60 (14) years and symptom duration of 63 (40) months. Our cohort consisted of 13% with moderate-high CDAs and 15% with moderate-high DAS28. Majority (77%) of CATCH participants had at least one major risk factor, 91% had > 1 minor risk factor, and 20% had 4 or more major and minor risk factors. Age > 65 (41%) and multiple comorbidities (51%) being the common major risk factor; with fewer, only 7% of the cohort requiring prednisone > 10 mg for minimum 4 weeks in the last 6 months.

Conclusion: The most common major risk factors for severe COVID-19 within an ERA cohort are age > 65 yrs, presence of multiple comorbidities including COPD, CAD and hypertension. Prioritizing vaccinations for these subset of ERA patients will become an important aspect for future management recommendations.

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Seronegative Rheumatoid Arthritis and Persistently High C-Reactive Protein: A Seven Year Misdiagnosis

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Objective: Whipple's disease is a rare multisystemic infection caused by *Tropheryma whipplei*, classically characterized by joint symptoms, chronic diarrhea, malabsorption and weight loss. Joint symptoms can often present years prior to development of characteristic disease with patients often initially misdiagnosed as rheumatoid arthritis. We present a case of Whipple's disease, developing classic symptoms after 7 years of immunosuppressive therapy, followed by a complicated course of treatment.

Methods: Case report and review of literature.

Results: A 67-year-old gentleman being followed for his non-erosive, seronegative rheumatoid arthritis, diagnosed 7 years prior and had failed hydroxychloroquine, leflunomide and methotrexate. He was treated with etanercept for 2 years and after loss of efficacy was switched to tofacitinib. His joint manifestations were well controlled clinically with this modification, but he had an unexplained elevation of his C-Reactive Protein (CRP), between 60 - 80 mg/L. Patient clinically deteriorated two years into his tofacitinib, developing shortness of breath and diagnosed with constrictive pericarditis and 2 months later, developed diarrhea. Subsequent CT imaging demonstrated diffuse colonic wall thickening best visualized at the transverse colon as well as diffuse low density abdominal retroperitoneal and small bowel mesenteric lymphadenopathy, suspicious for Whipple's disease, which was later confirmed on esophagogastroduodenoscopy. All disease modifying agents were held and ceftriaxone 2 g IV daily for 4 weeks was initiated followed by trimethoprim/sulfamethoxazole 160/800 mg PO BID for one year. Four months into treatment, his course was further complicated by readmission to hospital with fevers and elevated CRP in the low 100's mg/L, which revealed immune reconstitution inflammatory syndrome (IRIS) and treated with prednisone 1mg/kg, with complete resolution of his fever and CRP normalizing. During the re-admission, the patient also described extreme pain of the thighs bilaterally. Subsequent

magnetic resonance imaging demonstrated myositis; muscle biopsy showed sparse infiltration of the perimysial connective tissue by PAS-positive macrophages suggesting Tropheryma whipplei on the muscle biopsy. He was retreated with ceftriaxone and changed to hydroxychloroquine 200 mg PO TID and doxycycline 100 mg PO BID.

Conclusion: In summary, we are presenting a case of Whipple's disease, masquerading as symmetrical polyarthritis for 7 years, until development of classic symptoms. Treatment of this rare disease was further complicated by a rare manifestation of IRIS post antibiotic therapy and recurrence of his Whipple's in his muscles despite being on antibiotic therapies.

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Efficacy and Safety of Filgotinib in Methotrexate-Naïve Patients With Rheumatoid Arthritis: FINCH 3 52-Week Results

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Objectives: Filgotinib (FIL) is a potent, selective, oral JAK1 inhibitor. FINCH3 assessed FIL efficacy and safety in methotrexate (MTX)-naïve patients with rheumatoid arthritis (RA); Week 24 primary outcome results were previously presented. The objective of this study was to report FINCH3 (NCT02886728) results through Week 52.

Methods: This global, phase 3, double-blind, active-controlled study randomised MTX-naïve patients with moderately to severely active RA 2:1:1:2 to FIL 200mg once daily (QD) + MTX ≤ 20mg weekly (QW), FIL 100mg QD + MTX, FIL 200mg QD monotherapy + placebo, or placebo + MTX ≤ 20mg QW up to Week 52. Comparisons at Week 52 were not adjusted for multiplicity. Safety was assessed from adverse events and laboratory abnormalities.

Results: Of 1249 treated patients, 975 received study drug through Week 52. FIL efficacy was sustained up to Week 52. Proportions of patients achieving ACR20/50/70 (%) were increased with treatment with FIL 200 mg + MTX (n = 416; 75.0/62.3/47.8); FIL 100 mg + MTX (n = 207; 73.4/59.4/40.1); and FIL 200 mg monotherapy (n = 210; 74.8/61.4/45.2) versus MTX (n = 416; 61.8/48.3/29.8). FIL 200 mg + MTX, FIL 100 mg + MTX, and FIL 200 monotherapy also increased proportion achieving clinical disease remission by DAS28(CRP) < 2.6 CDAI, SDAI, and Boolean criteria; improved HAQ-DI; and halted radiographic progression versus MTX alone. Safety was consistent with Week 24 data. Safety outcomes through Week 52 for FIL 200 mg + MTX, FIL 100 mg + MTX, FIL 200 mg monotherapy, and MTX (%) were: adverse event rate 76.4, 79.2, 68.1 and 73.3; serious adverse events 6.3, 6.3, 8.1 and 6.7; serious infections 1.2, 1.4, 2.4 and 1.9; herpes zoster 1.4, 1.4, 1.9 and 1.0; VTE 0, 0, 0 and 1.0; MACE (adjudicated) 1.0, 0.5, 1.0 and 0.5; malignancy 0.2, 0, 0 and 1.0; and death 0.7, 0.5, 0 and 0.

Conclusion: Efficacy of FIL 200mg + MTX, FIL 100mg + MTX, and FIL 200mg monotherapy was sustained through Week 52, with faster onset and consistently numerically greater efficacy for FIL 200mg versus FIL 100mg. No new safety signals were observed.

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Characterisation of Depth of Response, Including 50% Improvement in ACR Components at Week 12 and Remission at Week 24, Following Treatment With Filgotinib Compared With Methotrexate or Adalimumab in Patients With Rheumatoid Arthritis

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Objectives: Filgotinib (FIL) an oral, potent, selective JAK1 inhibitor showed favourable efficacy at week (W)12 and W24 of treatment for rheumatoid arthritis (RA) compared with methotrexate (MTX) monotherapy (mono) in FINCH 3 (NCT02886728) and with placebo (PBO) or adalimumab (ADA) in FINCH 1 (NCT02889796). 50% clinical improvement from baseline at W12 is a key checkpoint for RA treatment. These post hoc analyses evaluated FIL treatment effect on improvement in ACR components at W12 and remission at W24 in FINCH 3 and FINCH 1.

Methods: FINCH 3 and FINCH 1 were global, phase 3, double-blind studies in patients (pts) with active RA. In FINCH 3, MTX-naïve pts was randomised 2:1:1:2 to once-daily (QD) oral FIL 200 mg + weekly MTX, FIL 100 mg + MTX, FIL 200 mg mono + PBO, or PBO + MTX mono up to W52. In FINCH 1, pts with inadequate response to MTX (MTX-IR) on a background of stable MTX were randomised (3:3:2:3) to oral FIL 200 or 100 mg QD, subcutaneous ADA 40 mg Q2W, or PBO up to W52. Post hoc analyses evaluated proportions of pts with 50% improvement from baseline in each ACR component and in all 7 ACR components (ACR50c) at W12, and proportions of pts with ACR50c at W12 achieving clinical remission at W24. Comparisons between treatments were not adjusted for multiplicity; subgroup comparisons are descriptive.

Results: 1249 pts in FINCH 3 and 1755 pts in FINCH 1 were analysed. A greater proportion of pts (%) in FINCH 3 and FINCH 1 receiving FIL 200mg+MTX (26.2 and 18.5, respectively), FIL 100mg+MTX (19.3 and 12.5, respectively) and FIL mono (22.9, FINCH 3) vs MTX mono (6.0, FINCH 3) or PBO+MTX (2.5, FINCH 1) achieved ACR50c at week 12 (P < 0.001). A numerically higher proportions of pts on FIL 200 mg+MTX vs FIL 100 mg+MTX (both studies) or ADA + MTX (FINCH 1) achieved ACR50c and individual components at week 12. Proportions of pts achieving CDAI ≤ 2.8 or Boolean remission at W24 were higher for pts with vs without ACR50c at W12.

Conclusion: In MTX-naïve and MTX-IR pts with RA, FIL treatment was more effective vs MTX (FINCH 3) or PBO (FINCH 1) for achieving ACR50c at W12-a potential predictor of remission at W24. Proportions of pts achieving ACR50c at W12 were numerically higher for pts receiving FIL 200 mg + MTX vs FIL 100 mg + MTX (both studies) and ADA + MTX (FINCH 1).

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Filgotinib Provided Rapid and Sustained Improvements of Work Productivity and Activity in Patients With Rheumatoid Arthritis who are Methotrexate-naïve: Results from the FINCH-3 Study

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Objectives: Filgotinib (FIL) is an oral, selective JAK1 inhibitor being investigated RA treatment. In FINCH 3 (NCT02886728), FIL+methotrexate (MTX), demonstrated rapid and significant improvements in RA signs/symptoms vs MTX monotherapy in MTX-naïve patients. This post-hoc analysis evaluated rate and magnitude of treatment response on work productivity and activity scores in RA patients from the FINCH 3.

Methods: Patients with active RA and MTX-naïve were randomized 2:1:1:2 received FIL 200mg +MTX, FIL 100mg +MTX, FIL 200mg +placebo (PBO), or MTX (+PBO) for up to 52 weeks (W). Activity impairment, work productivity impairment, presenteeism, and absenteeism were evaluated at baseline and then during treatment up to W52, using the self-administered 6-item Work Productivity and Activity Impairment Questionnaire: Rheumatoid Arthritis (WPAI:RA). The 4 subscale scores ranged from 0%-100%, with higher scores indicating greater impairment. Mean changes in WPAI:RA scores from baseline were quantified using least squares mean estimates returned by mixed-effects models for repeated measures; for estimates of the treatment effect on the score changes, the models included adjustment for the randomization stratification factors.

Results: Patients were (mean \pm SD) 53 \pm 14 years old, 80% female, and 42% employed. Compared with MTX alone, a significantly greater improvement from baseline in work productivity (except for absenteeism) from W4 (FIL100+MTX: -19.0; FIL200+MTX:-21.8; FIL200: -17.1; MTX:-6.6) to W12 (FIL100+MTX: -28.1; FIL200+MTX: -27.6; FIL200: -23.4; MTX: -19.5) and activity from W4 (FIL100+MTX: -17.8; FIL200+MTX: -23.2; FIL200: -19.7; MTX: -13.5) to W12 (FIL100+MTX: -28.1; FIL200+MTX: -32.5; FIL200: -30.5; MTX: -23.6); was observed in FIL and persisted through W52 with improvements reaching an MCID (7%). Although improvements in both work productivity and activity impairment scores were seen, the magnitude of improvement was directly related to percent of RA improvement by ACR as early as W4 and persisted throughout W52. In multiple regression analysis, higher baseline WPI score was associated with higher CRP ($+0.022 \pm 0.006$ per mg/dL) and greater tender joint count-68 (TJC68) ($+0.047 \pm 0.009$ per 10 joints) (all $P < 0.05$); same predictors were also associated with presenteeism (CRP $+0.018 \pm 0.005$ per mg/dL, TJC-68 $+0.032 \pm 0.008$ per 10 joints, both $p \leq 0.05$) but no similar associations were identified for absenteeism (all $P > 0.05$). Higher baseline activity impairment was associated with female gender ($+0.031 \pm 0.015$), CRP ($+0.019 \pm 0.003$ per mg/dL) and TJC-68 ($+0.034 \pm 0.005$ per 10 joints) (all $P < 0.05$).

Conclusion: FIL \pm MTX, versus MTX alone led to more rapid and sustained improvements in activity impairment, work productivity impairment and presenteeism in RA patients who were MTX-naïve.

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Effect of Filgotinib on Pain in Patients With Rheumatoid Arthritis: Results from Phase 3 Clinical Trials

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Objectives: Patients with RA often suffer substantial pain despite treatment with pain control as a top treatment goal. Filgotinib (FIL) -an oral JAK1 selective inhibitor- was efficacious and generally well tolerated in the FINCH RA clinical trial program. This FINCH post-hoc analysis was conducted to assess the impact of FIL on pain.

Methods: In FINCH 3 (F3), methotrexate-naïve patients with RA received

FIL 200mg +MTX, FIL 100mg +MTX, FIL 200mg, or MTX for up to 52 weeks (W). In FINCH 1 (F1) patients with an inadequate response to MTX (MTX-IR) on background MTX received FIL 200mg, FIL 100mg, adalimumab (ADA) 40mg, or placebo (PBO) for up to 52W; at W24, PBO patients were rerandomized to FIL 200 or 100mg. In FINCH 2 (F2), patients cs DMARDs with bDMARD-IR on background csDMARD received FIL 200, 100mg, or PBO 24W. Each study was analyzed separately. Patient-reported pain was assessed on a visual analog scale (VAS). Proportions of patients achieving moderate (30%), and substantial (50%) clinically important thresholds were analyzed, as were thresholds of 70% and 90%, and residual VAS pain scores of $\leq 10/20/40$ mm out of 100mm. Comparisons were not adjusted for multiplicity; nominal P values are presented.

Results: Baseline pain was high among all arms (mean VAS scores of 64-68 mm). Pain improved across patient populations. At W2, patients with pain reduction $\geq 30\%$, $\geq 50\%$, and residual pain ≤ 40 mm was significantly greater for all FIL arms versus PBO (F1/F2) or MTX (F3) (nominal $P < 0.05$). Pain was reduced by $\geq 90\%$ by W52 in approximately 25% of patients in F1/F3. Except for patients receiving FIL 100mg in the $\geq 30\%$ reduction analysis, significantly more bDMARD-IR patients on FIL had pain reduction at W24 compared to PBO in all analyses (F2; nominal $P < 0.05$). Significantly more MTX-naïve patients receiving FIL 200mg +MTX vs MTX monotherapy reported pain reduction for all measures at all time points (F3; nominal $P < 0.05$). Overall, more MTX-IR pts (F1) receiving FIL had pain reduction compared with patients on ADA, with significant differences noted for FIL 200mg for some measures at W2 through W30(nominal $P < 0.05$).

Conclusion: FIL 200 and 100mg provided rapid, clinically meaningful pain relief among a broad spectrum of RA patients and across several measures. The degree of improvement was substantial for many pts; $\geq 40\%$ of patients in all studies had a $\geq 50\%$ reduction in pain and nearly 25% had a 90% reduction in F1/F3.

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Functional Disability Is Associated With Anti-citrullinated Protein Antibodies in Indigenous First-degree Relatives of Rheumatoid Arthritis Patients

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Objectives: The preclinical stage of Rheumatoid Arthritis (RA) is characterized by seropositivity for anti-citrullinated protein antibodies (ACPA). We have previously shown that ACPA seropositivity is prevalent in the first-degree relatives (FDR) of RA patients. While ACPA is highly predictive of RA development in individuals who were selected by healthcare providers based on having joint symptoms such as arthralgia, the association between ACPA and self-reported symptoms in an unselected population of at-risk FDR has not been well studied. Because it has been proposed that the ACPA themselves may induce joint symptoms in the absence of joint inflammation, we sought to determine whether baseline and longitudinal ACPA seropositivity is associated with self-reported symptoms and functional impairment in a large, unselected, cohort of at-risk Indigenous FDR of RA patients.

Methods: Baseline demographics, Health Assessment Questionnaire (HAQ), and arthritis symptom survey data were obtained from a cohort of 607 unaffected FDR of RA patients. Associations between ACPA status and the self-report variables were analyzed by chi-square test. We used logistic regression to identify variables that were independently associated with ACPA seropositivity. An ordinal longitudinal outcome measure was defined in 325 FDR with (1) ACPA seronegative, (2) ACPA seroconversion, (3) ACPA seropositive and (4) inflammatory arthritis assessed at their last visit.

Results: 51 (8.4%) individuals were ACPA seropositive at baseline.

Joint symptoms were not more prevalent in ACPA seropositive FDR. Interestingly, all of the HAQ responses were higher in seropositive individuals, with difficulty walking on flat ground (31.4% vs 18.5%, $P = 0.043$) being significantly higher in ACPA seropositive individuals. Logistic regression modelling confirmed that difficulty walking was independently associated with baseline ACPA seropositivity (OR 2.58, 1.36-4.89), after adjusting for age, sex and community (Urban vs Rural). In the longitudinal analysis, median follow up time was 61 (IQR 54) months. Joint symptoms were not more prevalent in longitudinal outcome groups. Baseline difficulty walking on flat ground was higher in persistent ACPA-seropositive (36.4% vs 16.0%, $P = 0.037$) and in those who developed inflammatory arthritis (26.3% vs 16.0%, $P = 0.40$) compared with persistent ACPA-negative individuals.

Conclusion: Self-reported functional disability is associated with longitudinal preclinical outcomes in an at-risk FDR cohort, suggesting that ACPA may induce joint symptoms in the absence of inflammation. Overall, these data provide evidence that functional disability, rather than joint symptoms, is representative of pre-clinical RA symptomatology and may provide important insights into individuals at the highest risk to develop synovitis.

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Trends in RA Symptoms, Functional Impacts, and Work Status Prior to and during Early Months of the COVID-19 Pandemic: Results from the Canadian Early Arthritis Cohort (CATCH)

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Objectives: The COVID-19 pandemic and associated public health mitigation strategies have resulted in major disruptions to the lives of Canadians. We examined trends in work, mental and physical symptom impacts including emotional distress, pain, disability, fatigue, sleep, and social participation in adults with RA enrolled in the Canadian Early Arthritis Cohort (CATCH) prior to and during the early months of COVID-19 pandemic.

Methods: Data were from RA patients enrolled in CATCH who had completed the PROMIS-29 health survey and the Work Productivity and Activity Impairment (WPAI) questionnaires electronically, by phone or by paper mail between January 1-June 30, 2020. Descriptive statistics were used to summarize changes in work and trends in physical symptom and mental health domains in the months immediately prior to- (Jan, Feb) and during the early implementation period of national and provincial COVID-19 mitigation strategies (March to June).

Results: Participants ($N = 468$) were mostly white (89%) women (70%) with a mean (SD) age of 60 (15) years. 47% of the sample who reported working in 2019 were still working in 2020; 4% had stopped and 8% had started working in 2020, with the remainder (41%) not working in either year. Of those who reported working, most (74%) indicated they worked full time in 2019 and 2020. Analyses of monthly temporal trends across PROMIS-29 domains showed that mental health and physical symptom impacts were most severe in the month of April 2020. As compared with January 2020, in April higher proportions of participants reported feeling anxious (28% vs 40%), depressed (18% vs. 34%), fatigued (22% vs. 40%), and having difficulty sleeping (18% vs. 34%). Moreover, higher proportions of CATCH patients reported moderate-severe depression (7% vs. 20%), pain (23% vs. 38%), and disability (21% vs 34%). By June, the proportion of patients reporting moderate-severe symptoms were similar to proportions reported in the pre-pandemic months for all domains except physical function, where 29% continued to report moderate-severe impairments.

Conclusion: The COVID-19 pandemic and associated restrictions appeared to have only had modest impacts on overall changes in work status. However, by April 2020, there were notable impacts on physical, emotional and social health of adults with RA and the proportion of individuals reporting moderate-severe functional impairments remained higher up to 4 months after the start of the pandemic.

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Increased Rates of Hospitalizations and Emergency Room Visits in Rheumatoid Arthritis After Interstitial Lung Disease Onset

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Objectives: Interstitial lung disease (ILD) in rheumatoid arthritis (RA) is associated with significant morbidity and mortality. We assessed the risk of hospitalizations and emergency room (ER) visits in RA patients with new-onset ILD using longitudinal administrative health data from the United States.

Methods: New-onset adult RA subjects were identified in the MarketScan Commercial Claims database (2011-2018) based on physician and/or hospitalization diagnostic claims. RA was defined as the presence of ≥ 2 physician and/or 1 hospitalization claim (ICD9 714; ICD10 M05, M06) in a 2-year period. Incident ILD after RA diagnosis was identified based on ≥ 2 claims at least 1 month apart (ICD9 515, 516.3, 714.8; ICD10 M05.1, J84.1). Subjects with ILD before the first RA diagnosis were excluded. Hospitalization and ER visit rates were assessed in RA patients with and without ILD. To avoid capturing events occurring related to ILD onset itself, hospitalizations and emergency visits occurring within 3 months before/after the first ILD diagnosis were excluded. RA-ILD patients could contribute person-time to the non-ILD group from RA onset up to 3 months before ILD diagnosis. Rate ratios (RR) for hospitalizations and emergency visits were assessed using multivariate Poisson regression models adjusted for age, sex, and chronic obstructive disease (COPD) diagnostic codes in the year before RA diagnosis.

Results: Among 297,896 new-onset RA subjects followed for an average of 2.3 (standard deviation 1.7) years, 4951 patients (1.7%) developed ILD (ILD incidence rate 7.0/1000 patient-years). The hospitalization rate (per 100 patient-years) in RA-ILD was 24.0 (95% confidence interval, CI 23.1-24.9) and 15.6 (95% CI 15.5-15.7) in RA without ILD. Adjusting for age, sex, and baseline COPD, the hospitalization rate was significantly higher in RA-ILD (RR 1.50, 95% CI 1.45-1.56). The rate (per 100 patient-years) of ER visits in RA-ILD was 104.4 (102.5-106.3) and 95.3 (95.1, 95.5) in RA without ILD, adjusted RR 1.07 (95% CI 1.05-1.09).

Conclusion: The hospitalization rate in RA-ILD was 50% higher than in RA without ILD. ER visit rates were also significantly higher in RA-ILD versus RA without ILD. This highlights the morbidity of RA-ILD; future work will examine potential risk factors associated with hospitalization risk in RA-ILD.

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How Stable are Medication Beliefs and Concerns in Early RA?

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Objectives: At RA onset, DMARDs are essential to control inflammation and prevent disability. In established RA, specific beliefs about DMARD necessity and concerns about harm influence side effects and adherence. To examine how medication perceptions evolve over time, we evaluated the stability of RA medication beliefs around diagnosis and identified predictors of change 12 months later.

Methods: Data were from ERA patients enrolled in the Canadian Early Arthritis Cohort (CATCH) March 2017 and January 2020 who completed the Beliefs about Medicines Questionnaire at 0 and 12 months. Necessity and Concerns scales each have 5 statements regarding the need for prescribed medication to control RA and concerns about potential harms of taking them. We used Pearson correlation and multivariable regression to examine associations and predictors of change at 12-months.

Results: The 362 participants were mostly women (66%), of white racial background (83%), with a mean (SD) age of 56 (15) years, and symptoms of 6 (3) months. Compared with baseline, at 12-months ($n = 180$), mean Necessity beliefs were slightly higher (18.1 vs. 18.9; $P = .01$) and Concerns were slightly lower (15.2 vs. 14.3; $P < .01$). At baseline, weak ($|r| = 0.13$ to 0.27 ; $P < .05$) associations were evident between Necessity beliefs and minority status, CDAI, MTX use, and all HRQL domains except sleep. At 12 months, sleep, depression, and pain were positively though weakly related (r 's 0.15 to 0.20; $P < .05$), and participation ($r = -0.17$; $P < .01$) was inversely and weakly related to Necessity beliefs. At baseline, worse CDAI ($r = 0.11$), symptoms and mood ($r = 0.18$ to 0.32), function ($r = -0.23$), and participation ($r = -0.19$) were associated with higher Concerns (all p 's $< .01$). These relationships were somewhat stronger at 12-months ($|r| = 0.23$ to 0.38 ; $P < .05$), except physical function was no longer associated with Concerns. In multivariable regression, when starting treatment Necessity scores were significantly lower in minorities and increased with CDAI, MTX, and fatigue but decreased as sleep improved. No relationships were evident at 12-months. Higher Concerns when starting treatment were predicted by higher education, depression, and anxiety. At 12-months, higher Concerns were predicted by minority status and MTX use, emotional distress, better function and lower participation.

Conclusion: Our data suggest that ERA patients view medicines as necessary, but also have significant levels of concerns. Medication perceptions appear to be reasonably stable over the first year and are influenced by individual characteristics and RA and medication experiences. Specific interventions may be needed to systematically influence medication beliefs and concerns to improve acceptance, tolerance, and long-term adherence.

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Efficacy of Long-term Treatment With Baricitinib 2 mg in Patients With Active Rheumatoid Arthritis

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Objectives: The short-term efficacy of baricitinib was demonstrated previously.[1,2] The objectives of this post-hoc analysis were to evaluate long-term efficacy of once-daily baricitinib 2 mg in patients with active rheumatoid arthritis (RA) who were inadequate responders (IR) to conventional synthetic disease-modifying antirheumatic drugs (csDMARD) or biologic DMARDs (bDMARD).

Methods: Data from patients in two 24-week, phase III studies, RA-BUILD (NCT01721057, csDMARD-IR) and RA-BEACON (NCT01721044, bDMARD-IR), and one long-term extension (LTE) study (RA-BEYOND, NCT01885078) were analyzed (120 total weeks); all patients had a diagnosis of adult-onset RA as defined by the American College of Rheumatology/European League Against Rheumatism 2010 Criteria for the Classification

of RA.[3] The main outcomes of this analysis were achievement of low-disease activity (LDA; Simple Disease Activity Index [SDAI] ≤ 11), clinical remission (SDAI ≤ 3.3), Health Assessment Questionnaire Disability Index ≤ 0.5 , and safety. Non-responder imputation (NRI) and completer analyses were conducted on the modified intention-to-treat (mITT) population, which included patients who were randomized to baricitinib 2 mg in the RA-BUILD and RA-BEACON studies and who had received ≥ 1 dose of the study drug after randomization.

Results: A total of 684 patients in RA-BUILD and 527 patients in RA-BEACON were randomized. In RA-BUILD, 229 patients were randomized to baricitinib 2 mg; 180 of whom completed the study and entered RA-BEYOND. In RA-BEACON, 174 patients were randomized to baricitinib 2 mg; 117 of whom completed the study and entered RA-BEYOND. At week 120, based on the mITT population with data up to rescue, 27.5% of csDMARD-IR and 18.4% of bDMARD-IR patients treated with baricitinib 2 mg were in SDAI LDA; 13.1% of csDMARD-IR and 5.2% of bDMARD-IR patients were in SDAI remission (NRI). At week 120, 20.1% of csDMARD-IR and 10.9% of bDMARD-IR patients treated with baricitinib 2 mg met or exceeded the population normative value for physical function (NRI). The completer analysis results are not shown. Rates of adverse events of special interest were consistent with previous reports.

Conclusion: Conclusion: This analysis supports the long-term treatment sustained efficacy and safety of baricitinib 2 mg for up to 120 weeks. References: [1.] Dougados M, van der Heijde D, Chen YC, et al. Ann Rheum Dis. 2017;76:88-95. [2.] Genovese MC, Kremer J, Zamani O, et al. N Engl J Med. 2016;374:1243-52. [3.] Aletaha D, Neogi T, Silman AJ, et al. Arthritis Rheum. 2010;Sep;62(9):2569-81.

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Baricitinib 2-mg Provides Greater Improvements in Patient-Reported Outcomes across All Disease Activity Levels Compared to Placebo: Post-hoc Analyses of RA-BEACON and RA-BUILD Trials

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Objectives: Baricitinib (BARI) improved patient-reported outcomes (PROs) in patients with insufficient response or intolerance to ≥ 1 tumor necrosis factor inhibitors (TNFi) or other biological disease-modifying antirheumatic drugs (bDMARDs) as well as in patients with inadequate response (IR) to conventional synthetic DMARDs (csDMARDs).[1,2] The purpose of this analysis was to determine if BARI 2-mg provided greater improvement in PROs vs. placebo (PBO), across all levels of disease activity.

Methods: Data for these post-hoc analyses were taken from two phase 3 studies, RA-BEACON (NCT01721044; bDMARD-IR patients) and RA-BUILD (NCT01721057; csDMARD-IR patients). PROs assessed included pain (0-100 mm visual analog scale), physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F]) and duration of morning joint stiffness (MJS, minutes). Disease activity was assessed with the Clinical Disease Activity Index (CDAI) and categorized as: remission (≤ 2.8), low disease activity (LDA; > 2.8 to ≤ 10), moderate disease activity (MDA; > 10 to ≤ 22), high disease activity (HDA; > 22). To evaluate extent of benefit in PROs with BARI across disease activity levels at Week 12 relative to PBO, we used linear regression to model the relationship between change in PROs (response), and CDAI values (primary explanatory variable). Two additional variables included were treatment group and the interaction term between treatment and CDAI.

Results: At 12 weeks in bDMARD-IR patients, BARI 2-mg demonstrated greater improvements in pain, physical function, fatigue and MJS across

all disease activity levels vs. PBO group (mean estimated changes in pain, HAQ-DI, FACIT-F and MJS duration [BARI/PBO]; CDAI = 2.8: -32.8/-27.6, -0.7/-0.5, 13.0/11.4, -77.6/-37.5; CDAI = 10: -27.5/-22.7, -0.6/-0.4, 11.6/9.9, -67.3/-33.7; CDAI = 22: -18.7/-14.7, -0.4/-0.3, 9.3/7.3, -50.0/-27.2, respectively). In csDMARD-IR patients, BARI 2-mg provided greater improvement in pain, HAQ-DI, fatigue and MJS) for patients who achieved disease control (remission or LDA) compared to PBO group (mean estimated changes in pain, HAQ-DI, FACIT-F and MJS duration [BARI/PBO]: -38.3/-28.0, -0.8/-0.5, 12.2/10.5, -85.7/-43.1, respectively). BARI 2-mg showed greater reduction in pain and MJS duration vs. PBO in patients with MDA (BARI/PBO: -32.0/-23.1 and -68.5/-32.0) or HDA (-21.6/-14.9 and -39.9/-13.6, respectively).

Conclusion: BARI 2-mg provided greater improvements in pain, physical function, fatigue and MJS duration across all levels of disease activity in bDMARD-IR patients and csDMARD-IR patients who achieved remission or LDA. Greater reduction in pain and MJS duration were also observed in csDMARD-IR patients with MDA or HDA at Week 12. References: [1.] Smolen et al. *Ann Rheum Dis*. 2017;76(4):694-700. [2.] Emery et al. *RMD Open*. 2017;3(1):e000410.

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More than Half of Newly Diagnosed RA Patients are not Convinced of the Necessity of RA Medicines: Associations With RA Characteristics, Symptoms, and Function in The Canadian Early Arthritis Cohort (CATCH) Viviane Ta (McGill University, Montreal); Orit Schieir (University of Toronto, Notre-Dame-de-Grace); Marie-France Valois (McGill University, Montreal); Glen Hazlewood (University of Calgary, Calgary); Carol Hitchon (University of Manitoba, Winnipeg); Louis Bessette (Laval University, Quebec City); Diane Tin (Southlake Regional Health Centre, Newmarket); Carter Thorne (Southlake Regional Health Centre, Newmarket); Janet Pope (University of Western Ontario, London); Gilles Boire (Université de Sherbrooke, Sherbrooke); Edward Keystone (University of Toronto, Toronto); Vivian Bykerk (The Hospital for Special Surgery, New York); Susan Bartlett (McGill University, Montreal); CATCH Canadian Early Arthritis Cohort (CATCH) Investigators (Toronto)

Objectives: Although DMARDs are essential for controlling RA to reduce symptoms and disability, medication adherence is variable. Beliefs about the necessity of medications and safety concerns predict adherence and are modifiable. Little is known RA medications perceptions in newly diagnosed ERA patients. We examined associations among necessity beliefs and concerns, sociodemographic, RA characteristics, symptoms and function in ERA patients around the time of diagnosis.

Methods: Baseline data were analyzed from participants in the Canadian Early Arthritis Cohort (CATCH) who enrolled between 2017-2020 and completed the Beliefs about Medicine Questionnaire (BMQ) and PROMIS-29. All met ACR1987 or 2010 ACR/EULAR criteria and had active RA at enrollment. BMQ Necessity (N) and Concerns (C) scores were classified as high (≥ 20) or low (< 20) and categorized into: Accepting ($\uparrow N \downarrow C$); Ambivalent ($\uparrow N \uparrow C$); Sceptical ($\downarrow N \uparrow C$); and 4) Indifferent ($\downarrow N \downarrow C$). Groups were compared using ANOVA and chi-square tests.

Results: The 362 patients were mostly white (83%) women (66%) with a mean (SD) age of 56 (15), symptom duration of 6 (3) months, and 32% were obese ($BMI \geq 30$). 56% were DMARD-naïve or minimally exposed. Mean N and C scores were similar between men and women; 54% were classified as Indifferent, 31% Accepting, 9% Ambivalent, and 6% Sceptical. As compared to those classified as Accepting, significantly ($p < .05$) more Indifferent participants smoked, had a healthy weight, lower TJC, and there was a trend for lower CDAI. Groups were similar by sociodemographic, symptom duration, and DMARD/steroid use, except fewer Indifferent patients received MTX. Most (67-100%) worried about the long-term effects of their medications. Indifferent patients had statistically ($P < .05$) and meaningfully lower patient global, depression, anxiety, fatigue and pain interference, and higher function and participation scores (0.8-8.0 points). Depression and anxiety were highest in Ambivalent and Sceptical patients. Patients who were ambivalent or sceptical about medications were

concerned about dependency and disruption, and unclear about their role in controlling inflammation.

Conclusion: Around the time of diagnosis, most new RA patients worried about the long-term safety of their RA medications, and many were not convinced of their necessity. Many had low medication necessity beliefs and concerns, and only 31% had high necessity beliefs and low concerns around diagnosis. Lifestyle and lower CDAI, TJC, symptoms and functional impacts were associated with RA medication indifference. Exploring medication beliefs in newly diagnosed RA patients may help identify information gaps and provide opportunities to address concerns, potentially improving adoption and persistence over time.

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Rheumatologists vs Primary Care Physicians: Who Should Be in Charge of Discussing Influenza/Pneumococcal Vaccines With Rheumatoid Arthritis Patients?

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Objectives: Patients with rheumatoid arthritis (RA) have increased morbidity and mortality due to vaccine-preventable diseases (e.g., influenza). Inactivated vaccines are recommended in these patients. However, influenza and pneumococcal vaccine coverage is suboptimal. Physician advice is the most important predictor of increase in vaccine uptake among RA patients. It is unclear if rheumatologists (RHs) or primary care physicians (PCPs) should take the lead on discussing vaccines with RA patients.

Methods: Four focus groups among healthcare professionals (HCPs) were conducted at a large Canadian teaching hospital between 2016 and 2018. PCPs involved in RA care, RHs, and rheumatology nurses and residents participated. Encounters were audio-taped, transcribed verbatim, imported into MAXQDA software, and thematically analyzed. Perceptions of the relevance of addressing vaccination in RA and who should undertake this task were grouped and subsequently assessed.

Results: Twenty-six HCPs participated in the study (rheumatology nurses $n = 5$, 19.2%; rheumatology residents $n = 8$, 30.8%; PCPs $n = 6$, 23.1%; RHs $n = 7$, 26.9%). Most were females (65%) with a mean \pm SD age of 44 ± 11.4 years. All HCPs recognized the importance of discussing vaccination with RA patients but disagreed on who should be in charge of this task. Thirteen HCPs (50%) believed vaccination should be addressed by RHs, five (19.2%) by PCPs, and 8 (30.8%) did not comment on the topic. All PCPs (5/5), most rheumatology nurses (3/5), rheumatology residents (3/4), and half of RHs (2/4) were among the HCPs who reported the discussion about vaccines should be initiated by the RH. Reasons to support this were inadequate communication between HCPs, PCP's lack of awareness/knowledge of certain vaccines, not having a PCP, the role of RHs in management of RA, and patients' confidence in RHs. Two RHs who indicated that PCPs should discuss vaccination stated that lack of time was a barrier for them to undertake this task.

Conclusion: HCPs acknowledge the importance of discussing vaccination with RA patients. Most of them believe RHs should take the lead in this task. Improving communication between HCPs and enhancing awareness/knowledge of PCPs on vaccines in RA patients may promote influenza vaccine uptake in this group. Supported by a CIORA grant.

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Vasculitis in Patients With Rheumatoid Arthritis: A Descriptive Study

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Objectives: Patients with rheumatoid arthritis (RA) may present with features of vasculitis that do not fit classically described RA vasculitis. ANCA-associated vasculitis (AAV) has been observed in seropositive and seronegative RA patients, sometimes many years after their initial RA diagnosis [1]. There are also observations of patients with RA who develop symptoms of large-vessel vasculitis [2]. Until now, these descriptions have been limited to case reports or case series [3]. We aimed to characterize the presentation of vasculitis in patients with RA to better understand patient phenotypes associated with Poly autoimmunity.

Methods: Retrospective chart reviews were conducted of patients identified as having a diagnosis of both RA and vasculitis between 2003-2018 from a single local rheumatology practice (NK). Demographics, date of diagnoses, vasculitis type and clinical features, comorbid conditions and investigations related to diagnoses were extracted. Descriptive statistics and frequencies were used to characterize the population.

Results: Of 26 patients identified with RA and vasculitis, 17 (65%) were female. Average age of RA diagnosis was $51.7 \text{ years} \pm 15.1$ and mean time to from RA diagnosis to vasculitis onset was $7 \text{ years} \pm 12.3$. Five patients (19%) had GPA, 3 (12%) had GCA, 7 (27%) had MPA, one (4%) had PAN, one (4%) had renal rheumatoid vasculitis, 7 (31%) had LCV, and one (4%) had urticarial vasculitis. Twelve patients (46%) were either PR3 or MPO positive. The majority of patients (65%) were RF positive and 27% were CCP positive. Twelve patients (46%) had documentation of erosive damage on imaging. All patients with LCV had either seropositive or erosive RA. Interestingly, of the 7 patients with MPA, 57% ($n = 4$) were also seropositive RA and 43% ($n = 3$) had erosive disease on imaging. Two GPA patients were rheumatoid factor positive, and none had erosions on imaging.

Conclusion: A variety of vasculitis subtypes were observed. Patients with LCV had seropositive erosive disease, consistent with classic rheumatoid vasculitis. The arthritis of AAV is usually non-erosive, suggesting there may be an overlap syndrome present in these seropositive RA/MPA patients. Patients diagnosed with RA prior to GPA may have been mischaracterized. Analyzing more patients through large RA databases will improve characterization of prevalence and clinical features of vasculitis in patients with RA.

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Cognitive Impairment in Systemic Lupus Erythematosus Is Negatively Related to Participation and Quality of Life: A Systematic Review

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Objectives: The primary objective(s) of this study are to systematically review and synthesize the quantitative evidence on the relationship of cognitive impairment (CI) to either Health Related Quality of Life (HRQoL) or social role participation (SRP) in individuals living with systemic lupus erythematosus (SLE). Secondary objectives are to 1) explore the cognitive, HRQoL and SRP domains and measures used in the literature, and 2) examine SLE characteristics, socio-demographics, and geographic regions represented in the included literature.

Methods: This systematic review was guided by a registered *a priori* search protocol, the taxonomy of the International Classification of Functioning, Disability and Health (ICF) for CI and SRP, and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Electronic databases were searched in December 2018 and June 2020 from inception using a comprehensive search strategy (e.g., $n = 82$ cognition terms) completed by a librarian/information-specialist. Two reviewers independently completed all screening, selection and data extraction; a third reviewer resolved disagreements. The Mixed Methods Appraisal Tool

(MMAT) was used to critically appraise the quality of included studies. Data was synthesized and analyzed descriptively.

Results: Of the 7182 references screened, 14 articles were included. These studies collectively included 3144 SLE patients, ranging from 9-67 years of age, with the proportion of female participants ranging from 73-100%. Four of the included articles investigated the relationship between CI and HRQoL and all found CI had a negative relationship with HRQoL. Ten studies investigated the relationship between CI and SRP; eight found a negative relationship. SRP was reflected in the literature as education ($n = 7$), academics ($n = 3$) and valued life activities ($n = 1$). Fifty-three cognitive assessment tools, three HRQoL measures, and seven SRP measures were used across all studies. Due to the heterogeneity of measures used in the literature, results could not be pooled for meta-analysis.

Conclusion: The presence of CI is negatively associated with HRQoL and SRP in patients with SLE, and results indicate this relationship is an important area of SLE care to address. As only 14 studies were found, there is a need for more studies examining the associations between CI to HRQoL and SRP in individuals with SLE. This is especially necessary for studies that explore important life areas beyond that of academics or employment. Further research with consistent measures for CI, HRQoL, and SRP are needed to enable pooling of data and to allow for identification of effective methods to addressing this in SLE care.

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ANCA in Systemic Lupus Erythematosus: Prevalence and Clinical Implications

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Objectives: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease notable for its effect on nearly every tissue, association with a breadth of auto-antibodies. Anti-neutrophilic cytoplasmic antibodies (ANCA) are strongly associated with small-vessel vasculitis but their role in SLE is less clear. Our goal is to determine whether serum ANCA have clinical implications.

Methods: We included all SLE patients with at least two ANCA tests in the Lupus Clinic, between August 1979 and November 2019. Patients with 2 consecutive ANCA (both C and P ANCA) were considered exposed. Controls were never ANCA positive. Index date was time of the second ANCA. Vasculitis was defined by the SLEDAI-2K: ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, and biopsy/angiogram. Descriptive statistics were used to show patients' characteristics. Kaplan-Meier survival curves were plotted for outcomes of first vasculitis. Weibull parametric survival regression evaluated the effects of ANCA positivity on the outcome of vasculitis, adjusting for confounders.

Results: Of the 1426 patients tested for ANCAs on two occasions, 1091 (77%) had never tested positive, 145 (10%) patients tested positive twice and 190 (13%) patients tested positive once. Those that tested positive twice or more included 92 with only p-ANCA, 24 with only c-ANCA, and 29 with both. Median time between first and second ANCA was 12 months. Patients with either single ANCA positivity (either C or P) were largely similar to those with dual ANCA positivity. Kaplan-Meier survival curves show significantly higher cumulative index of vasculitis in the 145 patients with any ANCA positive compared to none ($P = 0.0491$). Survival regression models revealed that two or more p-ANCA positive (vs. ANCA negative patients) predicted the outcome of vasculitis after adjusting for SLEDAI-2K and prednisone treatment at index date (HR 1.78, 95% CI: 1.15-2.79) in the best fit multivariable model, while two or more c-ANCA positive did not reach significance in the other regression model. Looking into the nature of vasculitis, the proportion of patients with vasculitis within each of the ANCA subgroups were similar (p-ANCA 20.1%, c-ANCA 16.7%, mixed ANCA 20.7%), but only the p-ANCA group was significantly higher than those with no ANCA positivity (12.4%) partially due to small numbers.

Conclusion: In our cohort, approximately 10% of SLE patents have persistent ANCA positivity, predominantly p-ANCA. The presence of p-ANCA was associated with significantly more vasculitis, predominantly skin vasculitis.

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Longitudinal Relationships Between Cognitive Domains and Mood and Anxiety Symptoms in SLE

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Objectives: There is a consistent relationship between cognition and depression and anxiety in lupus. Together, mood, anxiety and cognitive symptoms represent among SLE's most common and disabling neuropsychiatric symptoms. Although the relationship between cognitive and mood symptoms is well established, less is known about i) which cognitive domains are most related to mood and anxiety symptoms, and ii) the longitudinal relationship between cognitive and mood and anxiety symptoms. The objectives of this study are to i) examine the relationship between neuropsychological performance across various domains and affective symptoms over time, and ii) investigate the overlap between classification of cognitive dysfunction and anxiety and depression in a well-characterized cohort of patients with SLE.

Methods: Data from a cohort of 301 patients with SLE were analyzed. Cognition was measured using a modified version of the ACR neuropsychological battery, and cognitive dysfunction was defined as z-scores ≤ -1.5 on two or more cognitive domains. Depression and anxiety were measured using the Beck Depression Inventory-II and the Beck Anxiety Inventory. Participants were classified as having depression if they scored greater than 17 on the BDI-II and anxiety if they scored greater than 18 on the BAI. All measures were performed at baseline, 6 month and 12 months. Data were analyzed using Multiple Factor Analysis.

Results: Anxiety and depression scores and neuropsychological performance were highly stable across time. Principal component analysis identified two dimensions that explained 42.2% of the variance in neuropsychological performance. The first dimension (33.1% of the variance) included primarily complex cognitive tests measuring executive function, verbal and visual memory, working memory and complex processing speed. The second dimension (9.1% of the variable) was primarily explained by measures of simple information processing speed or motor dexterity. Anxiety and depression scores were related to the first cognitive dimension in a stable manner across the three assessments, particularly to tests of verbal, visual and working memory. There was substantial overlap in participants classified as having cognitive dysfunction and anxiety and depression.

Conclusion: Depression and anxiety symptoms in SLE patients are related to a cognitive dimension incorporating memory, executive function and complex processing speed in a stable manner across one year, and many patients with cognitive dysfunction exhibit clinically significant anxiety and depression across time. Further clinical research should examine whether and to what extent cognition improves when anxiety and depression are treated, as well as the mechanistic links between anxiety and depression and CD in SLE.

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Validity and Reliability of Patient Reported Outcomes Measurement Information System Computerized Adaptive Tests in Systemic Lupus Erythematosus

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Objectives: The evaluation of Patient Reported Outcomes Measurement Information System (PROMIS) computerized adaptive test (CAT) in adults with systemic lupus erythematosus (SLE) is an emerging field of research. We aimed to examine the test-retest reliability and construct validity of the PROMIS CAT in a Canadian cohort of patients with SLE.

Methods: All consecutive adult (≥ 18 years old) with Lupus visiting a Canadian Lupus Clinic between July 2018-January 2020 were approached complete PROMIS CAT and 7 legacy instruments. Test-retest reliability of PROMIS was evaluated 7-10 days from baseline using intraclass correlation coefficient (ICC [2;1]). The construct validity of the PROMIS CAT domains was evaluated against the commonly used legacy instruments, and also in comparison to disease activity and disease damage using Spearman correlations. Time to completion of instruments were measured. A multi-trait-multimethod matrix (MMM) approach was used to further assess construct validity comparing selected 10 domains of PROMIS and SF-36 domains. Six a priori hypotheses were created to explore the relationships between select 10 PROMIS-CAT domains with corresponding SF-36 domains with at least a moderate correlation ($r > 0.3$): PROMIS-CAT Physical Function with SF-36 Physical Function and Role Physical. PROMIS-CAT Pain Behavior and Pain Interference with SF36 Bodily Pain. PROMIS-CAT Anger, Anxiety, and Depression with SF-36 Emotional Health scores. PROMIS-CAT Ability to Participate in Social Roles and Satisfaction with SF-36 Social Roles. PROMIS-CAT Fatigue with SF-36 Vitality. PROMIS-CAT Depression, Anxiety, Anger with SF-36 Mental Health.

Results: Of the 227 participants in the cohort, 90.3% were female, mean age at study enrolment was 48.6 ± 14.1 years, and mean disease duration was 18.5 ± 12.4 years. Moderate to excellent reliability was found for all domains [ICC [2;1] ranging from lowest, 0.66 for Sleep Disturbance and highest, 0.93 for the Mobility domain]. Comparing 7 legacy instruments with 14 domains of PROMIS CAT, moderate to strong correlations (0.51-0.91) were identified. The 14 domains of PROMIS CAT took approximately 11 minutes less to complete than the legacy instruments needed to assess the same domains, without the time needed for individualized grading. The MMM further established construct validity by showing moderate to strong correlations (0.55-0.87) between select PROMIS and SF-36 domains; the average convergent correlations were significantly greater than the average divergent correlations and all six a priori hypotheses were satisfied.

Conclusion: These results provide evidence on the reliability and validity of PROMIS CAT in SLE in a Canadian cohort.

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Serum Albumin as an Early Predictor of Proteinuria Recovery in Lupus Nephritis

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Objectives: Studies in lupus nephritis (LN) have shown proteinuria at 12 months is the best predictor of long-term renal outcomes, although recovery time often extends beyond 2 years. Our aim was to determine if serum albumin can serve as predictor of complete (CPR) and partial proteinuria recovery (PPR) in LN patients receiving standard treatment.

Methods: We studied all patients with follow-up visits at 6-9 and 18-21 months diagnosed with LN based on 24-hour urine proteinuria > 0.5 g/24 hours or a spot UPCr > 0.5 g/g associated with a prednisone start of ≥ 10 mg or escalation of ≥ 5 mg. CPR was defined as UPCr < 0.5 g/g. PPR was defined as UPCr < 1.0 g/g (if baseline ≤ 3.0 g/g) or UPCr ≤ 3.0 g/g (if baseline PCR > 3.0 g/g) by Rovin [LUNAR] criteria. We compared this to SLEDAI-2K which defines CPR as proteinuria < 0.5g/24 hours and SLEDAI-2K Responder Index-50 which defines PPR as a $\geq 50\%$ decrease in proteinuria from baseline. Complete recovery of serum albumin was defined as ≥ 35 g/L from baseline < 30 g/L, with partial recovery defined as ≥ 30 g/L but < 35 g/L from baseline < 30 g/L. ROC curves were generated to test if serum albumin is a predictor of combined proteinuria recovery endpoint (PPR+CPR as defined by Rovin criteria) at 6-9 and 18-21 months. AUC was analyzed for (a) albumin at baseline (b) absolute change from baseline to follow-up, and (c) percent change between baseline to follow-up.

Results: 161 patients with 6-9-month visits (83.9% female) were identified. Mean age and duration of lupus at the start of the study was 34.7 ± 12.6 and 5.2 ± 5.6 years. At 6-9-month visit, 22% of patients achieved PPR and 42% of patients achieved CPR (64% combined). Of 161 patients, 31 (19.3%) had baseline albumin < 30 g/L. Of 94 patients with an 18-21-month visit, 17% achieved PPR and 54% achieved CPR (71% combined). ROC curves showed albumin absolute change (AUC = 0.75) and percent change (AUC = 0.75) from baseline to 6-9 months predicted 6-9-month proteinuria recovery. Similarly, albumin absolute change (AUC = 0.78) and percent change (AUC = 0.78) from baseline to 18-21 months predicted proteinuria recovery at 18-21 months.

Conclusion: Absolute and percent change in albumin from baseline to 6-9 and to 18-21 months is a good predictor of proteinuria recovery and may serve as a readily accessible adjunct to proteinuria in LN response assessments.

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Optimal Initial Prednisone Dose for Remission Induction in Lupus Nephritis: A Propensity Score Matched Analysis

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Objectives: The existing ACR and EULAR guidelines for remission induction in lupus nephritis (LN) recommend initial prednisone doses of 0.3-1 mg/kg/day. However, recent observational studies reported non-inferior outcomes with significantly lower doses. The aim of this study was to compare the complete renal response rates in LN patients treated initially with ≤ 30 mg/day or ≥ 40 mg/day of prednisone.

Methods: Patients with new-onset LN and standard immunosuppressive treatment with azathioprine or mycophenolate mofetil or cyclophosphamide (Euro-lupus protocol) were followed for at least 12 months. Subjects were divided into medium (≤ 30 mg/day) and high prednisone groups (≥ 40 mg/day) and propensity score-matched based on demographic, clinical and laboratory variables as well as global and renal disease activity. Complete renal response was defined as proteinuria < 0.5 g/day and no worsening in renal function (serum creatinine $\leq 120\%$ from baseline). Glucocorticoid-related damage was also assessed.

Results: Two hundred and thirty-six patients (118 in each group) were included. Baseline characteristics were well-balanced between groups except Black patients' predominance in the high prednisone group (25.4% vs. 15.3%, $P = 0.04$) and higher frequency of LN class V in the medium dose group (35.6% vs. 22.9%, $P = 0.036$). Median prednisone doses were

45 mg/day and 20 mg/day for the high and medium dose groups respectively. Complete renal response rate at 12 months was higher in the high-dose group [57.6% vs. 37.1%, $P = 0.003$]. Similar findings were observed at two [75% vs. 40.3%, $P = 0.0002$] and three years [67.2% vs. 51.7%, $P = 0.144$] after LN diagnosis. High dose prednisone achieved better rates of complete response in both non-proliferative [69.2% vs. 15.4%, $P = 0.02$] and proliferative LN [57.6% vs. 37.4%, $P = 0.127$]. Patients in the high dose group received less cumulative glucocorticoids during the 2nd (5.2 ± 4 g vs. 6.6 ± 4 g, $P = 0.034$) and 3rd year (2.7 ± 2.3 g vs. 4.1 ± 3 g, $P = 0.008$). Glucocorticoid-related damage (new cataract, osteoporosis, osteonecrosis, diabetes) was not significantly different between groups at 12 (3.4% vs. 8.5% for the high and low-dose group respectively), 24 (10% vs. 16.7%) and 36 months (16.9% vs. 26.2%).

Conclusion: Higher initial prednisone doses (median 45mg/day) achieved significantly better rates of complete renal response at 12 and 24 months in new-onset LN. These patients received less cumulative glucocorticoids in the 2nd and 3rd year and did not accrue more glucocorticoid-related damage. Our findings suggest that the treatment of LN with initially high doses of prednisone leads to improved rates of renal response that, in turn, allows for faster glucocorticoid tapering compared to patients who were treated with lower doses.

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Gradual Glucocorticoid Withdrawal Is Safe in Clinically Quiescent Systemic Lupus Erythematosus

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Objectives: Systemic lupus erythematosus (SLE) patients are usually treated with glucocorticoids even during periods of clinically quiescent disease. A recent small randomized controlled trial showed that abrupt glucocorticoid withdrawal was associated with increased likelihood of flare in the next 12 months. The aim of the present study was to assess clinical flare rates and damage accrual in patients who tapered glucocorticoids gradually.

Methods: Lupus patients with two consecutive years of clinically quiescent disease were retrieved from our long-term longitudinal cohort. Individuals who maintained a low prednisone dose (5 mg/day) comprised the maintenance group whereas patients who tapered prednisone within these two years comprised the withdrawal group. Glucocorticoid tapering was monitored closely and occurred in 9-18 months after the first dose reduction. Patients were matched according to propensity score considering demographic, clinical, serological and therapeutic variables. All individuals were followed for two years after discontinuation (or corresponding date for the maintenance group). Outcomes included clinical flares (any increase in clinical SLEDAI-2K, any increase ≥ 4 and any increase in clinical SLEDAI-2K plus escalation in systemic therapy (glucocorticoids and/or antimalarials and/or immunosuppressives) as well as damage accrual.

Results: 204 patients (102 matched pairs) were included. Demographic, clinical, serological and therapeutic characteristics were all well-balanced between groups. Patients in the withdrawal group developed significantly less flares by any applied definition at 24 months compared to the maintenance group [33.3% vs. 50%, $P = 0.01$ for any clinical SLEDAI-2K increase, 12.7% vs. 26.5%, $P = 0.013$ for any increase ≥ 4 in clinical SLEDAI-2K and 14.7% vs. 27.5%, $P = 0.024$ for any flare with treatment escalation]. At 12 months, the withdrawal group also experienced less moderate-to-severe flares (requiring treatment escalation), although insignificantly. Regarding damage, less withdrawal patients accrued new damage at 24 months [6.9% vs. 17.6%, $P = 0.022$]. The difference in damage accrual was mostly glucocorticoid-related [2.9% vs. 11.8%, $P = 0.02$], while there was no significant difference concerning the non-glucocorticoid related damage [3.9% vs. 6.9%, $P = 0.317$].

Conclusion: Gradual glucocorticoid withdrawal was associated with significantly less clinical flares at 24 months compared to propensity score matched patients who maintained prednisone. Global and glucocorticoid-related

damage accrual was significantly less in the withdrawal patients. Gradual glucocorticoid withdrawal is safe in clinically quiescent SLE and should be attempted to reduce further damage.

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Efficacy of Biological Agents for the Management of Systemic Lupus Erythematosus: A Systematic Review and Network Meta-Analysis

Sierra Mendelsohn (University College Dublin, Dublin); Zaira Gonzalez (Western University, London); Juan Martinez (University Health Network, Toronto); Alfred Kim (Washington University School of Medicine, St Louis); Melanie Anderson (University Health Network Library Services, Toronto General 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: Biological agents may provide an efficacious and better tolerated therapy for Systemic Lupus Erythematosus (SLE) than current standard of care. However, only one agent, belimumab, has been approved for clinical use. The objective of this study is to systematically review the literature investigating biologics for SLE.

Methods: This systematic review and network meta-analysis (NMA) used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Comprehensive searches in three databases (Medline, Embase, Cochrane Central) were conducted to identify phase II and III RCTs in adults (≥ 16 years) with SLE, excluding lupus nephritis. Two reviewers independently screened references and full texts for inclusion on Covidence. Data was extracted using an excel form, and the Cochrane risk-of-bias tool (RoB 2) was used to appraise the risk of bias of RCTs. A Bayesian generalized linear hierarchical model was used in this NMA with binomial likelihood and logit link.

Results: A total of 5146 titles and abstracts were screened, 188 were retained and reviewed in detail, and 26 RCTs were included for the final analysis. All included RCTs had a low risk of bias based on the RoB 2. Twenty of the RCTs provided SLE Responder Index (SRI) outcome data reported as a primary outcome, secondary outcome, or post-hoc analysis. These 20 RCTs investigated the following biologics: belimumab, anifrolumab, ustekinumab, atacicept, baricitinib, blisibimod, epratuzumab, IL-2, lupuzor, PF-04236921, rontalizumab, sifalimumab, and tabalumab. Pooling for NMA indicated that belimumab [OR, 1.6; 95% CI, 1.1 to 2.4], anifrolumab [OR, 1.6; 95% CI, 1.0 to 2.7] and ustekinumab [OR, 3.5; 95% CI, 1.2 to 10.0] have greater odds of achieving SRI when compared to placebo. There was no evidence that other biologics were better than placebo. When compared to belimumab, anifrolumab [OR, 1.0; 95% CI, 0.57 to 1.9] and atacicept [OR, 1.0; 95% CI, 0.40 to 2.5] performed similarly; baricitinib, IL-2, PF-04236921, and ustekinumab trended towards greater odds of achieving SRI, except in all cases the confidence interval overlapped with one.

Conclusion: The NMA identified that belimumab, anifrolumab and ustekinumab demonstrated greater response in comparison to placebo, when measured using SRI. This systematic review identified that there was heterogeneity in the outcome measures and endpoints used. In the future, the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach will be applied to rate the quality of the evidence, and to gain insight into methodological pitfalls that could have negatively altered the results of RCTs.

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Identifying Cognitive Impairment in Patients With Systemic Lupus Erythematosus Using Bayesian Statistical Learning

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Mahta Kakvan (Toronto Western Hospital, Toronto); Nicole Anderson (Toronto Western Hospital, Toronto); Dennisse Bonilla (Toronto Western Research Institute, Toronto); May Choi (University of Calgary, Calgary); Marvin Fritzler (University of Calgary, Calgary); Dorcas Beaton (University of Toronto/Institute for Work and Health, Toronto); Patricia Katz (University of California San Francisco, 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 (CI) is usually operationalized on the American College of Rheumatology Neuropsychological Battery (ACR-NB) using a binary classification which may miss participants who have CI but score just below the cut-off. We explored continuous z-scores, instead of the binary approach of the ACR-NB, to facilitate the interpretability of the results. We aimed to classify patients using Hidden Markov Models (HMM) on existing data over time.

Methods: 301 consecutive SLE adult patients aged 18-65 years attending a single center were assessed for CI at baseline using the ACR-NB and 187 patients completed visits at 6 and 12 months. ACR-NB includes 19 tests and 6 cognitive domains. Age and gender matched normative data were used to obtain z-scores. Step 1: reduces the high-dimensional aspect of the ACR-NB tests using principal component analysis (PCA) to create a single component score which explains the most variance (1 dimension). Step 2: builds a 2-state and 3-state cognitive status based on a discrete-time HMM with the dimensionality reduction gained in step 1, adjusting this score by educational level and ethnicity. The HMM assumes that the change of the component score over time in patients with SLE can be segmented into distinct cognitive states, where each state captures if a patient is CI or not at time t, using the component score obtained at each time point. We used leave-one-out cross validation (loo-cv) to compare the resulting 2 and 3-state HMM. All the statistical learning was done from a Bayesian perspective.

Results: PCA identified 2 dimensions: The 1st (33.1% of the variance) included primarily complex cognitive tests and the 2nd (9.1% of the variable) was primarily explained by measures of simple information processing speed or motor dexterity. HMM analysis: The 3-state HMM showed a better predictive performance than the 2-state HMM, based on posterior predictive checks and loo-cv. A patient will be classified into one of these 3 states depending on their component scores, being negative scores associated with the most impaired state found in our analysis. We found higher education level associates with an increase mean component score. We also found that patients did not transition between these CI states over time.

Conclusion: This is the first framework which aimed to classify patients with SLE as CI or not using a semi-supervised method. This approach relies on the observed z-scores from the 19 tests on the ACR-NB and not on the binary classification.

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Is the Montreal Cognitive Assessment (MoCA) a Suitable Screening Tool for Assessing Cognitive Impairment in Patients With Systemic Lupus Erythematosus (SLE) Compared to the American College of Rheumatology Neuropsychological Battery (ACR-NB)?

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Toronto); 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: To determine whether the Montreal Cognitive Assessment (MoCA) is a suitable screening tool for assessing cognitive impairment (CI) in patients with systemic lupus erythematosus (SLE) compared to the American College of Rheumatology Neuropsychological Battery (ACR-NB).

Methods: Between January 2016 and July 2019, 300 patients with SLE completed the MoCA and ACR-NB on the same day. Patients with MoCA scores < 26 were considered CI. Based on ACR-NB, CI was defined as z-score ≤ -1.5 in \geq two cognitive domains. Area under curve (AUC) was calculated to assess the performance of the MoCA for detecting CI compared to ACR-NB. To further study the construct validity of the MoCA, two principal component analyses (PCA) were completed: the first PCA included 19 ACR-NB tests and MoCA total score; the second PCA included 19 ACR-NB tests and 7 MoCA domains (visual-spatial/executive, naming, attention, language, abstraction, delayed recall, and orientation). The purpose of the PCAs were to investigate the variance of CI explained by the MoCA (total score and domains), and to determine which factors MoCA and ACR-NB tests would load onto. Factors in the PCAs were retained if they had an Eigenvalue ≥ 1 . ACR-NB and MoCA loadings onto factors ≥ 0.35 were considered associated with that factor. Higher loadings (values closer to 1) indicate stronger associations.

Results: MoCA could not accurately predict CI with an AUC of 0.68 (95% confidence interval: 0.62-0.74). The first PCA retained six factors accounting for 67% total variance, with the most important factor accounting for 27% variance. Trails A, Stroop Colour, Stroop Word, Digit Symbol and Trails B from ACR-NB loaded onto the most important factor. MoCA total score had weak factor loadings on the first two factors but loaded onto factors 3 (37%) and 6 (44%) which accounted for 15% variance cumulatively. The second PCA retained 8 factors. MoCA Delayed Recall loaded 67% onto Factor 1 which accounted for 21% variance, with Hopkins Verbal Learning Test-Revised delayed recall, recognition, total recall, and Consonant Trigrams from ACR-NB. MoCA naming, abstraction, and orientation loaded onto factors 7 and 8 (8% variance cumulatively) but had nothing in common with ACR-NB tests.

Conclusion: Our findings do not support the use of the MoCA as a screening tool in this patient population. Selected MoCA domains may be better suited for screening in SLE rather than the total score. Further research will determine whether a new weighted scoring system can improve the performance of the MoCA in this patient population. Best Abstract on Clinical or Epidemiology Research By A Trainee - Phil Rosen Award.

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Systemic Lupus Erythematosus-related Intestinal Pseudo-obstruction (SLE-IPO): Case Report and Review of the Literature of a Rare and Potentially Fatal Complication

Julia Tan (University of British Columbia, Vancouver); Gary Xu (University of British Columbia, Vancouver); John Esdaile (University of British Columbia (Division of Rheumatology)/Arthritis Research Canada, Richmond) Introduction:

SLE-IPO is a rare, sometimes fatal complication of SLE, with less than 250 reported English cases.

Case: A 65-year-old male with SLE (oral ulceration, Raynaud's, pericarditis, interstitial lung disease (ILD), lymphopenia, and Coomb's hemolytic anemia) for 10 years was referred for diarrhea. He had positive ANA (1:1280), anti-RNP, anti-SSA, anti-SSB, dsDNA, ASMA, and low C3 (0.57) and C4 (0.09). He was receiving hydroxychloroquine and azathioprine.

In January 2020, he presented with diarrhea, malnutrition, and worsening ILD. Esophagogastroduodenoscopy, colonoscopy, and infectious workup were unremarkable. He was treated for small intestinal bacterial overgrowth. Prednisone 40mg taper was used to treat his ILD and azathioprine was switched to mycophenolate (2 gm/d). GI symptoms also improved.

In May 2020, he had a recurrence of GI symptoms, including emesis and 10kg weight loss. CT abdomen and pelvis revealed findings consistent with SLE-IPO. Infectious and metabolic workup was negative. He received IV methylprednisolone 1g for 3 days, and his GI symptoms resolved almost immediately. He was discharged on prednisone taper from 40 mg/d and mycophenolate.

Discussion: SLE-IPO, first described in 1993, is a late and severe complication of SLE. Patients commonly complain of abdominal pain and distension, nausea/vomiting, and weight loss. No specific autoantibodies are associated with SLE-IPO. CT typically demonstrates dilated bowel loops with air-fluid levels and bowel wall thickening, without an obstructing lesion in 60% of patients. Diagnosis is based on high clinical suspicion, concordant radiology and the exclusion of infection. However, misdiagnosis is common (54.1% in some studies) mainly due to non-specific symptoms. SLE-IPO responds robustly to systemic corticosteroids, which have been used as initial therapy in > 95% of the cases. Immunosuppressive agents, including cyclophosphamide, azathioprine, cyclosporin, and tacrolimus, have also been used as combination therapy in the majority of cases. Parenteral nutrition, prokinetic agents, and antibiotics may increase symptom resolution. Treatment should be started promptly as efficacy may decrease as atrophy and fibrosis progress. Both misdiagnosis and delayed treatment increase complications. Early series reported mortality up to 27.8%. With the increased availability of CT and recognition of SLE-IPO, recent reviews report a 6.7% mortality. SLE-IPO is a dangerous complication of SLE, which should be considered in SLE patients with signs of bowel obstruction. CT imaging should be performed to distinguish IPO from true obstruction. Laboratory, microbiological and endoscopic investigations will exclude other possible etiologies. Rapid institution of treatment is often lifesaving.

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External Validation of the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) as a Predictor of Mortality and Organ Damage Accrual in Systemic Lupus Erythematosus

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Objectives: The Systemic Lupus International Collaborating Clinics (SLICC) frailty index (FI) is a measure of susceptibility to adverse health outcomes among individuals with SLE. In the SLICC inception cohort, higher baseline SLICC-FI values were associated with increased risk of organ damage, hospitalizations, and mortality during follow-up. The current study aimed to externally validate the SLICC-FI in a prevalent cohort of individuals with established SLE.

Methods: This was a secondary analysis of data from a prospective cohort of adult SLE patients at a single academic medical centre. All participants met the revised ACR classification criteria for SLE and were assessed annually for medication use, comorbidities, disease activity [SLE Disease Activity Index 2000 (SLEDAI-2K)], organ damage [SLICC/ACR Damage Index (SDI)], health-related quality of life [Short-Form 36 (SF-36)], and other measures. For this analysis, the baseline visit was defined as the first visit at which both SDI and SF-36 data were available. To adapt the SLICC-FI for use in this dataset, the original definitions of some health deficits were modified. We calculated a baseline SLICC-FI score for each patient. Vital status and SDI score at last follow-up were recorded. Cox regression models estimated the association between baseline SLICC-FI values and mortality risk. Negative binomial regression models estimated the association of baseline SLICC-FI values with the rate of change in SDI scores per patient-year of follow-up. Multivariable models adjusted for relevant baseline characteristics.

Results: The 329 eligible SLE patients (96% of cohort) were mostly female (88%) with mean (SD) age 43.9 (14.4) years and median (IQR) disease duration 3.4 (1.2-13.3) years at baseline. Mean (SD) baseline SLICC-FI score was 0.17 (0.08), with 94 patients (28.6%) classified as frail (SLICC-FI > 0.21). Forty deaths occurred during mean (SD) follow-up of 10 (5.5) years. Mortality risk was significantly higher among frail individuals [Hazard Ratio (HR) 4.01; 95% CI 2.13-7.54]. Higher baseline SLICC-FI

values (per 0.05 units) were associated with increased mortality risk (HR 1.42; 95% CI 1.14-1.78), after adjusting for age, sex, education, medication use (corticosteroids, antimalarials, immunosuppressives), disease duration, smoking status, and baseline SLICC-FI score. Higher baseline SLICC-FI values (per 0.05 units) were also associated with increased organ damage accrual during follow-up (Incidence Rate Ratio 1.19; 95% CI 1.09-1.31), after adjusting for potential confounders.

Conclusion: Frailty, measured using the SLICC-FI, predicts organ damage accrual and mortality risk among individuals with established SLE. This external validation study provides additional support for the SLICC-FI as a useful prognostic tool in SLE.

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Systemic Lupus Erythematosus and Systemic Sclerosis Overlap With Paroxysmal Nocturnal Hemoglobinuria: A Case Report and Review of the Literature

Maria Powell (University of Calgary, Calgary); May Choi (University of Calgary, Calgary); Susan Barr (University of Calgary, Calgary); Marvin Fritztler (University of Calgary, Calgary)

Background: We describe a 75-year-old White female who was initially diagnosed with systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) overlap syndrome complicated by severe cytopenias, later confirmed to be secondary to paroxysmal nocturnal hemoglobinuria (PNH). In addition to the hematologic abnormalities, she met the 2019 ACR/EULAR classification criteria for SLE based on a positive ANA (1:640) on HEp-2 cells, inflammatory arthritis, and serositis, and the 2013 ACR/EULAR classification criteria for scleroderma based on sclerodactyly, Raynaud's phenomenon, abnormal capillary nailfolds, telangiectasias, pulmonary hypertension, high positive anti-CENP-A/B antibodies, and non-criteria manifestations of SSc including gastrointestinal reflux disease (GERD) and dysphagia.

Case: Her cytopenias consisted of direct antiglobulin test (DAT) negative hemolytic anemia (hemoglobin 80 g/dL), thrombocytopenia (platelet count 80×10^3), leukopenia (neutropenia with white blood cell count 3.0×10^3). She was started on prednisone and hydroxychloroquine for treatment of her suspected overlap syndrome. However, worsening cytopenias prompted further workup and revealed a PNH clone on flow cytometric analysis. Granulocyte clone measured 71.34%, monocyte clone measured 72.58%, and erythrocyte type 2 clone measured 0.79% and type 3 clone measured 14.53%. Bone marrow aspirate and biopsy showed a normocellular bone marrow with no morphologic evidence of myelodysplasia or aplastic anemia and normal cytogenetics. She was also noted to have hematuria without evidence red blood cells (RBCs) on urine microscopy. There was no clinical evidence of thrombosis. Eculizumab treatment was initiated for her PNH and her cytopenias improved.

Conclusion: PNH is a rare, acquired disease associated with hemolytic anemia, bone marrow failure, and thrombosis. It is caused by a mutation in phosphatidylinositol glycan A (PIGA) gene leading to deficiency in glycosyl phosphatidylinositol (GPI)-anchored proteins CD55 and CD59 predisposing to complement-mediated hemolysis. To our knowledge this is the first case report of PNH associated with SLE and SSc overlap. There are two case reports of PNH and scleroderma in the same patient; one case of PNH and localized scleroderma in a young woman and one report of an elderly male with aplastic anemia and scleroderma who later developed PNH. There are two case reports of PNH developing in patients with known SLE; one presenting with thrombosis and the other with DAT negative hemolytic anemia.

These cases and our patient highlight the need to consider a broad differential diagnosis, especially when a patient with features of overlapping conditions develops unexplained anemia and hematuria. Future studies are needed to better understand a potential link between PNH and autoimmune diseases.

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Pulmonary Arterial Hypertension in Systemic Sclerosis Is Nearly Always Accompanied by a Low Diffusing Capacity

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Objectives: Scleroderma (systemic sclerosis; SSc) has high morbidity and mortality. Pulmonary hypertension (PH) and pulmonary arterial hypertension (PAH) is common with a high mortality [1]. SSc patients are screened with pulmonary function tests (diffusing capacity of the lung for carbon monoxide; DLCO) [2]. Our objective was to analyze the DLCO% predicted and compare patients with and without PAH to determine if it is always low at time of PAH diagnosis.

Methods: The Canadian Scleroderma Research Group (CSRG) database was used containing more than 1300 SSc patients with a mean disease duration of 8 years. All patients over 18 years of age, with a confirmed diagnosis of SSc, and DLCO recorded at least twice were eligible for enrolment into this nested case control study. Diagnosis of PH was verified using several algorithms within the database including right heart catheterization, use of PH medications and physician response of 'yes' to question has this patient been diagnosed with pulmonary hypertension. Sensitivity, specificity and positive (PPV) and negative predictive values (NPV) were calculated for DLCO% predicted < 50% and presence of PH/PAH. Continuous variables were expressed with means \pm standard deviation. P-waves < 0.05 were considered statistically significant.

Results: At time of PH diagnosis, the mean DLCO% predicted was 47% (N = 30) vs no PH 73% (N = 960) $P < 0.0001$, and proven documented PAH also showed the differences (PAH, N = 22 DLCO% predicted 51% vs. PAH negative (N = 968) DLCO% pred 72%, $P < 0.0001$). The OR of a DLCO% predicted less than 60 was 4.7 for PAH and 7.6 for PH (both $P < 0.001$) and even higher if DLCO < 50% (OR 11.5 for PH and 7.6 for PAH). In those with PH, DLCO > 80% conferred a positive predictive value (PPV) of 0.3% compared to those with DLCO < 50% with PPV of 13.2%. In those with PAH, DLCO > 80% was PPV of 0.3% and DLCO < 50% correlated with PPV of 8.3%. In addition, the PH groups with DLCO < 50% and DLCO < 60% had negative predictive values at 98.7% and 98.9%, respectively.

Conclusion: A low DLCO is associated with a high odds of PH/PAH in SSc and the NPV is very high at both DLCO < 50% predicted and < 60% predicted. This may aid in determining who should receive a right heart catheterization in SSc patients.

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The Fecal Microbiome Differences Between Patients With Systemic Sclerosis With And Without Small Intestinal Bacterial Overgrowth

Daniel Levin (McMaster University, St. Catharines); Maggie Larche (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Giada De Palma (McMaster University, Hamilton); Elena Verdu (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Barbara Baker (McMaster University, Hamilton); Premysl Bercik (McMaster University, Hamilton)

Objectives: Gastrointestinal manifestations of systemic sclerosis (SSc) affect up to 90% of patients, with symptoms including diarrhea and malnutrition. Small intestinal bacterial overgrowth (SIBO) is a condition associated with increased numbers of pathogenic bacteria in the small bowel and is often found in patients with SSc. While currently unknown, it is suggested that dysregulation of the fecal microbiota may lead to the development of SSc and SIBO. Our study aimed to describe the fecal microbiota of patients with SSc and compare it between those with and without a diagnosis of SIBO. We also compared the fecal microbiota of SSc patients to healthy controls to understand the association between particular bacterial taxa and clinical manifestations of SSc.

Methods: 29 patients with SSc underwent breath testing to assess for SIBO, provided stool samples to determine taxonomic assignments and completed the UCLA Scleroderma Clinical Trial Consortium GIT 2.0 which details symptoms and quality of life factors. Stool samples were compared between SSc patients with and without SIBO, and between patients with SSc and a healthy cohort (HC, n = 20), aged 18-80 years.

Results: Fecal microbiome analyses demonstrated differences between SSc patients with and without SIBO and differences in the diversity of species between HCs and patients with SSc. Trends were also observed in Anticentromere Antibody (ACA+) SSc patients, including higher *Alistipes indistinctus* spp. levels associated with increased methane levels at breath gas testing, and higher *Slakia* spp. levels associated with increased rates of fecal soiling.

Conclusion: Our results suggest that changes to the fecal microbiome occur in patients with SIBO and SSc when compared to HCs. As a cross-sectional study, the potential role of an altered microbiome on the development of SSc pathophysiology was not considered and needs to be further investigated. Best Abstract By A Medical Student.

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Diagnosis of Pulmonary Hypertension Preceding the Confirmation of Early Systemic Sclerosis: A Case Report

Shahna Tariq (University of Alberta, Edmonton); Jan Tervaert (University of Alberta, Edmonton); Mohammed Osman (University of Alberta, Edmonton)

Case: A 45-year-old female was referred for evaluation of a 3-year history of Raynaud's phenomenon on a background of familial cardiomyopathy, a recent pulmonary embolism (> 1 month prior to the assessment), and pulmonary hypertension on echocardiogram (RVSP > 70 mm Hg with preserved biventricular function). Nailfold video capillaroscopy (NVC) revealed enlarged capillaries (approximately 2.6 capillaries/digit 30-50 microns in apical diameter, and 2.3 capillaries/digit > 50 microns in apical diameter) and microhemorrhages (approximately 1.3/digit) consistent with an early systemic sclerosis (SSc) pattern. Serological assessment revealed a positive ANA (homogeneous pattern) with no SSc-specific autoantibodies, nor other markers associated with other connective tissue diseases (e.g., hypocomplementemia, anti-phospholipid antibodies, or a positive Coombs test). Right heart catheterization revealed elevated mean pulmonary artery pressures (37 mm Hg) elevated pulmonary vascular resistance (11.1 Wood units) and elevated right ventricular systolic pressure (70 mm Hg) with normal right atrial and pulmonary capillary wedge pressure (6- and 4-mm Hg, respectively) - confirming the presence of pulmonary arterial hypertension. An extensive malignancy work-up was non-contributory.

Discussion: Abnormal nailfold capillaries are associated with vascular involvement in connective tissue diseases and are increasingly being used in the diagnosis and management of systemic sclerosis. Our case demonstrates the utility of NVC in the assessment of pulmonary hypertension in patients without an established connective tissue disease - particularly early on in their disease course. Although PAH is often a complication of longstanding SSc, studies employing NVC as a risk stratification tool in patients with connective tissue disease and suspected PAH maybe important in its early diagnosis.

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A Review of PAH Screening Practices of Patients in the Canadian Scleroderma Research Group Registry: Is It Time to Revise the Guidelines?

Curtis Sobchak (McMaster University, Hamilton); Sandeep Dhillon (McMaster University, Hamilton); Jessica Kapralik (McMaster University, Hamilton); Nader Khalidi (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Nathan Hambly (McMaster University, Hamilton); Gerard Cox (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: Pulmonary arterial hypertension (PAH) affects approximately 10% of patients with systemic sclerosis (SSc) and is associated with a high mortality despite available therapies. Screening is important to facilitate early diagnosis and early intervention has been shown to improve long-term outcomes. The general availability and non-invasive nature of echocardiography make it a feasible option for PAH screening, with guidelines

recommending an annual echocardiogram. Using data from the Canadian Scleroderma Research Group (CSRG) database, we determined the proportion of SSc patients who underwent annual echocardiograms for PAH screening.

Methods: Data was obtained from the CSRG, a national longitudinal registry of SSc patients > 18 years old. We included patients irrespective of underlying comorbidities, and with a minimum of three visits (baseline plus ≥ 2 follow-ups). We considered a patient to have an annual echocardiogram if the echocardiogram was performed within 18-months of the baseline and follow-up visits throughout the entire duration of follow-up. We characterized the study population at baseline (sex, ethnicity, age at diagnosis, tobacco use, years with SSc prior to first CSRG visit, antibody profile (anti-centromere, anti SCL-70, anti-RNA polymerase III) and comorbidities (diabetes, rheumatoid arthritis, peripheral vascular disease) and compared characteristics between those who did versus did not undergo annual echocardiograms throughout the study duration. We determined the proportion of patients who underwent annual echocardiography for 2-, 5-, and 10-years.

Results: Of 1698 patients in the CSRG, 1223 (72.0%) patients had ≥ 3 registry visits. Of these patients, 360 (29.4%) underwent echocardiography annually for the entire duration of their follow-up. Sex, ethnicity, age at diagnosis, tobacco use, years with SSc prior to first visit, antibody profile and prevalence of comorbidities were similar between those who did versus did not have annual echocardiograms. Of those followed for ≥ 2 years, 61.7% had annual echocardiograms. Of those in the registry for ≥ 5 -years, 38.0% had annual echocardiograms and 6.7% of those in the registry for ≥ 10 -years had annual echocardiograms.

Conclusion: This study demonstrated that approximately 30% of SSc patients underwent annual PAH screening throughout the entire CSRG follow-up and suggests that, as patients are followed for a longer duration, fewer patients undergo annual screening. Study limitations include annual echocardiograms not being recorded in the CSRG database and changed practices based on CSRG data suggesting that annual echocardiograms may not be appropriate. Investigating disease progression and incidence of PAH in this population is the next step to understanding for whom annual screening may be appropriate.

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Placental Fibrin Deposition and Thrombosis Leading to Intrauterine Growth Restriction: A Case Report of a Young Woman With Eosinophilic Fasciitis

Milica Tanic (McMaster University, Hamilton); Karen Beattie (McMaster University, Hamilton); Maggie Larche (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Jorge Arredondo (Hamilton Health Sciences and McMaster University, Hamilton); Samih Salama (McMaster University and St. Joseph's Healthcare Hamilton, Hamilton)

Background: Eosinophilic fasciitis (EF) is an autoimmune disease closely related to Systemic Sclerosis (SSc). It causes inflammatory fibrosis characterised by skin edema/induration, inflammatory arthritis and joint contractures. In contrast to SSc, EF typically does not involve internal organs.

Case: We present a 32-year-old female who developed a right upper extremity indurated area over nearly one year which progressively spread to areas including thighs and buttocks over several months. The area became hyperpigmented, thickened and painful on sun exposure. There were no features suggesting connective tissue disease including no Raynaud's, skin tightness, dilated nailfold capillaries, digital or oral ulcers.

Skin biopsy within a few months of presentation revealed fibroadipose tissue with focal chronic inflammation. Repeat biopsy showed abundant mucin deposition in the superficial and deep dermis with sparse lymphocytic infiltrate suggestive, but not diagnostic, of SSc. There were no eosinophils in the tissue and no clinical features of SSc. Anti-nuclear antibodies were negative, C-reactive protein and erythrocyte sedimentation rate were normal. Magnetic resonance imaging demonstrated dermal thickening associated with subcutaneous stranding and fascial and muscle edema. A third biopsy including fascia showed prominent inflammatory infiltrate

and fibrosis/thickening of dermis collagen consistent with a diagnosis of EF. Treatment with prednisone and mycophenolate induced clinical remission. After 15-months she gave birth to her 4th child. Pregnancy was complicated by fetal intrauterine growth restriction (IUGR); placental biopsy showed extensive fibrin deposition of the placental parenchyma and intervillous thrombi.

This case suggests that EF, like many other autoimmune diseases, may confer increased risk for adverse pregnancy outcomes. Patients with SSc, a disease similar to EF, are at increased risk for pre-eclampsia and IUGR. A study of 3 women with SSc revealed severe placental fibrosis and strong immunohistochemical positivity for vascular endothelial growth factor compared to healthy controls. They also described chorionic villous infarcts, similar to thrombotic disease seen in our patient. Interestingly, placental fibrosis, a feature described in SSc, is common in pre-eclampsia, a hypertensive/vascular disorder of pregnancy.

Conclusion: As suggested by this case, visceral fibrosis may occur occultly during pregnancy in EF. Furthermore, pathological overlap between pre-eclampsia and EF/SSc suggests that EF may affect placental vasculature. Finally, placental fibrinoid deposition and thrombosis, as seen in our patient, may warrant therapies like anticoagulation, immunosuppression or elective early delivery. This has clear implications for pre-conception counselling and obstetrical risks management in patients with EF.

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A Rare Case of Systemic Sclerosis and ANCA Associated Vasculitis Overlap

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Background: Although 10% of patients with systemic sclerosis (SSc) have positive antineutrophilic antibody (ANCA) serology, association with ANCA associated vasculitis (AAV) is exceptionally rare. We present a case of fever of unknown origin (FUO) in a SSc patient on maintained on Rituximab who is ultimately diagnosed with biopsyproven AAV.

Case: 56-year-old male with 10-year history of diffuse SSc (Scl-70 positive) manifested by generalized scleroderma, Raynaud's phenomenon with ulceration, gastric reflux, usual interstitial pneumonia, and secondary Sjogren's Syndrome presented to hospital with a 1-month history of fevers, abdominal pain, and productive cough. His SSc was stable on Rituximab 1g twice a year (last dose was 5 months before symptom onset). This patient had failed multiple courses of outpatient antibiotics and was admitted to hospital with fever, WBC > 20, and CRP 236. Intensive infection workup including bacterial, fungal, mycobacterial culture, EBV, CMV viral load, and serology for rare infections such as Coxiella, strongyloides were unremarkable. Chest CT was unchanged from baseline, echocardiogram was normal, and CT abdomen initially demonstrated non-specific colonic enteritis, but colonoscopy was unremarkable. After weeks in hospital, the patient's fevers spontaneously remitted, and his WBC and CRP improved. He was discharged with potential viral etiology as cause of FUO.

Unfortunately, the patient quickly represented to hospital with recurrent fevers. Work up revealed an elevated creatinine of 164 mmol/L (previously 105 mmol/L) and a new active urine sediment with red blood cells. Blood work was significant for an elevated anti-myeloperoxidase (MPO) antibody of 511 U/mL by ELISA, and a normal CD19 count of $0.14 \times 10^9/L$. Renal biopsy confirmed crescentic pauci-immune glomerulonephritis. The patient was thus diagnosed with SSc-ANCA overlap and treated with high-dose glucocorticoids and IV cyclophosphamide. He clinically improved and was discharged.

Conclusion: SSc-ANCA overlap is rare, affecting 0.2-0.4% of SSc patients in the previous literature. Typically, these patients are Scl-70 positive,

MPO positive, and have limited SSc (79-88%). Glomerulonephritis is the most common organ involved. Diagnosis of SSc-ANCA overlap can be challenging since vasculitis manifestations such as digital ischemia and renal failure can be misattributed to SSc. Further confounding our case, the patient was already treated with Rituximab, the maintenance agent of choice in AAV. Positive ANCA serology is fairly common in SSc (10%); however, physicians should be vigilant for features of AAV.

Conclusion: We describe a rare case of biopsy-proven SSc-AAV overlap. This case is highly atypical given our patient was on maintenance therapy with Rituximab.

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Interim Analysis: Validation of the GCA Probability Score (GCAPS) in a Canadian Population

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Objectives: The diagnosis of giant cell arteritis (GCA) can be challenging and may lead to excessive invasive temporal artery biopsies (TAB) and high-dose corticosteroids. In up to 76% of cases, management is unchanged following TAB and up to 85% of patients experience corticosteroid associated side effects. The GCA probability score (GCAPS) may improve and complement clinical decision making. GCAPS was developed in the United Kingdom and is the first risk stratification tool validated against ultrasound and TAB. Based on clinical variables, GCAPS has a cut-off of 9.5 out of a possible score of 32 with a sensitivity of 95.7% and specificity of 86.7%, which could help avoid unnecessary interventions in low-risk patients. This is the first study to assess and validate GCAPS in a Canadian population.

Methods: Patients aged ≥ 50 with a clinical suspicion of GCA and at least one of the following were included: c-reactive protein (CRP) ≥ 5 mg/L, new-onset headache, jaw claudication, fever, pain and/or stiffness in the hips and/or shoulders, temporal artery tenderness, or recent visual impairment. Patients were excluded if they had a previous diagnosis of GCA, were taking over 10 mg of glucocorticoids for more than 4 weeks prior to ultrasound, had TAB performed prior to ultrasound or were unable to provide informed consent. Participants were prospectively enrolled from a single centre in Vancouver, British Columbia. Data including demographics, signs and symptoms suggestive of GCA, glucocorticoid use, DMARD use, inflammatory markers, ultrasound, CTA, MRI, and TAB was collected.

Results: We present preliminary data from our study. Of the 73 patients recruited, GCAPS variables associated with low-risk of GCA were the following: age < 65 (13.7%), male gender (38.4%), symptom onset > 6 weeks (37%), no headache (28.8%), no polymyalgia rheumatica symptoms (58.9%), ≤ 1 constitutional symptom (89.0%), no ischemic symptoms (38.4%), no visual signs (86.3%), no cranial nerve palsy (98.6%), temporal and large artery score of 0 (83.6% and 94.5% respectively), CRP < 25 mg/L (42.5%), and the presence of an alternative diagnosis (1.4%). In our data set, 28.8% did not demonstrate any vasculitic changes on ultrasound and 64.4% had a negative TAB. Using clinical diagnosis at 6 months as the GCA diagnostic gold standard, we will calculate the sensitivity and specificity for various GCAPS cut-offs using area under the receiver operating characteristic curve.

Conclusion: This study will help clarify whether GCAPS is a feasible tool to aid standard clinical decision making in low risk GCA cases in the Canadian population.

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Cervical Ulceration Caused by Granulomatosis With Polyangiitis: A Case Report and Review of the Literature

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Background: Granulomatosis with polyangiitis (GPA) is an antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis characterized by necrotizing granulomatous inflammation of small and medium sized vessels, most commonly affecting the upper respiratory tract, lungs, and kidneys. Involvement of the cervix is rare in GPA, with only twelve reported cases. We present a patient with a cervical ulcer found to be caused by GPA on biopsy.

Case: Our patient is a 31-year-old female with an initial diagnosis of seropositive rheumatoid arthritis in 2016, previously treated with hydroxychloroquine and methotrexate and maintained on sulfasalazine monotherapy. In the fall of 2019 she presented with sinusitis, nodular scleritis, migratory polyarthritis and tenosynovitis, papular elbow lesions, petechial rash, and dyspnea associated with transient ground glass opacities on CT chest. Investigations revealed persistent low-grade hematuria and ANCA-Proteinase 3 antibody titre > 8, resulting in a diagnosis of GPA. She was treated with prednisone and rituximab (March 3rd and 19th). She presented with vaginal bleeding on March 9th, 2020 and cervical ulcer biopsy performed on April 29th, 2020 showed areas of geographic necrosis, vasculitis comprised of eosinophils and nuclear debris in the walls of medium-sized blood vessels with a significant eosinophilic infiltrate consistent with GPA. Azathioprine was added in August 2020 with improvement of her cervical ulcer seen on examination in September 2020.

Conclusion: Twelve cases of cervical involvement in GPA have been reported. The differential diagnosis includes malignancy, infections, sarcoidosis and other vasculitides including isolated vasculitis of the female genital tract, giant cell arteritis, and Behcet's disease. In this case, histology ruled out malignancy and infectious screening was negative. Clinical data favored GPA over other vasculitides. Of the previously reported cases, five had cervical involvement at initial presentation. Two patients were receiving azathioprine at the time of presentation. Five cases had no other organ involvement when they developed cervical inflammation. Six patients were treated with cyclophosphamide and prednisone - four had resolution of symptoms, one was lost to follow up, and one died shortly after initiation of therapy. Other successful therapies included azathioprine [1] and methotrexate and prednisone [1]. One patient failed treatment with methotrexate but responded to rituximab and prednisone. One patient died of an unknown cause prior to treatment, and two patients did not have treatment response clearly described.

Conclusion: We report a case of biopsy-proven cervical ulceration caused by GPA treated with prednisone, rituximab and azathioprine.

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Comparison of Two Rituximab Regimens for Induction of Remission in Antineutrophil Cytoplasmic Antibody-associated Vasculitis: Systematic Review and Meta-analysis

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Objectives: Recommended induction therapies for severe antineutrophil cytoplasmic antibody-associated vasculitis (AAV), granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), include cyclophosphamide or rituximab (RTX). Two RTX regimens are available: the 4-dose AAV regimen at doses of 375 mg/m² I.V. weekly, and the 2-dose rheumatoid arthritis (RA) regimen at doses of 1000 mg I.V. on day 1 and 15. Although the AAV regimen is the most extensively studied, many clinicians use the RA regimen to reduce infusion frequency, dose, and cost. No clinical trial directly compares these two regimens. The objective of this meta-analysis was to compare the efficacy and safety of these two RTX regimens for the induction of remission in severe AAV.

Methods: A systematic review was performed to identify studies using the AAV and/or RA rituximab regimens for remission induction in severe AAV. Patients were excluded if they received concomitant cyclophosphamide or plasma exchange. The primary endpoint was the proportion of patients in complete remission at 6 months, defined as a BVAS of 0 and/or as the absence of disease activity on clinical assessment. The pooled estimate was obtained using meta-analysis methods for proportions with random effects. Secondary endpoints included ANCA status, B cell depletion, mean prednisone dose, infections, and death.

Results: Out of the 3619 studies identified, 27 met inclusion criteria: 1 RCT, 4 prospective cohorts, 9 retrospective cohorts and 13 case series. A total of 506 patients were included for analysis: 361 treated with the AAV regimen and 145 with the RA regimen. Mean age was 50 years, 52% were women, and 86% were ANCA-positive. Relapsing disease at inclusion accounted for 83% and 92% of patients in the AAV and the RA regimen group, respectively. Overall, complete remission at 6 months was achieved in 88 % (95% CI: 78-95) of patients. There was no significant difference between the AAV and RA regimens, complete remission reaching respectively 85% (95% CI: 70-96) and 91% (95% CI: 79-99). Results remained consistent after the exclusion of low-quality studies. At 6 months, mean prednisone dose was 8.1 mg and comparable in both groups. Both regimens led to a similar proportion of patients with infections (12% in both) and death (1% vs. 0%), respectively, at 6 months, with insufficient data to conclude on other secondary endpoints.

Conclusion: No difference was found in terms of efficacy and safety between the 4-dose AAV and the 2-dose RA rituximab regimens for induction of remission in severe AAV.

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