**1**

**Long Term Originator Infliximab Treatment is Predictive of Retention in Stable Rheumatic Disease Patients in Canada**

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**Objectives:** To evaluate long-term retention patterns of stable rheumatic disease (RD) patients treated with REMICADE® (infliximab [IFX]).

**Methods:** Using IMS Brogan's™ database of private and public insurance claims data, our analysis included RD patients with: (1) first IFX claim between Jan 2008-May 2015; (2) no IFX claims 12 months prior to the initial claim; (3) ≥1 claim for any other drug 12 months after the initial IFX claim; and (4) ≥1 claim for any non-IFX drug 4 months after May 2015. Retention was measured at 12-month intervals and unadjusted odds ratios calculated at the 95% confidence interval within and between cohorts of RD patients. Within-group analysis compared 12 month retention by number of years on IFX. Analyses considered cohorts of patients according to age, gender, insurance type, and previous biologic experience.

**Results:** A total of 1,672 had ≥2 years of claims history and had been on IFX for ≥1year. Within-group comparisons showed that a patient's probability of being retained on IFX in subsequent 12-month periods increased concurrently with elapsed time on IFX. Patients on IFX for 2, 3, 4 and 5 years showed significantly higher retention in the subsequent year compared to patients on IFX for only 1 year ($P < 0.05$). Similar trends were observed for females, in the 19-64 age range, within naïve and experienced cohorts, and by those patients with private insurance coverage. Retention at 12-month intervals up to and including 5 years was significantly better at each interval for biologic-naïve vs experienced patients and public insurance vs private insurance patients in the between-group analyses.

**Conclusion:** Real world patients treated with IFX have excellent long-term treatment retention. Longer time on IFX appears to predict better future retention, becoming statistically significant after 2 years. The results were robust and consistent amongst various subgroups of stable Canadian rheumatology patients.

**2**

**Methotrexate Use in Patients: Self-Reported Coping Mechanisms**

Dawn Richards (Canadian Arthritis Patient Alliance, Toronto); Laurie Proulx (Canadian Arthritis Patient Alliance, Ottawa); Linda Wilhelm (Canadian Arthritis Patient Alliance, Midland); Nathalie Robertson (Canadian Arthritis Patient Alliance, Ottawa); Annette McKinnon (Canadian Arthritis Patient Alliance, Toronto); Janet Gunderson (Canadian Arthritis Patient Alliance, Glaslyn); Don Mohoruk (Canadian Arthritis Patient Alliance, Coquitlam)

**Objectives:** Methotrexate is one of the first medications prescribed to manage inflammatory and other types of arthritis. This key medication is used with non-biologics or biologics. As people who live with arthritis, we know firsthand that many people have difficulties tolerating methotrexate, so do not use it as prescribed and may not benefit maximally from it. We asked people how they cope with taking their methotrexate so that we can build and share resources based on this information.

**Methods:** CAPA drove this project with financial and in-kind support from many arthritis stakeholders. One Board member acted as project manager to construct an online survey. Methods to achieve input and feedback for the draft survey included phone calls and emails. Feedback was gathered from patients (members of the CAPA Board) and the survey was reviewed by a rheumatologist. Once finalized and agreed to, the survey was translated in to

French. Subsequent distribution and promotion of the bilingual survey were achieved through CAPA's efforts (email blast to membership, social media promotion on Twitter and Facebook) and with stakeholders' help via online dissemination tools (and included efforts of other patient organizations, individual patients, and the Arthritis Society).
**Results:** At the time of submission, over 250 respondents (88% female, 12% male) had participated in the online survey. Approximately 80% of responses were from Canada and most responses were from people living with rheumatoid arthritis. Nearly 50% of survey respondents indicated that they "do not like taking methotrexate, but it helps me manage my arthritis." The most popular methods to tolerate methotrexate include switching from the pill form to an injectable form, taking methotrexate right before bed, and taking folic acid. Nearly 80% of respondents answered that they have not talked to their physician or pharmacist about finding the most appropriate solution for them with respect to taking methotrexate. An extensive analysis of the results will be presented.
**Conclusion:** Using an online survey, CAPA learned from people living with arthritis about how they cope with taking methotrexate, a seminal medication used in the treatment of arthritis. The survey responses will be used to inform resources that are medically reviewed about managing to take methotrexate. Through sharing information from other patients, we hope that this will encourage others to try these tips or to have an honest conversation with their doctor or pharmacist to help them find their own most appropriate solutions. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**3**

**The Objective Gap: A Survey of Patient and Health Care Professionals' Priorities for Inflammatory Arthritis Treatment**

Ed Ziesmann (The Arthritis Society (Ontario Division), Toronto); Ahmad Zbib (The Arthritis Society, Toronto); Douglas Emerson (The Arthritis Society, Toronto)

**Objectives:** More than one million Canadians live with inflammatory arthritis (IA). An online survey was provided to health care professionals (HCPs) and patients with IA across Canada to identify priorities in terms of treatment outcomes.
**Methods:** Participants were surveyed online and asked a series of questions about the objectives for treatment and whether they felt that various aspects of coping with arthritis were adequately addressed in the clinical setting.
**Results:** 235 patients and 108 HCPs responded to the survey. Patients and HCPs agreed that the impact of arthritis on the mind, family and the social and economic aspects of arthritis were not addressed well in clinical practice. Patients perceived that their physicians' priorities were to limit the effect of the condition on their body (52%) and enable them to live an independent life (27%). Physicians perceived that their patients' priorities were similar, 32% and 54% respectively. Patients were more likely than HCPs to identify pain relief as a priority following initiation of a biologic (39% and 15% respectively). HCPs were more likely than patients to prioritize getting on with a normal life (52% and 29% respectively) and reducing joint inflammation (24% and 8% respectively).
**Conclusion:** Results suggest that patients and HCPs view the goals for care quite differently. People with IA are also looking for more support than the traditional clinical appointment is structured to provide. Further studies are needed that address the gap between how HCPs treating IA measure the progress of treatment, and how patients experience their disease. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**4**

**Development of Guidelines for Radiographically-Guided Intra-Articular Steroid Injections in a Community Rheumatology Group Practice**

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**Objectives:** Radiographically guided steroid injections are procedures often requested by community-practicing Rheumatologists. The purpose of this study was to develop and establish a set of guidelines to determine the conditions in which radiographically-guided injections would be most beneficial for patients when compared to clinically-guided injections.

**Methods:** All patients referred from a community-based Rheumatology clinic in Brampton for radiographically guided injections at Brampton Civic Hospital between January – December 2014 were identified. A subset of this group consisting of patients who had shoulder and knee injections was further sub-analyzed. The patients' charts were retrospectively reviewed for data on gender, age, body mass index (BMI), diagnosis, injection history, injection location(s), type of steroid used, and dose of each injection. Follow-up data relating to the injection (patient status, improvements and complications following injection), as well as duration between re-injections were collected. For patients who had radiographically-guided shoulder and knee injections, data was also collected on prior medications, steroid injections to the joint and outcomes before radiographically-guided steroid injection.

**Results:** A total of 118 patients had 134 injections. Patients tolerated the injections well with approximately 67% noting a benefit. Actual pain scores were recorded in <10% of patients and duration of benefit was quantified in 16% of patients. There was no significant difference between the different joints injected. Hip and shoulder joints that were injected with 80mg Depomedrol had a significantly higher chance of improvement compared with lower doses ($P<0.05$). In the case of shoulder and knee injections which derived no benefit from clinically-guided injections, 54% had benefit when injected with radiographic guidance.

**Conclusion:** Based on the above data, a preliminary set of quality improvement guidelines were developed for the group of clinicians that participated. 1. Standardize chart documentation to indicate the level of pain in the joint both pre and post-injection, the percentage of improvement in the injected joint and the duration of reported improvement. 2. Refer patients for radiographically guided injections if the 1st clinically injection of the knee or shoulder failed. 3. Refer patients for radiographically guided injections if the joint is difficult to access (hip, sacro-iliac joint, or facet joints,) or the joint is complex/ damaged . 4. Refer patients to radiology for aspiration of fluid from complex and deep joints. 5. Discuss among peer group the proper techniques and approaches for both basic and complex joint injections. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**5**

**A Needs-based Rheumatologist Education Program on Treating to Target in Psoriatic Arthritis and Spondylarthropathy: Insights, Challenges, and Future Directions**

Janet Pope (Western University, London); Linda Wang (Western University, London); Paul Tingey (Queensland University, Ipswich); Angela Montgomery (Mississauga); Arthur Karasik (Toronto); Pauline Boulos (Dundas); Vandana Ahluwalia (William Osler Health System, Ontario Rheumatology Association, Brampton); Maggie Larche (McMaster University, St Joseph's Healthcare Hamilton, Hamilton); Sara Haig (Western University, London); Nikhil Chopra

(London); Gina Rohekar (University of Western Ontario, London); Sherry Rohekar (Western University, London)

**Objectives:** To determine if comparative practice data and education for rheumatologists would change physician behavior for monitoring and treating psoriatic arthritis (PsA) and spondyloarthritis (SpA).

**Methods:** Participating rheumatologists each performed a chart audit on 20 patients with PsA and SpA. Accredited education (determined by a survey and chart audits) and results of chart audits (comparing to other rheumatologists) were provided for each participant (intervention). Eight months later, a repeat chart audit by each participant was conducted on another 20 PsA and SpA patients. Changes in measurements collected, treatment given and patient characteristics pre and post intervention were analyzed.

**Results:** Nine rheumatologists received the intervention. At baseline, most routinely monitored PsA and SpA for clinical and laboratory markers. In PsA, there was no change post-intervention in performing SJC (96%), TJC (>91%), ESR (>70%), CRP (>73%), and CDAI (25%). In SpA, there were increased measurement of inflammatory markers (54% pre vs. 61% post for CRP), more NSAID use and decreased physical exam measures and HAQ but no significant changes. There were no major treatment differences pre and post intervention including NSAIDs, DMARDs and biologics.

**Conclusion:** The rheumatologists frequently performed measurements of disease activity, did not change significantly with educational intervention so there may have been little room for improvement and many patients were already in a low disease state. Calculation of composite scores did not increase in PsA. The validity of physical exam and BASDAI as a measurement of disease activity were noted as concerns in applying a treat-to-target approach in SpA. Supported by a CIORA grant. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**6**

**Evaluation of Patient Satisfaction with the On-TRAAC Clinic; Benefits of a Joint Approach**

Janet Roberts (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton); Joanne Homik (University of Alberta, Edmonton); Walter Maksymowych (University of Alberta, Edmonton); Jill Hall (University of Alberta, Edmonton); Kathy Cotton (Alberta Health Services, Edmonton); Rashmi Mandhane (Alberta Health Services, Edmonton); Edna Hutchings (CaRE Arthritis, Edmonton); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton)

**Objectives:** The University of Alberta Division of Rheumatology has launched a new multidisciplinary clinic, the On-TRAAC Program (On Treating Rheumatoid Arthritis – Providing Access to Care), providing aggressive T2T disease modification and co-morbidity management in a shared-care model of rheumatologists and advanced care practitioners (ACP). Primary Objective: To evaluate patient satisfaction in patients enrolled in the On-TRAAC program compared to those treated in general rheumatology clinics through a patient satisfaction survey. Secondary Objective: To evaluate measures of disease activity over time in the ON-TRAAC group.

**Methods:** Methods: We performed an observational cross-sectional survey study using a modified version of the Leeds Satisfaction Questionnaire (mLSQ), a validated and reliable tool developed for inflammatory arthritis (IA) outpatient clinics, to compare satisfaction between the two patient groups: On-TRAAC and the traditional model of care (TMC). The questionnaire's

subscales include: provision of information, empathy with the patient, attitude towards the patient, communication, technical competence and overall satisfaction. A sub-group analysis of patient satisfaction over time in the On-TRAAC group was also performed. Markers of disease activity including DAS 28-CRP, HAQ (Health Assessment Questionnaire) and CRP were assessed over time in the ON-TRAAC group.
**Results:** Results: A total of 82 patients completed the survey (34 patients in the On-TRAAC group and 48 in the TMC). The average age of the participants was 53 years and included 27 males and 55 females. The overall satisfaction score was 4.36 in the TMC group and 4.46 in the On-TRAAC group (higher values represents higher satisfaction). Twenty-seven patients in the On-TRAAC group performed the survey at least twice and showed improved satisfaction on subsequent visits with an initial overall satisfaction score of 4.43 and follow up score of 4.53. No statistically significant differences were noted between groups, or within the On-TRAAC group. Within the On-TRAAC group, markers of disease activity including DAS 28 CRP, HAQ and CRP all showed improvement between baseline and follow-up visits.
**Conclusion:** While patients in both treatment groups were very satisfied with their care, patients in the ON-TRAAC group were at least as satisfied with their care as those in the TMC. This has important implications as it lends support to the use of this alternate model of care in the provision of services to those with IA, which has potential benefits from both a clinical and health economics perspective. Larger patient numbers with longer follow-up are needed to provide meaningful comparisons between these different models of care. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**7**

**Anti-Homocitrullinated Protein Antibody Isotype Usage in Rheumatoid Arthritis Patients and their Unaffected First Degree Relatives**

Lillian Barra (The University of Western Ontario, London); Sallie ElHayek (The University of Western Ontario, London); Ewa Cairns (The University of Western Ontario, London); David Bell (The University of Western Ontario, London)

**Objectives:** The majority of Rheumatoid Arthritis (RA) patients express anti-citrullinated protein antibodies (ACPA). Unaffected first degree relatives of RA patients (FDR) also express ACPA, commonly of the IgA isotype. Recently, it has been found that RA patients and FDR also express IgG anti-homocitrullinated protein antibodies (AHCPA). It is unknown whether other isotypes are expressed. We aim to investigate the AHCPA isotype profile in RA patients and their unaffected FDR.
**Methods:** Subjects were recruited from a tertiary care rheumatology clinic (London, Canada); all were examined by a rheumatologist and completed a questionnaire for demographics, co-morbidities and joint symptoms. FDR and healthy controls (HC) were excluded if they had swollen joints. Serum was obtained at time of rheumatologist assessment. Serum AHCPA targeting homocitrullinated fibrinogen was determined using an in-house enzyme linked immunoabsorbant assay (ELISA). Fibrinogen was homocitrullinated by incubating with potassium cyanate and confirmed by western blot. Anti-CCP was measured by ELISA (Euroimmun©) and RF by ELISA (Inova©) or nephelometry. FDR were genotyped for HLA-DR4 alleles encoding the shared epitope.
**Results:** The study included 125 RA, 61 FDR and 40 HC. Demographics for FDR and HC were similar. Compared to HC, RA patients were older (median age 59 (IQR 16) vs. 52 (IQR 21) years, p=0.0026) and more likely to be current or past smokers (64% vs. 36%, p=0.0036). Median age for FDR was 54 (IQR 18) years and 30% had a history of smoking. 20% of FDR

expressed IgG AHCPA, compared to 30% in RA patients and 5% in HC (p=0.0010 for RA vs. HC). Levels of IgG AHCPA in FDR were similar to RA (median 71.3 (IQR 75.9) and 69.5 (IQR 99.6) RU/ml, respectively). FDR rarely expressed IgM (8%) and did not express IgA AHCPA. 20% of RA and 13% of HC subjects expressed IgM, but very few expressed IgA AHCPA (<7% in both groups). AHCPA was significantly associated with anti-CCP2 (OR: 3.23; 95%CI: 1.33, 7.87) and RF (OR=4.29, 95% 1.70, 10.79) in RA but not FDR or HC. AHCPA expression in FDR was not significantly associated with joint symptoms, smoking or the shared epitope.

**Conclusion:** IgG AHCPA is the most commonly expressed isotype in RA and FDR. The significance of IgG AHCPA expression in FDR is unclear as it was not associated with joint symptoms or other risk factors for RA (smoking or the shared epitope). Longitudinal studies are needed to determine whether AHCPA is meaningful in populations at risk for RA.

**8**

**Patient, Rheumatologist, and Extended Role Practitioner (ERP) Perspectives on the Implementation and Impact of an Allied Health Rheumatology Triage (AHRT) Initiative in Ontario Rheumatology Clinics**

Laura Fullerton (Ontario Best Practices Research Institute, University Health Network, Toronto); Sydney Brooks (The Arthritis Society, Toronto); Raquel Sweezie (The Arthritis Society, Toronto); Vandana Ahluwalia (William Osler Health System, Ontario Rheumatology Association, Brampton); Claire Bombardier (Ontario Best Practices Research Institute, University of Toronto, Toronto General Research Institute, Toronto); Anna Gagliardi (University of Toronto, Toronto General Research Institute, Toronto)

**Objectives:** Early treatment with traditional and/or biologic DMARDs is critical for the prevention of irreversible joint damage and long-term disability in patients with IA. While the recommended time from referral to rheumatologist is 4 weeks, only 38% of RA patients in Ontario are seen within this timeframe and fewer than 50% receive treatment with a DMARD within 6-months of symptom-onset. Triage is the process of identifying the urgency of a patient's condition and ensuring they are seen in a timely manner. Advanced Clinician Practitioners in Arthritis Care (ACPAC) are extended role practitioners (ERPs) with specialized training in joint examination who can assess, triage, and manage patients with MSK conditions. This research evaluates the impact of integrating ACPAC-trained ERPs into 6 rheumatology clinics. Qualitative research was used to assess patient, rheumatologist, and ERP perspectives on the clinical/logistical impact of this intervention, facilitators/barriers of success, and recommendations for future application.

**Methods:** Semi-structured telephone interviews (n=22) were held with all participating rheumatologists (n=6), ERPs (n=6), and a sample of patients (n=10) from each clinical site. Interviews were approximately 30-60 minutes in length, audio-recorded, and transcribed verbatim. Data were collected from Dec 15, 2015-Aug 15, 2016. Transcripts were analyzed using basic qualitative description. Two independent researchers compared coding and achieved consensus. Data were tabulated by theme and clinical site to identify trends and facilitate interpretation.

**Results:** Patients, rheumatologists, and ERPs consistently reported reduced wait-times to rheumatology care, diagnosis, and treatment for those with IA. The role of ERPs in taking medical history, conducting joint exams, and ordering lab work/imaging was reported to improve clinical efficiency by providing rheumatologists with the information needed to diagnose/treat in the first appointment. Rheumatologists and ERPs reported high agreement in joint assessment

outcomes, and a belief that the intervention improved quality of care for IA and non-IA patients. Patients reported high satisfaction with ERP assessments, valuing: early joint examination/lab work, urgent referral if needed, and the provision of information, support, and management strategies. Facilitators of success included: supportive clinical staff, regular ERP and rheumatologist communication, and knowledge of EMR systems. Recommendations included: extending ERP roles to include stable patient follow-up, and ERP care between scheduled rheumatology appointments.
**Conclusion:** Patients, rheumatologists, and ERPs expressed high agreement that the triage intervention reduced wait-times to rheumatology consult, diagnosis, and treatment for patients with IA; as well as improved clinical efficiency and quality of care. Findings support the integration of ACPAC-trained ERPs in rheumatology models of care. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**9**

**Automated Data Extraction from Electronic Medical Records in Rheumatology: An Ontario Best Practices Research Initiative Pilot Project (OBRI)**

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**Objectives:** To assess the feasibility of extracting clinical data from Ontario rheumatologists' Electronic Medical Records (EMR), and evaluate the integrity of the data for quality improvement and research purposes.
**Methods:** Four community rheumatologists currently participating in the Ontario Best Practices Research Initiative (OBRI) and using the Accuro EMR, agreed to participate. Fig.P Software Incorporated installed a data sync program into the rheumatologists' EMRs and developed algorithms to extract the same data as routinely collected by OBRI via faxed case report forms (CRFs). After identifying OBRI participants within each EMR, demographic data, enrollment and follow up assessment dates, primary outcomes (patient/physician globals, tender/swollen joint counts), comorbidities and medications were extracted. Data extracted by Fig.P was compared to data previously received and entered in the OBRI database. Data was only compared for OBRI patients enrolled after the rheumatologist started using their EMR.
**Results:** Feasibility: Fig.P worked with each rheumatologist to identify where the data of interest was being entered into their EMR. While Fig.P successfully extracted data from all test sites, new computer programming/algorithms were required for each site. Data Integrity: In total, 107 OBRI patients were identified by Fig.P. The identification of OBRI patients within the EMR varied from 23% - 100% across the four sites. Enrollment dates could only be extracted for 0-43% of the patients. Patient demographics extracted by Fig.P (including patient name, address, telephone number, date of birth, and gender) matched data in the OBRI database in 67% - 100% of cases. Agreement in patient and physician globals ranged from 34% - 94% and from 56% - 94% for tender and swollen joint counts, across the four sites. Documentation of comorbidities and medications in the EMR were not associated with dates and were therefore not compared to data found in the OBRI database.
**Conclusion:** Clinical data extraction from Accuro is feasible, however there is great variability

in how rheumatologists are documenting patient assessments within their EMR. Patient demographics and primary outcomes can be accurately extracted from Accuro. Assessments/values documented on the OBRI CRF were not always entered into the EMR in a standardized manner, accounting for the poor agreement at some sites. To support rheumatology care quality improvement, we recommend implementation of the agreed upon core set of clinical variables currently being finalized by the Arthritis Alliance of Canada and the development of a consensus on standardization data entry for those variables within all EMR platforms. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**10**

**The Effect of Triage Assessments on Identifying Inflammatory Arthritis and Reducing Rheumatology Wait Times in Ontario: The ORA Allied Health Rheumatologist Triage (AHRT) Project**

Sydney Brooks (The Arthritis Society, Toronto); Claire Bombardier (Ontario Best Practices Research Institute, University of Toronto, Toronto General Research Institute, Toronto); Mary Bell (University of Toronto, Toronto); Angela Cesta (University Health Network, Toronto); Laura Fullerton (Ontario Best Practices Research Institute, University Health Network, Toronto); Arthur Karasik (Toronto); Tetyana Kendzerska (University of Toronto, Toronto); Raquel Sweezie (The Arthritis Society, Toronto); Jessica Widdifield (McGill University, Montreal); Vandana Ahluwalia (William Osler Health System, Ontario Rheumatology Association, Brampton)

**Objectives:** We evaluated the influence of triage assessments by Extended Role Practitioners (ERPs) for improving timeliness of rheumatology consultations for patients with suspected inflammatory arthritis (IA). Wait time (time from primary care referral to rheumatology consultation) was compared for those patients who were triaged and expedited by an ERP versus usual care (comparators not triaged).

**Methods:** Rheumatologists identified patients with possible IA from their wait lists through a paper triage process. Patients were included if there was not enough information on the referral to determine urgency, i.e. 'grey zone' patients. Patients were adults newly referred by a family physician or nurse practitioner within the previous month. An ERP established a weekly triage clinic in each rheumatologist's office and assessed each patient using a standardized tool to identify patients for an expedited rheumatologist consult. Non-expedited patients (patients without a suspected IA diagnosis) went back on the waiting list to receive the next available routine appointment. The time from referral to the first rheumatologist consultation was determined, comparing patients who were expedited to those who were not and to patients in a usual care control group identified through a retrospective chart review.

**Results:** Seven rheumatologists participated in the study. Among 390 'grey zone' patients identified from the rheumatologists' wait lists, 218(56%) met inclusion criteria and received an ERP triage assessment (female: 70%; mean age (SD): 53 (14)). The ERP suspected IA in 114/218 patients (52%) and of those, 82% were expedited for an appointment with the rheumatologist. The median (IQR) time from referral to first rheumatologist consultation was 37.0 (24.5-55.0) days for expedited patients versus 105 (71.0-135.0) days for non-expedited patients. Four rheumatologists provided usual care control group data. In these four sites, there was a significant difference comparing the wait time for the expedited patients (n=55) and the usual care control group (n=331): 35.0 (23.5-52.5) days and 58.0(24.0-104.0) days respectively.

**Conclusion:** Triage by an ERP resulted in a high number of patients with suspected IA receiving

more timely consultations. Time to see a rheumatologist was accelerated for patients with suspected IA and wait times were improved compared to usual practice. These results suggest that an ERP working in a triage role in a rheumatologist's office can improve timeliness of rheumatology consultations for 'grey zone' patients with IA. This may lead to improvements in access to care and improved clinical outcomes. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**11**

**Factors Associated with Decisions to Transition to a Different Biologic, including Biosimilar: The Patients' Perspective**

Elizabeth Badley (Arthritis Community Research and Evaluation Unit, Toronto); Monique Gignac (University of Toronto/Institute of Work and Health, Toronto); Deanna Bowlby (Toronto); Ken Gagnon (Montréal)

**Objectives:** To better understand: a) patients' perspectives in transitioning to a different biologic, including biosimilars; b) information and resource needs of patients that would support them in taking an active and informed role in biologic treatment decisions.

**Methods:** This study was led by The Arthritis Society (TAS) in partnership with the Canadian Spondylitis Association, Crohn's and Colitis Canada, Canadian Arthritis Patient Alliance, Gastrointestinal Society, Canadian Psoriasis Network, and Arthritis Community Research and Education Unit (ACREU). Patients were recruited through partner agencies. Eligibility including having received at least two biologics for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease, and/or ulcerative colitis. Focus groups were held in Vancouver, Prairies (online), Toronto, Montreal (French) and Atlantic (online). The 44 participants completed a pre-survey. They also viewed a brief video on biosimilars mid-way through the focus group to ensure participants were familiar with basic information about these medications.

**Results:** A diversity of diseases was represented at each focus group, several participants reported multiple diseases and the majority reported a form of inflammatory bowel disease. The duration of the disease varied with approximately 50% reporting longer than 8 years duration. Participants ranged in age, the majority being 50 years of age or less, with approximately 25% being under 35 years. Over two thirds were women. Most participants reported being only somewhat/not very confident in their knowledge of biosimilars and noted the need for credible information. Almost all felt it was very important to be fully informed and engaged in any decision to switch biologic and that their physician must approve a switch in their biologic, including to a biosimilar. About 50% were somewhat or very comfortable with switch to a biosimilar if approved by their physician. Approximately 50% reported being not very/not at all comfortable/not sure with a physician being required, based on price, to prescribe a biosimilar for person not on the originator biologic. There was acceptance of biosimilars as a treatment option, although much less acceptance of switching from a currently effective biologic to its biosimilar.

**Conclusion:** Greater access to information to increase knowledge, confidence and ability to engage in decisions to switch biologics is needed. Although patient-centred care was important to participants, most expected their physician to lead medication decisions, to be well informed and make decision based on their patients' best interest. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**12**

**Disseminated Histoplasmosis in a Patient with Antecedent Extrapulmonary Sarcoidosis**

Britney Jones (University of Alberta, Edmonton); Alison Clifford (University of Alberta, Edmonton)

**Background:** Sarcoidosis is a multisystem granulomatous disorder of unknown etiology that may present with diverse manifestations. Infection with Histoplasma capsulatum, a fungus endemic to the US and South America, may closely mimic the features of sarcoidosis. Treatment for these diseases varies greatly, highlighting the importance of establishing the correct diagnosis.

**Case Presentation:** A 42-year-old male with an antecedent biopsy-proven diagnosis of extra-pulmonary sarcoidosis was evaluated for new dyspnea, reticular pulmonary infiltrates and splenomegaly. The initial diagnosis of sarcoidosis was made in Australia 4 years earlier, when he presented with diffuse lymphadenopathy. Excisional lymph node biopsy revealed granulomas, and serum ACE was positive. Treatment with prednisone and plaquenil resulted in clinical improvement, however, one year later, he developed sudden onset left vision loss due to panuveitis. This responded quickly to increased prednisone, and low dose methotrexate (MTX) was added. He moved to Alberta 6 months prior to presentation, and was stable on 5 mg prednisone daily and MTX 15 mg weekly. Several days before presentation, he developed sudden onset high fever (>39 degrees Celsius), dyspnea, and fatigue. Investigations revealed leukopenia (WBC 2.8 $x10^9$/L), cholestatic liver enzyme elevations (GGT 463 U/L, ALP 200 U/L), and interstitial changes on CXR. Abdominal ultrasound revealed massive splenomegaly and abdominal lymphadenopathy. Hypoxia developed (O2 sats 86%), requiring hospital admission. Methotrexate was held, and CT chest confirmed extensive mid and lower lung subpleural reticulation with ground glass opacification, sparing of the upper lobes, and small, calcified mediastinal lymph nodes. Bronchoscopy fluid was negative for viruses, bacteria, and mycobacteria. One of 2 BAL cultures grew yeast, initially attributed to contamination, and transbronchial biopsy revealed poorly-formed, non-necrotizing granulomas, with negative GMS stains, suspicious for pulmonary sarcoidosis. Ophthalmologic exam was unremarkable. The patient initially improved with cessation of methotrexate and a course of empiric antibiotics and was discharged home, but subsequently relapsed with fevers, rigors, headache and pancytopenia. Three weeks later, Histoplasma capsulatum was isolated from the BAL. The patient was treated with IV amphotericin B followed by oral itraconazole, with resolution of his symptoms. Travel history was remarkable only for frequent biking through the river valley where excavation was being performed.

**Conclusions:** The differential diagnosis of sarcoidosis is broad and should be carefully considered in patients with an established diagnosis if clinical status deteriorates. Granulomatous infections are especially important to rule out prior to increasing immunosuppression to prevent unnecessary complications.

**13**

## Anakinra for Treatment of Severe Idiopathic Pericarditis: Experience in a Series of Seven Patients

Arielle Mendel (McGill University, Montreal); Vartan Mardigyan (McGill University, Montreal); Laeora Berkson (McGill University, Montreal)

**Objectives:** Anakinra, an IL-1 receptor antagonist, is a promising treatment for steroid-dependent recurrent idiopathic pericarditis, but knowledge of when to initiate and how to taper this therapy is limited. Our objective was to evaluate the use and outcomes of anakinra for idiopathic pericarditis at our institution, to assess the optimal role for this medication in the therapeutic armamentarium.

**Methods:** A retrospective chart review was conducted of consecutive cases of idiopathic pericarditis managed jointly by rheumatology and cardiology at a tertiary care center in Montreal, Quebec, from January 2013-October 2016. Cases treated with anakinra were reviewed for details on their presentation and clinical course.
**Results:** Seven of 19 patients referred for idiopathic pericarditis received treatment with anakinra (3 male, 4 female). All patients had typical positional or pleuritic chest pain and mean CRP at presentation was 177.3 (95% CI 133.4–221.2). Five had hemodynamically significant pericardial effusions, 3 required pericardiocentesis, and 2 had imaging evidence of pericardial constriction. Initial therapy consisted of colchicine and corticosteroids in most; DMARDs were added in 3 cases. Anakinra was started a median of 9 months (3 weeks – 6.5 years) after initial diagnosis due to corticosteroid dependence or DMARD failure. Patients who required pericardiocentesis appeared to start anakinra earlier compared to those who did not (6.1 months vs. 12.8 months, NS). Clinical resolution of pericarditis was documented 3 weeks after starting anakinra (95% CI, 1.3–4.6 weeks), and corticosteroids were discontinued after a mean of 4 months. Mean duration on anakinra is 7.7 months (95% CI 2.8 – 12.6). Although 4 patients have been able to taper anakinra to less than 7 days per week, none have yet been able to discontinue the drug. The 12 patients not treated with anakinra were more often male (83.3% vs. 42.8%), had less hemodynamically significant pericarditis (33.3% vs. 71.4%), and had more frequent ANA positivity (33.3% vs 0%) compared to anakinra recipients. Three no longer require any medications, while others remain on prednisone, colchicine, and/or NSAIDs.
**Conclusion:** In agreement with published literature, anakinra is effective in the treatment of refractory idiopathic pericarditis. This series demonstrates the spectrum of therapeutic success with anakinra, as early as 1 month and as late as 6 years into the disease course. Special consideration may be given to anakinra in cases of tamponade, constriction, or when tapering of initial therapy is unsuccessful. Further study of the optimal time to initiate and taper anakinra is needed.

**14**

**Lack of Pro-inflammatory Cyto/chemokines in ANA+ Individuals with Insufficient Criteria for a Diagnosis of Systemic Autoimmune Rheumatic Disease (SARD)**

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**Objectives:** Patients with SARD often have a prolonged pre-clinical phase during which they are anti-nuclear antibody (ANA) positive but lack clinical symptoms. It has been proposed that progression from asymptomatic autoimmunity to clinical disease is accompanied by immunologic changes that could be used as predictors of disease development. Our objective is to identify cyto/chemokine abnormalities in ANA+ individuals who lack sufficient criteria for a diagnosis of SARD.
**Methods:** ANA+ individuals who: 1) lacked clinical symptoms of SARD (ANS); 2) had a least one clinical symptom of SARD (UCTD); or 3) had a recently diagnosed steroid and immunosuppressive naïve SARD were recruited, and compared with ANA- healthy controls (HC). The levels of 30 cyto/chemokines were measured, 29 by Luminex and one (BAFF) by

ELISA. Peripheral blood interferon (IFN)-induced and BAFF gene expression was quantified by NanoString. The normalized levels of 5 ubiquitously expressed IFN-induced genes were summed to produce an IFN5 score.
**Results:** Cyto/chemokines were measured in plasma samples from 145 individuals (21 HC, 37 ANS, 28 UCTD, and 59 early SARD). The plasma levels of four cyto/chemokines, IP-10, eotaxin, BAFF, and TNF-a, were significantly elevated in early SARD patients when compared to HC (Bonferroni corrected p = 0.0001, 0.0006, 0.003, 0.033, respectively). The levels of IP-10, eotaxin, and TNF-a were not significantly elevated in ANS and UCTD individuals as compared to HC. Although there was a trend to elevated serum BAFF levels in UCTD and ANS individuals, this only achieved statistical significance in UCTD patients (p = 0.037 and 0.065, respectively). However, ANS individuals had significant elevations of BAFF RNA in their peripheral blood (p = 0.009). We have previously reported that all ANA+ subsets have significantly elevated IFN5 scores. The levels of IP-10, serum BAFF, and BAFF RNA were positively correlated with IFN5 scores in ANA+ individuals, suggesting that these pro-inflammatory factors are induced by type I IFN. For ANA+ individuals lacking a SARD diagnosis, the levels of IP-10, TNF-a, and BAFF RNA were positively correlated with the ANA titer, while IFN-a2 and IP-10 demonstrated an association with the number of different autoantibody specificities detected.
**Conclusion:** Although elevated levels of several pro-inflammatory factors are seen in early SARD, significant increases in these factors are not generally seen in the subset of ANA+ individuals who lack sufficient criteria for a SARD diagnosis. Instead, elevations in these factors, particularly those associated with type I IFN, appear to parallel serologic and clinical progression.

**15**

**Prior Sun Exposure and Skin-Specific Auto-antibodies are Associated with Skin Disease in Systemic Lupus Erythematosus**

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**Objectives:** Patients with systemic lupus erythematosus (SLE) have various presentations. Almost 80% of SLE patients manifest lupus-specific skin lesions. A pathogenic link between skin inflammation and SLE has been proposed but not yet shown. Preliminary animal and human data suggest that sunburns may promote the development of SLE: In the Non-obese diabetic mouse, repeated high-intensity sun exposure promotes SLE. Skin-specific antibodies have been detected in patients with SLE and animal models of SLE. We hypothesized that skin-directed antibodies are present in adults with SLE associated with a history of significant sun exposure, possibly reflecting immune activation in the skin and a role in the development of systemic disease.
**Methods:** Consent for blood collection was obtained from three populations; SLE patients with a history of lupus specific skin lesions as cases (n=15), SLE patients without a history of lupus specific skin lesions (n=5) and atopic dermatitis patients (n=3) as negative controls. Antidesmoglein-3 antibody levels in serum were determined by ELISA, and flow cytometry

analysis was performed on peripheral blood mononuclear cells. Patients completed a validated and scored sun exposure questionnaire addressing sun exposure history prior to disease onset. The calculated sun exposure score and the ELISA data were analyzed using Mann-Whitney U test.
**Results:** Analysis of the questionnaire score shows a history of significantly increased sun exposure prior to disease onset in SLE patients with skin disease when compared to SLE patients without skin disease (median score = 60 versus 32, respectively; $p<0.05$). Anti-desmoglein-3 autoantibodies titers were higher in the serum of SLE patients with skin disease than in patients without skin disease (median = 0.463 versus 0.087 IU, respectively; $p<0.05$).
**Conclusion:** Thus, SLE patients with skin disease have a history of higher antecedent sun exposure, consistent with the hypothesis that sun exposure may be an environmental trigger for disease. The resulting immune activation of the skin may be reflected in aberrant skin-specific antibody production. Our findings require confirmation in a larger sample, but these preliminary results contribute to understanding the environmental triggers promoting SLE.

**16**

**Canadian Study of Adherence Outcomes in Adalimumab Patients: Three-Year Results from the COMPANION Study in Rheumatology Patients**

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**Objectives:** HUMIRA® (adalimumab, ADA) is a TNF-alpha inhibitor indicated for various inflammatory autoimmune diseases including rheumatoid arthritis (RA) and spondyloarthritis (SpA). Patients receiving ADA in Canada are eligible to enroll in the AbbVie Care patient support program (PSP) providing personalized services. This retrospective study assessed the impact of specific factors, including PSP services and patient characteristics, on persistence and adherence to ADA over a 3-year period in the overall cohort of patients (all indications) and in RA and SpA patients specifically.
**Methods:** ADA PSP patients were linked to the IMS longitudinal pharmacy transaction database using a probabilistic matching algorithm. Patients starting ADA between July 2010 and August 2012 were indexed and tracked for 36 months to calculate days until end of persistence (>90 days without therapy), censored for persistence through month 36. Cox regressions and multivariable logistic regression models provided hazard ratios (HR) and adjusted odds ratios (OR) to measure the association between patient characteristics/PSP services and persistence and adherence, respectively. Adherence was measured using the medication possession ratio (MPR) (>=80% MPR). Additional analyses were performed on patients who were persistent up to when specific PSP services were introduced in a separate cohort.
**Results:** A final sample of 4,772 patients (including 918 RA and 1,028 SpA patients) was selected. In the overall cohort (all indications), older age groups had significantly greater odds of adherence (40-49, 50-59, 60-69, 70+; OR = 1.3, 1.4, 1.4, 2.1, $p<0.05$ for all comparisons) relative to the 30-39 years age group. In a subset of patients (n=2,866) who were persistent when ongoing care coach calls were available, those receiving this service were 65% less likely to stop therapy (HR=0.35, $p<0.01$) and 38% more adherent (OR = 1.38, $p<0.01$) compared to those without it. Among this patient subset, RA and SpA patients (n=1,125) who received this service were 61% more persistent (HR=0.39, $p<0.01$) and showed a trend towards better adherence

(OR=1.34, p=0.065) compared to those without it.
**Conclusion:** Ongoing care coach calls provided by the AbbVie Care PSP significantly correlate with greater patient persistence and adherence over 36 months. Moreover, patients aged between 30 and 39 years appear to have lower adherence compared to older age groups. These results may help refine services that improve treatment adherence.

**17**

**Epidemiology of Lupus Nephritis in Inflammatory Bowel Disease**

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**Objectives:** Concurrent lupus nephritis (LN) and inflammatory bowel disease (IBD) is exceedingly rare, and the association between the two is poorly understood. The aim of this study is to identify factors associated with concomitant LN and IBD.

**Methods:** Patients hospitalized from 2004 to 2012 were identified using the Nationwide Inpatient Sample and ICD 9 codes for IBD (555.0, 555.1, 555.2, 555.9, 556.0, 556.1, 556.3, 556.4, 556.5, 556.6, 556.8, 556.9) and LN (583.81). IBD patients with LN were compared with those without LN. The Pearson's $\chi 2$ test and paired t-test were used for categorical and continuous variables respectively. Statistical analysis was performed using SAS version 9.3 (SAS Institute, Cary, North Carolina).

**Results:** We identified 268,170 patients with Crohn's disease (CD) and 152,804 patients with ulcerative colitis (UC). Among the CD and UC groups, we further identified 318 and 299 patients with LN respectively. Compared to CD patients without LN, the CD-LN group had significant associations with hypertension (36.2% vs. 29.1%, p=0.004), hyperlipidemia (35% vs. 13.1%, p <0.0001), obesity (13.2% vs. 5.7%, p<0.0001), chronic diastolic heart failure (HF; 2.1% vs. 0.3%, p<0.0001), anemia of chronic disease (9.4% vs. 3.4%, p<0.0001), renal osteodystrophy (2.9% vs. 0.2%, p <0.0001), secondary hyperparathyroidism (2.1% vs. 0.1%, p<0.0001), hepatitis C (2.4% vs. 0.6%, p <0.0001), transaminitis (1.2% vs. 0.4%, p= 0.009), acute tubular necrosis (ATN; 3.8% vs. 0.5%, p<0.0001) and depression (12.9% vs. 9.7%, p=0.04). Smoking (10.9% vs. 18.4%, p=0.001) and anal fistulas (0% vs. 1.5%, p=0.02) had significantly lower associations. Similarly, the UC-LN group compared to UC patients without LN had stronger associations with hyperlipidemia (48.2% vs. 19.3%, p<0.0001), obesity (16.6% vs. 6.1%, p<0.0001), chronic systolic HF (1.5% vs. 0.3%, p<0.0001), chronic diastolic HF (1.2% vs. 0.4%, p=0.02), atrial fibrillation (14.1% vs. 8.7%, p=0.001), pulmonary hypertension (0.9% vs. 0.1%, p<0.0001), anemia of chronic disease (7.1% vs. 2.8%, p<0.0001), ATN (3.4% vs. 0.9%, p<0.0001), esophageal bleeding varices (0.3% vs. 0.03%, p=0.002), ischemic colitis (2.2% vs. 0.9%, p=0.01) and ileal conduit (0.3% vs. 0.03%, p=0.01). Smokers (4.9% vs. 8.7%, p=0.02) and patients with colectomy (0% vs. 1.97%, p=0.01) had significantly lower associations. Both CD and UC patients had a higher mortality when associated with LN (2.4% vs. 1.0%, p=0.02 and 4.3% vs. 2.3%, p=0.01).

**Conclusion:** In patients with IBD, LN should be suspected when admitted to the hospital with proteinuria, hematuria and renal failure as it carries a significantly higher mortality.

**18**

**Discontinuation of Biologic Drugs 1-year Before Pregnancy and During Pregnancy: A Real-World Comparison between Inflammatory Bowel Disease and Rheumatoid Arthritis**

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**Objectives:** Recent evidence suggests that rheumatoid arthritis (RA) remission during pregnancy may not be as common as previously believed. Use of biologic drugs during pregnancy has been studied more extensively in inflammatory bowel disease (IBD) than in RA, and evidence to date suggests that they are relatively safe in IBD. Our objectives were to compare patterns of biologics discontinuation before and during pregnancy in women with IBD or RA, and determine factors associated with discontinuation.

**Methods:** Our data source consisted of British Columbia administrative data on women with ≥1 pregnancies between 01/01/2002 and 12/31/2012, including all physician visits, hospital admissions, and dispensed medications, linked to a Provincial Perinatal Registry. Pregnant women with IBD or RA exposed to biologics were identified as having ≥1 ICD9/10 codes for IBD or RA prior to pregnancy, and ≥1 biologics prescriptions from one year before pregnancy until delivery. Using information on prescription dates and pregnancy start dates, we determined the use of biologics as binary (on/off treatment) in multiple 90-day exposure windows starting from one year prior to each pregnancy, until date of delivery; drug discontinuation was defined as having no prescriptions for any biologics during a 90-day window. Associations between disease type and time-dependent drug discontinuations were investigated using multilevel logistic regression models, fitted with binomial generalized estimating equations to account for the correlation between multiple pregnancies in the same woman over the 10-year study period. Covariates considered included maternal age, Charlson Comorbidity Index, number of concomitant disease modifying drugs, immunosuppressants, glucocorticoids, and numbers of hospitalizations and outpatient visits over the two years prior to pregnancy.

**Results:** There were 134 pregnancies in 121 women (mean maternal age 31.8 [SD 4.61]), with RA (52%) or IBD (48%) who were using biologics before or during pregnancy. In the year prior to pregnancy, adjusted odds of drug discontinuation were no different between those with RA versus those with IBD (aOR:1.07, 95%CI:0.70-1.64, p=0.76). However, over the course of pregnancy, women with RA were two times more likely to discontinue biologic therapy than women with IBD (aOR:2.02 [95%CI:1.50-2.70], p<0.0001); with older women being less likely to discontinue their biologics (aOR:0.76, 95%CI:0.62-0.92, p=0.006).

**Conclusion:** Despite controlling for comorbidity, concomitant drugs, and healthcare utilization, women with RA are twice as likely to discontinue their biologics during pregnancy, compared to those with IBD. This warrants further investigation into the implications for stopping therapy, as disease control is known to directly affect pregnancy outcomes in RA patients.

**19**

**Leflunomide-Induced DRESS Syndrome in the Setting of Undifferentiated Spondyloarthropathy**

Matthew Piche (Western University, London); Jason Lee (Western University, London); Sara Haig (Western University, London)

**Objectives**: Present a case of leflunomide-induced DRESS syndrome in the setting of undifferentiated spondyloarthropthy and review the current literature regarding this clinical scenario so as to contribute to the understanding of this condition.
**Methods**: Electronic and paper chart review was performed. Time course began with initial presentation to tertiary care hospital to most recent rheumatologic follow-up. Consultation notes, progress notes, laboratory findings, genetic testing, biopsy and imaging reports were analyzed. Clinical presentation, and outcome were ascertained via chart review. Case reports regarding leflunomide-induced DRESS syndrome were accessed via PubMed through searching "Leflunomide DRESS".
**Results**: 22-year-old female with a history of undifferentiated spondyloarthropathy diagnosed at age 13, characterized by bilateral uveitis, knee, feet and neck pain. Previously treated with Celebrex, Methotrexate and Enbrel, which she stopped on her own. On transfer of care to adult rheumatology she was initially treated with Naproxen but experienced ongoing joint pain, so was started on leflunomide 20mg PO OD. 1 month later she presented to ER with nausea, abdominal pain, emesis and a raised, erythematous, blanchable macular rash. Laboratory investigation demonstrated a leukocytosis of $30.5x10^9$/L, eosinophilia of $11.7x10^9$/L, HgB 119g/L, MCV 75.4fL and platelets $264x10^9$/L, AST 447, ALP 466, GGT 123, and total bilirubin 143.8umol/L. CT chest demonstrated diffuse ground glass opacity. Bronchoscopy was performed and was unremarkable. Further workup included weakly positive ANA, negative pANCA, negative cANCA, and negative rheumatoid factor. Hepatitis serologies were negative. Skin biopsy demonstrated subacute spongiotic dermatitis. Clinical Pharmacology was consulted and pharmacogenomics was performed to assess for CYP2C19 genotyping. The patient was found to have a poor metabolizer status for this enzyme thus making it possible that reduced leflunomide metabolism capacity might have contributed to her clinical picture of DRESS syndrome. The patient was treated with prednisone 60mg PO OD with subsequent taper and hold of leflunomide. All serologic parameters, including liver enzymes, eventually returned to baseline with prednisone treatment and cessation of leflunomide.
**Conclusion**: Leflunomide induced DRESS syndrome is rare with a handful of cases documented in the literature. This case report contributes to the understanding and treatment of leflunomide induced DRESS syndrome as it outlines the clinical presentation, serologic investigation, and biopsy findings of a patient presenting with DRESS syndrome in the setting of poor metabolizer status for CYP2C19 enzyme.

**20**

## Mononeuritis Multiplex Possibly Related to IgG-4 Case Report and Review of the Literature

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IgG4-related diseases (IgG4-RD) are gaining recognition but remain poorly understood, with features of both autoimmune disorders and allergic disorders. While commonly recognized in the pancreas, salivary glands, and lacrimal glands, increasingly cases affecting other tissues are described. Features of IgG4-RD include: subacute painless swelling, dense tissue infiltration of IgG4 plasma cells and small lymphocytes, storiform fibrosis, obliterative phlebitis, tissue eosinophilia, elevated serum IgG4 levels, and responsiveness to glucocorticoid therapy.
A previously healthy 47-year old male presented with mononeuritis multiplex initially with unilateral peroneal neuropathy, and rapidly progressed to include bilateral ulnar neuropathies. Imaging and laboratory investigations were unremarkable, including negative ANCA, ANA, RF,

ENA, cryglobulin screen, and normal CRP, SPEP, ACE level, and free kappa lambda chain assay. Infectious work-up including Hepatitis B and C, syphilis, HIV, and Lyme disease were negative. His electromyography demonstrated severe ulnar nerve axonal damage that was rapidly progressive with complete atrophy of the abductor digiti minimi muscle, and a persistent peroneal nerve palsy. Sural nerve biopsy revealed non-specific inflammatory infiltration (lymphoid predominant) with the presence of eosoinophils; the initial biopsy was not stained for IgG4.

He subsequently developed recurrent episodes of pancreatitis. Computerized tomography scan of the pancreas was modestly enhanced with clear delineations, and concerns for primary autoimmune pancreatitis could not be ruled out.

Given his rapid progression of neuropathy, he received intravenous immunoglobulins, glucocorticoids and cyclophosphamide induction, and transitioned to methotrexate maintenance therapy. His peripheral neuropathy gradually improved and he had no further episodes of pancreatitis. Serum IgG-4 level was elevated at 1.00g/L while on methotrexate, which raised suspicion for IgG-4 RD. However, his sural nerve could not be re-stained for IgG-4 levels and a repeat biopsy was not indicated.

Our patient presented with possible IgG4-RD as the etiology for his mononeuritis multiplex and recurrent pancreatitis. We reviewed one comparable case of IgG-4 related mononeuritis multiplex with electrophysiological evidence of axonal neuropathy and skin fibrosis described by Ohyama et al. (2013), where skin and sural nerve biopsies exhibited IgG-4 positive plasma cells. He improved symptomatically and biochemically with prednisone. Another case of severe peripheral neuropathy was described by Suzuki et al. (2016), with elevated serum IgG4 levels, sural nerve biopsy with obstructive thromboangiitis, and bone marrow biopsy with blood vessel occlusion by IgG4 positive plasma cells. However, symptoms failed to improve with steroid therapy. Taken together, as IgG4-RD gains recognition, it should be included in the investigation of mononeuritis multiplex.

**21**

**Tocilizumab Treatment Leading to Remission of Rapid Onset Nephrotic Syndrome in AA Amyloidosis Secondary to an Unknown Chronic Inflammatory Disorder**

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AA amyloidosis (AA) is a complication of prolonged inflammation from various causes that can lead to organ damage. Treatment is directed primarily at controlling the underlying inflammatory disease. We report the use of IL-6 inhibition to treat AA in a patient with an unknown inflammatory disorder.

A 71-year-old female with a past medical history of hypothyroidism and resected childhood scrofula was referred for AA. Two years prior to presentation, she was diagnosed with polymyalgia rheumatica (PMR) based on atypical symptoms of sudden onset extremity weakness, diffuse myalgias and arthralgias, and elevated C-reactive protein (CRP) (143.3 mg/L). She received prednisone for 1 year but developed recurrent arthralgias and new onset peripheral edema after its discontinuation. She was referred to rheumatology as her presentation was inconsistent with PMR. CRP remained elevated (121.0 mg/L) but renal function (Cr=42 umol/L) and urine albumin-to-creatinine ratio were normal. Autoantibodies, complements, serum protein electrophoresis, and free light chains were normal. X-rays showed no joint erosions. Prednisone 10 mg daily was continued but she was lost to rheumatology follow-up and continued to have ongoing symptoms. Approximately 1 year later, nephrotic syndrome

developed with pedal edema, urine protein-to-creatinine ratio (UPCR) of 1148.0 mg/mmol and normal renal function (Cr=34 umol/L). A renal biopsy revealed amyloidosis with positive immunocytochemical staining for amyloid A protein. Due to severe nephrotic syndrome she was initiated on monthly intravenous tocilizumab (8 mg/kg), a monoclonal antibody against IL-6 receptor. CRP prior to tocilizumab initiation was 14.5 mg/L and normalized to 0.6 mg/L after 1 month of therapy with marked improvement in proteinuria (UPCR=163.2 mg/mmol) after 8 months of treatment. Complete remission of proteinuria was achieved at 14 months of treatment (UPCR=44.4 mg/mmol) and renal function remained normal throughout treatment.
Serum amyloid A (SAA), an acute phase reactant protein, is a component of amyloid fibrils in AA. IL-6 plays a synergistic role in SAA expression in vitro, while IL-6 blockade substantially decreases SAA production. Reduction of serum SAA levels to normal range with anti-inflammatory treatment in AA has been correlated with stabilization or improvement in organ function as well as reduced mortality. Case reports of tocilizumab use in AA from various inflammatory disorders have demonstrated efficacy in renal outcomes. This case adds to growing observational data that tocilizumab is an effective treatment option for AA and can be considered in rapidly progressive cases even when the underlying disease is unknown.

**22**

**The First Case of Bacillus Calmette-Guérin Induced Small-Vessel Central Nervous System Vasculitis**

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**Objectives:** To present an unrecognized vascular complication of Bacillus Calmette-Guérin (BCG) therapy administered for bladder carcinoma. We also review the vascular and rheumatologic manifestations of mycobacterial infections, the potential infectious mimickers for primary central nervous system (SNC) vasculitis, as well as the available diagnostic modalities for SNC vasculitis.

**Methods**: Case Report

**Results**: We report the case of an 89 year old Caucasian man treated with intravesical BCG for relapsing high-grade bladder carcinoma. The patient presented with recurring episodes of right upper limb paresthesia, clumsiness, and dysarthria. Initial workup, including anti-neutrophil cytoplasmic antibodies, antinuclear antibodies, inflammatory markers, computed tomography of the head, cerebral angiography, transthoracic echocardiography, carotid Doppler ultrasound, holter monitoring, electroencephalography, lumbar puncture with flow cytometry, as well as tuberculin skin testing and interferon-gamma release assay, was normal. Magnetic resonance imaging revealed multiple predominantly left-sided frontotemporal micronodular peri-vascular lesions. Left frontal lobe biopsy showed non-necrotizing granulomatous vasculitis. Ziehl staining was negative. Initially, the patient was treated for primary SNC vasculitis with corticosteroids and immunosuppressors. The patient's drowsiness, confusion, paraphasia and hemiparesis relapsed during attempts to taper the corticosteroids. Six months later, he developed bilateral mycobacterial endophtalmitis. Urine, blood, and vitreous cultures were positive for mycobacteria, later identified as Mycobacterium bovis. A retrospective diagnosis of BCG-induced central nervous system vasculitis was made. The patient was treated with high-dose corticosteroids, moxifloxacin, isoniazid, ethambutol, and rifampicin.

**Conclusion**: BCG is a live attenuated form of Mycobacterium bovis widely used as tuberculosis vaccination and intravesical therapy for superficial forms of bladder cancer. Systemic

complications are very rare and have been described as case reports or case series. Cases of endophtalmitis, meningitis, aortitis or mycotic aneurysms have been described, including one case of CNS vasculitis affecting the base of the brain. Systemic infections are usually present within weeks but can manifest months or years after the last instillation. In disseminated forms of BCG infections, referred to as BCGitis, histopathology usually reveals granulomatous inflammation. The diagnostic performance of mycobacterial culture and PCR-based assays is less than 50%, making this a diagnostic challenge. Despite therapy, mortality seems to be highest, more than 15%, in patients with vascular involvement. This is, to our knowledge, the first case of BCG-induced small-vessel CNS vasculitis. Mycobacterium bovis infection is rare and findings are often nonspecific, making diagnosis very difficult. Other infectious and non-infectious entities must be ruled-out appropriately before considering this diagnosis.

**23**

**Incomplete Presentation of Heerfordt-Waldenstrom Syndrome**

Jeff Gong (University of Calgary, Calgary); Paul MacMullan (University of Calgary, Calgary)

Sarcoidosis is a granulomatous disease of unclear etiology. It is a systemic disease with various clinical manifestations and organ involvements – a disease of 'a thousand faces'. The most common presentation is Lofgren's syndrome, which is characterized by fever, arthritis, erythema nodosum, and hilar lymphadenopathy. Heerfordt-Waldenstrom syndrome is a rare form of sarcoidosis, presenting with fever, uveitis, facial palsy, and parotid gland enlargement. Here we present a case of a 48-year-old Chinese female with a two-year history of query Bell's palsy and recent erythematous lesions on her lower extremities, who presented with acute peri-auricular pain, bilateral parotiditis, and fever. Physical examination revealed bilateral parotid gland swelling and lower leg erythematous lesions. Infectious and inflammatory workup were all negative. CT chest showed subtle left upper lobe centrilobular nodularity. Biopsies of the skin, lung nodule, and parotid gland demonstrated non-caseating, non-necrotizing granulomas consistent with sarcoidosis. With the constellation of symptoms and investigative results, she was diagnosed with Heerfordt-Waldenstrom syndrome. Treatment with glucocorticosteroid led to resolution of her ear pain and parotid swelling and improvement of her leg lesions.

**24**

**Paraneoplastic Raynaud's Phenomenon in an ANA Positive Patient**

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**Introduction:** Paraneoplastic Raynaud's is a rare entity that tends to progress rapidly without response to conventional therapies. Typically, Raynaud's present prior to diagnosis of malignancy, resolves with cancer treatment and recurrence may indicate relapse.

**Case description**: A 68 year-old male with T3, N1 cholangiocarcinoma diagnosed in June 2015 presented with asymmetric distal fingertip ischemia. He had undergone tumor excision in July 2015 and received 5 cycles of gemcitabine. His last dose was in January 2016 after which he experienced swelling, pain, numbness and bluish discoloration of fingertips. The symptoms worsened with exposure to cold and progressed to necrosis over the next 3 months. There was no history of symptoms of connective tissue disease (CTD) or prior episodes of cyanosis. On physical examination there was violaceous to necrotic discoloration of the finger pads of the 2nd,3rd and 4th fingers bilaterally. There was no sclerodactyly, no ulcerations but some bullous change in the affected fingers. Nailfold capillaries were normal. A clinical diagnosis of secondary Raynaud's phenomenon was made and the patient was started on amlodipine. Initial

investigations showed positive ANA (1:640, speckled) with negative ENA panel. aPL, ANCA and cryoglobulins were negative. Despite treatment with warfarin and calcium channel blocker, symptoms progressed. Sildenafil was added with symptom improvement. He was also prescribed nitroglycerin patches but he did not use them. Repeat imaging studies showed tumor progression. He then required 7 cycles of Cis-platinun and capecitabine that decreased tumor size by 77%. Amlodipine and sildenafil were continued during chemotherapy. Over the course of 3 months there was complete resolution of finger ischemia. He continues to have Raynaud's with numbness and discoloration, but digital amputation was avoided.

**Discussion**: Our case illustrates the etiological complexity of secondary Raynaud's phenomenon: CTD, vasculitis, drug-induced and paraneoplastic. We speculate that gemcitabine, often cited associated with finger necrosis secondary to direct endothelial damage, was perhaps the initial triggering stimuli of our patient's severe Raynaud's phenomenon possibly compounded by his autoimmune background. Our patient's improvement of ischemia and necrotic lesions coincided with Cis-platinun/capecitabine induced tumor-size reduction. We cannot rule-out then the possibility that the release of vasoactive substances by the tumor itself may also play a role in the pathogenesis of our patient's vascular manifestations.

**25**

**Strongyloides Presenting as Diffuse Alveolar Hemorrhage in SLE: A Case Report**

Saara Rawn (McMaster University, Hamilton); Stephanie Garner (McMaster University, Hamilton); Mark Matsos (McMaster University, Hamilton)

**Objectives:** Differentiating diffuse alveolar hemorrhage caused by infection or SLE activity can be clinically difficult in an acutely ill patient. Management differs significantly as SLE is a multi-system disease that often requires escalation of immunosuppression (1). Our goal is to outline the importance of considering endemic parasites in SLE patients on immunosuppression presenting with diffuse alveolar hemorrhage.

**Methods:** Case report

**Results:** A 33-year-old Vietnamese female presented with one week of nausea, vomiting and diarrhea. She was originally diagnosed with SLE at the age of 12 and one month prior to her current presentation had been determined to have biopsy proven, stage IV lupus nephritis. One month ago, her dsDNA was 77, CRP 6.1, C3 0.69 and C4 0.2. She was negative for tuberculosis and was started on Prednisone 50 mg daily and Cellcept 1000 mg twice daily.

On this admission, her hemoglobin was 83 and she had an elevated creatinine at 151. She was pan-cultured, started on empiric antibiotics, and an initial inflammatory work-up was ordered. The next day, she developed hemoptysis with a hemoglobin of 63. A chest CT showed ground glass opacities in keeping with diffuse alveolar hemorrhage. The initial autoimmune work up showed: dsDNA 10, CRP 70, C3 0.73, C4 0.2, and pANCA/cANCA negative. Initial bacterial cultures and acid-fast bacilli tests were negative. After consultation with infectious disease and nephrology she was started on pulse steroids out of concern for lupus pneumonitis. Hematology determined thrombotic thrombocytic purpura to be unlikely.

Several days into her admission, she developed hematochezia and hypoxic respiratory failure. A broader infectious work up revealed disseminated Strongyloides stercoralis. Ivermectin was initiated and steroid therapy was significantly tapered. The patient recovered and returned home to the community with close follow-up.

**Conclusions:** Herein, we describe a case of diffuse alveolar hemorrhage in a patient with SLE from a region endemic to Strongyloides. In the literature, Strongyloides hyperinfection syndrome in SLE patients on immunosuppression is a risk factor for sepsis and death (2). This illustrates

the importance of considering endemic parasites in the differential for SLE patients on immunosuppression who present with diffuse alveolar hemorrhage or gastrointestinal complaints. Additionally, further research is required to determine the utility of parasite prophylaxis for SLE patients from endemic regions prior to initiating immune compromising regimens (3).

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**26**

**Innate Lymphoid Cells (ILCs) are Differentially Distributed in Inflammatory and Non-inflammatory Joint Diseases**

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**Objectives:** To enumerate the different subsets of ILCs in peripheral blood and synovial fluids of patients with inflammatory and non-inflammatory joint effusions.

**Methods:** Innate lymphoid cells (ILC) are immune cells of the lymphoid lineage not expressing specific antigen receptors. They are classified into three subsets: ILC1 (Natural Killer (NK) cells and ILC1) secrete IFN-γ and TNF-α; ILC2 secrete IL-4, IL-5, IL-9, IL-13, and amphiregulin; ILC3 (Lymphoid Tissue Inducer (LTi) and NK cell activating receptor (NCR+) ILC3) secrete IL-17A and IL-22. Patients with confirmed synovial effusion presenting at the Centre hospitalier universitaire de Sherbrooke (CHUS) signed an informed consent form. Cells from joint effusions were separated by Ficoll-density gradient centrifugation, stained for ILC, and analysed using a BD FACS Aria III flow cytometer. For cytokine detection, cells were stimulated for 6h with PMA/ionomycin prior to cell staining. The distribution of ILC subtypes according to various diagnoses is presented in cells/ml and ratios of ILC subtypes per ml of synovial fluid relative to peripheral blood. The protocol was approved by the CRC-CHUS ethics committee.

**Results:** Synovial fluids and blood from 48 patients with various diagnoses were analyzed. The highest concentrations (cells/mL) of ILC cell subtypes found in the synovial fluids were: ILC1: 7; ILC2: 70; LTi: 4 X104; NCR+ ILC3: 1.3 X105; NK: 5. Synovial fluids relative to peripheral blood frequently presented ratios of ILC cell subtypes ≤1, suggesting little preferential homing in the joints. However, synovial fluids (relative to blood) were enriched 45 and 7 times for NCR+ ILC3 in Juvenile Idiopathic Arthritis (JIA) and spondylarthropathy patients, respectively, and 8 and 6 times for LTi in Psoriatic Arthritis and Rheumatoid Arthritis (RA) patients, respectively.

**Conclusion:** 1- LTi and NCR+ ILC3 subtypes are the ILC most abundant in synovial fluids. •ILC1 and NK cells are rare in synovial fluids and unlikely to be involved in pathogenesis;ILC2 remain infrequent, even when enriched in synovial fluid (e.g. in JIA, RA and gout). 2- Relative to their concentrations in peripheral blood, LTi and NCR+ ILC3 subtypes are markedly enriched in synovial fluids of patients with autoimmune-mediated diseases, notably LTi in RA and Psoriatic Arthritis, and NCR+ ILC3 in spondylarthropathy and JIA. The abundance of these IL-17 secreting cells in synovial fluids from these diseases is especially intriguing. 3- We observed significant heterogeneity within patients with the same clinical diagnosis. 4-The pathophysiological implications of the differential distribution of subtypes of ILC cells across diseases and within clinical diagnoses remain unclear.

**27**

**Elevated 14-3-3η Levels Predict more Rapid Radiographic Progression in Patients with**

**Recent-Onset Inflammatory Arthritis in Clinical Remission**

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**Objectives:** 14-3-3η is a joint-derived serum protein that up-regulates pro-inflammatory factors. We have previously reported that baseline 14-3-3η levels ≥0.50 ng/ml (HIGH 14-3-3η) were predictive of radiographic progression over 5 years. Our objective was to verify if the persistence of HIGH 14-3-3η at 18 months in recent-onset polyarthritis patients in REMISSION predicts more rapid radiographic progression over the following years, up to 42 months.

**Methods:** Serum 14-3-3η titres were assessed at baseline and at 18 months into disease, a median of 14 months after diagnosis and initiation of treatment. Three definitions of 'clinical remission' at 18 months were used: Swollen Joint Count (SJC) =0; SJC + Tender Joint Count (TJC) =0; ACR/EULAR Boolean definition. The progression of radiographic damage (Erosion and Total Sharp/van der Heijde (SvH) scores) in patients with LOW (<0.50 ng/ml) or HIGH (≥0.50 ng/ml) 14-3-3η were compared using the Mann-Whitney test. P values <0.05 were considered significant.

**Results:** Out of 331 patients, 36.0% of which had HIGH 14-3-3η at Baseline, 308 had complete data up to 5 years. Median age was 60 years, 62% women. Depending on the stringency of the definition used, variable numbers of patients reached remission at 18 months: 162 (53%) had SJC=0; 108 (35%) SJC+TJC=0; and 56 (18%) Boolean. Remission at 18 months was negatively associated with persistence of HIGH 14-3-3η since HIGH 14-3-3η were then present in 32/162 (19.7%) SJC=0 patients; 22/108 (20.4%) SJC+TJC=0 and 13/56 (23.2%) Boolean. Compared to patients in remission with LOW 14-3-3η, patients in remission with HIGH 14-3-3η at 18 months had numerically faster subsequent progression with all definitions. For example, in patients with Boolean remission, erosion progression over 42 months was 7.2 ±13.1 vs 1.5 ±3.3 and progression of Total score 9.2 ±14.5 vs 2.8 ±4.4 units. However, due to low numbers and limited power, differences in progression were statistically significant only for the less strict definitions of remission and over the following year: Erosions (SJC=0, p=0.0042, SJC+TJC=0, p=0.0236), Total score (SJC=0, p=0.0146; with a trend for SJC+TJC=0, p=0.077). None of the comparisons over 42 months or of those involving Boolean reached significance.

**Conclusion:** The persistence of HIGH 14-3-3η levels appears to decrease the odds of reaching remission in polyarthritis patients. HIGH 14-3-3η levels in patients in remission appears associated with more rapid radiographic (especially erosive) progression over the following year. A larger study is required to validate these findings, especially with the most stringent criterion of Boolean remission.

**28**

**The Effect of a High-Fat Diet on Arthritis Using a Mouse Model of Rheumatoid Arthritis**

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University of Western Ontario, London )

**Objectives:** Rheumatoid Arthritis (RA) is a chronic autoimmune disorder that is characterized by the production of antibodies that target citrullinated proteins (ACPA). Citrullination is a post-translational modification catalyzed by various isoforms of peptidyl arginine deiminase (PAD), which is upregulated in inflammation. Obesity is a pro-inflammatory state that has been shown to be a risk factor for RA; however, the etiology of this association is currently unknown. We aim to describe the effect of a high-fat diet on arthritis using a mouse model of RA.

**Methods:** Mice expressing human leukocyte antigen DRB1*0401 (DR4tg) are known to develop arthritis starting at day 45 and peaking at day 70 after immunization with PAD2-citrullinated fibrinogen (CitFib). We fed DR4Tg mice and C57BL/6 (B6) controls a high-fat, high-cholesterol (HFHC) diet or standard chow for 70 days, and immunized them at day 0 and 21 with PBS, unmodified fibrinogen (Fib) or PAD4-citrullinated fibrinogen (CitFib). Mice were monitored weekly for weight gain and joint swelling (change in ankle width using calipers). Serum IgG anti-CitFib antibody responses were measured using an in-house ELISA. Protein sequences determined by mass spectrometry of in-house PAD2-CitFib were compared to commercial PAD4-CitFib.

**Results:** HFHC-fed male B6 mice (n=6) gained significantly more weight than chow-fed B6 mice at day 70 (n=6) ($p<0.05$). DR4tg mice did not gain weight when fed a HFHC (n=13) compared to a chow diet (n=13). Caloric intake and ACPA levels did not differ among groups. At day 70, there was no swelling or histologic signs of arthritis in any mouse group (n=20). PAD2-citrullinated fibrinogen was found to have 19 more citrulline residues than PAD4-citrullinated fibrinogen. A citrullinated peptides known to bind to DRB1*0401 and initiate T and B cell responses was not present in the PAD4-CitFib.

**Conclusion:** Feeding DR4tg mice a HFHC diet did not increase weight gain or antibody responses compared to regular chow. PAD4-CitFib immunized DR4tg mice did not develop arthritis, potentially due to differences in the degree or location of citrulline residues compared to PAD2-CitFib. Future studies will examine the effect of a HFHC diet on PAD2-citrullinated fibrinogen immunized DR4tg mice and the contributing immune mechanisms.

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## Determining whether Citrullinated and Homocitrullinated Lipoproteins have a Role in Rheumatoid Arthritis-Associated Atherosclerosis by Promoting Proinflammatory Cytokine Release from Macrophages

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**Objectives:** Rheumatoid arthritis (RA) patients are at an increased risk of developing cardiovascular disease (CVD) compared to the general population, although the exact mechanism of CVD pathogenesis in RA is unknown. The majority of RA patients express antibodies that target citrullinated proteins. Citrulline is structurally similar to homocitrulline, and homocitrullinated (carbamylated) low-density lipoproteins (HcitLDL) have been identified in atherosclerotic plaques. A prior study showed that HcitLDL promotes the formation of lipid-laden macrophages, which are implicated in the pathogenesis of atherosclerosis; however, the effects of citrullinated LDL (CitLDL) and HcitLDL on cytokine release from human macrophages are unknown. We aim to investigate whether macrophages exposed to CitLDL or

HcitLDL secrete proinflammatory cytokines, namely TNF-alpha and IL-6.
**Methods:** CitLDL was made by modifying human LDL using rabbit skeletal peptidyl arginine deiminase (PAD2), while homocitrullination was achieved by incubating human LDL with potassium cyanate. Cells from a human monocyte cell line (THP1) were plated at a density of 4*10^5 cells/well then cultured with 10 ng/mL phorbol-12-myristate-13-acetate (PMA) for 7 days to induce differentiation to M1-type macrophages. The differentiated monocytes were subsequently treated with 10 µg/mL CitLDL, HcitLDL, unmodified LDL, commercial acetylated LDL (AcLDL), or lipopolysaccharide (LPS). Cell supernatants were collected at 0, 2, 4, 6, 8, 10, 12, 16, 18, 20, and 24 hours post-incubation, and TNF-alpha and IL-6 cytokine concentrations were measured in duplicate using commercial enzyme-linked immunosorbent assay (ELISA) kits. The time course experiments were performed at least in duplicate.
**Results:** Citrullination and homocitrullination of LDL were confirmed via western blot. Peak secretion of TNF-alpha occurred at 6 hours for the AcLDL (1.74 ng/mL) and LPS (2.81 ng/mL) treatments, while peak secretion of IL-6 occurred after 24 hours for both AcLDL (0.25 ng/mL) and LPS (1.18 ng/mL). At 10 µg/mL, LDL, CitLDL, and HcitLDL did not induce TNF-alpha or IL-6 secretion at any time point.
**Conclusion:** In a human monocyte cell line differentiated to an M1 macrophage phenotype, the maximal secretion of TNF-alpha occurred 6 hours after AcLDL exposure, while maximal secretion of IL-6 occurred much later. At the same concentration, CitLDL and HcitLDL did not induce release of these proinflammatory cytokines. Future work will focus on treating macrophages with different concentrations of CitLDL and HcitLDL to determine whether these modified LDLs could contribute to proinflammatory cytokine release and have a potential role in the pathogenesis of RA-associated atherosclerosis.

**30**

**Phenotype Assessment of Adult Offspring Carriers of the SQSTM1/P392L Mutation in Familial Forms of Paget's Disease of Bone**

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**Objectives:** Paget's disease of bone (PDB) is a common bone disorder in Canada. Genetic factors play an important role in PDB. In the French-Canadian population, a mutation P392L within SQSTM1 gene was involved in 46% of familial forms. In New-Zealand, the emergence of PDB in offspring inheriting SQSTM1 mutations was reported to be delayed by a decade compared to their parents. We aimed at assessing the phenotype of offspring carriers of the SQSTM1/P392L mutation in our French-Canadian cohort.
**Methods:** We reviewed research records from adult offspring carriers of this mutation aged <80 years and their affected parent. In parents, we collected data on sex, age at diagnosis, number of affected bones, total serum alkaline phosphatase levels (tALPs) expressed as a ratio to the midpoint to normal range. PDB extended phenotype assessment relying on tALPs, total body bone scan and skull and pelvis radiographs, was performed in offsprings at inclusion in 1997 to 2009. We recently started an extended phenotype reassessment of these offsprings by bone imaging, if not done during the past 8 years.
**Results:** We recruited 96 adult offsprings in 16 different large kindreds: 54.2% were men, mean age was 59.3±9.8 years, ranging from 36 to 78 years. The offsprings originated from 57 affected parents, 52.6% were men. At initial evaluation of parents, mean age at diagnosis was 59.3±10.5 years, ranging from 43 to 83 years. They had 6.6±5.2 affected bones and tALPs were 6.7±11.6.

In offsprings, tALPs were measured at 0.98±0.3, at a mean age 44± 10 years. Total body bone scans, performed at 45±10 years, were negative for PDB in 70% of cases and uncertain in 30%. Radiographs, performed at 46±11 years, were uncertain for 3 in the skull and one for the pelvis. Preliminary analysis of the phenotypic update in 18 offsprings provided negative bone scan in 78% of cases, uncertain in 11% and positive in 11%. Radiographs were uncertain (skull n=1; pelvis n=2) or positive (skull n=1; pelvis n=1) in two sisters, aged of 73 and 74. They had indeed polyostotic PDB: pelvis and right femur for one and skull and pelvis for the other. Their affected mother had PDB involving 7 bones, diagnosed at the age of 64.
**Conclusion:** The occurrence of PDB in offspring carriers of the SQSTM1/P392L mutation also appears to be delayed in our French-Canadian population. These findings may reflect age-dependent penetrance of SQSTM1 mutation or interaction with unknown environmental factors.

**31**

**Clinical Audit of Hydroxychloroquine Dosing and Toxicity Screening in Patients with Inflammatory Arthritis and Connective Tissue Diseases**

Sahil Koppikar (Queen's University, Kingston); Henry Averns (Kingston)

**Objectives:** To determine whether appropriate hydroxychloroquine (HCQ) dosing and toxicity screening is elicited during regular clinical encounters for patients with inflammatory arthritis and connective tissue diseases.
**Methods:** A prospective clinical audit was conducted at eight Canadian rheumatology practices in eastern Ontario. Audit standards were based on the American College of Rheumatology (ACR) and American Academy of Ophthalmology (AAO) recommendations. Best practice standards included appropriate weight based dosing of hydroxychloroquine and subsequent monitoring for toxicity. We audited 90 appropriate patient encounters, spread out over the eight practices using a standardized screening form. The results presented are prior to the audit intervention, which is currently ongoing.
**Results:** Among the 90 patients enrolled in the study, 80% were female with an average age of 58 years. Patients were on hydroxychloroquine for an average duration of 76.7 months, with rheumatoid arthritis (60%) and systemic lupus erythematosus (23.3%) being the most common diagnoses. A total of 58 patients (64.5%) were considered high risk for retinal toxicity based on AAO criteria including age, duration of use, renal or liver dysfunction and pre-existing retinal disease. Three out of four audit standards were not met. No patients in our audit had hydroxychloroquine retinopathy and therefore, the last standard could not be assessed. Only 68% of patients were being appropriately dosed based on ideal body weight (Devine formula). Furthermore, 19% of patients were on a prescription dose that was greater than 10% of the recommended dosage. Only 88% of patients had a baseline ophthalmologic exam in the first year of treatment, while guidelines suggest all patients should have one. Within the hydroxychloroquine retinopathy high-risk cohort, 91% of patients were getting yearly eye exams. Results post-intervention are pending a re-audit in November 2016.
**Conclusion:** Our guideline-based standards of appropriately dosing hydroxychloroquine and monitoring for retinopathy are not being met in typical patient encounters. The current system can be improved and the next step is to provide clinicians with a weight-based dosing chart that includes monitoring requirements. This intervention will be applied over three months and a re-audit will be conducted. The results will be compared to pre-intervention outcomes. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**32**

**Canadian Rheumatologists' Perceptions on Clinical Audits**

Sahil Koppikar (Queen's University, Kingston); Henry Averns (Kingston)
**Objectives:** Clinical audits are quality improvement processes that seek to improve patient care through systematic reviews of care against explicit criteria. While common practice internationally, the Royal College of Physicians and Surgeons of Canada does not currently mandate clinical audits be completed. Therefore, it is unclear how many Canadian physicians actually conduct these audits. The purpose of this study was to evaluate Canadian rheumatologists' perceptions and involvement in clinical audits, perceived benefits and barriers, and its impact on improving patient care.
**Methods:** Rheumatology was chosen due to its practice environment and guidelines being amenable to clinical audits. All licensed rheumatologists in eastern Ontario were invited to participate in the study. An anonymous online survey questionnaire was used to evaluate rheumatologists' attitudes looking at perceived benefits, barriers and facilitating factors around clinical audits. The survey involved multiple choice options and responses on a 5-point Likert scale. Weighted average scores (WAS) were calculated for relevant questions. Basic demographic data was also collected.
**Results:** Among the 22 participants, 14 had university affiliations, with an average time in practice of 11-15 years. Overall, most rheumatologists (21/22) did not have clinical audits embedded as part of their routine practice. Interestingly, while 17 participants were aware that clinical audits were reportable to the RCPSC for MOC credits, only 8 had ever taken part in one previously. Of those that had participated before, areas audited mostly involved screening guidelines around investigations or treatment effectiveness and safety. Rheumatologists that had completed clinical audits previously mostly agreed that it helped improve patient care in their practices with a WAS of 4. All 22 rheumatologists either agreed or strongly agreed that clinical audits have the potential to improve patient care with a WAS of 4.27. Other major benefits included the ability of audits to provide professional satisfaction (3.77), improve delivery of health services (4.05), and achieve the standard of care (4.27). The biggest barriers to conducting clinical audits were lack of time (3.41), shortage of staff (3.36), and a lack of expertise with clinical audits (3.0). Fifteen rheumatologists were willing to participate in future audits with 11 of them wanting EMR tools to help facilitate the process.
**Conclusion:** While Canadian rheumatologists recognize the benefits of practice reflection programs in patient care and safety, there are clear barriers limiting the implementation of clinical audits. Most rheumatologists are willing to participate in clinical audits provided they are given appropriate resources. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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## Efficacy and Safety Analysis by Overall Anti-drug Antibody Result up to Week 30 in Patients with Rheumatoid Arthritis Treated with SB2 (an Infliximab Biosimilar) or Reference Infliximab in a Phase III Study

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**Objectives:** SB2 is approved by the European Medicines Agency as a biosimilar of the reference infliximab (INF). The clinical results of this phase III study have been reported. The objective of this study is to compare the efficacy and safety results including infusion related reaction by anti-

drug antibody (ADA) status up to Week 30 in patients with rheumatoid arthritis (RA) treated with SB2 or INF.
**Methods:** This study is a randomized, double-blind phase III study. A total of 583 patients with RA were treated with 3 mg/kg of SB2 or INF with background methotrexate (MTX). Efficacy, safety and immunogenicity were measured. The immunogenicity was measured using electrochemiluminescence with SB2 single tagged assay.
**Results:** The proportion of patients who developed ADA up to Week 30 were 55.1% in SB2 and 49.7% in INF. All efficacy parameters including ACR response rates were comparable between SB2 and INF treatment groups up to Week 30. There was a trend towards decreased efficacy in ADA positive subgroups compared with ADA negative subgroups in both treatment groups (ACR20 response rate in ADA positive subgroup: 56.6% in SB2 vs. 59.4% in INF; ACR20 response rate in ADA negative subgroup: 72.7% in SB2 vs. 71.2% in INF). Safety profiles were also comparable between SB2 and INF in both ADA positive and negative subgroups. Within each treatment group, safety profiles were comparable between ADA positive and negative subgroups. Two patients (1.6%) treated with SB2 and 4 patients (2.7%) treated with INF in the ADA negative subgroups, and 8 patients (5.1%) treated with SB2 and 9 patients (6.2%) treated with INF in the ADA positive subgroups reported an infusion related reaction.
**Conclusion:** Regardless of the overall 30-week ADA status, efficacy results were comparable between SB2 and INF. Efficacy tends to be lower in ADA positive subgroup compared with ADA negative subgroup. The safety profile including infusion related reactions were also comparable between SB2 and INF regardless of ADA status, but a higher proportion of patients reported infusion related reactions in ADA positive subgroup compared to ADA negative subgroup in both treatment groups.

**34**

**High Disease Activity is a Predictor of Depression and Persistent Depression in Early Rheumatoid Arthritis: Results from the Ontario Best Practices Research Initiative (OBRI)**

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**Objectives:** Prior studies have shown that the prevalence of depression among individuals with rheumatoid arthritis (RA) may be as high as 40% but persistence of depression over time is relatively unknown. Uncontrolled inflammation may drive severe disease and, in turn, inflammation and high disease activity are hypothesized to mediate depressive symptoms. The aims of this analysis were to: (1) describe the prevalence of depression at baseline and determine how often depression persists over time; (2) evaluate if high disease activity is associated with depression in early RA (ERA).
**Methods:** We selected RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) with ERA (≤ 1 year disease duration) and at least one follow-up visit. Depression was ascertained by patient self-report at baseline and over the first 2 years of follow-up. The association between baseline disease activity measured by the Clinical Disease Activity Index (CDAI) and depression at baseline or persistent depression (defined as self-reported depression at 1 and 2 years of follow-up), was evaluated with multivariate logistic regression, adjusted for

potential confounders.
**Results:** 722 patients with ERA at OBRI enrolment (73.9% female) were included with a mean (SD) age of 56.2 (13.8) years. Mean (SD) disease parameters were: CDAI: 22.2 (13.9); DAS28: 4.5 (1.6); physician global: 4.6 (2.4), and HAQ disability Index: 1.1 (0.7). Almost one-third of patients (26.7%) reported depression at baseline, while 20.7% had persistent depression.. Persistent depression was significantly higher (23.1%) in patients with moderate/high disease activity (CDAI>10) at baseline compared with those with low disease activity (CDAI ≤10) (12.3%, p=0.02). After adjusting for potential confounders (sex, rheumatoid factor status, prior use of DMARDs, HAQ disability index), increased CDAI at baseline was significantly associated with depression at baseline (adjusted OR: 1.03; 95%CI: 1.01-1.04, p=0.001). Furthermore, increased CDAI at baseline was identified as an independent predictor of persistent depression after 2 years (adjusted OR: 1.03; 95%CI: 1.01-1.05, p=0.004). Female gender (adjusted OR: 1.96; 95%CI: 1.06-3.62, p=0.03) and prior use of DMARDs (adjusted OR: 0.49; 95%CI: 0.29-0.82, p=0.001) were also associated (positively and negatively, respectively) with persistent depression.
**Conclusion:** Depression in ERA is common and higher disease activity at baseline is significantly associated with the probability of depression. Furthermore, initial high disease activity was associated with persisting depression. Further analyses will explore the relation between changes in disease activity over time and risk of depression.

**35**

**Impact of Concomitant Use of Disease Modifying Antirheumatic Drugs and Methotrexate Administration Route on Durability of Biologic Treatment: Results from the Ontario Best Practice Research Initiative (OBRI) Cohort**

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**Objectives:** Prior controlled clinical trials and observational studies have suggested that concurrent DMARD therapy enhances the efficacy of TNF inhibitors. Furthermore, differences in the effectiveness and survival of subcutaneous vs. oral methotrexate have been previously shown. We aimed to assess the impact of concomitant DMARD use and methotrexate route of administration on time to biologic discontinuation in RA patients initiating biologic treatment in a large Canadian observational cohort.
**Methods:** Patients enrolled in the Ontario Best Practice Research Initiative (OBRI) that initiated biologic therapy and had at least one follow-up assessment were included in the primary analysis. Patients using combination therapy with biologics and MTX were also included for the subgroup analysis. The impact on biologic discontinuation due to (i) any reason, (ii) inefficacy, and (iii) safety, was assessed with multivariate Cox regression using concomitant DMARD use (primary analysis) and MTX route of administration (secondary analysis) as time-dependent covariates.
**Results:** Among the 748 patients included in the primary analysis, 116 (15.5%) received biologic monotherapy and 632 (84.5%) were on combination therapy. Mean (SD) age and

disease duration were 55.5 (12.7) years and 9.5 (9.9) years, respectively, while the majority were females (79.1%), without any significant differences between groups. Over a mean (SD) follow-up of 1.8 (1.6) years biologic discontinuation was reported for 38.6% of patients. Upon adjusting for potential confounders (socio-demographics, health insurance information, disease parameters, prior and concomitant medications), no significant differences were observed between combination therapy with DMARDs vs. biologic monotherapy in discontinuation due to any reason [HR (95%CI): 0.90 (0.68-1.20)], inefficacy and safety reasons [0.95 (0.66-1.38)], or inefficacy [1.45 (0.89-2.39), 0.14]. However, patients on combination therapy had significantly lower hazard of discontinuation due to safety reasons as compared to patients on monotherapy [0.47 (0.28-0.78), 0.004]. In the subgroup analysis, upon adjusting for potential confounders and taking into consideration MTX dose, no statistical association between route of MTX administration and biologic durability was observed.
**Conclusion:** This analysis showed that, unlike registries from other countries, concomitant use of DMARDs is not associated with durability of biologic treatment in Canadian routine clinical practice. However, a lower hazard for discontinuation due to safety reasons was observed in patients on combination therapy suggesting potential survivor bias. Furthermore, neither route of administration nor dose of MTX were significant predictors of biologic durability despite the fact that previous studies have shown differences in efficacy when a biologic was used as monotherapy, with suboptimal doses of concurrent MTX.

**36**

**Multimorbid Conditions Linked with Inflammation are Prevalent Around the Time of RA Diagnosis and Associated with Disease Activity in the First Year of Follow Up: Results from the Canadian Early Arthritis Cohort**

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**Objectives:** Estimate the prevalence of nine multimorbid conditions previously linked with inflammation around the time of RA diagnosis, and associations with RA clinical characteristics, treatment strategies, and trajectories of disease activity in the first year of follow up.
**Methods:** Data were analyzed from early RA (ERA) patients (<1-year symptom duration) enrolled in the Canadian Early Arthritis Cohort (CATCH) who met 1987 or 2010 ACR/EULAR RA criteria, and had at least two DAS28 measures available in the first year. We examined baseline multimorbidity with the following conditions associated with inflammation: 1) cardiovascular disease (CVD), 2) diabetes, 3) cancer, 4) pulmonary disease, 5) bowel disease, 6) other rheumatic diseases, 7) psoriasis, all obtained from patient-reports of a doctor diagnosis of each condition, 8) obesity (BMI>= 30) and 9) depressive symptoms (RAND-12 <42). Other baseline covariates included: age, sex, race, education, smoking, symptom duration and RA treatment. We compared baseline clinical characteristics in RA + each condition vs. RA alone as well as adjusted effects of each condition on early treatment with steroids and DMARDs using logistic regression. Adjusted associations of multimorbid conditions with DAS28 trajectory over the first year of follow up were estimated using linear growth models.
**Results:** The sample included 1595 patients with a mean(sd) age of 54(15) years, symptom

duration of 6(3) months, and 1153 (72%) were female. At baseline 1434 (92%) were treated with conventional DMARDs (majority with methotrexate (76%)) and 33 (2%) with a biologic. Over 7/10 ERA patients reported at least one other multimorbid condition, and 1/ 3 reported multiple (2+) conditions. Patients with multimorbid conditions were often older and had more severe RA at baseline, with variations by condition. RA+CVD and RA+ depressive symptoms were associated with a 60% and 90% higher odds of steroid use at baseline, respectively, relative to RA alone ($p<.001$). In fully adjusted growth models, presence of diabetes, other rheumatic diseases and depressive symptoms were associated with higher baseline DAS28 scores and less DAS28 improvement over time; pulmonary disease, bowel disease, psoriasis and obesity were associated with less DAS28 improvement over time, and CVD and cancer were associated with higher DAS28 scores at baseline only (all $p<0.05$).

**Conclusion:** ERA patients frequently reported multimorbid conditions linked to inflammation that were associated to varying degrees with early disease presentation, treatment, and worse DAS28 trajectories over time. Further, study is needed to determine if integrated treatment approaches addressing multimorbid rather than single inflammatory conditions may yield better outcomes.

**37**

**Exploring the Management of Cardiovascular Risk by Rheumatologists, Cardiologists, and Primary Care Providers in Patients with Inflammatory Arthritis: A Quality Improvement Study**

Richard Norman (University of Toronto, Toronto); Amanda Steiman (Mount Sinai Hospital, Toronto)

**Objectives:** There is mounting evidence that patients with inflammatory arthritis, including RA, AS, and PsA, are at increased risk of cardiovascular disease, and that this risk is under recognized and undertreated. One modifiable cardiovascular risk factor is dyslipidemia, for which there is no specific, evidence-based guidance for management in patients with inflammatory arthritis. As the first step in arriving at an ad hoc, locally consistent approach to lipid management in these patients, we surveyed academic rheumatologists, cardiologists and primary care providers to identify how dyslipidemia is managed, by whom, and knowledge gaps to be bridged.

**Methods:** An online questionnaire was distributed to rheumatologists, cardiologists and primary care providers at five academic teaching hospitals in Toronto, Canada. Domains covered included practice type, perceptions of cardiovascular risk in patients with inflammatory arthritis, preferred resources (e.g. guidelines), and clinical approach to managing dyslipidemia. A series of patient vignettes was included to assess decision-making regarding lipid management. Descriptive analyses have been performed to date.

**Results:** Data collection is ongoing. Preliminary results were collected from 32 practitioners (8 rheumatologists, 8 cardiologists, and 16 primary care providers). Primary care providers were most likely to be the lipid managers (78%). Rheumatologists virtually always entrusted other providers with management. Practitioners referred to a variety of guidelines for lipid management, although none applied the weighted Framingham (EULAR) approach for patients with RA. 56% of practitioners incorrectly identified the appropriate screening age for patients with inflammatory arthritis, as set out in local guidelines. The majority (63%) of practitioners estimated they spent two minutes or less addressing cardiovascular risk during a typical patient encounter. For the patient vignettes, there was marked variability between providers (both within and between specialties) regarding thresholds for treatment. Practitioners estimated

cardiovascular risk as being similar between two matched vignettes, one with traditional cardiovascular risk factors and one with RA.
**Conclusion:** These preliminary results support the need for guidance and consistency in lipid management in patients with inflammatory arthritis. There are several potential avenues for improvement, including engaging primary care providers in knowledge translation activities, as these practitioners are most likely to manage lipids. There was considerable variability of approach in the pilot cohort thus far. This observation may translate to disparities in clinical outcomes. There is a strong need for clear, evidence-based guidelines for management of lipids and cardiovascular risk in patients with inflammatory arthritis. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**38**

**Multiple Statistical Imputation of Missing Data in a Real World Clinical Cohort Increased Sample Size and Power with Minimal Deviations Enhancing the Clinical Research Potential of the Observational Dataset**

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**Objectives:** Real-world observational studies occur amid the context of day-to-day clinical care where missing data including data not collected or patients lost at follow-up are unique when compared to clinical trials. Clinical trials use large budgets and strict control of clinical practice to avoid missing data. In order to continue to reflect the realities of clinical care, imposing strict guidelines on care to reduce missing data is not preferable. We sought to use the current best practices in clinical observational research, multiple statistical imputation (MSI), to assess the difference in data quality when MSI was used compared to when data were simply left missing.
**Methods:** Core variables were selected based on their frequency of use by researchers querying data from the Ontario Best Practices Research Initiative, an observational clinical cohort of adult patients with incident or prevalent active rheumatoid arthritis (RA ) in Ontario (n=3075) with n=56 rheumatologists contributing patients. The variables selected were patient demographics, RA disease activity (DAS28, CDAI), and HAQ score. MSI works by replacing the missing values for each patient with a plausible substitute based on the complete data from all patients that are similar to the patient with the missing data value. In order to determine if MSI improved data quality we used statistical models (Generalized Linear Models) to compare an identical analysis in the OBRI dataset including missing data, then again in the OBRI dataset with no missing data due to MSI.
**Results:** A total of 3075 patients were included in the study, with 47,703 visits. Results using the original data with missing values compared to the complete data after imputation were almost identical Db=0.0013-0.02, with a reduced standard error 0.15-0.08. Clinically, this means the models had a small difference in DAS28 of less than 1% and a decrease in standard deviation of 41% for clinical research using MSI data instead of datasets containing missing data.
**Conclusion:** Because the differences in models were small, results from the MSI dataset were functionally identical yet had narrower confidence intervals. Therefore, the use of MSI in the OBRI clinical cohort increased sample size and power while minimizing standard deviation and

confidence intervals enhancing the clinical research potential of the observational dataset. MSI represents the most methodologically rigorous approach to missing data thus minimizing error in clinical results. Future analyses from querying the OBRI database will rely on MSI.

**39**

**The Efficacy of an Osteoporosis Clinic in a Community Hospital Setting: A Retrospective Chart Review and Telephone Survey**

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**Objectives:** Patients with fragility fractures secondary to osteoporosis are at increased risk of subsequent fractures, morbidity and mortality. The Osteoporosis (OP) Clinic at Markham Stouffville Hospital (MSH) was set up in July 2015 to screen, diagnose and treat patients with fragility fractures. The goal of this study was to identify differences in OP screening and treatment initiation between patients seen in the OP clinic versus usual care to determine care gaps in secondary fracture prevention.

**Methods:** A retrospective chart review and telephone interview was conducted on 40 patients who had sustained a hip fragility fracture from September 2015 to July 2016. 20 of those patients were referred to the OP clinic through fracture clinic, while the remaining patients received usual care (i.e. follow-up with family practitioner after fracture clinic). Patients with dementia, a palliative condition or those in long-term care facilities were excluded from the study.

**Results:** Mean age of patients in the OP clinic group was 79.3 compared with 81.5 in the usual care group. 80% of patients in the OP clinic group were female compared with 75% in the usual care group. Risk factors for osteoporosis were present in the OP clinic group: previous glucocorticoid use (20%), parental hip fracture (5%), currently smoking (5%), >3 alcoholic drinks per week (5%). Mean BMD T-score for the OP clinic patients was -2.28. BMD information was not available for the usual care group. Bisphosphonate/RANKL inhibitor was prescribed to 60% (12/20) of OP clinic patients who were deemed eligible, of which 80% filled the prescription within 15.8 days. 7/20 patients were on OP drug therapy prior to OP clinic referral, and in all cases, the existing OP medication was continued or switched to another drug class. Self-reported compliance with prescribed treatment was 75% at 3 months. In the usual care group, 10/20 patients had a BMD test scheduled after their fracture. 5/20 patients were taking OP treatment prior to their fracture. Following usual care, one additional patient was initiated on OP treatment.

**Conclusion:** A significant care gap exists in secondary fracture prevention between the OP clinic and usual care groups. As such, better screening and subsequent intervention is needed for patients with fragility fractures. This study also highlights the efficacy of an OP clinic in a community hospital setting. Future directions include inclusion of OP clinic referral in pre-printed order sets and education endeavours to engage family practitioners in OP management for patients with fragility fractures. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**40**

**Presence and Frequency of Power Doppler Signals are Associated with Higher Leeds Foot Impact Scale Scores in Early Rheumatoid Arthritis Patients**

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**Objectives:** There is a lack of evidence elucidating the clinical value of ultrasonography (US) for the functionality and quality of life of patients with early Rheumatoid Arthritis (RA). This study assessed the relationship between Power Doppler ultrasound (PDUS) scores in the metatarsophalangeal (MTP) joints of patients with early RA and clinical outcomes related to their feet and overall general health.
**Methods:** Patients between 18 and 85 years who were newly diagnosed with RA (treatment naïve, ACR criteria) were eligible. Consenting participants completed the Leeds Foot Impact Scale (LFIS) and the Health Assessment Questionnaire (HAQ), which included domains addressing pain, fatigue, and global arthritis activity (GL). Swollen and tender joints were assessed for MTPs 2-5 of both feet by a rheumatologist. This same rheumatologist also performed and interpreted PDUS scans of the same joints of each participant. PDUS of each MTP was graded on a scale of 0-3 (OMERACT criteria), and results from both feet were summed to reflect the severity of inflammation. A Mann-Whitney test compared each clinical outcome in the presence/absence of PD findings in the feet. Linear regression analyses determined the associations between clinical outcomes and a) the total number of joints with PD signals ≥1, and b) the severity of total PD scores.
**Results:** This study included 40 patients [n=32 female, mean (SD) age=52.1 (10.4) years]. Patients with a PD score ≥1 in any MTP joint (n=16) had significantly higher LFIS scores than patients with no positive PD signal (U=113, p=0.029). A significant positive correlation was found between the number of joints with PD signals ≥1 and LFIS (standardized ß=0.312, p=0.050). The severity of PD scores significantly correlated with the swollen joint count (standardized ß=0.312, p=0.050), but not with the tender joint count. No significant correlations were found between PD and any of domains (pain, fatigue, and GL) of the HAQ.
**Conclusion:** In this small sample of early RA patients, PD findings correlated with several clinical outcomes. Patients reported significantly more functional impairments in the LFIS when their MTP joints showed the presence of PD signaling, and when patients had more inflamed joints in the feet. It appears that that the number of inflamed MTP joints rather than the extent of inflammation is a correlate of feet functionality in an early RA population.

**41**

**A Randomized Single-blinded Controlled Trial of Ischemic Preconditioning for the Treatment of Raynaud's Phenomenon (RP)**

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**Objectives:** Raynaud's phenomenon (RP) consists of episodic vasospasms of digital arteries with underlying dysfunction of vascular endothelium. Ischemic preconditioning (IPC) is a therapeutic strategy protective against future ischemia, with brief cycles of ischemia and reperfusion resulting in circulating endogenous compounds being released from ischemic cells. IPC can be induced by inflating and deflating a standard blood pressure cuff placed on the upper arm in repeated bursts. We hypothesized that IPC would be more effective than sham in RP treatment, with decreased frequency, duration, and/or severity of RP episodes (primary outcomes). Secondary outcomes included scores from the Disability Arm Shoulder and Hand (DASH), Health Assessment Questionnaire Disability Index (HAQ-DI), and 15-point pain scale. Sample size required 13 patients to find 6 fewer RP attacks per week at 80% power.
**Methods:** This was a randomized controlled, single-blinded cross-over trial. The active

intervention of inflating the cuff on the upper arm (200 mmHg) and sham (60 mmHg) were performed 3 times per week for 2 weeks, with a 2-week washout period between active and control (sham) interventions. Cuff inflation was performed 4 times for 2.5 minutes, with 2.5 minutes between inflation of BP cuff. Participants completed a daily diary recording number of RP episodes, duration, and a 10-point severity score. Participants of age 18 years or older with at least 7 RP episodes per week over a 2-week pretreatment period and a systolic blood pressure of at least 80 mmHg were recruited. Participants with new or changed RP treatment in the pretreatment period and during the study were excluded.
**Results:** 18 patients were enrolled (17 with secondary RP and 1 with primary RP); mean age 60.8 (SD 9.4), 89% female; and mean number of RP attacks/2 weeks in screen was 16.9 (SD 11.3). With IPC versus control, results were not significant (NS) including an increase of 0.5 RP episodes/week (SD: 10.0; p=0.42), decrease of 55.6 minutes per week (SD 516.4; p=0.33), and a decrease in average severity of 0.4 points (of 10) (SD 12.9; p=0.44). Secondary outcomes were also NS [DASH score decrease of 0.07 (SD 10.08, p=0.49), HAQ-DI increase of 0.48 (SD 2.61, p=0.10), and pain increase by 0.69 (of 15) (SD 2.83, p=0.16)].
**Conclusion:** No differences between IPC and control were found. This could be due to lack of effect of IPC on RP, too few treatments, sham also being effective, or the drop in RP frequency being too low to be clinically relevant.

**42**

**Lupus Erythematosus, Antibodies against Mitochondrial DNA and their Clinical Associations**

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**Objectives:** Knowing that double membrane containing cardiolipins is present in mitochondria and that mitochondria extruded from cells promote inflammation in systemic lupus erythematosus, we issued the hypothesis that the presence of antibody against mitochondrial DNA and whole mitochondria is 1) higher in patient with lupus versus controls and 2) may be associated with thrombosis and 3) level of disease activity.
**Methods:** In this cross-sectional cohort study, we used the serum and data from 2 SLE registries (Toronto and Quebec City) and a control group. We developed assays to measure antibodies against whole mitochondria (AMA) and mitochondrial DNA (AmtDNA) and tested each subjects and controls for IgG antibodies. Our main outcome variables were defined as thrombosis event and SLEDAI score ≥ 4. We compared the mean of antibodies from a SLE group to the controls with a linear mixed model. Odds ratio with 95% confidence interval [OR (CI)] were derived from bivariate and multivariate logistic regressions. Models were adjusted for disease duration, age, BMI, antimalarial and prednisone treatment.
**Results:** Data from a total of 247 participants was captured (181 in Toronto and 66 in Quebec) and 44 controls. The mean comparison between SLE vs controls showed a statistically significant difference for AmtDNA_IgG [mean (0.74 ± 0.02) vs (0.62 ± 0.02) and AMA_IgG [mean (1.49 ± 0.04) vs (1.19 ± 0.06)] p<0.0001 for both for OR 29 (4 - 226) and 3 (2 – 6). Forty-eight of these participants had had confirmed thrombotic events and the SLEDAI score was ≥ 4 for 85 patients. The association of thrombotic event with AmtDNA was significant OR 0.12 (0.01 – 1.47) p=0.10 [0.02][1] for Quebec and with AMAIgG OR 0.49 (0.25 – 0.98) p= 0.04

[0.06]1 for Toronto. There was a significant association with SLEDAI≥4 in both groups, which seems to be due to its increased dsDNA item. [1] 1st value is bivariate and the 2nd multivariate.
**Conclusion:** IgG Antibodies against mitochondria seems more abundant in lupus patients than in controls and preliminary findings on the AMA suggest that this antibody may be associated with a protective effect against thrombosis in these patients. It would be interesting to compare our tests to the increased dsDNA associated with disease activity. The fact that our results are based on a single measure in time limits the current analysis and we are working at collecting longitudinal informative biospecimen in the MRAS Biobank and Data Repository in Quebec City.

**43**

**Incident Autoimmune Inflammatory Myositis in Systemic Sclerosis – Results of a Longitudinal Study**

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**Objectives:** Studies of autoimmune inflammatory myopathies (AIM) in systemic sclerosis (SSc) have numerous limitations. We undertook this study to identify predictors and outcomes of incident AIM in a large, multi-center SSc cohort using prospective, standardized data collection.
**Methods:** Subjects in the Canadian Scleroderma Research Group registry who did not have AIM, defined as the presence of inflammatory myositis or overlap with polymyositis / dermatomyositis recorded by a study physician, at baseline were identified. The cumulative incidence of AIM was determined. Baseline characteristics of subjects with and without incident AIM were compared to identify clinical and serological predictors of AIM. Kaplan Meier and Cox proportional hazards models were used estimate survival.
**Results:** 1182 SSc subjects with a mean follow up of 4.4+2.6 years were included, of which 69 (6.2%) developed new onset AIM during follow up. A cumulative incidence curve demonstrated that AIM developed at a constant rate of 1.3/100 patient-years. There were no differences in age and sex at baseline between those who did and did not develop AIM. Subjects who developed AIM were more likely to have diffuse cutaneous disease (58% vs 34%, p<0.0001), tendon friction rubs (32% vs 11%, p<0.0001) and inflammatory arthritis (49% vs 28%, p=0.0003) at baseline compared to those who did not. Interestingly, subjects who developed AIM were already more likely to have muscle weakness[VL1] (26% vs 14%, p=0.006), higher creatinine kinase[VL2] (110 vs 87 u/L, p=0.05) and lower FVC %predicted (88% vs 92%, p=0.09) without any difference in ILD (28% vs 30%, p=0.67) at baseline compared to those who did not. Subjects who developed AIM were less likely to have anti-centromere antibodies at baseline compared to those who did not (27% vs 42%, p=0.02). There were no statistically significant differences in the rates of anti-topoisomerase (24% vs 16%), -PM-Scl (5% vs 4%) or -U1RNP (9% vs 5%) autoantibodies between the two groups. There was no difference in the risk of mortality in those who developed AIM compared to those who did not (unadjusted log-rank p=0.52 and adjusted hazard ratio 1.19 (95% CI 0.38, 3.77).
**Conclusion:** This study provides robust estimates of the magnitude, predictors and outcomes of AIM in SSc. Notably, SSc subjects who develop AIM may have sub-clinical muscle disease prior to their diagnosis of AIM. Given the relative rarity of AIM in SSc, these findings may help clinicians caring for people with SSc make timely diagnoses of AIM, initiate treatment promptly

and optimize outcomes.

**44**

**A Retrospective Study of Osteoporosis Medication Adherence in Patients who Attended an Interprofessional Osteoporosis Therapeutic Program after Sustaining a Fragility Fracture**

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**Objectives:** Osteoporosis (OP) is both an economic strain and a growing threat to our aging population. Treatment rate following fragility fracture, a complication from osteoporosis, remains low. Non-adherence to OP prescription is well documented with greater than 50% of patients considered as poorly persistent within 12 months. Educating patients about both the risks and benefits of each medication by addressing fears and side effects proactively may help adherence. Our program offers an interprofessional team approach to osteoporosis care including timely investigation post fragility fracture, consultation with specialist and allied healthcare team, and holistic education opportunity. Objectives of this study were to determine 1) order rate, 2) initiation rate and 3) persistence rate of OP prescription at 6 and 12 months after attendance in OP clinic.

**Methods:** Patients with fragility fractures referred by the Fracture Clinic Screening Program-Ontario Osteoporosis Strategy, and attended OP clinic from January 2015 to June 2016 were included in this study. Retrospective chart review was conducted to collect data on relevant covariates including age, gender, fragility fracture site, attendance of the OP Therapeutic Education Program and pattern of OP prescription use 6 months and 12 months after attending OP Clinic. Initiation and persistence rate of OP prescription were determined from dispensing history via the Ontario Drug Benefit database (Drug Profile Viewer) as available.

**Results:** Of the 321 patients referred, 231(72%) were seen in OP clinic with mean age 69 (SD 11), 93% female. Bone Mineral Density (BMD) testing was expedited for 205 (64%) patients. Most common fracture sites were wrist (43%), humerus (16%) and hip (15%). Amongst those who attended OP clinic, 47% were at high risk and 45% were at moderate risk per the Canadian Association of Radiologists and Osteoporosis Canada (CAROC) criteria. Order rate of OP prescription was 86% in high risk group and 28% in moderate risk group. Of the 72 treatment naïve patients, dispensing history was available for analysis in 45 patients. Initiation rate within 60 days post clinic was 88.4% (40/45), persistence rate of OP prescription use was 81.5% (31/38) at 6 months and 100% (22/22) at 12 months post clinic.

**Conclusion:** High prescription order rate was seen in the high risk group and the respective lower rate in moderate risk group may reflect patient's preference to postpone medication use. Initiation and persistence rates appeared to be high but larger sample is needed to confirm findings. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

**45**

**An Ongoing Commitment to Evaluate Inter-rater Reliability in Joint Count Assessment and Provider Global Assessment as Supported by an Interprofessional Arthritis Care**

**Team**

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**Objectives:** Joint count assessment is an integral component in diagnosing and ongoing evaluation of rheumatoid arthritis (RA). The presence of variability between assessors in joint count assessments has been well documented. Since we take a team based approach to arthritis care, it is important to evaluate the extent of variability in joint counts between individual assessors and make ongoing effort to minimize this gap. This is a follow-up study to the previous project where correlation of swollen joint count (SJC) amongst a large interprofessional arthritis care team was found to be moderate with Intraclass Correlation Coefficient (ICC) of 0.51. The goal of this study is to estimate the congruence in a) swollen joint count assessment and b) provider global assessment (PrGA), both being American College of Rheumatology core set measures for improvement in RA disease activity.

**Methods:** In first part of the study, assessors performed a 28 SJC on each patient independently. In the second part, assessors completed a provider global disease activity worksheet where four scenarios were given with the following parameters: age, VAS scores (pain, fatigue, sleep, patient global), duration of morning stiffness, mHAQ, tender joint count, swollen joint count, grip strength. Assessors assigned a score of 1 to 10 based on their impression of overall RA disease activity. Upon study completion, patient volunteers and assessors gathered for debrief, and answered a survey for attainment of qualitative feedback.

**Results:** Three patients participated in the SJC assessment (mean age 67.3 ± 18.6). Two of the three patients have a diagnosis for RA (<1 year) and one patient has a diagnosis for psoriatic arthritis (>3 years). All patients (100%) were taking DMARD(s). Thirteen assessors participated, including 4 rheumatologists and 9 clinicians from 3 other health disciplines. The ICC of 28 SJC amongst 12 assessors was 0.86, indicative of good correlation. With respect to PrGA, the ICC amongst 13 assessors was 0.96, also indicative of good correlation. Review of satisfaction survey completed by assessors showed 100% agreed the study fostered a culture of trust and demonstrated commitment to quality improvement, and 100% support a full team intervalidation study annually.

**Conclusion:** There appears to be a trend of improvement in inter-rater reliability 28 SJC assessment (from ICC 0.51 to 0.86). Repeating the evaluation of SJC and PrGA assessment amongst team members periodically may help to maintain reliability and continue fostering a culture of trust. Bigger sample size is needed to confirm findings.

**46**

**Bridging the Information Gap: Developing an Educational Resource on Pregnancy and Parenting with Arthritis**

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**Objectives:** An educational resource was developed regarding pregnancy and parenting with arthritis which is the second phase of a project led by the Canadian Arthritis Patient Alliance (CAPA). Results of a CAPA-led survey on pregnancy and parenting indicated a high need for information for people living with arthritis when faced with these important life decisions. The topics identified through this survey guided the development of this web-based resource.
**Methods:** The results of a CAPA-led survey were analyzed to determine the relative importance of the topics identified by respondents. Priority was placed on developing content for the topics identified by respondents as "very important" and "important". One Board member acted as project manager to design the web page, analyze the survey results, develop the content and obtain input on the content from various stakeholders including people living with arthritis, researchers and rheumatologists. Methods to obtain input and feedback for the resource were through collaborative software tools (Balsamiq), e-mails, phone calls and in person meetings. Feedback was gathered from stakeholders and incorporated into the educational resource.
**Results:** An educational resource on pregnancy and parenting with arthritis was developed in consultation with people living with arthritis, researchers and rheumatologists. The resource addresses key gaps in information identified through a CAPA survey for people living with arthritis and those in their network of support. Ongoing efforts will be made to add to the resource and promote it to the wider community including other patient organizations, health care professionals and researchers. Monitoring the use of the resource will be done through social media and website metrics as well as surveys.
**Conclusion:** CAPA developed an on-line resource for people living with arthritis regarding pregnancy and parenting. CAPA aims to raise the profile of this issue and help people living with arthritis engage in more dialogue with their healthcare providers during these critical life events. An educational resource can be an effective tool for people living with arthritis as they navigate through uncharted territory. In turn, it is expected that use of the resource will facilitate better health care decisions for themselves and their families, improve communication with health care professionals, enable shared decision making and reduce overall stress for people living with arthritis and their families. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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## Comparison between Continuing SB4 (Etanercept Biosimilar) and Switching from Reference Etanercept to SB4: Long-Term Safety and Efficacy of SB4 from a Phase III Study

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**Objectives:** SB4 is approved by the European Medicines Agency as a biosimilar of the etanercept reference product (ETN). The phase I study results and 52-week results of phase III study have been reported previously. The objective of this study is to evaluate the long term safety, immunogenicity, and efficacy of continuing SB4 vs. switching (as will occur in clinical practice) from ETN to SB4 in patients with moderate to severe rheumatoid arthritis (RA).
**Methods:** The phase III randomised, double-blind study period consisted of 52 weeks of

treatment with either weekly dose of subcutaneous 50 mg SB4 or ETN with background methotrexate (MTX) in patients with moderate to severe RA. After 52 weeks of treatment, patients in Czech Republic and Poland were enrolled into the open-label, extension period and received SB4 for an additional 48 weeks. Efficacy, safety, and immunogenicity were assessed up to week 100.

**Results:** At week 52, 245 patients from the randomised, double-blind study period enrolled into the extension study: 126 patients continued to receive SB4 (SB4/SB4) and 119 patients switched from ETN to SB4 (ETN/SB4). From the SB4/SB4 group and ETN/SB4 group, respectively, 119 (94.4%) patients and 113 (95.0%) patients completed 100 weeks of treatment. SB4 was well tolerated and the safety profile was comparable between SB4/SB4 and ETN/SB4 during the extension period. The proportion of patients who experienced any adverse events after switching was 47.6% in SB4/SB4 and 48.7% in ETN/SB4. During the extension period, neither active tuberculosis nor injection site reaction was reported and 1 patient (0.8%) from SB4/SB4 and 1 patient (0.9%) from ETN/SB4 developed anti-drug antibodies. The American College of Rheumatology (ACR) responses were sustained and comparable between SB4/SB4 and ETN/SB4. At week 100, the ACR20 response rates were 77.9% vs. 79.1%, ACR50 response rates were 59.8% vs. 60.9%, and the ACR70 response rates were 42.6% vs. 41.7% in SB4/SB4 and ETN/SB4, respectively. Other efficacy endpoints were also comparable between the two groups. The radiographic progression assessed by modified Total Sharp Score was minimal and comparable between SB4/SB4 and ETN/SB4 (0.45 vs. 1.00).

**Conclusion:** SB4 was well tolerated and effective over 2 years in patients with RA. Efficacy, safety, and immunogenicity were comparable between the SB4/SB4 and ETN/SB4 groups and switching from ETN to SB4 had no treatment emergent issues such as increase in adverse events, increase in immunogenicity, or loss of efficacy.

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**Impact of Anti-Drug Antibodies on Efficacy and Safety up to Week 24 from A Phase III Study Comparing SB5 (An Adalimumab Biosimilar) with Reference Adalimumab in Patients with Moderate to Severe Rheumatoid Arthritis Despite Methotrexate Therapy**

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**Objectives:** SB5 is a biologic agent developed as a biosimilar of the reference adalimumab (ADL). The 24-week efficacy and safety results from a phase III study in patients with rheumatoid arthritis (RA) have been reported previously. Immunogenicity to monoclonal antibodies may affect patients' safety and efficacy. The objective of this study is to compare the efficacy and safety by anti-drug antibody (ADA) in patients with RA treated with SB5 or ADL up to week 24.

**Methods:** In this randomized, double-blind, phase III study, patients with moderate to severe RA despite methotrexate treatment were randomly assigned to receive 40 mg of either SB5 or ADL administered subcutaneously every other week. Efficacy, safety, and immunogenicity were measured.

**Results:** The proportion of patients with detectable ADA up to week 24 was 32.8% in SB5 and 31.5% in ADL. The ACR responses and other efficacy endpoints were comparable between SB5 and ADL up to week 24 both within patients with detectable ADA and within patients without

ADA. In the SB5 treatment group, there was a trend towards decreased efficacy (ACR20, ACR50, ACR-N, change in DAS28 from baseline, and in patients with remission based on DAS28, SDAI or CDAI) in patients with detectable ADA compared to patients without ADA. In the ADL treatment group, there was a trend towards decreased efficacy for patients in remission based on DAS28, SDAI or CDAI in patients with detectable ADA compared to patients without ADA, but other efficacy endpoints were comparable. The safety profiles of SB5 and ADL were generally comparable and the proportion of patients with any treatment-emergent adverse events in SB5 and ADL, respectively, were 34.1% vs. 31.4% in patients with detectable ADA and 36.5% vs. 44.3% in patients without ADA. Similarly, the proportion of patients who experienced an injection site reaction in SB5 and ADL, respectively, was 4.5% vs.1.2% in patients with detectable ADA and 2.2% vs. 3.8% in patients without ADA.
**Conclusion:** Patients with detectable ADA were more likely to have reduced efficacy compared to those without ADA. Efficacy was comparable across treatment groups within patients with detectable ADA and within patients without ADA. The safety profile was generally comparable regardless of the presence of ADA.

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**Criterion-related Validity of European Scleroderma Study Group Activity Index in an Early Scleroderma Cohort**

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**Objectives:** To explore whether disease activity, as measured by European Scleroderma Study Group Activity Index (EScSG-AI), correlates with serological and morphological signs of T-lymphocyte activation and capillary damage assessed over time in systemic sclerosis (SSc); and estimate the effect of disease activity on the risk of subsequent organ damage in a large SSc cohort.
**Methods:** Predictive validity: of 421 SSc patients from the CSRG database with disease duration of ≤3 years, 197 who had no evidence of endstage organ damage initially and available 3-year follow-up were included. Disease activity was assessed by EScSG-AI with two variability measures: adjusted mean (am) EScSG-AI (the area under the curve of AI over observation period), and persistently active disease/flare (PAD/Flare). Outcomes were based on the Medsger severity scale and included accrual of a new severity score (Δ≥1) overall and within specific organ systems, or reaching a significant level of deterioration in health status. Concurrent validity: 1) sIL-2R serum levels were studied by ELISA in 68 and 40 pts at baseline and 1-year FU, respectively; 2) microvascular pathology - in 78 (baseline) and 47 (FU) SSc pts using nailfold video capillaroscopy; 3) lymphocyte phenotyping - in 45 skin biopsies.
**Results:** After adjustment for covariates, amEScSG-AI was the most consistent predictor of risk across the study outcomes over 3 years in diffuse SSc (dcSSc): disease progression defined as Δ≥1 in any major internal organ, significant decline in FVC and DLCO, severity of visceral disease, and HAQ-DI worsening. In multivariate analysis, progression of lung disease was predicted solely by amEScSG-AI, while severity of lung disease – by amEScSG-AI, older age, modified Rodnan skin score (mRSS) and initial severity. EScSG-AI was associated with the patient- and physician-assessed measures of health status, and overpowered mRSS in predicting disease outcomes. T-lymphocyte activation marker (sIL-2R) and the number of T-lymphocytes in skin infiltrates were higher in active vs inactive SSc. Compared to baseline values, the mean sIL-2R levels significantly dropped at FU in pts with reduction in EScSG-AI (3975±2275 pg/ml

vs 7055±3630 pg/ml, p<0.003), but remained persistently high in those with PAD/Flare (5570±3625pg/ml, p=0.4). PAD/Flare was accompanied by further loss of capillaries (5.6±1.4 loops/mm, p<0.05).
**Conclusion:** EScSG-AI was closely linked to serological and morphological signs of Th2 activation. The activity burden over the observation period quantified with amEScSG-AI predicted the risk of deterioration in health status and development of severe organ involvement in dcSSc patients, suggesting that EScSG-AI is responsive to changes in disease activity.

**50**

**Experience with Tofacitinib in Canada: Rheumatoid Arthritis Patient Characteristics and Treatment Patterns from 2014 to 2016**

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**Objectives:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). This study characterizes patients with RA newly prescribed tofacitinib 5 mg twice daily (BID) in Canada and treatment patterns for tofacitinib use in Canadian clinical practice between June 2014 and August 2016.
**Methods:** A descriptive analysis of patient-reported demographic and medication history was performed for patients with RA newly prescribed tofacitinib and enrolled in the Canadian eXel support program, which provides support to physicians and patients, by facilitating access and patient education during treatment with tofacitinib.
**Results:** Between June 2014 and August 2016, 2749 patients with RA were newly prescribed tofacitinib and enrolled in the eXel support program. As of 31 August 2016, 1739 (63.3%) patients were actively receiving therapy, 200 (7.3%) were in the process of initiating therapy, 647 (23.5%) were no longer active in the program following treatment initiation and 163 (5.9%) did not initiate therapy. Reasons for treatment discontinuation included: lack/loss of efficacy (251/647 [38.8%]), other health issues (179/647 [27.7%]), and patient decision to try another therapy (91/647 [14.1%]). Based upon patient-reported information at baseline, the mean (standard deviation [SD]) age was 59 years (SD:12), the majority of patients were female (80.4%) and the mean disease duration was 14 years (SD:11). The majority of tofacitinib patients were residing in Ontario (35.4%), Quebec (23.1%), Alberta (9.9%) and Nova Scotia (7.9%) with 23.8% from the remaining provinces of Western and Atlantic Canada. Of the 2183 patients with available medication history, 439 (20.1%) were biologic-naïve and 1744 (79.9%) had used biologic disease-modifying antirheumatic drugs (bDMARDs) in the past. Of the patients who had received prior bDMARD therapy, the mean number was 2.2. Over 2014, 2015 and 2016, the use of tofacitinib in patients who had received ≤1 prior bDMARD has increased (36.2%, 37.9% and 47.1%, respectively).
**Conclusion:** Among Canadian patients with RA prescribed tofacitinib, most had received prior bDMARD treatment and had a long disease duration. Approximately 20% were biologic-naïve patients and an increase in the prescribing of tofacitinib to patients with ≤1 prior biologic failure was observed. Utilization of tofacitinib has been changing in Canada over the 2 years of observation.

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**Persistence of Tofacitinib in the Treatment of Rheumatoid Arthritis in Open-Label, Long-Term Extension Studies up to 8 Years**

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**Objectives:** Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). Time on treatment in long-term extension (LTE) studies is considered a composite measure of safety and efficacy for disease-modifying antirheumatic drugs (DMARDs), as discontinuation is often due to lack of efficacy (LOE) and/or adverse events (AEs). This analysis estimated drug survival of tofacitinib up to 96 months (8 years) and describes reasons for discontinuation.
**Methods:** Data were pooled from two LTE studies (NCT00413699 [ongoing; March 2015 data-cut] and NCT00661661 [completed April 2014]) of patients with RA who participated in Phase (P)1/2/3 tofacitinib studies. Of the 6,553 patients randomized in P1/2/3 studies, 4,867 patients (74.3%) received treatment in LTE studies with tofacitinib 5 or 10 mg twice daily (BID) as monotherapy or with background DMARDs. Kaplan-Meier analyses estimated drug survival in patients who withdrew from the LTE for any reason, due to LOE or due to AEs, including patients who had previously responded to and tolerated treatment in P1/2/3 studies. Ongoing patients were censored as of March 2015 and LTE completers at their end-of-study date.
**Results:** 4,867 patients were treated for a mean (maximum) duration of 3.0 (7.9) years in the LTE. The median drug survival for all tofacitinib-treated patients was 5.0 years (95% confidence interval 4.7, 5.2), for tofacitinib with background DMARDs was 4.9 (4.5, 5.2) and as monotherapy was 5.1 (4.6, 5.9) years. Similar median survival was observed between tofacitinib doses: 5.2 (4.8, 5.7) and 4.8 (4.5, 5.2) years for 5 and 10 mg BID, respectively. The discontinuation rate due to LOE was considerably lower than due to AEs (LOE: 3.1%, 3.5%, 3.0%; AEs: 21.6%, 25.2%, 20.0% for all tofacitinib, 5 or 10 mg BID, respectively). The most commonly reported reasons for discontinuation due to AEs were infections/infestations (8.8%, 8.5%, 8.9%), investigations (4.2%, 5.6%, 3.5%), and neoplasms (benign, malignant, unspecified) (3.2%, 4.4%, 2.8%) for all tofacitinib, 5 or 10 mg BID, respectively. Median survival was generally similar for patients receiving all tofacitinib, 5 or 10 mg BID with respect to monotherapy/combination therapy, and across selected baseline characteristics.
**Conclusion:** Drug survival in LTE studies provides important information on long-term safety, efficacy, and tolerability. Median survival of tofacitinib was ~5 years, with discontinuation more commonly associated with AEs than LOE. Similar survival was observed for tofacitinib 5 and 10 mg BID, monotherapy/combination therapy, and selected baseline characteristics. These data support tofacitinib use for long-term RA management.
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## Treatment Response to Methotrexate and Conventional Disease Modifying Anti-Rheumatic Drugs (DMARDS) in Seropositive and Seronegative Patients with Early Rheumatoid Arthritis: Results from CATCH (Canadian Early Arthritis Cohort)

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**Objectives:** Rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) may affect treatment response in early rheumatoid arthritis (ERA). Hence, differences in treatment response to methotrexate (MTX) and DMARDs in seropositive versus seronegative (RF and/or ACPA) patients with ERA were investigated.

**Methods:** Data were analyzed from patients enrolled in the Canadian Early Arthritis Cohort (CATCH), a prospective multi-site study of patients with ERA who had symptoms <1 year, not in remission at baseline (DAS≥2.6), and had available RF, ACPA, and DAS28 at baseline and at 3-6 months follow-up. Two-tailed t-tests and tests for proportions were used to compare differences in ΔDAS28/HAQ-DI/%DAS28 remission at 3-and 6-months in patients who were RF+ vs. RF-, ACPA+ vs. ACPA-, and RF + or ACPA+ vs. RF-ACPA-, respectively, treated with either: MTX monotherapy, MTX + hydroxychloroquine (HCQ), MTX + sulfasalazine (SSZ), triple therapy (MTX + HCQ + SSZ) and MTX + leflunomide (LEF).

**Results:** There were 1245 patients; baseline mean(SD) age was 55 (1), 906 (73%) were female; mean(sd) DAS28 was 5.3 (1.2), 774 (64%) were RF+, 553 (58%) were ACPA+ and 856 (76%) were seropositive (RF+ and/or ACPA+). Baseline disease activity and distributions of MTX-based treatment strategies did not significantly differ by serology. However, serology was associated with differences in treatment response to specific therapies. After 3-months, triple therapy was associated with a greater reduction in DAS28 in RF+ (mean ΔDAS28: - 1.95) vs. RF- (mean ΔDAS28: - 1.10) [mean difference in ΔDAS28 RF+ vs. RF-: -0.85, 95% CI: -1.37 to -0.33), ACPA+ (mean ΔDAS28: -1.86) vs. ACPA- (mean ΔDAS28: -1.15) [mean difference in ΔDAS28 ACPA+ vs. ACPA-: -0.71, 95% CI: -1.22 to -0.20] and seropositive (mean ΔDAS28: -1.98) vs. seronegative (mean ΔDAS28: -0.73) [mean difference in ΔDAS28 seropositive vs. seronegative: -1.25, 95% CI: -1.81 to -0.70] and was associated with higher DAS28 remission in RF+ (40%) vs. RF- (21%), p = 0.03. However, RF+ patients had worse responses to treatment with MTX+LEF (p = 0.04). RF+ (p = 0.06), ACPA+ (p = 0.09) and seropositive patients (p = 0.11) had non-significant trends towards better response to MTX + HCQ than their seronegative counterparts. Results were similar in multivariable analyses adjusted for baseline age, sex, education, symptom duration, comorbidities, smoking, HAQ-DI, DAS28 and steroid use. Differences were no longer significant using 6-month endpoints.

**Conclusion:** Early treatment response to triple therapy was better in seropositive ERA patients, whereas MTX + LEF had a better response in seronegative ERA patients.

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**Results of a Phase IIb Study of Vobarilizumab, an Anti-Interleukin 6 Receptor Nanobody®, in Patients with Moderate-to-Severe Rheumatoid Arthritis Despite Treatment with Methotrexate**

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**Objectives:** This phase IIb study of vobarilizumab, a Nanobody consisting of an anti-IL-6R domain and an anti-human serum albumin domain, was designed to assess the efficacy and safety of several dose regimens in adults with moderate to severe RA despite methotrexate therapy.

**Methods:** In this 24-week double-blind global study, patients were randomized 1:1:1:1:1 to receive subcutaneously administered placebo or one of four dose regimens of vobarilizumab in addition to methotrexate. The primary endpoint was the proportion achieving an ACR20 response at Week 12. Patients with missing ACR20 response were treated as non-responders. The secondary endpoints included assessments of higher levels of ACR response and disease activity (DAS28CRP). Adverse events and routine safety parameters including laboratory assessments were recorded. Early discontinuation was mandatory for patients with <20% improvement in both swollen and tender joint counts at Weeks 12, 16 or 20. Only patients who completed the study could enroll in a 2-year open-label extension study.
**Results:** A total of 345 patients were enrolled (placebo N=69, vobarilizumab 75mg q4w N=69, 150mg q4w N=70, 150mg q2w N=68, or 225mg q2w N=69). Demographics and baseline characteristics were similar across groups with mean baseline DAS28CRP between 5.8 and 6.2. At Week 12, statistical significance for the primary endpoint analysis was not achieved with ACR20 responses of 62%, 75%, 81%, 78% and 72% reported in the placebo and vobarilizumab dosing arms, i.e., the proportions achieving ACR20 responses did not increase significantly by increasing dosing regimen. ACR50 and ACR70 responses of up to 45% and 21% were achieved (placebo 28% and 9%). Responses continued to increase through Week 24. A sustained impact on disease activity was observed with up to 49% of patients achieving DAS28CRP<2.6 at Week 24 (placebo 16%). Of all vobarilizumab treated patients, 3.6% experienced at least one SAE during the treatment period with no dose dependency (placebo 5.8%). One death, considered not related to study treatment, was reported. Grade 3 toxicity for liver enzymes (AST 0.7%, ALT 1.8%) and neutrophils (1.1%) was infrequent and independent of dose.
**Conclusion:** In patients with active RA despite methotrexate, treatment with vobarilizumab (150mg q4w, 150mg q2w and 225mg q2w) had a positive impact on disease activity with a compelling safety profile. A striking placebo effect was observed and is under investigation. Overall, the results support the advancement of vobarilizumab into phase III of development.

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**Results of a Subgroup Analysis by Access to Biologics in a Phase IIb Study of Vobarilizumab, an Anti-Interleukin 6 Receptor Nanobody®, in Patients with Moderate-to-Severe Rheumatoid Arthritis Despite Treatment with Methotrexate**

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**Objectives:** In this phase IIb study of vobarilizumab, a Nanobody consisting of an anti-IL-6R domain and an anti-human serum albumin domain, an unexpectedly high response to placebo on ACR20 was observed. A subgroup analysis was performed to better understand the results.
**Methods:** In this 24-week, double-blind global study, patients were randomized 1:1:1:1:1 to receive subcutaneously administered placebo or one of four dose regimens of vobarilizumab in addition to methotrexate. The primary endpoint was the proportion achieving an ACR20 response at Week 12. Early discontinuation was mandatory for patients with <20% improvement in both swollen and tender joint counts at Weeks 12, 16 or 20. Only patients who completed the study could enroll in a 2-year open-label extension study. In a post-hoc subgroup analysis the proportion of patients achieving an ACR response at Week 12 was calculated separately for the subset of countries with access to biologicals (e.g., USA, Belgium, Spain) and for the subset

without such access.
**Results:** A total of 345 patients were enrolled (placebo N=69, vobarilizumab 75mg q4w N=69, 150mg q4w N=70, 150mg q2w N=68, or 225mg q2w N=69). Demographics and baseline characteristics were similar across groups with mean baseline DAS28CRP between 5.8 and 6.2. At Week 12, ACR20 responses of 62%, 75%, 81%, 78% and 72% were reported in the placebo and vobarilizumab dosing arms. In the subset of countries with widespread access to biologicals, 40% (6/15) of patients in the placebo group achieved an ACR20 response while in the subset without such access a response of 69% (37/54) was observed. Responses in the vobarilizumab dosing arms were 75%, 83%, 72%, and 56%, compared to 76%, 81%, 80%, and 77% in the two subsets, respectively.
**Conclusion:** In patients with active RA despite methotrexate, treatment with vobarilizumab (150mg q4w, 150mg q2w and 225mg q2w) had a positive impact on disease activity. Overall, a striking placebo effect was observed, driven by patients in the subset of countries without widespread access to biologics. This may have been a result of the forced discontinuation for non-responders and consequent loss of access to treatment. This will be addressed in the phase III development of vobarilizumab.

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**Physical Activity and Sedentary Behaviour in Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis**

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**Objectives:** Patients with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are at increased risk for premature cardiovascular disease. As sedentary behaviour and lack of physical activity (PA) are known cardiovascular risk factors, we studied habitual PA levels in SLE and RA patients, in comparison to healthy controls.
**Methods:** For this cross-sectional study, RA and SLE patients were recruited from rheumatology clinics at an academic medical center from April 2013 to December 2014. Age- and gender-matched healthy controls were recruited through local advertising. RA and SLE patients met the respective ACR classification criteria and disease activity was assessed by the DAS-28 and SLEDAI-2K, respectively. PA was assessed by self-report patient questionnaires and measured objectively by triaxial accelerometers worn during waking hours for seven consecutive days. Minutes per day of sedentary, light, and moderate-vigorous physical activity (MVPA) were recorded and compared between SLE, RA, and healthy control participants using ANOVA.
**Results:** There were 59 participants: 20 SLE patients, 19 RA patients, and 20 healthy controls. Disease activity was quiescent in both patient groups. All three groups demonstrated high levels of sedentary behaviour, with mean (SD) sedentary time of 10.1 (1.3) hours/day, or 76.4% of total accelerometer wear time. Total MVPA (mean ± SD, minutes/day) was significantly lower in SLE (34.5 ± 22.7) and RA (41.5 ± 21.3) patients compared to controls (64.9 ± 22.4) ($p<0.001$). Furthermore, Canadian physical activity guidelines for MVPA (≥ 150 minutes/week) were less frequently met by SLE (2/20, 10.0%) and RA (3/19, 15.8%) patients compared to healthy controls (9/20, 45.0%) ($p=0.02$). There was no significant difference between SLE, RA and control participants in the amount of time spent in sedentary behaviour ($p=0.80$) or light activity ($p=0.17$). Self-reported PA data correlated poorly with accelerometry data, with all participants over-reporting time spent performing MVPA, and underestimating sedentary time.
**Conclusion:** Given the increased cardiovascular risk, low MVPA levels and high sedentary behaviour identified by accelerometry among RA and SLE patients, despite well-controlled

disease, is concerning. Investigation of factors, other than disease activity, that impact PA and sedentary behaviour in RA and SLE patients is required, in order to design effective interventions to target this modifiable cardiovascular risk factor in these vulnerable patient populations.

**56**

**Patient Centered Approach to Disease Modification in Scleroderma: Results from the faSScinate Trial of Tocilizumab Compared to Placebo in Active Diffuse Cutaneous Systemic Sclerosis**

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**Objectives:** Patient Acceptable Symptom State (PASS) as an absolute state of well-being and has shown promise as an outcome measure in many rheumatologic conditions. We assessed whether PASS may be an effective in active diffuse cutaneous SSc.

**Methods:** Data from the faSScinate trial were used, which compared tocilizumab vs. placebo over 48 weeks followed by an open-label tocilizumab period to 96 weeks. Three different types of PASS questions were evaluated at weeks 8, 24, 48 and 96 including would a current state be acceptable over time as yes vs. no response, and Likert scales about how acceptable a current state is if remaining over time. Additional outcomes assessed included mRSS, HAQ-DI, MD and Pt global VAS, CRP and ESR. PASS question #1: "Considering all of the ways your scleroderma has affected you over the last week, how acceptable would you rate your level of symptoms?" PASS question #2: "Think about all the ways that your scleroderma has affected you during the last week. If you were to remain for the next few months as you were in the last week, would this be acceptable to you?" PASS question #3: "Has there been a change in how you would describe your level of functional impairment since you started the study?"

**Results:** At baseline, the placebo group consisted of 44 patients, and tocilizumab group had 43 patients. At baseline, 33% achieved PASS for all three PASS questions, with the proportion increasing to 69%, 71% and 78%, respectively at 96 weeks. Changes in PASS scores showed a moderately negative correlation with HAQ-DI, Pt and MD global VAS. PASS asking 'Considering all of the ways your scleroderma has affected you how acceptable would you rate your level of symptoms?' showed significant correlations with patient-reported outcomes and differentiating placebo vs. tocilizumab at 48 weeks (P=0.023).

**Conclusion:** PASS may be used as patient-centered outcome in SSc especially as a 7-point Likert scale. Further validation through larger clinical trials is required before being able to apply this concept to clinical practice.

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**Pulmonary Arterial Hypertension and Pulmonary Fibrosis Screening in Systemic Sclerosis in Clinical Practice: Choosing Wisely or Missed Opportunities?**

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**Objectives:** Patients with Systemic Sclerosis (SSc) are at increased risk of developing pulmonary arterial hypertension (PAH) and pulmonary fibrosis (PF). Early detection of PAH allows for appropriate therapeutic intervention and improves survival, and as such, screening guidelines since the year 2006 suggest annual transthoracic echocardiogram (TTE) and pulmonary function testing (PFT) for patients with SSc. Recent research suggests PAH screening among Canadian rheumatologists is sub-optimal, but to date no independent chart review assessing this has been published. Our goal was to assess adherence to screening guidelines for PAH in SSc patients in Hamilton based rheumatologists by independent chart review.

**Methods:** 21 rheumatologists in the Hamilton area were contacted to participate. Patient charts were reviewed that contained the words “systemic sclerosis”, “scleroderma”, or “SSc”, and among those charts, patients with a diagnosis of SSc were included. Charts were then reviewed from the year 2006 onward to assess whether on an annual basis patients were screened for symptoms of PAH (dyspnea, exercise intolerance, chest discomfort), underwent a screening TTE, and underwent screening PFT’s. Patients were excluded if they already had been diagnosed with PAH. Whether appropriate follow up to abnormal screening tests with a cardiologist or respirologist was made was also evaluated.

**Results:** a total of 6 rheumatologists agreed to participate. 119 patients’ charts were reviewed in total. Annual screening for PAH symptoms was very common (97% of patients, 115/119). Annual PAH screening via TTE (76%, 90/119) and PFT (77%, 91/119) was less common. Positive screening tests in the form of elevated RVSP (>40 mmHg) on TTE (9% of patients, 11/119) or diffusion capacity less than 60% on PFT (9%, 11/119) was uncommon. All patients with abnormal TTE (100%, 11/11), and nearly all with an abnormal PFT (91%, 10/11) received appropriate follow up with respirology or cardiology.

**Conclusion:** Rheumatologists consistently assess symptoms of PAH in patients with SSc , but are less likely to order regular screening TTE’s and PFT’s, with almost one quarter of patients not receiving them annually. This may be due to an overreliance on symptomatology to rule out PAH, but may also be due to a lack of awareness of specific guidelines regarding PAH screening in SSc. When PAH screening is abnormal, rheumatologists are effective at arranging appropriate follow up. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**An Audit of ANCA Testing at a Canadian Tertiary Care Centre: Are we Over-utilizing ANCA as a Diagnostic and a Monitoring Tool?**

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**Objectives:** To evaluate the indications for testing and re-testing of anti-nuclear cytoplasmic antibodies (ANCA) at The Ottawa Hospital over 1 year.

**Methods:** We searched The Ottawa Hospital biochemistry database and reviewed the records of patients with positive ANCA (defined as elevated myeloperoxidase [MPO] or proteinase 3 [PR3] titers) tested between April 1, 2014 and March 31, 2015.
**Results:** 1889 ANCA tests were performed in the study year. 112 patients had at least 1 positive ANCA in the study year and 169 total tests were positive. Indications for first-time ANCA testing: 69 patients had first-time positive ANCA in the study year, with 35 (51%) anti-MPO positive, 31 (45%) anti-PR3 positive, and 3 (4%) doubly positive. The indications for testing were suspicion for AAV in 20 patients (29%), suspicion for unspecified vasculitis in 20 (29%), suspicion for an inflammatory condition in 25 (36%), and unknown in 4 (6%). Overall, 27 patients (39% of first time positives) were diagnosed with AAV corresponding to 80%, 40%, 12%, and 0% of patients tested for these indications, respectively. Thirty-one (45%) patients had other inflammatory/infectious etiologies (most commonly inflammatory bowel disease (n=5), lupus (n=4), and inflammatory eye diseases (n=3)), and non-inflammatory diagnoses accounted for the remaining 11 (16%). Patients with AAV had significantly higher mean maximum PR3 and MPO titers than those with non-AAV diagnoses (1138 vs. 145 and 323 vs. 119 respectively, $p<0.05$ t-test). Indications and outcomes of repeat ANCA testing: 120 repeat ANCAs were performed in the study year; 84 of these were done on 44 patients with AAV and 36 on 24 patients with other diagnoses. Altogether, 80% of patients with AAV were re-tested in the study year (between 1-6 times, median 2 tests) vs. 42% of those with non-AAV conditions (between 1-5 times, median 1). Routine monitoring (as opposed to testing for changed clinical status) accounted for 72% of all repeat tests (n=86). Management was changed in 9% of all patients at the time of repeat ANCA, 34% of all re-tests performed for changed clinical status and 1% of re-tests conducted routinely.
**Conclusion:** Despite widespread ANCA testing, few patients who start with low clinical suspicion for AAV are diagnosed with AAV following ANCA testing. Serial ANCA testing is common practice but is not supported by clear evidence, and few ANCA re-tests subsequently lead to change in management. Clarification of guidelines on effective ANCA ordering may limit unnecessary hospital laboratory costs and patient bother. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Anti-Topoisomerase Antibodies are Negatively Associated with Smoking in Systemic Sclerosis**

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**Objectives:** Few studies have examined the effect of smoking in SSc. One study reported that smoking was not associated with the onset of SSc[1], while another reported that smoking had a negative impact on the progression of vascular, gastrointestinal and respiratory manifestations of SSc[2]. Interestingly, a negative association was reported between smoking and anti-

topoisomerase I antibodies (ATA) in the former study (OR 0.648, 95% CI 0.421-0.998, P=0.049)[1]. We undertook this study to replicate this finding in a large, multinational SSc cohort.
**Methods:** An international (Canada n=1287, Australia n=505, US n=299) cohort of 2091 SSc subjects was formed, socio-demographic and clinical variables were harmonized, and sera were tested for ATA, anti-centromere (ACA) and anti-RNA polymerase III (ARA) antibodies using a line immunoassay (Euroimmun GmbH, Lübeck, Germany). Exposure was measured as first-hand ever (current or in the past) or never cigarette smoking. Associations between smoking and ATA were assessed in the individual cohorts then meta-analyzed using the R 'meta' package to generate pooled estimates. Between-cohort heterogeneity was evaluated by Q (p-value < 0.10 indicating heterogeneity) and I2 (value of 0% indicating no, and larger values increasing heterogeneity) statistics. All models were adjusted for age, sex and race (white vs non-white).
**Results:** Baseline characteristics of the Canadian and Australian cohorts were similar (87% females, mean age 57 years, mean disease duration 11 years, approximately 1/3 with diffuse cutaneous disease (dcSSc)). The US subjects were also predominantly women (83%), but they were younger (mean age 49 years), had shorter disease duration (mean 2.5 years) and were more likely to have dcSSc (59%). There were 60%, 47% and 48% ever smokers and ATA were present in 15%, 18% and 15% of the Canadian, Australian and US subjects, respectively. In adjusted logistic regression analysis, ATA was negatively associated with ever smoking in all 3 cohorts: OR 0.60 (95%CI 0.43, 0.83) in Canadian, OR 0.48 (95% CI 0.29, 0.80) in Australian and OR 0.59 (95% CI 0.29, 1.17) in US subjects. The pooled OR was 0.56 (95% CI 0.43, 0.73; Q-test p=0.79, I2 0%). %). Of note, there were no associations between smoking and either ACA (pooled OR 1.06, 95% CI 0.77, 1.45; Q-test p=0.1588, I2 46%) or ARA (pooled OR 1.15, 95% CI 0.87, 1.51; Q-test p=0.5970, I20%).
**Conclusion:** We found robust evidence of a negative association with ATA and smoking exposure in a large international SSc cohort. Further studies will be required to determine the mechanisms underlying these associations.

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**Modeling the Cost-effectiveness of Rituximab Use Compared to Tumor Necrosis Factor Inhibitors (anti-TNF) Agents as a Second-line Therapy in Patients with Rheumatoid Arthritis (RA) in Quebec, Canada Using RHUMADATA Registry Data.**

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**Objectives:** No guidelines are currently available for selecting a particular biologic agent and for switching from one agent to another. In a recent study, rituximab demonstrated better long-term retention rate than three tumor necrosis factor inhibitors (anti-TNFs) (adalimumab, etanercept and infliximab) as a second-line agent in Rheumatoid Arthritis (RA) patients unsuccessfully treated with prior anti-TNF. We conducted a cost-utility analysis to compare rituximab and three anti-TNFs (adalimumab, etanercept and infliximab) used as second-line therapy in terms of direct RA-related costs borne by the public health care system and outcomes, measured as Quality Adjusted Life Years (QALYs).
**Methods:** Four two-state (e.g., "on second-line treatment" and "after failing second-line treatment") Markov models reproduced the 6-years long course of patients treated either with adalimumab, etanercept, infliximab or rituximab. Baseline patient characteristics, transition probabilities, cost and treatment effectiveness were estimated for each group of patients based on

the data from a clinical registry RHUMADATA®. We included RA patients who failed one prior anti-TNF and started the second-line treatment either with adalimumab, etanercept, infliximab or rituximab between January 1st, 2007 and January 1st, 2013. Only patients who had complete data on baseline and follow-up Health Assessment Questionnaire (HAQ) scores were included in this preliminary analysis. Transition probabilities for rituximab and the combined anti-TNFs were obtained from Kaplan-Meier survival estimates of the 6-year drug retention rates. Unit costs (2016 CAD) from Quebec, Canada were applied to value RA-related healthcare resources used (e.g., biologic agent and rheumatologist visits costs), which were measured on an item-by-item basis. Treatment effectiveness was measured in QALYs calculated from the Health Assessment Questionnaire (HAQ) scores over follow-up time. Both costs and effectiveness were discounted at 5% rate per year.

**Results:** Out of 130 RA patients identified, 96 patients were included in this preliminary analysis. Over 6 year follow-up, rituximab as a second-line treatment was associated with cost of $18,312 and effectiveness of 2 QALYs and was dominant (both more effective and less costly) over treatment with adalimumab, etanercept, and infliximab, which were associated with cost of $22,022, $21,976 and $26,502, and effectiveness of 1.98 QALYs, 1.97 QALYs and 1.76 QALYs, respectively.

**Conclusion:** Based on results of the preliminary analysis, the second-line rituximab therapy was more effective and less costly when compared to adalimumab, etanercept and infliximab. The joint uncertainty surrounding the cost and effectiveness of rituximab compared to adalimumab, etanercept and infliximab will be estimated in probabilistic sensitivity analysis.

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**Repeat Testing of Antibodies and Complements in Systemic Lupus Erythematosus: When is Enough?**

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**Objectives:** Patients with systemic lupus erythematosus (SLE) frequently undergo repeat testing for antibodies against extractable nuclear antigens (anti-ENA) and other markers, but it is not known whether this is necessary or cost-effective. This study aims to characterize the frequencies of changes in anti-ENA results on repeat testing and also anti–double-stranded-DNA (anti-DNA) and complement C3 and C4.

**Methods:** Chart review at one site of 130 SLE patients enrolled in the 1000 Canadian Faces of Lupus prospective registry with annual antibody and complement testing. We determined the frequency of seroconversion (changes) on the next test and over the entire follow up given one or multiple consistent results and the cost to detect these changes. Consecutive consistent results within the same calendar year were counted as only one result.

**Results:** Overall, 89.4% of patients had no changes in anti-ENA screen results from the first available test, 3.3% changed from negative to positive and 7.3% from positive to negative (n = 123). Following a single anti-ENA test, 3.9% (n = 280) of negative results changed to positive and 4.2% (n = 263) of positive changed to negative on the next test. After multiple consistent tests, the frequencies of anti-ENA changes progressively declined and none were observed after five or more consistent tests. No changes from the first test were observed in anti-DNA and C3 and C4 in 60.2 (n = 130) and 83.3 and 75.4% (n = 126) of patients respectively. The frequencies of an abnormal result in the year following a normal test were 7.9 (n = 573), 7.6 (n = 737), and 7.6% (n = 727) respectively. A negative next test result was more frequent following an anti-

DNA titre ≥ 3 times normal (41.3%, n = 63) than positive anti-DNA results overall (24.5%, n = 273; $p < 0.01$). Using the US Medicare National Limit, after two consistent negative anti-ENA tests, the cost to detect one change was estimated to be above $2000 US dollars. Following up to seven consistent years, detecting a negative-to-positive anti-DNA change always cost below $900. Detecting low complement C3 or C4 following one normal result cost $218.79 and $216.12 respectively; these increased above $400 following two to seven consistent years, but never exceeded $2600.

**Conclusion:** Anti-ENA results change infrequently, especially following consistent negative tests. The high cost and lack of evidence that changes affect management suggest routine annual repeats of anti-ENA tests are unnecessary. Anti-DNA and complements change more frequently. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Pituitary Granulomatosis with Polyangiitis: A Case Series and Review of the Literature**

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**Background**: Granulomatosis with polyangiits (GPA) is a granulomatous, necrotizing vasculitis affecting small-vessels. Pituitary involvement in GPA is rare.

**Objectives:** (1) To describe two cases of pituitary GPA; (2) To perform a literature review of pituitary GPA and describe the clinical characteristics and management of previously reported cases.

**Methods:** We performed a chart review followed by a literature search of the following databases: Medline, Embase, Scopus, and Proquest. Keywords for "granulomatosis with polyangiitis" and "pituitary" were used.

**Results:** Case 1: A 52 year-old woman was diagnosed with GPA in January 2010 on the basis of recurrent sinusitis, peripheral neuropathy, and positive cANCA with elevated anti-PR3. Treatment included corticosteroids and cyclophosphamide IV for 6 months. In December 2010, the patient developed severe headaches with visual blurring. MRI brain showed a large sellar and suprasellar mass favoring hypophysitis. Pituitary hormone testing revealed central diabetes insipidus and central hypothyroidism. The patient received pulse methylprednisolone followed by oral prednisone and rituximab. Histology from endoscopic transphenoidal resection showed necrotic tissue with numerous inflammatory cells. The patient has since been in remission on methotrexate with persistent pituitary dysfunction.

Case 2: A 36 year-old woman presented in July 2014 with acute bilateral hearing loss in the context of sinus symptoms, hypoxemic respiratory failure, and pulmonary nodules. Positive PR3-cANCA led to a diagnosis of GPA. Treatment included pulse methylprednisolone for 3 days followed by oral prednisone and rituximab. A CT head performed for recurrent sinusitis and subsequent MRI revealed a pituitary mass without compression of adjacent structures. Pituitary hormone testing was within normal range. The mass decreased significantly in size on serial MRI scans over the next 2 years while on therapy. The patient remains in remission on maintenance azathioprine.

Our literature review yielded 64 cases of pituitary GPA. Of these, 71% were female with mean age 42 years (range 13 to 77). The majority of patients demonstrated cANCA, anti-PR3 positivity. Diabetes insipidus, hypogonadism and hypothyroidism were the most common manifestations of pituitary dysfunction. All patients received corticosteroids with immunosuppressive therapy (cyclophosphamide, rituximab and methotrexate were used).

Although many patients achieved remission of GPA, pituitary dysfunction was often irreversible.
**Conclusion:** Pituitary dysfunction is a rare finding in GPA. A growing number of cases have been reported in the literature demonstrating effectiveness of standard immunosuppressive regimens in inducing remission of GPA, although pituitary dysfunction and need for hormone supplementation is often irreversible.

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**Predictors of Canadian Adult Rheumatologist Clinical Workload and Working Hours**

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**Objectives:** To evaluate predictors of rheumatologists' self-reported clinical work hours and patient volumes based on results of the first national workforce survey in rheumatology.
**Methods:** The Stand Up and Be Counted survey was conducted in 2015, capturing workforce characteristics of Canadian rheumatologists. In this analysis, only adult rheumatologists who did not participate in Tele-health services were included to facilitate interpretation of practice volumes (n=255). Univariate analysis was conducted to evaluate the relationship between: demographic variables (sex, age, practice type (academic vs. community), billing practice (fee for service (FFS) vs. other remuneration plan), years in practice, retirement plans, and measures of workload (hours worked per week, number of clinics per week (measured in ½ days) and patient volume (number of new and follow-up consults seen per week). Significant relationships from the univariate analysis were considered in multivariate linear regression, with the exception of highly correlated variables. We evaluated the relationship between practice type, sex, age and working hours and clinical volumes using multivariate linear regression for each workload measure. $P<0.05$ was considered significant.
**Results:** Male rheumatologists reported conducting a higher number of ½ days in clinic (8 vs. 6, $p=0.046$) and seeing more new patients seen per week (15 vs. 11, $p=0.001$) compared to females, but hours worked and number of follow-up visits seen per week did not significantly differ between sexes. Community rheumatologists reported having more ½ day clinics (8 vs. 4), new (15 vs. 8) and follow-up visits (55 vs. 35) per week (all $p<0.01$), but total hours worked per week was not significantly different from academic colleagues. FFS rheumatologists reported a higher number of ½ day clinics per week ($p<0.001$) and more follow-ups ($p=0.04$) compared to other remuneration plans. None of the measures of workload varied by rheumatologist age, years in practice or retirement plans. In multivariate analysis, community practice remained a significant independent predictor of higher patient volumes, longer working hours and more clinics per week. Sex remained an independent predictor, with female rheumatologists holding 0.6 fewer clinics per week and seeing 8.5 fewer follow-up patients per week than males but this did not affect the duration of working hours or new patient consultation volume.
**Conclusion:** Practice type and rheumatologist sex are predictors of self-reported clinical workload. These factors should be considered in workforce planning as the proportion of female rheumatologists has increased over time and alternative billing practices have been introduced in

many centres.

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**Challenges in Measuring Wait Times for Rheumatology Care in Canada: A Demonstration Using Four Models of Care**

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**Objectives:** To test the feasibility of reporting on the waiting time (WT) performance measure for rheumatoid arthritis (RA) in four different models of care across Canada.

**Methods:** Four models of care in five practice locations were evaluated: the Rheumatic Health Unit (RHU) Central Triage Model of Care (Newfoundland); The Arthritis Program (TAP) at Southlake Regional Hospital (Ontario), The Early Arthritis Clinic (EAC) in the William Osler Health System (Ontario), The Siksika Arthritis Screening Project (SASP) and the Urban Aboriginal Arthritis Care Program (UAACP, Alberta). Sequential RA cases were included at all sites except TAP, where only patients enrolled in a national early arthritis cohort were included as a method of identifying RA cases. Cases seen in the emergency department, self-referrals and transfers of care were excluded. The median and 90th percentile WTs in days (d) for rheumatologist care were calculated for new RA consults using the time between referral receipt and the first visit. The percentage of cases meeting a benchmark of <4 weeks was calculated. WTs were reported yearly for 2014 and/or 2015.

**Results:** While 4 of the programs maintained databases, none had all available information and chart reviews were required to collect data on referral and consultation dates. WTs for the two Alberta sites could not be calculated due to the low numbers with traditional physician referrals, as at least one third of the population used self-referral in the model of care. WTs are therefore only reported in three models. The longest WTs were observed in the RHU in 2014 (n=60 cases), with median WTs of 142d, 90th percentile of 200d and only 8% of cases meeting the WTA benchmark. This improved in 2015 (n=72) with a median WT of 74d, 90th percentile of 137d; however, only 11% met the WTA benchmark. In contrast, the 2015 EAC (n=80) WTs were substantially lower (median 45d, 90th percentile 83d, 25% met the WTA benchmark [CEHB1] ). TAP had the lowest WTAs: in 2014 (n=29) the median WT was 34d, 90th percentile 85d with 31% meeting the WTA benchmark, in 2015 (n= 25) this improved to a median of 21d, 90th percentile of 57d with 64% meeting the benchmark.

**Conclusion:** Our review has shown extensive variation in waiting times to care for patients, with only a single site reporting a median wait time <4 weeks. Measuring waiting times routinely in an automated fashion is recommended to encourage system improvements. Supported by a CIORA grant. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Rheum4U – Preliminary Results of Piloting a Web-based Tool for Quality Improvement in Rheumatology Clinics**

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**Objectives:** To develop an electronic platform (Rheum4U) for use alongside a hospital-based electronic medical record (EMR) at the University of Calgary, to integrate clinical data capture with additional demographic information and outcomes (e.g. patient-reported outcomes). This platform will support enhanced clinical applications, quality improvement initiatives and observational research.
**Methods:** Rheum4U was developed in 5 phases. Phase 1: a working group of rheumatology division members (n=13) active in research/quality improvement efforts performed a prioritization exercise to determine which data elements were necessary and desired in the platform. Phase 2: the data element specifications were finalized and supplied to the platform developer (EPICORE, Edmonton, Alberta). Alpha testing was performed to correct initial bugs. Phase 3: n=18 testers (including physicians, nurses and recruited non-patient lay-testers) were involved in Beta testing for usability. Phase 4: administrative and clinical staff and managers provided input on implementation, which informed clinic "dry runs" of Rheum4U. Phase 5: Rheum4U was piloted in 2 rheumatology clinic sites (n=8 rheumatologists) to determine feasibility, efficiency and acceptability.
**Results:** Phase 1-3: The Rheum4U platform data elements were set to include patient-reported information, including demographics (including ethnicity, biologic sex, household income, education and marital status), health history (including comorbidities, alcohol use, smoking and marijuana use), functional status assessment (CLINHAQ, which includes pain, fatigue, sleep and a patient global evaluation of disease activity), quality of life (EQ-5D), and Work Productivity and Activity Impairment questionnaire (WPAI). Healthcare provider data elements included global evaluation of disease activity, disease activity measures (joint counts), blood pressure, height, weight and medications. During Phase 4, it was identified that different models of care used at the two clinic sites necessitated different assignment of tasks for data entry by physicians and nurses as well as different patient recruitment strategies by administrators. Also nursing staff and managerial turnover at one site created additional implementation challenges and highlighted the need for ongoing educational initiatives. During initial pilot testing, Phase 5, the duplication of data entry into both the EMR and Rheum4U (especially for medication data) was highlighted as a concern by providers; however, having readily available calculated disease activity and functional status scores was of high clinical utility.
**Conclusion:** Rheum4U pilot testing highlights challenges and benefits of a web-based tool for clinical care, quality improvement and research in the clinic and provides valuable information to inform full implementation of the platform in rheumatology clinics in Calgary. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.
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## Assessing System-Level Performance Measures for Early Rheumatoid Arthritis in the Canadian Early Arthritis Cohort Study (CATCH): An 8-Year Observational Cohort Study

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**Objectives:** The Arthritis Alliance of Canada developed 6 system-level performance measures for inflammatory arthritis. This study assesses 3 of these measures in early RA (ERA) patients enrolled in the Canadian Early Arthritis Cohort (CATCH).

**Methods:** ERA patients enrolled between January 2007-February 2015 who met 1987 or 2010 ACR/EULAR criteria and had < 1 year of symptom duration at cohort entry and had >1 year of follow-up were included. Measures were computed annually and stratified by enrollment year and included: i) percentage of patients with RA seen in yearly follow-up (fixed 12 and 14 month windows from baseline), ii) annual percentage of RA patients treated with a disease-modifying drug (DMARD, proportion of patients with at least one record of DMARD or biologic use) and, iii) time from new RA diagnosis to initiation of DMARD therapy, as well as the percentage prescribed DMARDs within 2 weeks of diagnosis.

**Results:** 1763 ERA patients were included with a mean age of 54 years, 73% were female and 82% were Caucasian. At enrolment, mean disease duration was 5.7 months and DAS28 was 5.1. Over 8 years, the number of patients seen in yearly follow-up declined from 100% to 88%. Over follow-up, 42% of patients had 0 gaps in care of >12 months, and 64% had 0 gaps >14 months. Over 8 years the percentage of ERA patients on a DMARD declined from 95% to 86%. Over this period, the percentage receiving DMARD treatment within 14 days of diagnosis increased from 75% to 80%. Median time to DMARD therapy was between 0 and 1 days (50th percentile) during all years of measurement indicating treatment occurred at time of diagnosis; and the 90th percentile ranged between 66 to 122 days.

**Conclusion:** Overall there was high adherence to performance measures in CATCH. Small declines in performance that were noted over time occurred with increasing length of patient follow-up. The decline in DMARD use may be due to low disease activity, among other factors which will be explored in future analysis. A limitation of the study is that the percentage seen in yearly follow-up may have been biased, as follow-up dates were per protocol leading to higher adherence. This study represents a “best-case scenario” for capturing performance measures from systematically collected data demonstrating the feasibility of rapid DMARD initiation. Our findings are useful for benchmarking while testing the measures in other settings nationally and data sources. Supported by a CIORA grant. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Effects of a Web-based Patient Decision Aid on Biologics for Rheumatoid Arthritis: A Proof-of-Concept Study**

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**Objectives:** Patient decision aids are designed to present benefits/harm of treatment options and clarify individuals' preferences. We have developed a user-friendly decision aid, ANSWER-2, for patients with rheumatoid arthritis (RA) who are considering biologic and small molecule agents. A main feature of ANSWER-2 is the trade-off exercise which helps patients consider value-sensitive options (e.g., the mode and frequency of medication administration). We aimed to assess the effect of ANSWER-2 on patients' perceived decision quality and self-management capacity.

**Methods:** We used a pre-post study design. Participants were recruited from rheumatologists' clinics, patient groups and social media. Individuals were eligible if they: 1) had a physician diagnosis of RA, 2) had been recommended to start/switch to a new biologic or small molecule agent, and 3) had internet access. Access to ANSWER-2 was provided immediately after enrollment. Participants completed outcome measures before and within 2 days after using ANSWER-2. They included: 1) Decisional Conflict Scale (DCS; 0-100, scores < 25 are associated with follow-through with decisions), 2) Partners in Health Scale (PIHS; 0-88, lower = better), and 3) Medication Education Impact Questionnaire (MeiQ; 6 subscales, higher score = better). We used paired t-test or Wilcoxon signed-rank test to assess differences pre and post intervention.

**Results:** 50 participants were enrolled [40 women; mean age=49.6 years (SD 12.2); median disease duration=5 years (Q1; Q3: 2; 10)]. The mean DCS was 45.9 (SD 25.1) pre-intervention, and 25.1 (SD 21.8) post-intervention (change: -21.2, 95% CI: -28.1, -14.4; $p < 0.001$). Before using ANSWER-2, 20% of participants scored < 25, compared to 52% after the intervention. Similar results were observed in the PIHS [pre: 25.3 (SD 14.8); post: 20.4 (SD 13.0); change: -3.7, 95% CI: -6.3, -1.0; p=0.009]. Findings from MeiQ were mixed, with statistically significant differences found only in the self-management sub-scales: 1) Self-management Ability [pre: 26.7 (SD 5.3); post: 28.0 (SD 4.9); change: 1.3, 95% CI: 0.0, 2.5; p=0.048]; 2) Self-management Role & Responsibility [pre: 31.8 (SD 3.3); post: 32.6 (SD 2.8); change: 0.9, 95% CI: 0.2, 1.6; p=0.012]; 3) Self-management Support [pre: 17.5 (SD 4.4); post: 18.9 (SD 3.2); change: 1.1, 95% CI: 0.2, 2.0; p=0.019].

**Conclusion:** Patients' perceived decision quality and self-management capacity improved after using ANSWER-2. Our results were similar to other studies evaluating patient decision aids in chronic diseases. Future research comparing ANSWER-2 with other education material will provide further insight into the value of patient decision aids in RA management.

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## Magnetic Resonance Imaging Measures of Disease Activity in Rheumatoid Arthritis Patients Treated with Multiple Regimens of DMARD Therapy

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**Objectives:** Magnetic resonance imaging (MRI) in rheumatoid arthritis (RA) is more sensitive than other techniques in evaluating disease activity levels. Few studies have illustrated the impact of conventional and biologic DMARDs on the MRI findings of RA. The objectives of this study were to compare MRI findings among groups of RA patients treated with different medication regimens over a two year study period.
**Methods:** MRIs were acquired of the dominant hand of 51 RA patients from a single clinic at baseline and follow-up over an average of 23 months. RAMRIS score and clinical disease activity scores (CDAI) for bone marrow edema, erosion and synovitis was performed for the 2nd through 5th MCP joints at baseline and follow-up. Based on the drug history obtained, patients were grouped into four categories: 1)DMARD mono-therapy with methotrexate (MTX), 2)DMARD mono-therapy with hydroxychloroquine (HCQ), 3)DMARD multi-therapy (multiDMARD), and 4)Biologic and conventional DMARD multi-therapy (DMARDbio). Multivariable linear regression analyses were conducted to determine differences in RAMRIS scoring at follow-up. The analyses were adjusted for baseline values.
**Results:** The MTX, HCQ, DMARDbio and multiDMARD groups had 12, 5, 21 and 13 patients respectively. Average CDAI scores at baseline were 10.9, 7.3, 19.0 and 36.5 for MTX, HCQ, multiDMARD and DMARDbio groups respectively. The RAMRIS scores at follow up were significantly higher in the multiDMARD groups for all components of RAMRIS and for synovitis in the DMARDbio group. Statistical significance was compared to changes in the MTX group ($p < 0.05$).
**Conclusion:** In this prospective cohort we noted a significant difference in RAMRIS scoring in the multiDMARD therapy group. The baseline CDAI score of the multiDMARD group was higher than the MTX group. The need for multiple DMARDs during this study period may have been because of the higher disease activity in this group. Despite multiple therapies, there was worsening of disease activity based on the RAMRIS scores in this group, which likely was accounted for by the significantly higher baseline disease activity. The MTX group was a suitable control considering the stable RAMRIS scores from baseline to follow-up. The DMARDbio group had the highest CDAI score of 36.5. There was a significant difference in RAMRIS synovitis score in the DMARDbio group versus MTX group. This would suggest that biologic DMARD therapy has higher efficacy in suppressing disease activity versus multiple csDMARD therapy. Further studies will be needed to determine the impact of therapy on disease activity as measured by MRI studies.

**69**

**Clinical Usefulness of 18F-Fluorodeoxyglucose Positron Emission Tomography in the Management of Giant Cell Arteritis: A Systematic Review and Meta-analysis**

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**Objectives:** Background: 18F-fluorodeoxyglucose positron emission tomography (PET) was proposed as a diagnostic tool for giant cell arteritis (GCA). Objective: To review the utility of the PET modality in comparison with ultrasound (US) and magnetic resonance imaging (MRI) for the diagnosis of GCA.
**Methods:** Methods: MEDLINE, Sciendirect, Scopus, The Cochrane Library and The Centre for

Reviews and Dissemination (through November 2014) were searched. Articles using PET, US or MRI for the diagnosis of GCA were included. Studies had to include a reference standard such as the American College of Rheumatology criteria, biopsy of the temporal artery or general clinical follow up. Assessment of the quality of evidence was conducted using Grading of Recommendations, Assessment, Development and Evaluation (GRADE).
**Results:** Results: Fifty three articles were selected for meta-analysis. Pooled sensitivity and specificity were calculated through the bivariate diagnosis random-effects meta-analysis. Pooled sensitivity and specificity of PET were (68% [95% CI, 41% to 86%]) and 95% [95% CI, 83% to 99%]), respectively. Pooled sensitivity and specificity of PET/CT were 78% (95% CI, 64% to 86%) and 90% (95% CI, 72% to 97%), respectively. Based on indirect comparison, performance of the other aforementioned technology was generally similar. Quality of the evidence for PET, PET/CT and MRI was rated as very low. As for ultrasonography, quality was low. Major concerns were: use of a reference standard not likely to identify correctly GCA patients, initiation of glucocorticoids prior to image acquisition that may cause false negative and lack of standardized criteria with PET and PET/CT.
**Conclusion:** Conclusions: As the results of performance of imaging modalities are equivalent, uncertainties remain about the choice of an alternative to temporal biopsy. However, PET or PET/CT may represent a valuable tool for the examination of large vessels, especially when inflammation targets specifically these regions.

**70**

**A Case Series of Two Presentations of Skull Base Inflammatory Pseudotumor Sparing the Orbit and a Review of the Literature Focusing on Steroids and Immunosuppressive Induction Regimens**

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**Purpose:** To review the medical management of two cases of biopsy-proven IgG4 negative inflammatory pseudotumor (IPT) of the skull base, and to assess the prevalence of skull base IPT with a focus on treatment modalities and outcomes.
**Methods:** We conducted a retrospective case review of patients with skull base IPT. We also performed a literature review of IPT cases in English articles available in PubMed, Medline, and Google Scholar.
**Results:** Two patients over a 12-month period experienced progressively worsening neurological deficits. Imaging revealed a soft tissue mass of the skull base and biopsies of these lesions were in keeping with IPT. One patient's symptoms improved on high dose oral prednisone therapy with adjuvant azathioprine, while the other patient required multiple IV pulse steroids and induction with agents including cyclophosphamide, rituximab, and mycophenylate mofetil. The literature review revealed twenty cases of IgG4 negative IPT of the skull base. Patients were managed with varying doses of initial corticosteroid therapy and tapering regimens, with two cases involving adjuvant cyclophosphamide. Eight patients treated with corticosteroids showed no evidence of disease activity at follow-up. Nine patients treated with corticosteroids had improved symptoms. One patient showed progressive disease with corticosteroid treatment. One patient remained on low dose corticosteroids. The two patients treated with adjuvant cyclophosphamide showed stable disease at follow-up. There was one death with corticosteroid mono-therapy related to complications of subsequent radiation treatment.
**Conclusion:** The findings suggest that there is a relatively good prognosis for treatment of IPT

with medical modalities. Corticosteroids with adjuvant immunosuppressive therapy may be considered in patients with refractory disease. There are currently no guidelines for induction regimens, identifying it as an area for future exploration.

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**Definitions of Scleroderma Renal Crisis: A Scoping Review**

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**Objectives:** Scleroderma renal crisis (SRC) is a rare life-threatening complication of systemic sclerosis. The absence of a gold standard definition of SRC has hindered our understanding of this problem. The primary objective of this scoping review was to identify and map the range of criteria used to define SRC in order to guide the development of a consensus definition for SRC.

**Methods:** A scoping review was conducted using the Arksey and O'Malley framework. The search for published literature was conducted in three databases: Medline, Embase and non-Ovid Pubmed. A two-stage screening process was used to assess the relevance of papers identified in the search. Papers were eligible for inclusion if they were full-length articles in English whose main topic of study was SRC or scleroderma renal disease. Two reviewers independently screened eligible papers for final study selection. Data was extracted on (1) formal definitions of SRC used in the papers, (2) clinical predictors of SRC (limiting to original studies of at least 50 SSc subjects), and (3) items that distinguish SRC from its differential diagnoses. A web-based survey of members of the Scleroderma Clinical Trials Consortium was used to identify unpublished definitions of SRC.

**Results:** The search identified 408 papers that met study inclusion criteria. Among these, only 78 reported a formal definition of SRC, of which 37 were original studies (excluding case reports). In total, 38 original definitions of SRC were identified from 33 original studies, 9 reviews and 2 editorials. There was significant heterogeneity in definitions. As a rule, though, in addition to new-onset hypertension and renal failure, other common items used to define SRC included hypertensive encephalopathy and seizures, microangiopathic hemolytic anemia and characteristic changes on kidney biopsy. Clinical predictors significantly associated with SRC were reported in 19 original studies of at least 50 subjects and included shorter disease duration, diffuse cutaneous involvement, high skin score, large joint contractures, anti-RNA polymerase III positivity and recent exposure to corticosteroids. Seventy-five (75) studies addressed differential diagnoses of SRC, including ANCA-associated glomerulonephritis and thrombotic thrombocytopenic purpura, among others. The web-based survey identified unpublished definitions of SRC that were largely consistent with the results of the published literature.

**Conclusion:** Criteria used to define SRC are used in a minority of studies and are heterogeneous. In view of the increasing number of clinical trials in systemic sclerosis, a consensus definition of SRC is urgently needed to standardize data collection on SRC.

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**Are hs-cTnT, NT-proBNP, and CRP Predictors of Cardiac and Pulmonary Outcomes in Systemic Sclerosis? Preliminary Findings from the Canadian Scleroderma Research Group**

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(Montreal); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal)

**Objectives:** Cardiopulmonary disease is the principal cause of mortality in systemic sclerosis (SSc) and early detection is therefore an important goal. High sensitivity cardiac troponin T (hs-cTnT), B-type natriuretic peptide (NT-proBNP) and C-reactive protein (CRP) have emerged as potential biomarkers of cardiopulmonary disease in SSc. However, studies to date are limited by small, selected samples, and cross-sectional study designs. The aim of this study was to determine the independent predictive ability of hs-cTnT, NT-proBNP, and CRP in a large, mulit-center sample of SSc subjects followed prospectively.

**Methods:** Subjects from the Canadian Scleroderma Research Group registry with data on hs-cTnT, NT-proBNP, and CRP were identified. hs-cTnT and NT-proBNP were analyzed in a central lab, while CRPs were performed in local labs. Outcomes of interest were death, systolic dysfunction (LVEF<50% or medications for heart failure), arrhythmias (pacemaker/ICD or anti-arrhythmic medications), PAH (mPAP≥25 and PCWP≤15 determined by RHC) and PH (SPAP >45 but not PAH). Univariate and multivariate analyses using Cox proportional hazard models were generated for each outcome. hs-cTnT and NT-proBNP were analyzed continuously using log transformed variables. Multivariate models were adjusted for demographic (age, sex) and clinical (dyspnea, DLCO %predicted, diabetes and hypertension) covariates.

**Results:** We included 332 subjects with mean follow-up of 6±2.1 years. Study subjects were predominantly women (89.8%) with mean age of 58.4±11.3 years, mean disease duration of 12.9±9.2 years, and of which 38.6% had diffuse skin involvement. Forty-seven (47, 14%) subjects died during follow up, 22 (6.6%) developed systolic dysfunction, 10 (3%) arrhythmias, 18 (5%) PAH and 21 (6.3%) PH. In univariate analyses, elevated hs-cTnT at baseline was associated with risk of death and PH, elevated NT-proBNP was associated with death and arrhythmias, and elevated CRP was associated with death and PH (all p values<0.05). In multivariate analyses, the only independent association was that of elevated CRP with death (HR 1.39, 95%CI 1.00-1.92).

**Conclusion:** hs-cTnT , NT-proBNP and CRP were associated with cardiopulmonary outcomes in univariate analyses. Only CRP was independently associated with death in multivariate analyses. This could suggest either no additional predictive power of NT-proBNP and hs-cTNT beyond routine clinical parameters or lack of power. A larger sample would be required to resolve this uncertainty and such a study is currently being planned. This research has the potential to inform the development of evidence-based screening tools for cardiac and lung involvement in SSc.

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**Microangiopathic Hemolytic Anemia in Systemic Sclerosis: Scleroderma Renal Crisis or Thrombotic Thrombocytopenic Purpura?**

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**Introduction:** Microangiopathic hemolytic anemia (MAHA) is a potentially life-threatening condition. In the setting of systemic sclerosis (SSc), MAHA suggests scleroderma renal crisis (SRC); however, thrombotic thrombocytopenic purpura (TTP) should be considered.

**Objectives:** To describe a case of TTP in the setting of SSc to highlight important aspects of diagnosis and management.

**Case:** A 55 year-old Caucasian woman with a history of treated parotid lymphoepithelial

carcinoma presented with new onset puffy fingers, Raynaud's, digital ulcerations, dyspnea and retinal hemorrhages. Examination revealed swelling and skin thickening of fingers to wrists, fissuring at the fingertips, splinter hemorrhages, and bibasilar inspiratory crackles. Blood pressure was 130/70 mmHg.
Investigations revealed normocytic anemia (Hgb 106 g/L), thrombocytopenia (Plt 64x10**9/L), mild elevation in creatinine (95 umol/L) with bland urinalysis, and elevation in ESR (33 mm/h) and CRP (11 mg/L). LDH was mildly elevated (376 U/L); bilirubin and coagulation parameters were normal with haptoglobin undetectable. Peripheral blood smear revealed 2.3% schistocytes. ANA was positive with negative anti-dsDNA, Smith, Ro, La, RNP, centromere and Scl 70 antibodies.
The patient was admitted for management of possible normotensive SRC and captopril was initiated. High resolution CT chest demonstrated bibasilar ground glass opacifications, pulmonary function tests revealed diminished DLCO (Adj) 61%, and echocardiogram showed normal pulmonary pressures. Anti-polymerase RNA III and anti-Ro52 antibodies were strongly positive.
After 3 days of captopril, thrombocytopenia mildly worsened (Plt 46x10**9/L) but hemoglobin was stable. With increasing percentage of schistocytes on blood smear, an ADAMTS13 level was found to be undetectable (<0.03 U/mL) - in keeping with TTP. Captopril was discontinued and plasma exchange (PLEX) with prednisone 80 mg was initiated. Platelets normalized after 4 treatments; however, systolic blood pressure and creatinine rose (160 mmHg and 130 mmol/L), raising concerns for concomitant SRC. PLEX and prednisone were tapered, captopril was resumed and rituximab (375 mg/m2 IV weekly x 4) was administered. Blood pressure and renal function returned to baseline, her blood work has remained stable. Pre-PLEX ADAMTS13 inhibitor was later reported as positive.
**Conclusion:** SRC and TTP are difficult to differentiate in the setting of SSc. Both present with MAHA, thrombocytopenia, and renal involvement. Although hypertension points to SRC, this feature may be absent in 5% of patients. Rapid assays for ADAMTS13 are useful for confirming TTP. Management of TTP in SSc is challenging due to the need for judicious use of corticosteroids. Rituximab may be a useful therapy in the concurrent management of TTP and SRC.

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**Immune-mediated Necrotizing Myopathy with Underlying Central Core Disease: A Case Report**

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**Objectives:** Central core disease (CCD) is a rare congenital myopathy that presents with varying degrees of muscle weakness ranging from asymptomatic individuals to severe disability. It is most commonly caused by mutations in the skeletal muscle ryanodine receptor (RYR1) gene with primarily an autosomal dominant inheritance with some cases of sporadic mutations. This case report reviews a case of immune-mediated necrotizing myopathy (IMNM) in a patient with previously undiagnosed CCD and highlights the challenges in diagnosis and management of these two disorders.
**Methods**: Written consent was obtained to conduct the case review. All medical charts and laboratory tests were reviewed and summarized, highlighting the pertinent findings.
**Results:** A 57 year-old Caucasian female was admitted to the intensive care unit for hypoxic

respiratory failure following a witnessed aspiration during assessment for a fall causing a hip fracture. She was difficult to extubate with evidence of low respiratory volumes leading to findings of new interstitial lung disease and profound muscle weakness, although initial elevations in her creatine kinase (480 U/L) were modest. Prior history revealed muscle weakness and fatigue since childhood that progressed more rapidly in the months prior to her admission accompanied by dramatic weight loss. Her family reported a history of multiple orthopedic surgeries for foot deformities in childhood and developmental delay not otherwise specified. Electromyography showed evidence of chronic myopathic changes associated with some necrotic features. Muscle biopsy confirmed an IMNM with an underlying CCD. Her serology showed a negative anti-HMGCR, high positive Anti-Ro52 and a weak positive Anti-PL-12. She required treatment with multiple immunosuppressive agents including intravenous immunoglobulins, prednisone, mycophenolate mofetil and eventually Rituximab. Her treatment course was complicated with prednisone induced psychosis, probable myocarditis, and recurrent aspiration. An extensive work-up for underlying malignancy was negative.

**Conclusion:** To the best of our knowledge, CCD has not been reported simultaneously with IMNM despite CCD being one of the most common congenital myopathies. During work-up of any suspected myopathy, it is important to determine the temporal course of symptoms, including the presence of childhood weakness. In our case, additional clinical clues to a concomitant underlying CCD included orthopaedic complications with foot deformities and developmental delay. Orthopedic deformities are commonly found in patients with CCD including scoliosis, congenital hip dislocation, foot deformities, and joint contractures. Other clinical signs include motor developmental delay and malignant hyperthermia susceptibility. Our case highlights the importance of a muscle biopsy in diagnosis.

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**Antisynthetase Syndrome Triggered by Golimumab Treatment for Rheumatoid Arthritis**

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**Background:** Less than a dozen cases of anti-TNF induced anti-synthetase syndrome have been described in the literature. Etanercept, adalimumab and infliximab have all been implicated but there have not been any published cases resulting from golimumab use. We report a case of golimumab-induced anti-synthetase syndrome.

**Case:** In 2013, a 41-year old male was diagnosed with high titre anti-CCP+ RF+ rheumatoid arthritis. He was ANA negative, and had no clinical or immunologic features of myositis, connective tissue disease, or lung disease at the time. After treatment with NSAIDS, hydroxychloroquine, methotrexate, and leflunomide was unsuccessful in suppressing disease activity, and avoiding IM/PO steroid use, golimumab 50 mg s.q. monthly was started fifteen months after diagnosis. Two months later, he was admitted to hospital with fever, multiple pulmonary emboli, diffuse ground glass opacity on chest CT, myalgias, a diffuse maculopapular rash, and mechanics hands. Serology showed a weakly positive ANA in a speckled pattern, creatine kinase ~500, and the presence of Anti-Jo1 antibodies. He was diagnosed with anti-synthetase syndrome and pulmonary emboli.

His RA medications were stopped and he was started on high dose steroids, azathioprine, and IVIg. Nerve conduction studies confirmed myopathic changes.

**Discussion**: TNF inhibitors may play a triggering role in the anti-synthetase syndrome. Including our case, the average age of patients with anti-TNF associated anti-synthetase syndrome is 45.7 (range 30-63). The 2-month interval between diagnosis and duration of anti-TNF therapy is in keeping with other reports in the literature (average 13

months, range 2-36).
**Conclusion**: Anti-synthetase syndrome is a rare but devastating complication of anti-TNF therapy reported in limited case series in the literature. Overlap syndromes of RA and myositis complicate diagnosis. A high index of suspicion and close clinical monitoring is essential when starting patients on such therapy.

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**Successful Treatment of Statin-Induced Autoimmune Myopathy without Corticosteroids**

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**Objectives:** Our objective was to describe the clinical phenotype and successful treatment regimens of patients with statin-induced autoimmune myopathy (SI-AIM) treated without corticosteroids (CSs).

**Methods:** Our study included all patients from the Université de Montréal AIM cohort with a documented anti-3-hydroxy-3-methylglutaryl-CoA reductase (anti-HMGCR) autoantibody. We selected statin-exposed patients who did not receive any CSs during the course of their treatment and performed a retrospective review of medical records. Remission was defined as a serum creatine kinase (CK) level <500 U/L.

**Results:** From a cohort of 45 anti-HMGCR positive AIM patients, 42 were previously exposed to statins, of whom 8 patients (4 men, 4 women, mean age 59 years) were not treated with CSs and therefore selected for study. Three clinical stages of myopathy were recognized: stage 1 (serum CK elevation, normal muscle strength, normal EMG), stage 2 (CK elevation, normal strength, myopathic EMG) and stage 3 myopathy (CK elevation, proximal muscle weakness, myopathic EMG). Three out of 8 patients presented and were treated in stage 1 myopathy after a mean statin discontinuation time of 23 months (range 5-54 months). The remaining 5/8 patients presented in stage 3 myopathy. The mean time between statin cessation and treatment initiation was 5 months (range 0-10 months), with one patient improving to stage 2 myopathy upon statin discontinuation. MTX monotherapy induced remission in all 3 patients presenting in stage 1 myopathy and in 1 patient in stage 2 myopathy. The mean time to remission was 7 months (range 4-13 months). In the remaining 4 patients with stage 3 myopathy, IVIG was successfully used in 3 patients to induce remission with either MTX or MTX+AZA, whereas 1 patient responded to a MTX+AZA combination alone. The mean time to remission for stage 3 myopathy was 10 months (range 1-21 months). MTX monotherapy (n=5) or a MTX+AZA combination (n=1) were able to maintain remission for at least 6 months in the 6 patients available for analysis. Thus, all 8 patients did not require CSs to achieve remission.

**Conclusion:** Eight patients with SI-AIM were successfully treated with immunosuppressive and/or immunomodulating agents but without CSs. Four patients with normal strength (i.e. in stage 1 or 2) responded to MTX monotherapy. In patients with proximal muscle weakness, combination therapies with MTX+IVIG, MTX+AZA or MTX+AZA+IVIG were successfully used and thus, appear reasonable induction strategies in stage 3.

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**Seropositive Rheumatoid Arthritis Associated Myositis Presenting with Dysphagia and Dysarthria**

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**Purpose:** To present a case of biopsy proven Rheumatoid Arthritis (RA) associated Inflammatory Myositis, presenting with dysphagia, dysarthria and without proximal muscle weakness.

**Methods:** A case report is presented as well as a review of the literature for cases of inflammatory myositis presenting with only bulbar symptoms.

**Case:** A 70-year-old woman with a history of well controlled rheumatoid arthritis on Hydroxychloroquine presented with progressive dysphagia. She had mild dysarthria with an associated facial droop. She denied symptoms of limb weakness. There were no clinical features of Dermatomyositis. Creatinine Phosphokinase was persistently elevated above 1100 U/L. Videofluoroscopic swallow study was consistent with cricopharnygeal dysfunction. Initial work up including EMG, brain/c-spine MRI, and serological testing for neuromuscular and inflammatory causes were unremarkable. After 3 years of disease, EMG testing was repeated on the upper extremities, which found abnormalities consistent with a myopathy. A muscle biopsy was consistent with a diagnosis of an inflammatory myositis. High dose oral prednisone and Methotrexate lead to normalization of the patient's creatinine kinase, and after 2 months there was mild improvement of her symptoms.

**Conclusion:** Rheumatologists should be aware of this rare presentation of RA associated Myositis presenting with dysphagia and dysarthria. Diagnosis requires collaboration with neuromuscular specialists and neuropathologists.

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**Patient Preferences for Disease Modifying Anti-Rheumatic Drug Treatment of Rheumatoid Arthritis: A Systematic Review**

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**Objectives:** To systematically review studies reporting patients' preferences for traditional and biologic disease modifying anti-rheumatic drugs (DMARDs) in RA.

**Methods:** We conducted a systematic literature search in five electronic medical databases (Medline, CENTRAL, EMBASE, Psychinfo, and HealthStar) from inception to October, 2015 using MeSH headings and keywords for RA and patients' preferences. We included English-language studies that measured patients' preferences for health outcomes or other attributes relevant to DMARD decisions, and studies that examined patients' choices for different treatment options. We extracted and summarized study characteristics and outcome data to identify common themes. All screening and data abstraction was conducted in duplicate.

**Results:** Of 6261 abstracts screened, 346 underwent full-text review and 19 studies were

ultimately included. The 19 studies used a variety of methods to measure preferences including: standard gamble (n=2), time trade-off (n=4), willingness to pay (WTP) (n=6), conjoint analysis (n=5), visual analog scale (n=2), risk benefit trade-off (n=1) and Arthritis Impact Measurement Scales (AIMS-2) (n=1). The studies varied in size from 25 to 1024 patients, average age ranged from 50-70 years, and disease duration from 7 to 15 years. The majority of patients in most studies were Caucasian. The treatment attributes that patients were asked to consider included: treatment benefits (n=6); treatment harms, including both rare adverse events and more common but less serious side effects (n=6), dosing (n=3) and cost (n=1). The specific attributes considered, the way in which they were described, and the options presented, varied widely. In general, avoiding adverse events were rated as more important than treatment benefits, but there was considerable heterogeneity in the results across the studies. Serious but rare adverse events were generally viewed as more important than more common 'nuisance' side-effects. The cost of treatment was rated as the most important attribute in only 1 study and dosing was generally less important than both treatment benefits and harms. Patient characteristics associated with greater risk aversion included: worse functional status (n=3), older age (n=3), lower income (n=2), greater pain (n=2), and black ethnicity (n=1).

**Conclusion:** Patients with established RA appear to be generally risk averse, valuing the avoidance of harm as more important than treatment benefits, but preferences varied widely. This demonstrates the importance of assessing patients' preferences in treatment decision-making.

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## The OMERACT RA Flare Questionnaire (RA-FQ) is Responsive to Change in RA Symptoms and Impacts

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**Objectives:** We have previously provided evidence of the construct validity and reliability of the RA Flare Questionnaire (RA-FQ), a new measure that quantifies the symptoms and impacts of RA flares. This study, evaluates responsiveness or sensitivity to change of the RA-FQ in a clinical trial and two observational studies of RA patients who were initially in remission or low disease activity.

**Methods:** RA patients in two observational studies [CATCH in Canada (n=896) and STPR in France (n=138)], and an RCT in the Netherlands (DRESS; n=178) completed the 5-items, a self-assessment of whether they were in flare at the time (yes/no), and if so, the severity and duration. Within each cohort, we selected patients who said they were not in flare and had a DAS28 <3.2 at the first visit (V1). Flare at the next study visit (V2) was defined three ways: 1) patient report (yes/no); 2) patient report-stringent (Boolean: patient report yes AND severity ≥4/10 AND duration > 7 days [to increase likelihood this represented true increase in inflammatory disease activity]; and c) DAS definition often used in studies (DAS28 < 3.2 at V2 required increase of 1.2; DAS ≥ 3.2 at V2 required increase of 0.6). We compared the mean change in RA-FQ scores and other PROs and clinical indicators of disease activity between flaring and non-flaring

patients. Effect size was estimated using Cohen's standardized mean difference. We hypothesized that at V2, RA-FQ scores, clinical indicators, and PROS would be similar in patients not in flare at both visits, and would be clinically significantly higher in those who were classified as flaring at V2.
**Results:** The mean difference in RA-FQ scores at Visit 2 ranged from 7.3 (95% CI 1.4, 13.2) in the French trial using the DAS definition to 19.6 (95% CI 16.7, 22.6) in the Canadian trial using the patient report-stringent. The standardized mean difference effect sizes ranged from 0.82 to 1.95, and were largest for patient report-stringent in 2 of 3 studies. Mean difference effect sizes were also strong (range 0.84–2.42) for patient global, MD global, HAQ, DAS28, and other clinical indicators except ESR.
**Conclusion:** Data from clinical and observational studies support the responsiveness of the RA-FQ in detecting change over time. The robust psychometric properties of the RA-FQ suggest it reliably detects clinically relevant worsening of RA symptoms and impacts consistent with an increase in disease activity, and support its use in research and clinical care.

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**"I Just Want My Life Back": Physical Function and Fatigue are Critical Targets for Improving Participation and HRQL in Rheumatoid Arthritis**

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**Objectives:** The primary goal of treatment for rheumatoid arthritis (RA) is to maximize health-related quality of life (HRQL) through symptom and damage control, and normalize function and participation in social and life activities. Although fatigue is recognized as one of the most debilitating symptoms of RA, little is known about how fatigue impacts participation. We hypothesized that fatigue, along with pain, mood, disease activity, and disability would be associated with reduced participation.
**Methods:** RA patients enrolled in an observational study at an academic center completed PROMIS measures assessing fatigue, physical function, mood (depression and anxiety), pain interference, sleep disturbance, and participation. RA clinical indicators were also collected at the visit. Variance inflation factors were examined to evaluate collinearity among variables. Covariates/confounders independently associated with participation included pain, mood (depression, anxiety), sleep, disease activity (CDAI), and physical function. Multiple regression models that did and did not include pain were compared using likelihood ratio tests with SPSS and R.
**Results:** Participants were mostly female (82%) and white (83%) with mean (SD) age of 56 (13) years; 24% had ≤ high school, 29% had RA ≤ 5 years with 13% ≤ 2 years, and 22% were disabled. Mean CDAI was 7.9 (7.8). Most were in CDAI remission (n=56; 32%) or LDA (n=67; 38%); 39 (22%) were in MDA and 14 (8%) in HDA. Mean PROMIS fatigue was 53.9 (10.0); fatigue increased across CDAI levels from 46.2 (8.6) in remission to 64.0 (9.6). Only those with HDA had mean sleep, depression or anxiety scores > 55 (i.e., above population norms). In the full model, fatigue, depression, CDAI, and physical function were significant independent predictors of reduced participation in social roles and activities ($F(2, 162) = 29.75$, $p<.001$, adjusted $r2=.54$). Contrary to our hypothesis, pain was not associated with participation in univariate or multivariate models.
**Conclusion:** Our results suggest that in RA patients, high levels or fatigue are common;

conversely, depression, anxiety, and sleep disturbance were elevated only in people with HDA. Disability and fatigue appear to have the greatest impact on participation in social roles and activities. RA treatments and interventions that attenuate fatigue and improve mood in people with active RA may improve their ability to participate in social and life situations restoring a sense of normalcy and improving HRQL. Funding: PCORI IP2-PI0000737 and SC14-1402-10818, CIHR 312205.

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**How much is the Obesity Epidemic Affecting Physical Function in RA?**

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**Objectives:** Aggressive, early treatment of RA with new therapeutic agents has dramatically improved the management of RA. However, many studies have failed to show greater improvements in function or disability reduction between targeted control vs. less-aggressive care. The prevalence of obesity is increasing dramatically world, and may be even higher in RA patients. Because obesity is also a risk factor for disability, we evaluated the extent to which excess weight may independently contribute to poorer physical function (PF) in RA.

**Methods:** RA patients enrolled in an observational study at an academic Inflammatory Arthritis Clinic completed the patient global, pain VAS, and PROMIS measures assessing PF, pain, fatigue, sleep, and depression. RA clinical indicators were also collected at the visit. Outcomes were compared in obese and non-obese patients using t-tests and chi-square. Multiple regression was used to evaluate the effects of pain, fatigue, and BMI on PF, after controlling for age and disease activity.

**Results:** Participants were mostly female (82%) and white (83%) with mean (SD) age of 55 (13) years; 24% had ≤ high school; RA duration 12 (9). Mean CDAI was 8.1 (8.1). Most were in CDAI remission (n=57; 32%) or LDA (n=64; 36%); 40 (23%) were in MDA and 16 (9%) in HDA. 49 (28%) were classified as normal weight (BMI 18.5-24.9), 46 (26%) were overweight (BMI 25-29.9), and 82 (46%) were obese (BMI≥ 30). Men had a significantly higher mean BMI than women (33.6 [ 8.4] vs. 29.5 [7.2], p = .006). As compared to non-obese participants, obese participants had a significantly ($p<.05$) higher CDAI (6.1 [6.9] vs. 10.4 [8.9]; p=.000, respectively) and worse PF, pain, fatigue, sleep, and depression (mean differences -5.0, -4.6, 4.6, 3.8, 2.9, 3.6, and -4.7, respectively). In regression analyses, pain, fatigue, and BMI (but not sleep or depression) were inversely related to PF, after controlling for age and disease activity. In the final model, pain, fatigue and BMI were significantly and inversely related to PF ($\beta$=-.39, -.24, and -.153, respectively) after controlling for age and disease activity ($F(5, 170) = 55.5$, p=.000, adjusted $r^2$=.61).

**Conclusion:** Our results suggest that excess weight also contributes to poorer PF in addition to pain and fatigue. As the prevalence of obesity continues to escalate in RA populations, weight loss may be increasingly important to improve not only physical health, disease activity, and response to treatment, but also pain, fatigue, and PF.

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**Efficacy and Safety of Switching from Adalimumab to Baricitinib: Phase 3 Data in Patients with Rheumatoid Arthritis**

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**Objectives:** Baricitinib is an oral JAK1/JAK2 inhibitor under investigation for the treatment of patients with moderate to severe RA.1,2 In the 52-week Phase 3 RA-BEAM study, baricitinib 4 mg once daily (QD) showed clinical improvements compared to placebo and to adalimumab in MTX-inadequate-responder (IR) patients.2 The objective of this analysis was to evaluate efficacy and safety in patients from RA-BEAM who changed treatment from adalimumab to baricitinib either after rescue in RA-BEAM or switch after entering a long-term extension study (RA-BEYOND).
**Methods:** In RA-BEAM (completed September 2015), 1305 patients were randomized 3:3:2 to placebo, baricitinib 4 mg QD, or adalimumab 40 mg every 2 weeks. At Week 16 or subsequent visits, IRs (lack of ≥20% reduction in tender and swollen joint count) were rescued to open-label baricitinib 4 mg. At Week 52, patients could enter RA-BEYOND, where all patients received baricitinib 4 mg and remained blinded to their randomized treatment in RA-BEAM. No adalimumab washout period was applied for rescue or switch from adalimumab to baricitinib. Efficacy analyses evaluated both rescued and not rescued RA-BEAM patients who entered RA-BEYOND ≥24 weeks before the present data cutoff. Safety analyses included patients not rescued in RA-BEAM who entered RA-BEYOND.
**Results:** A total of 51 patients were rescued from adalimumab to baricitinib 4 mg in RA-BEAM; at Week 52, 67%, 49%, and 24% achieved ACR20, ACR50, and ACR70, respectively. Among patients who completed RA-BEAM without rescue, 381/394 (97%) baricitinib, and 238/241 (99%) adalimumab patients entered RA-BEYOND. Of these, 185 (continued baricitinib) and 108 adalimumab (switched to baricitinib) patients reached the 24-week time point and were included in the RA-BEYOND efficacy analysis; 340 (continued baricitinib) and 211 adalimumab (switched to baricitinib) patients were included in the RA-BEYOND safety analysis. Patients who switched from adalimumab to baricitinib showed improvements in disease control through 12 weeks post-switch in RA-BEYOND, without evidence of worsening through the following 12 weeks. Exposure-adjusted incidence rates for total treatment-emergent adverse events (TEAEs) and infections, including serious events, were similar for patients who switched from adalimumab to baricitinib and those who continued on baricitinib.
**Conclusion:** Switching from adalimumab to baricitinib without adalimumab washout was associated with improvements in disease control during the initial 12 weeks post-switch, without an increase in overall TEAEs, serious adverse events or infections, and without subsequent evidence of worsening. References: 1Dougados M et al. Ann Rheum Dis 2015;74(S2):79. 2Taylor PC et al. Arthritis Rheumatol 2015;67(S10):3927-3928.

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**Previous Use of Conventional Disease-Modifying Antirheumatic Drugs and Response to Baricitinib**

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**Objectives:** Baricitinib, an oral JAK1/JAK2 inhibitor, is in development for patients with moderate to severe RA.1,2 This post hoc analysis of 2 completed Phase 3 studies aimed to determine if previous failure of cDMARDs altered the response to baricitinib in RA patients and to evaluate the effect of concomitant steroid use and prognostically unfavorable factors on the efficacy of baricitinib.

**Methods:** Patients with ≥6 swollen and tender joints and no prior biologic DMARD use were eligible for study inclusion. In RA-BUILD, cDMARD-inadequate responder (IR) patients with hsCRP ≥3.6 mg/L were randomized to placebo or baricitinib (2 or 4 mg) once daily (QD).1 In RA-BEAM, MTX-IR patients with X-ray erosions and hsCRP ≥6.0 mg/L were randomized to placebo QD, baricitinib 4 mg QD, or adalimumab 40 mg biweekly.2 Patients continued background cDMARD (including MTX). The primary endpoint in both trials was ACR20 at Week 12 for baricitinib 4 mg vs. placebo.1,2 This analysis included placebo (N=716) and baricitinib 4 mg (N=714) patients and assessed number of previous cDMARDs, concurrent corticosteroid use, and effect of poor prognostic factors (high disease activity by Simplified Disease Activity Index [SDAI]>26), RF/ACPA positive, and radiographic erosions).

**Results:** In placebo patients, 40%, 34%, and 23% previously used MTX alone, MTX + 1 cDMARD, and MTX + ≥2 cDMARDs, respectively; in baricitinib 4 mg patients the rates were 46%, 29%, and 23%. Oral corticosteroids were used in 56% of placebo and 55% of baricitinib patients at baseline; patients continued use throughout the studies. Regardless of treatment assignment, most patients had 2 or 3 prognostically unfavorable factors (95% in placebo; 96% in baricitinib patients). The primary objectives were met for both studies.1,2 The clinical efficacy of baricitinib 4 mg over placebo at 12 weeks and the percentage of patients with van der Heijde modified Total Sharp Score (mTSS) change from baseline ≤0 at 24 weeks were both similar regardless of the number of cDMARDs previously used, the concomitant use of corticosteroids, or the presence of prognostically unfavorable factors. Rates of serious adverse events and discontinuation due to adverse events were comparable regardless of the number of cDMARDs used, corticosteroid use, or the number of risk factors.

**Conclusion:** Baricitinib has demonstrated clinical efficacy in a wide range of patients with varying exposure to cDMARDs, concomitant use of corticosteroids, serologic status, and baseline disease activity. References: 1Dougados M et al. Ann Rheum Dis 2015;74(S2):79. 2Taylor PC et al. Arthritis Rheumatol 2015;67(S10):3927-3928.

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## Effect of Personalized Diet and Exercise Recommendations in Early Inflammatory Arthritis: A Randomized Trial

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**Objectives:** Physical activity and diet positively influence disease activity and cardiovascular risk in patients with rheumatoid arthritis (RA). We tested the effect of a brief individualized counseling intervention on physical activity levels and fitness, and dietary intake, compared to standard of care.

**Methods:** Thirty patients with inflammatory arthritis (<1 year duration) were randomized to standard of care or the intervention which consisted of individualized visits with a dietetic intern and physiotherapist at two time points to review age-specific strategies on diet and exercise.

Primary outcomes included anthropometric measurements (height, weight, waist and hip circumference), nutritional intake, physical activity (pedometer steps) and physical fitness. Disease activity measures and biochemical testing (blood pressure measurement, inflammatory markers, cholesterol profile and random glucose) were collected. Change from baseline to six months in these outcomes were assessed using paired t-tests between groups.
**Results:** Thirteen patients in the intervention group and 10 in the control group completed the study. At baseline the two groups were well matched in demographics including age (49 years), gender (71% female standard care, 93% female intervention), seropositive (86%), mean BMI (27.2 kg/m2 standard care, 25.4 kg/m2 intervention) and functional disability as measured by the HAQ (mean 1.0 (SD 0.9), intervention 0.6 (SD0.4)). However, the standard of care group did have higher DAS28 scores than the intervention group at baseline (mean DAS28 5.5 (SD 1.4) standard care, mean DAS28 3.5 intervention $p<0.001$). There were numerical trends to larger improvements in the intervention group for pedometer steps per week (intervention + 9,583, standard care +6,696) and the six-minute walk test distance (mean increase 45.7 meters intervention, mean increase 6.8 meters standard care), but these differences were not statistically significant. Biochemical markers including the LDL also improved to a greater degree in the intervention group but without reaching statistical significance (-0.23 (SD 1.53) intervention, mean change -0.09 (SD 1.11) standard care $p= 0.8$). There was no difference between the two groups in change in BMI. Nutritional intake (vitamin C, iron, fibre, vitamin A and folate) improved in the intervention group but did not reach statistical significance.
**Conclusion:** Poor enrolment and high dropout rates in this short-term study highlight the difficulty of behavioral change. Those continuing in the study and who received the intervention demonstrated a non-significantly improved activity and nutritional intake that may benefit long-term outcomes. Supported by a CIORA grant.

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**Longitudinal Trajectories of the Weighted Lansbury Articular Indices and Standard Joint Counts are Similarly Correlated with Trajectories of Physical Function in Early Inflammatory Arthritis**

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**Objectives:** Residual disease activity impacts functional status in early rheumatoid arthritis (ERA). The impact of large or small joint activity on function is likely task dependent. The Lansbury Articular Index (LAI) weights joints by size allowing estimates of large joint disease burden. The Health Assessment Questionnaire (HAQ) seems to weigh upper extremity tasks more than lower extremity or weight bearing tasks. We sought to determine associations of LAI with HAQ and whether changes in the LAI trajectory more closely reflected the evolution of the HAQ trajectory than the standard joint count measures
**Methods:** We used data from subjects followed in a multicentre Early Arthritis Cohort. Arthritis activity measures (DAS28, tender28 joint count (tjc28), swollen28 joint count (sjc28), function (HAQ), QoL (SF12 physical (PCS) and mental (MCS) scores) and work status were captured per study protocol. The LAI based on 28 joints was calculated separately for swollen (LS28) and

tender (LT28) joint counts. The impact of LS28, LT28 on baseline disability status was modeled using logistic regression. Individuals' trajectories for each measure (HAQ, DAS28, TJC28, SJC28, LT28,LS28) were visualized with LOESS plots and marginal trajectories by variable plotted. Each measure's longitudinal trajectory was fitted using the best fitting fractional polynomials. Each individual disease activity trajectory was then jointly modelled with the HAQ longitudinally. Correlations between each pair of joint trajectories (HAQ with TJC28 or SJC28 or LT28 or LS28) were calculated.
**Results:** ERA subjects (n=2133, 73% female; baseline mean (SD) Age 53(15) years, DAS 5.1(1.4)) were followed for median (IQR) 24(10,48) months. At last visit 44 % were in remission (DAS28<2.6). Combining all visits, the LS28 correlated with SJC28 (r= 0.9 p<0.0001), PCS (r=-0.4 p<0.0001) and HAQ (r= 0.4 p<0.0001). The LT28 correlated with the TJC28 (0.9 p<0.001), PCS (r=-0.5 p<0.0001) and HAQ (0.5 p<0.0001). Disability at baseline (6% of cohort) was associated with higher LT28 (OR 1.003 p=0.001) and higher TJC28 (OR 1.071 p<0.0001) in separate logistic regression models that included age. The HAQ trajectory was highly correlated with the trajectories for DAS28 (r=0.83), LT28 (r=0.83), and TJC28 (r=0.85) and less strongly with trajectories for LS28(r= 0.59) and SJC28 (r=0.61)
**Conclusion:** The trajectories of HAQ and both Lansbury and standard joint counts are highly correlated over time in ERA. The LAI performed similarly to standard joint counts. Although type of occupation was not addressed and likely influences the impact of lower extremity involvement, both LT28 and TJ28 associated with baseline work disability.

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**Qualitative Inquiry on Treatment Preferences for Rheumatoid Arthritis Pharmacotherapy: An Indigenous Patient Perspective**

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**Objectives:** To explore what factors influence Indigenous patients when making treatment decisions for management of rheumatoid arthritis (RA).
**Methods:** Ten in-depth interviews were conducted (n=9 females, n=1 male) with self-identified Indigenous patients with RA, using a constructivist qualitative approach. Both on- and off-reserve patients were recruited. A semi-structured guide was used in the interviews, which were audio-recorded and transcribed verbatim. Using a team approach, a content analysis was first performed to identify narratives describing decision-making preferences for taking RA medications. We then proceeded with a constant-comparison analysis to identify and synthesize treatment preferences patients have and what actions they take regarding medication utilization.
**Results:** Trust, medical knowledge, health experiences and fear were key influences in the decision-making and actions Indigenous patients took when a medication was recommended. Acceptance and adherence to a medication occurred when a high sense of trust existed. The concept of trust was framed in narratives of perceiving drug benefit, understanding the medication mechanism of action and adverse effects, trusting the physician making the recommendations, and perceived involvement in making decisions about care. Considerations and actions to modify recommended treatment were influenced by patients' personal medical knowledge and their health experiences, which gave them confidence to self-regulate dosages to balance benefits and risks. The decision to reject a prescription was illustrated by narratives of fear, which was mediated by perceptions of drugs' harms to the body and potential for

dependency.
**Conclusion:** Indigenous patient considerations to use recommended RA medications were influenced by factors of trust, medical knowledge, health experiences and fear. Evidently, these factors are expressed in the acceptance, modification or rejection of prescribed medications. Our results imply that optimizing use of RA medications could be achieved through: a) building relationships of trust between patients and physicians, b) increasing capacity for self-management, c) communicating thorough information about medication benefits, adverse effects and mechanisms of action, and d) involving patients in decision making about care.

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**Body Mass Index does not Impact Abatacept Retention in Biologic-Naïve Patients with Rheumatoid Arthritis who have Poor Prognostic Factors: A 12-Month Interim Analysis of an Observational, Prospective Study**

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**Objectives:** In patients with RA, obesity may impair clinical response to anti-TNF agents.1,2 In contrast, BMI does not appear to impact treatment retention or clinical response to abatacept (ABA);3 however, data on the effects of BMI are limited for patients with poor prognostic factors (radiographic erosion or RF/anti-citrullinated peptide antibody [ACPA] double seropositivity). Previously, poor prognostic factors were found to positively impact ABA retention, independently of treatment line.4 The current analysis tested the impact of BMI on ABA retention in biologic-naïve patients with RA who had poor prognostic factors at baseline.

**Methods:** ACTION is a 2-year, international, observational study of patients with RA who initiated IV ABA in routine clinical practice. Time to ABA discontinuation in biologic-naïve patients was estimated using Kaplan–Meier survival analysis. Clinically relevant variables, known risk factors, and potential predictive factors with significance in univariate models ($p \leq 0.20$) and no collinearity, were entered into multivariate Cox proportional hazards regression models. Prognostic factors of ABA retention were assessed in subgroups of patients with and without radiographic erosion at baseline. As comorbid obesity has previously been linked to a decreased likelihood of joint damage progression in patients with RA who are ACPA positive,2 BMI status was forced into the multivariate model after stratification for RF/ACPA double-seropositive versus double-seronegative status.

**Results:** Here we report 1-year results for 677 biologic-naïve patients with ≥1 prior conventional synthetic DMARD failure who enrolled into the ACTION study in two cohorts: 122 from Europe and Canada between May 2008 and December 2010; 555 from across Europe between September 2010 and December 2013. Data from the two enrollment cohorts were pooled owing to similar baseline characteristics. The 12-month ABA crude retention rate (95% CI) in biologic-naïve patients was 78.14% (74.72, 81.16). When forced into the multivariate model, BMI did not significantly impact ABA retention in the subgroups of patients who were RF/ACPA double seropositive ($p=0.142$) or double seronegative ($p=0.518$) at baseline.

**Conclusion:** Real-world evidence shows that RF/ACPA double seropositivity is predictive of abatacept retention in biologic-naïve patients.4 BMI does not significantly impact abatacept

retention, even in subgroups of patients with poor prognostic factors such as RF/ACPA double seropositivity. 1. Gremese E, et al. Arthritis Care Res 2013;65:94–100. 2. Iannone F, et al. Joint Bone Spine 2015;82:187–91. 3. Nüßlein HG, et al. Clin Exp Rheum 2016;34:489–99. 4. Alten R, et al. Ann Rheum Dis 2016;75 (Suppl 2): 202.

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**Evaluation of the Association Between C-Reactive Protein and Anti-citrullinated Protein Antibody in Rheumatoid Arthritis: Analysis of Two Clinical Practice Data Sets**

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**Objectives:** The association between inflammatory markers such as CRP or ESR and joint damage has been widely established in RA. Autoantibodies such as RF and anti-cyclic citrullinated peptide (anti-CCP) are also associated with severe joint damage. However, there are limited data on the association between markers of inflammation and autoantibodies. The objective of this analysis was to evaluate the association between CRP and anti-CCP using clinical practice data sets.

**Methods:** Two data sets were used: a single academic center, prospective, observational cohort registry of patients with RA, and the Optum Clinformatics Data Mart (Optum), which includes the Optum Medicare data. The registry was established in 2003 and primarily comprises patients with established RA. In Optum, patients with two ICD-9 codes for RA (714.0) and a prescription for a DMARD between Jan 2007 and Dec 2014 were identified. For inclusion in the current study, patients were required to have anti-CCP and CRP baseline values. Patients meeting inclusion criteria were placed into CRP groups by quartiles and anti-CCP positivity was evaluated in each group. Additional sensitivity analyses were conducted by grouping patients into two CRP groups, i.e., CRP ≥5 vs <5 mg/L. Multivariate logistic and linear regression for anti-CCP positivity were evaluated with CRP as an independent variable and controlling for baseline covariates.

**Results:** A total of 1309 patients from the registry and 3798 from Optum were included in the analysis. Patients in the high (vs low) CRP groups were older (mean 60.1 vs 51.4 yrs in registry; 60.0 vs 54.4 yrs in Optum), had more males (23 vs 13% in registry; 30 vs 21% in Optum) and a greater proportion of patients was anti-CCP positive. Based on multivariate logistic models, patients in CRP group 3 vs group 1 (odds ratio [95%CI] 2.08 [1.43,3.03], p<0.001) and group 4 vs group 1 (1.87 [1.23,2.84], p=0.003) had significantly higher odds of being anti-CCP positive in the registry. Similar findings were observed in Optum: group 2 vs group 1 (1.37 [1.15,1.63], p<0.001); group 3 vs group 1 (1.68 [1.42,2.00], p<0.001); and group 4 vs group 1 (2.09 [1.76,2.48], p<0.001). The findings from the linear regression model and sensitivity analysis were consistent with those of the logistic regression model.

**Conclusion:** Analyses based on two independent data sources indicate that there is an association between CRP and anti-CCP levels in patients with RA. Patients with a high CRP level are more likely to be anti-CCP positive, with a higher anti-CCP level.

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**Association of Anti-citrullinated Protein Antibody Positivity and Titer Levels to Low Hand BMD, and the Consequence of Low Hand BMD on DAS28 (CRP) Remission in Established Rheumatoid Arthritis: Findings from a US Observational Cohort**

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**Objectives:** Hand bone mineral density (BMD) loss is an independent predictor of radiographic joint progression,1 and a potential indicator of vertebral and non-vertebral fracture risk.2 The relationship between hand BMD loss and anti-cyclic citrullinated peptide-2 antibodies (anti-CCP2, a surrogate of anti-citrullinated protein antibodies [ACPA]) in patients with established RA is unclear. Therefore, we evaluated this association to assess joint progression and fracture risk in patients with established RA.

**Methods:** Patients enrolled in a single academic center, prospective, observational cohort registry of RA patients, established in 2003, were included. The registry comprises mostly patients with established RA; digitized hand radiographs were collected at baseline and every 2–3 yrs over 15 yrs from which hand BMD was measured using digital X-ray radiogrammetry (DXR–BMD). The current cross-sectional analysis is based on available data of DXR-BMD and anti-CCP2 measured within 6 months. Anti-CCP2–IgG-positive (+) patients (≥20 U/mL) were distributed into equal groups (Gp1–3), representing increasing anti-CCP2 concentrations. Associations between DXR–BMD and anti-CCP2 status and titers were explored in univariate and multivariate regression analyses controlling for covariates (age, RA duration, BMI, smoking status, use of steroids, biologic DMARD, and osteoporosis medication). The association between DAS28 (CRP) remission (<2.6) and bone loss was analyzed in patients with DXR–BMD ≥0.5 and <0.5.

**Results:** A total of 149 patients (all women) were included (47 anti-CCP2 negative [–], 102 anti-CCP2+ [34 per group]). Age (mean: 60–63 yrs), BMI (mean: 26–29 kg/m2), DAS28 (CRP; median 3.7–4.2) and biologic DMARD use (43–56%) did not differ by anti-CCP2 status (+/–) or titer group; mean disease duration was greater in the three anti-CCP2+ titer groups versus the anti-CCP2– group ($p=0.0215$). DXR–BMD was higher in the anti-CCP2– versus the anti-CCP2+ groups ($p<0.0001$ for left and right hand). DXR–BMD decreased with increasing anti-CCP2 titer increase ($p<0.001$ for left and right hand). Patients with low DXR–BMD were less likely to be in DAS28 (CRP) remission (DXR–BMD ≥0.5, 36.5% vs DXR–BMD <0.5, 18.8%; $p<0.05$). Even after controlling for baseline confounding factors, the odds of being in remission were significantly lower for patients with DXR–BMD <0.5 versus ≥0.5 ($p=0.0496$).

**Conclusion:** These data suggest that anti-CCP2+ patients with established RA, particularly those with high anti-CCP2 titers, have lower hand BMD and patients with lower hand BMD are less likely to be in remission. Such patients could be at increased risk of joint progression and fracture. 1. Hoff M, et al. Ann Rheum Dis 2009;68:324–9. 2. Haugeberg G, et al. Ann Rheum Dis 2004;63:1331–4.

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## Serious Infections in RA Offspring Exposed to TNF Inhibitors

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**Objectives:** Most TNFi are actively transported across the placenta, reaching higher fetal than

maternal blood levels. Thus, we evaluated serious infections in RA offspring exposed to TNFi in the pre-conception and/or gestational period compared to unexposed RA offspring, as well as to children from the general population.
**Methods:** The "PregnAncies in RA mothers and Outcomes in off-spring in the United States (PAROUS)" cohort includes all women with ≥1 hospitalization for delivery after RA diagnosis, identified through MarketScan database (2011-2014), and a randomly selected control group of women, matched ≥4:1 for age, year of delivery, and state of residence. Only women continuously enrolled within MarketScan for ≥12 months prior to delivery and with available child linkage were included in PAROUS. We defined TNFi ex-posure based on ≥1 filled prescription during pregnancy and/or the preconception period. We ascertained serious infections in the offspring based on ≥1 hospitalization with infection as a primary diagnosis, ≤12 months of life. We performed multivariate analyses, adjusting for maternal demographics, co-morbidities, pregnancy complications, and drugs.
**Results:** We identified 2455 RA offspring and 11 018 matched controls. Among RA offspring, 290 (11.8%) were exposed to TNFi during pregnancy, 109 (4.4%) were unexposed during pregnancy but exposed in the preconception period, and 2056 (83.7%) were unexposed both during the pregnancy and preconception periods. The percent of serious infections in RA offspring with no TNFi exposure was identical (2.1%, 95%CI1.5,2.8) to non-RA offspring (2.1%, 95%CI1.9,2.5) while the percent of serious infections in RA offspring with TNFi exposure was 3.1% (95%CI2.0,6.8). With regards to TNFi exposure in the third trimester, the percent of serious infections was 2.8% (95%CI0.7,8.4), while for TNFi exposure in the preconception period only, it was 1.8% (95%CI0.3,7.1). In multivariate analyses, we were unable to determine a substantially increased risk of serious infections in RA offspring exposed to TNFi versus non-RA offspring [OR for TNFi pregnancy 1.4 (95%CI0.5,3.7), OR for TNFi preconception 0.9 (95%CI0.2,4.4)]. The OR estimates for serious infections in RA offspring exposed to TNFi during pregnancy versus unexposed RA offspring were also imprecise (OR 1.2; 95%CI0.6,2.6) as were the results when we restricted TNFi exposure to the third trimester (OR 1.0; 95%CI0.3,3.4).
**Conclusion:** We were unable to demonstrate a marked excess risk for serious infections in RA offspring exposed to TNFi during pregnancy, including the third trimester, versus unexposed RA offspring.

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## Resilient Coping Associated with Functional Outcome in Patients with Rheumatoid Arthritis

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**Objectives:** The purpose of this study is to: 1) investigate the relationship between resilience and self-reported functional impairment in the RA patient population and 2) determine the predictors of resilience in the RA patient population.
**Methods:** Participants completed the Brief Resilience Coping Scale (BRCS) and the Health Assessment Questionnaire (HAQ), along with demographics questionnaire, Pain Coping Inventory (PCI), Pain Catastrophizing Scale (PCS), depression questionnaire (PHQ-9), Perceived Stress Scale (PSS), Multidimensional Scale of Perceived Social Support (MSPSS). A RA disease activity score (DAS) was also completed by their rheumatologist. Bivariate correlation and stepwise regression were conducted.

**Results:** 155 patients were included in the study. Resilience was inversely correlated with HAQ scores (r -.20), indicating that higher resilience was associated with better self-reported functional status. Living with a spouse or partner, higher levels of education, better understanding of RA and higher levels of perceived social support were related to higher resilience. Higher levels of depression, pain catastrophizing and passive coping were associated with lower levels of resilience. Understanding of the disease, level of education, and depression were independent predictors of resilience.
**Conclusion:** Resilience is associated with better self-reported functional status in RA patients. Depression, level of education and level of understanding of RA are predictors of resilience.

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**Examining the Role of Sleep on Fatigue in People with Early Rheumatoid Arthritis**

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**Objectives:** To explore the associations between self-reported fatigue and objective measures of sleep in patients with early rheumatoid arthritis (RA), taking into account demographics, presence of joint inflammation, and reported functional limitation.
**Methods:** 30 individuals diagnosed with RA in the previous year were recruited into a 1-year prospective cohort study examining microstructural bone health and physical activity. Participants completed outcome measures at baseline and 12 months: Multidimensional Assessment of Fatigue questionnaire (MAF0-50), 28 tender/swollen joint count, and Health Assessment Questionnaire (HAQ; baseline only). Sleep quality (efficiency) and quantity (minutes per day) were measured with SenseWear Mini TM accelerometers for a week. We performed a secondary analysis with data collected at both time points. Associations between sleep quality/quantity, personal characteristics, disease activity, and fatigue were examined using Pearson's correlation. Backward stepwise regression was used to identify predictors of fatigue. From the list of candidate variables, several were excluded due to collinearity or very weak correlation with fatigue. Remaining variables were entered into a hierarchical model.
**Results:** Participants were 80% female, and on average 53.3 (SD 13.7) years old, with a BMI of 27.9 (SD 6.6). The average HAQ was 0.59 (SD 0.60), and 30% of participants had no tender/swollen joints. Despite low disease activity, they reported clinically important fatigue levels at baseline [MAF0-50: 21.6 (SD 10.7)] and 12 months [19.6 (SD 15.2)]. Average sleep time and efficiency were 433 minutes (SD 58) and 84% (SD 6) at baseline, respectively. Fatigue was negatively correlated with age ($r = -0.48$, $p=0.014$), sleep efficiency ($r=-0.40$, $p=0.056$), and sleep time ($r=-0.11$, $p=0.615$), and positively correlated with presence of tender/swollen joints ($r=0.684$, $p<0.001$), at baseline. Presence of active joints and age were the strongest predictors of fatigue at baseline (adj. $R2=0.62$, $F(2,21)=19.35$, $p<0.001$). Adding sleep time and sleep efficiency to the model increased R2 by 0.09 (change $F(2,19)=3.03$, $p=0.072$). The overall model had an adj. R2 of 0.68 ($F(4,19) = 13.07$, $p<0.001$). Although the total variance explained by the model declined at 12 months (adj. $R2 = 0.37$), it was still significant ($F(4,18)=4.21$, $p=0.014$), and the contributions from sleep time and efficiency stayed relatively constant.
**Conclusion:** Our findings are consistent with the previously reported association between self-reported sleep disturbance and fatigue in early RA: even after accounting for the stronger predictors, objectively measured sleep efficiency and sleep time help predict fatigue. These results highlight the importance of addressing sleep in managing fatigue among people with RA.

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**Exploring the Role of Apolipoprotein A1 in Assessing Cardiac Risk in Rheumatoid Arthritis**

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**Objectives:** Cardiovascular disease (CVD) is a major cause of morbidity and mortality in rheumatoid arthritis (RA), with risk indices like the Framingham Risk Score underestimating CVD risk in RA. This is largely attributed to "the lipid paradox" in which traditionally atherogenic lipid levels decrease with increased RA disease activity. We explore the relationship between levels of the HDL subcomponent apolipoprotein A1 (apoA1) and disease activity, lipid levels, and CVD in an early inflammatory arthritis (EIA) cohort.

**Methods:** 22 patients matched for age and DAS28ESR(3variable) from our single center EIA cohort had systematic annual assessment of disease activity, lipid levels, and medical comorbidities. Using a standardized ELISA kit, apoA1 titres were determined from four serial serum collections. Changes in these levels were compared with fluctuations in DAS28ESR(3variable) and lipid levels in both non-CVD and CVD patients (as determined by annual comorbidity assessment) using non-parametric tests.

**Results:** The mean age of the 22 patients was 62.7 years, with serial samples collected over a mean follow-up period of 34.4 months. Average DAS28ESR3var scores varied non-significantly between the CVD (3.06) and non-CVD (2.91) groups, and all subjects met ACR criteria for seropositive RA diagnosis. Five subjects developed CVD after a median (IQR) of 64 (42, 104) months. There were non-significant differences in initial ApoA1 titres (47.28 vs 107.86 ng/mL, p=0.23) and average annual change in ApoA1 (-8.57 vs -8.09, p=0.47) between the groups. ApoA1 levels showed poor correlation with HDL (-0.130 mmol/L, p=0.25), LDL (+0.10 mmol/L, p=0.37), Total Cholesterol (-0.02 mmol/L, p=0.84), and Triglycerides (+0.20 mmol/L, p=0.08) over time. They also didn't correlate with DAS28ESR3var (-0.17, p=0.88) or DAS28CRP3var (-0.11, p=0.32). Between the CVD and non-CVD groups there was non-significant differences in average Total Cholesterol (5.17 vs. 4.67, p=0.11), HDL (1.54 vs 1.77, p=0.59), and LDL (2.79 vs 2.47, p=0.17). Within the CVD group, there were significantly higher apoA1 levels after the CVD event than before (65.45 vs. 31.83, p<0.01)

**Conclusion:** ApoA1 levels do not associate with RA disease activity, CVD risk, or lipid levels in EIA. Although levels significantly rose in CVD patients after their cardiac event, this may be attributed to the effects of post-event statin therapy. Alternate measures of lipid metabolism may be more predictive of CVD in RA patients.

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**Real-World Analysis of Cost-Effectiveness among Patients with Rheumatoid Arthritis who Switched from a Tumor Necrosis Factor Inhibitor to Another Targeted Disease-Modifying Antirheumatic Drug**

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**Objectives:** Patients with rheumatoid arthritis (RA) who have an inadequate response to a tumor

necrosis factor inhibitor (TNFi) can switch to another targeted disease-modifying antirheumatic drug (DMARD), either by changing to another TNFi ("cycling") or by switching to a new mechanism of action ("new MOA switching") biologic. Given potential differences in outcomes conditional on choosing either of these strategies, this study examined the cost per effectively treated patient in the first year after TNFi cycling or new MOA switching.
**Methods:** This claims-based analysis included a cohort of patients with RA in the Truven Health Analytics MarketScan Commercial database who either cycled from a TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, or infliximab) to another TNFi or switched to a new MOA biologic (abatacept or tocilizumab) or targeted oral DMARD (tofacitinib) between January 2010 and December 2014. A validated claims-based algorithm was applied to estimate treatment effectiveness for the 12-month post-switch period based on six criteria: 1) adherence ≥80%; 2) no index biologic dose increase; 3) no addition of a synthetic DMARD (leflunomide, methotrexate, sulfasalazine, or hydroxychloroquine); 4) no switch to another targeted DMARD; 5) no new/increased oral glucocorticoid use/dose; and 6) intra-articular injections on <2 days. Costs were calculated from healthcare claims based on the paid amount for targeted DMARDs, adjusted for inflation according to price changes for the individual medications during the study period. Cost per effectively treated patient was defined as the average 12-month post-index cost for targeted DMARDs divided by the number of patients categorized by the algorithm as effectively treated. Bivariate analysis was conducted to compare treatment effectiveness and costs between TNFi cyclers and new MOA switchers.
**Results:** A total of 8,517 patients were included (5,997 TNFi cyclers and 2,520 new MOA switchers). TNFi cyclers and new MOA switchers had similar age (mean±SD, 49.7±9.6 vs 51.0±9.3 years), sex (female, 81.2% vs 83.9%), and Deyo-Charlson index score (mean±SD 1.4±0.8 vs 1.5±1.0). Costs and treatment effectiveness significantly favored new MOA switchers over TNFi cyclers ($33,008 vs $38,456, $p<0.001$; and 26.0% vs 23.3%, $p=0.008$, respectively), resulting in higher cost per effectively treated patient for TNFi cycling vs new MOA switching ($165,200 vs $126,991). Differences in adherence, subsequent treatment switches, and dose increases were major drivers of cost effectiveness.
**Conclusion:** After prior exposure to TNFi, switching to a new MOA rather than cycling to another TNFi was associated with significantly better treatment effectiveness and lower drug costs, resulting in lower cost per effectively treated patient.

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## Clinical and Radiographic Outcomes After 3 Years of Sarilumab in Patients with Rheumatoid Arthritis

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**Objectives:** Sarilumab is a human mAb blocking the IL-6Rα. Sarilumab + MTX demonstrated significant improvements in RA signs and symptoms, physical function, and inhibition of radiographic progression in the 1-year phase 3 MOBILITY study (NCT01061736). This analysis examined 3-year clinical and radiographic outcomes and safety in patients who completed MOBILITY and entered the open-label extension (OLE) study EXTEND (NCT01146652).
**Methods:** Patients in MOBILITY were initially randomized to placebo or sarilumab 150 or 200

mg q2w subcutaneously for up to 1 year. Early rescue with open-label sarilumab 200 mg q2w was allowed for insufficient response after week 16. After completion of MOBILITY, patients were eligible for enrollment in EXTEND, in which all patients received sarilumab 200 mg q2w + MTX. DAS28-CRP and CDAI assessed clinical efficacy. Radiographs from patients at baseline and subsequent second and third years were centrally read by 2 readers independently. Linear extrapolation was applied at year 3 for patients who had data at year 2 and from an unscheduled visit between years 2 and 3 but not at year 3. Statistical analysis at year 3 was performed on the basis of patients' original randomized treatment assignment, regardless of whether they were rescued during the double-blind period (MOBILITY).
**Results:** Of the 1197 randomized patients in MOBILITY, 901 participated in EXTEND. At year 3, after all patients had received open-label sarilumab for 2 years, percentages of patients achieving DAS28-CRP <2.6 or CDAI ≤2.8 were similar in patients originally treated with either dose of sarilumab or placebo, though the initial sarilumab 200 mg group exhibited the most favorable outcomes. Improvements were maintained within each group from year 2 to year 3. Three-year radiographic data were available for 755 patients; linear extrapolation was used in 29. At year 3, mTSS in the initial placebo and sarilumab 150 and 200 mg groups was only slightly increased since year 2. TEAEs occurred in 89.7% of patients over 3 years. The most common TEAEs (≥10%) were neutropenia (19.4%), increased alanine aminotransferase (13.0%), and upper respiratory tract infections (12.7%). Infections were the most frequently reported serious AE (4.2/100 patient-years).
**Conclusion:** Active treatment with sarilumab 200 mg q2w resulted in durable clinical response and stabilization of radiographic progression over 3 years irrespective of prior treatment, though the initial sarilumab 200 mg group showed the most favorable outcomes. Adverse events were consistent with the anticipated effects of IL-6 inhibition and the known safety profile of sarilumab.

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**Sarilumab Dose Reduction in an Open-label Extension Study in RA Patients**

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**Objectives:** Sarilumab is a human mAb blocking the IL-6Rα. In the phase 3 MOBILITY (NCT01061736) and TARGET (NCT01709578) studies, sarilumab (150 or 200 mg subcutaneously q2w) demonstrated efficacy in adults with active, moderate-to-severe RA. In both studies, infections, neutropenia, injection site reactions, and increased transaminases were among the most common treatment-emergent adverse events. Laboratory changes were consistent with IL-6 signaling blockade. This analysis examined laboratory changes and treatment continuation after sarilumab dose reduction observed through January 2016 in EXTEND (NCT01146652), an open-label, follow-up study evaluating long-term safety and efficacy of sarilumab with or without concomitant conventional synthetic DMARDs.
**Methods:** Adults with RA who previously participated in sarilumab studies were eligible. Patients who entered into EXTEND initially received sarilumab 150 mg weekly. After dose

selection for phase 3 studies, patients were switched to or initiated on sarilumab 200 mg q2w. Per protocol, investigators could reduce the sarilumab dose from 200 mg q2w to 150 mg q2w for absolute neutrophil count (ANC) ≥0.5 to 1.0 Giga/L, platelet count ≥50 to 100 Giga/L, or alanine aminotransferase (ALT) ≥3 to 5 × upper limit of normal. Dose reductions were also performed at the investigator's discretion. Efficacy data from EXTEND were analyzed before and 24 weeks after dose reduction for MOBILITY (n=173) and TARGET (n=60) patients.
**Results:** As of the January 2016 interim analysis (N=1864), dose reduction from sarilumab 200 mg q2w to 150 mg q2w had occurred in 17.2% of patients (n=321). The most common reasons for dose reduction were decreased ANC (10.7%; n=199) and increased ALT (4.1%; n=76) levels. The most common non-laboratory reason for dose reduction was infection (0.4%; n=8). At the time of analysis, 76.9% of patients (n=247) whose dose was reduced were continuing treatment, with a median treatment duration of 2.3 years after dose reduction. Improvements in ANC and ALT levels were observed over the 6 months after dose reduction. Sarilumab efficacy was maintained in MOBILITY and TARGET patients 24 weeks after dose reduction as assessed by ACR20 response rates (83.1% and 85.1%, respectively) and improvements in HAQ-DI scores (-0.68 and -0.82, respectively).
**Conclusion:** In patients whose sarilumab dose was reduced from 200 mg q2w to 150 mg q2w, there was an improvement in laboratory abnormalities and continuation of treatment for the majority of patients. Improvements in signs and symptoms of RA and physical function were maintained after dose reduction.

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**Efficacy of Sarilumab Plus csDMARDs in Rheumatoid Arthritis Patients who had an Inadequate Response to One or More than One Prior TNF Inhibitor**

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**Objectives:** In the phase 3 TARGET study (NCT01709578), sarilumab (150 or 200 mg subcutaneously [SC] q2w) plus conventional synthetic DMARDs (csDMARDs) demonstrated efficacy in adults with active, moderate-to-severe RA and inadequate response to TNFis. Consistent with IL-6 inhibition and the safety profile of SC sarilumab, infections, neutropenia, injection site reactions, increased lipids, and increased transaminases were among the most common treatment-emergent adverse events. This prespecified analysis examined whether the efficacy of sarilumab plus csDMARDs was affected by the number of prior TNFis.
**Methods:** Adults with active, moderate-to-severe RA with inadequate response or intolerance to ≥1 TNFi were randomized to receive placebo (n=181), sarilumab 150 mg q2w (n=181), or sarilumab 200 mg q2w (n=184) SC plus csDMARD(s) for 24 weeks. Efficacy by number of prior TNFis (1 vs >1) was analyzed for the coprimary endpoints of ACR20 response at week 24 and mean change from baseline in HAQ-DI at week 12. Additional post hoc analyses evaluated the secondary endpoints of ACR50/70. Treatment-by-subgroup interactions were analyzed using a logistic regression model for ACR20 at week 24 and a mixed-effect model for repeated measures for HAQ-DI at week 12; treatment-by-subgroup interaction with $P<0.05$ was considered significant.

**Results:** A majority of patients (76.8%) reported prior use of only 1 TNFi; 23.2% of patients used >1 TNFi. Most patients discontinued TNFi treatment because of inadequate response (92.3%). ACR20 responses were numerically greater in patients receiving either dose of sarilumab in both the 1 and the >1 prior TNFi groups at week 24 relative to placebo patients. Responses in placebo and sarilumab groups were numerically higher in the group that failed 1 TNFi. Similar results were observed with ACR50/70 responses. The mean change from baseline in HAQ-DI at week 12 was greater in sarilumab patients than in placebo patients in both prior TNFi exposure groups. Interaction test analyses indicated no significant treatment-by-subgroup effect in the proportion of patients with 1 or >1 prior TNFi who achieved ACR20 at week 24 (P=0.1215) or in mean change from baseline in HAQ-DI at week 12 (P=0.1767).
**Conclusion:** Efficacy of sarilumab was observed in patients with inadequate response to TNFis, irrespective of the number of prior TNFi therapies. In harder-to-treat patients (ie, patients with prior exposure to >1 TNFi), sarilumab 200 mg q2w was associated with a greater numerical trend in ACR20/50 response when compared with sarilumab 150 mg q2w.

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**Onset of Action of Sarilumab in Patients with Rheumatoid Arthritis in 2 Phase 3 Studies**

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**Objectives:** Sarilumab plus MTX has demonstrated efficacy in patients with RA and inadequate response to MTX (MOBILITY; NCT01061736), while sarilumab plus conventional synthetic DMARDs (csDMARDs) demonstrated efficacy in patients with RA and inadequate response or intolerance to tumor necrosis factor (TNF) inhibitors (TARGET; NCT01709578). Among the most common treatment-emergent adverse events in both studies were infections, neutropenia, injection site reactions, and increased transaminases. This analysis of MOBILITY and TARGET study data assessed the time to onset of clinical efficacy of sarilumab and the durability of response over 24 weeks.
**Methods:** Adults with active, moderate-to-severe RA were randomized to 1 of 3 groups receiving subcutaneous sarilumab 150 or 200 mg or placebo q2w plus background MTX (MOBILITY) or csDMARDs (TARGET). Clinical efficacy was evaluated in these patients at weeks 2, 4, 8, 12, and 24 in a post hoc analysis. ACR20/50/70 response rates were analyzed using the 2-sided Cochran-Mantel-Haenszel test stratified by prior biologic use and region (MOBILITY) or by region and number of prior TNF inhibitors (TARGET); nonresponder imputation was applied for patients who started rescue medication or discontinued the study. Changes from baseline in HAQ-DI, DAS28-CRP, and CDAI were analyzed with a mixed model for repeated measures; no data were imputed.
**Results:** Baseline demographic and disease characteristics were similar between treatment groups in both studies. Improvements in ACR20 responses were observed as early as week 2 in both studies, with nominal P<0.05 observed at week 8 for all sarilumab-treated groups in both studies. Similar trends were observed for ACR50 and ACR70 responses. Greater reductions in DAS28-CRP mean change from baseline vs placebo were observed with both doses of sarilumab by week 2 in both studies (nominal P<0.05). Similarly, numerical improvements in HAQ-DI and

CDAI were observed with both doses of sarilumab vs placebo by week 4 in both studies (nominal P<0.05). Improvements in all efficacy parameters were sustained through the end of each study (ie, week 52 for MOBILITY and week 24 for TARGET). The most common treatment-emergent adverse events at week 12 were infection and neutropenia, consistent with the safety profile previously reported for the entire study periods.
**Conclusion:** Sarilumab rapidly improved signs and symptoms of RA in patients with inadequate response to MTX (MOBILITY) or TNF inhibitors (TARGET), and improvements were sustained through the end of treatment.

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**Understanding the Impact of Early Rheumatoid Arthritis on the Feet: Pain, Activity Limitations and General Health**

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**Objectives:** This cross-sectional study assessed the association between clinical findings in the metatarsalphalangeal (MTP) joints of patients with early rheumatoid arthritis (RA) and i) the Leeds Foot Impact Score (LFIS) and ii) the pain and fatigue components of the Health Assessment Questionnaire (HAQ) as well as the global and total HAQ scores.
**Methods:** Individuals 18-85 years old with early RA (ACR criteria) who were treatment naive were recruited . The metatarsophalangeal (MTP) joints 2-5 of both feet were examined by an experienced rheumatologist who assessed and recorded tenderness and swelling in each joint. Participants completed the HAQ and the LFIS questionnaires. The HAQ assesses pain, fatigue and global health while the LFIS assesses two domains associated with RA: impairments/footwear (21 items related to foot pain and joint stiffness and footwear related impairments), and activities/participation (30 items related to activity limitation and participation restriction). Higher scores for HAQ domains indicate higher levels of pain and fatigue while higher LFIS scores are associated with more impairment and limitations. Linear regression analyses assessed associations between number of tender/swollen joints (maximum 8) and each of the LFIS, HAQ pain (0-10), HAQ fatigue (0-10), HAQ global (0-10), and total HAQ (0-3). Regression analyses also examined the association between the LFIS score and each HAQ domain.
**Results:** Included in the study were 40 participants (n=32 women), mean (standard deviation (sd)) age = 52.0 (10.4) yrs. Eighteen participants had ≥1 swollen joint and 31 participants had ≥1 tender joint. The mean numbers (sd) of swollen and tender joints were 1.2 (1.7) and 3.9 (2.9), respectively. The mean (sd) LFIS score was 23.4 (13.8). Means (sd) for HAQ domains were: pain 5.5 (2.8); fatigue 5.5 (3.2); global 5.5 (2.9) and total 1.1 (0.7). Analyses showed significant associations between number of tender joints, but not swollen joints, and LFIS (β=0.452, p=0.003), pain (β=0.342, p=0.031) and fatigue (β=0.329, p=0.038). Significant associations were found between LFIS scores and each of pain (β=0.704, p<0.001), fatigue (β=0.547, p<0.001), HAQ global (β=0.622, p<0.001), and total HAQ (β=0.628, p<0.001).
**Conclusion:** These results suggest that individuals with more tender MTP joints have significantly greater impairments and activity limitations than those with fewer tender joints. Interestingly, the number of swollen joints does not seem to be associated with such impairments and limitations. The significant associations between the LFIS and HAQ domains emphasize the overall impact of foot impairments on quality of life in patients with RA.

**100**

**Assessing the Correlation between Early Erosions in Rheumatoid Arthritis (EERA) Software and the EULAR-OMERACT Rheumatoid Arthritis Scoring System (RAMRIS) for Quantifying Erosions in the MTP Joints of Patients with Early RA**

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**Objectives:** Magnetic resonance imaging (MRI) is a sensitive and specific method for detecting bone erosions in patients with early rheumatoid arthritis (RA). Early detection, primarily in the metacarpophalangeal (MCP) joints and metatarsophalangeal (MTP) joints, is crucial for treatment and successful patient outcomes. The EULAR-OMERACT RA scoring system (RAMRIS) is used to semi-quantitatively assess bone erosions from MRI scans. Early Erosions in Rheumatoid Arthritis (EERA) software can be applied to MRI scans to quantify bone erosions and does not require a trained radiologist. We assessed the correlation between EERA and RAMRIS scores for erosions in the MTP joints of patients with early RA.

**Methods:** Patients with early RA (DMARD naïve) were recruited. Each patient underwent an MRI scan (1.0 Tesla peripheral MRI) of MTPs 2-5 of the most symptomatic foot. MRI scans were scored for erosions using a semi-quantitative scale (0-10 for each erosion) by a blinded, musculoskeletal trained radiologist. Two trained non-radiologist readers (MJ and SS), applied EERA software to MRI scans to semi-automatically quantify erosion volume (mm3) . Spearman's rho was calculated to compare EERA and RAMRIS scores for erosions in the MTP joints .

**Results:** Analyses included MRI scans of the clinically more symptomatic foot [(right:left): 24:9] of 33 participants [female: 27, mean (SD) age: 51.0(10.6) years., EERA detected erosions in 84.8% of participants. RAMRIS detected erosions in 94.6%, 29.7%, and 10.8% with cut off values of 1, 2 and 3, respectively] . The mean erosion volume per participant was 70.97 mm3, and mean baseline RAMRIS erosion score per participant was 5.1 (4.6). Spearman's rho coefficients of 0.293 ($p<0.01$) and 0.215 ($p<0.01$) were calculated for each reader and showed weak correlation between RAMRIS erosion scores and EERA erosion volumes.

**Conclusion:** MTP joint erosion volumes measured by non-radiologists using EERA software exhibited weak correlation with RAMRIS erosion scores assessed by an experienced radiologist. While both scoring systems identified a high number of erosions in this population, there was only a weak correlation between RAMRIS and EERA for MTP erosion measurement. This may suggest that the EERA software does not accurately assess the extent of erosive damage in the MTP joints of patients with early RA. Future studies should aim to enhance the EERA software by developing imaging algorithms to reliably assess MTP erosions, as it does in the MCP joints.

**101**

**Assessing the Reliability of Early Erosions in Rheumatoid Arthritis (EERA) Software for Quantifying Erosions in the Metatarsophalangeal (MTP) Joints of Patients with Early Rheumatoid Arthritis (RA)**

Sydney Scheffler (McMaster University, Hamilton); Matthew Jessome (McMaster University, Hamilton); George Ioannidis (McMaster University, St. Joseph`s Healthcare Hamilton, Hamilton); Jonathan Adachi (McMaster University, St. Joseph`s Healthcare Hamilton,

Hamilton); Karen Beattie (McMaster University, Hamilton); Maggie Larche (McMaster University, St Joseph's Healthcare Hamilton, Hamilton)
**Objectives:** The Early Erosions in Rheumatoid Arthritis (EERA) software was developed to accurately and efficiently quantify erosive damage in the metacarpophalangeal (MCP) joints of patients with early rheumatoid arthritis (RA). The MCPs and metatarsophalangeal (MTP) joints are commonly affected in early RA and are monitored for disease progression. The ability of EERA software to assess erosions in the hand has shown to be valid and reliable, however the software has not been applied to Magnetic Resonance Imaging (MRI) scans of the feet. The objectives of this study were to assess the inter- and intra-rater reliability of EERA software for quantifying erosions in the MTP joints and to compare the reliability of EERA software for quantifying erosions in the MCP joints with the MTP joints of patients with early RA.
**Methods:** MRI scans of the most clinically affected foot were acquired from patients diagnosed with early RA using a 1.0 Tesla peripheral MRI scanner. Two trained, independent readers (MJ and SS) used the software to evaluate and sum the volumes (in mm3) of erosions in the 1st to 5th MTP joints. One reader (SS) measured erosion volumes a second time, one week after the first analysis, blinded to the initial results. Inter- and intra-rater reliability were assessed using Bland-Altman plots and intra-class correlation coefficients (ICC) with 95% CI.
**Results:** The study included 38 participants female: 30, mean age (sd): 51.6 (10.1 ) years]. EERA reliability was poor between the two readers, with an inter-rater reliability ICC of 0.093 (95% CI -0.120 to 0.338) and 0.299 (95% CI -0.013 to 0.562) at the first and second time points, respectively. Intra-rater reliability was fair, with an ICC of 0.434 (95% CI 0.132 to 0.662). A preceding study found excellent reliability of EERA software for quantifying erosions in the MCP joints with an inter-rater reliability ICC of 0.945 (95% CI 0.887 to 0.959) and intra-rater reliability ICCs of 0.993 (95% CI 0.982 to 0.997), 0.979 (95% CI 0.949 to 0.992), and 0.933 (95% CI 0.834 to 0.973).
**Conclusion:** EERA is significantly more reliable when measuring erosions in the MCP joints than the MTP joints of patients with early RA. The poor reliability of EERA software in the foot joints suggests the imaging algorithms are highly sensitive to the MCP joint compared to the MTP joints because of the unique morphologies.

**102**

## Do Psoriasis Patients Who Participate in Clinical Research Differ from Those Who Do Not?

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**Objectives:** Psoriasis is a chronic skin condition that affects 2-3% of the population. People with psoriasis have an increased risk of developing psoriatic arthritis. To understand this disease, the Toronto Western Hospital (TWH) has established 2 cohorts of patients: patients with psoriasis without psoriatic arthritis (PsC cohort) and patients with psoriatic arthritis (PsA cohort). Patients registered in these cohorts participate in clinical research studies. TWH dermatologists also treat patients with psoriasis who are not in clinical research (Clinic cohort). The aim was to determine whether the clinical features and outcomes of psoriasis patients who participate in clinical research are the same as those who do not. If the two groups prove to be similar, then the knowledge from clinical research can be generalized to patients seen in clinical practice.
**Methods:** The PsC and PsA cohorts are defined as patients enrolled in clinical research whose

follow-up assessments are based on a standardized protocol. The Clinic cohort patients are not enrolled in research. The information on the patient's disease history (age of onset, extent of psoriasis), demographic and social history (gender, employment, smoking), medication (past and current), and comorbidities (cardiovascular, respiratory, musculoskeletal) was collected from their charts. The Clinic cohort information was compared to both the PsC and PsA cohorts using one-way ANOVAs and logistic regression to test association of variables.
**Results:** Each cohort included 200 patients. Analysis of the demographic and social history variables showed an overall similarity between the Clinic cohort and the PsA and PsC cohorts. Likewise, the comorbidities of the patients in the Clinic and research cohorts were similar. Therapies used by patients in the PsA and the Clinic cohorts were more similar than the treatments used by PsC and the Clinic cohorts. Interestingly, the Clinic cohort was treated more with topical treatments than the PsC cohort; whereas, the PsC cohort was found to be treated more with NSAIDs than the Clinic cohort. This is likely due to the fact that the patients in the PsC cohort were treated by dermatologists outside of TWH.
**Conclusion:** The demographics, social history and comorbidities were similar between the Clinic cohort and the research cohorts. Thus, it is possible to generalize the results of the research studies using the Psoriatic Arthritis and Psoriasis Cohorts to patients who are not involved in clinical research. As might be expected for a dermatology clinic, more clinic patients were treated with topical therapy than in the research cohorts.

**103**

**Active Arthritis is Associated with Elevated 14-3-3 eta Titres in Systemic Lupus Erythematosus**

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**Objectives:** Arthritis is common in systemic lupus erythematosus (SLE) but unlike in rheumatoid arthritis (RA), is generally non-erosive. 14-3-3 eta, a chaperone protein that activates pro-inflammatory pathways is emerging as a novel biomarker for erosive RA and is present in up to 60% of RA patient sera. We investigated clinical associations of serum 14-3-3 eta in SLE, focusing on arthritis.
**Methods:** Sociodemographics, ACR classification criteria, and SLEDAI scores were recorded prospectively in consenting patients with SLE. Arthritis as assessed by the SLEDAI was categorized as active (n=78), inactive (n=138) and never present (n=45). Serum levels of 14-3-3 eta were measured by ELISA and considered positive if the titre was above 0.19 ng/ml (as per the manufacturer). We report descriptive statistics and logistic regression models testing the independent association of 14-3-3eta with arthritis state.
**Results:** Of the 265 SLE patients studied, the majority were female (92%) and Caucasian (67%) with a mean (SD) age of 51.7(14) years, a median (interquartile range IQR) disease duration of 8 (4,10) years, a median (IQR) number of ACR criteria 6 (5,7), and a median (IQR) SLEDAI score of 4(2,7) at the time of sera collection. Two hundred and sixteen (81%) had active or inactive arthritis and 65 (22%) were positive for 14-3-3 eta. The median (IQR) 14-3-3 eta titre of positive samples was 0.6 ng/ml (0.34, 1.82). No differences in the percentage of 14-3-3 eta positivity were seen between any two of the three arthritis groups (active 22 /78 (28%), inactive 27/138 (20 %), and never present 10/48 (20%), nor were there differences in 14-3-3 eta positivity for other

individual SLEDAI criteria. However, patients with active arthritis had the highest 14-3-3eta titers (top quartile of the population median) (active arthritis versus inactive arthritis p=0.03; active arthritis versus inactive/never present p=0.04). In multivariable regression models, 14-3-3eta titre in the top quartile of the population median was predictive of active (versus inactive/never) arthritis (OR 3.6, 95% confidence interval 1.33 to 9.98), independent of other variables, including ethnicity (Caucasian versus non-Caucasian) and SLEDAI score. There was no correlation of 14-3-3 eta titer with number of ACR criteria nor SLEDAI score.
**Conclusion:** SLE patients are less likely to be positive for 14-3-3eta than RA patients. In SLE, 14-3-3eta titers are predictive of active arthritis, independent of other markers of disease activity. Our next goal is to explore the association of 14-3-3eta with erosive arthritis in SLE.

**104**

**Management of Rheumatoid Arthritis in a Public Referral Hospital of Ethiopia**

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**Objectives:** Early diagnosis and institution of DMARDs are fundamental to prevent joint damage in rheumatoid arthritis (RA). Most treatment guidelines recommend Methotrexate (MTX), alone or in combination with other DMARDs. Treatment guidelines are often difficult to apply in resource-limited countries due to competing health priorities and lack of rheumatology capacity. As an initial step in addressing rheumatology care needs in Ethiopia, we reviewed current RA treatment practices in the adult rheumatology clinic at Black Lion Hospital (BLH) where care is provided by Internists and Internal Medicine residents.
**Methods:** In September 2016, after ethics approval, medical charts of a convenient sample of 51 patients diagnosed with RA were reviewed. Data on patient demographics, disease phenotype, medication use and side effects was extracted from the charts. We report descriptive statistics.
**Results:** Six patients with presumptive RA deemed to have a non-RA diagnosis by the rheumatologists were excluded. The remaining 45 patients with RA had a mean (SD) age at first visit of 36 (13) years and were followed for a median Interquartile range (IQR) 2 (0, 4.75) years. The majority were female (87%), resided in Addis Ababa (60%) and 55% received government subsidized health care. Most patients had polyarthritis (85%) and 27/38 (84%) were Rheumatoid Factor (RF) positive. Radiographic findings of RA were seen in 77% of the 26 patients with available X-ray reports. Most patients (94%) were on prednisolone with a median dose at last visit of 8.75 (5,10) mg/day. The median (IQR) for the maximal daily dose of prednisolone used or prescribed was 15 mg/day (10,30). Steroid side effects were recorded in 42% of patients. Chloroquine (taken by 56%) and MTX (taken by 78%) were the only DMARDS used. Only 19 patients were on combination DMARDs. The median (IQR) for the maximal MTX dose used was 7.5 mg/week (IQR 7.5,10), the median dose at last visit was 6.25 (IQR 0,10). MTX therapy was often interrupted due to lack of access (30%) and /or cost (23%).
**Conclusion:** Compared to Canadian and European cohorts, RA patients followed in the rheumatology clinic at the largest referral hospital in Ethiopia had a greater proportion of patients using persistent corticosteroids with high rates of steroid induced side-effects and a limited use of DMARDs (i.e. MTX). Initiatives to increase rheumatology capacity, provide rheumatology training to general practitioners, internists, and development of RA management

recommendations relevant to resource limited areas may expand practices that should improve outcomes for persons with RA.

**105**

**Barriers to the Use of MTX in Ethiopia: Survey of Pharmacy Providers**

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**Objectives:** Methotrexate (MTX) is the mainstay of Disease Modifying Anti-Rheumatic drugs (DMARDs) used to treat rheumatoid arthritis (RA). Its use has been shown to slow radiographic progression and improve clinical outcomes in at least 50% of RA patients. Multiple barriers exist to the use of MTX in African countries with a low Human Development Index such as Ethiopia. This survey of Ethiopian Pharmacy Providers (EPP) was conducted to inform on the availability and the patterns of use of MTX.

**Methods:** In September 2016, Pharmacy Providers attending the Essentials of Pharmacy Practice course, provided by the Ecumenical Pharmaceutical Network and the Ethiopian Catholic Secretariat in Addis Ababa, completed a survey on their experience with dispensing MTX for the treatment of rheumatic conditions.

**Results:** All of the twenty-three EPP that attended the course completed the survey. Most (78%) of the EPP were pharmacy technicians whereas 22% were pharmacists from 6 of the 11 Ethiopian regions. Seven (32%) of the respondents work in a hospital based pharmacy, 12 (55%) in a health centre pharmacy and 3 (14%) in other areas (i.e. clinic pharmacy). The number of years of practice (median (range) of the pharmacy technicians and pharmacists was 4 (1-8) and 10 (6-15) respectively. MTX was available in only 3/23 pharmacies (13%; 2 were hospital pharmacies) and was only available as oral tablets. In addition, six EPP reported that MTX was available in the hospital pharmacy of their region. Only 2/23 (9%) pharmacists have dispensed MTX and in both cases it was not for use in patients with rheumatic conditions. Only 3/23 (13%) of the EPP reported feeling comfortable educating patients on how to take methotrexate. Counselling was provided by 1/7 EPP who indicated that they were not comfortable with educating patients on how to take MTX vs 2/3 of those who felt comfortable with MTX education (p=0.2). No EPP reported having provided counseling on contraception or MTX-alcohol interactions.

**Conclusion:** There is an urgent need to bridge the gap of RA treatment between developed and emerging countries. This survey identified two key aspects limiting the use of MTX in Ethiopia: a) availability of the drug in pharmacies, and b) confidence of designated pharmacists in supplying and counseling patients for methotrexate. Improved MTX access and recommendations for counselling are needed to increase the confidence of pharmacists when dispensing MTX.

**106**

**Successful Treatment of Eosinophilic Fasciitis with a Tumor Necrosis Factor Inhibitor**

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A 52 year old woman presented with one month of upper and lower extremity edema, arthralgias in her hands and feet, and paraesthesias. Past medical history was notable for uterine fibroids,

thyroidectomy due to Hashimoto's thyroiditis on levothyroxine, and a positive TB positive skin test in the context of previous BCG immunization.
A complete blood count revealed mild eosinophilia (0.84 x 109/L-1.7 x 109/L). Blood and stool cultures, viral serologies, HIV testing, serum protein electrophoresis, and peripheral blood film were normal. ANA, RF, ENA, dsDNA, and ANCA were negative. Complement and ACE levels were normal. X-rays of her chest, hands, and feet and echocardiogram were unremarkable. MRI demonstrated bilateral wrist tenosynovitis.A bone marrow biopsy showed normal trilineage hematopoeisis but an increase in eosinophilic and megakaryocytic precursors with normal flow cytometry and cytogenetic testing. Deep fascial biopsy demonstrated edema with a predominantly histiocytic infiltrate. Periodic Acid-Schiff and Ziehl-Neelson staining were negative. Taken together these findings were suggestive of granulomatous eosinophilic fasciitis.
Prednisone 1 mg/kg resulted in a rapid reduction of the extremity edema and complete resolution of her peripheral eosinophilia. Attempts to taper below 10 mg/day resulted in recurrent symptoms, which did not respond to the addition of either Methotrexate and Azathioprine.
Golimumab 50 mg SC monthly was commenced, given the pathological features (granulomatous features on histology. She experienced a rapid reduction in residual symptoms (stiffness and restricted flexion). Despite tapering off corticosteroids completely over the next six months, this improvement has been maintained for over two years.

**107**

**Purpuric Dermatitis Herpetiformis in a Patient with SLE**

Raphael Rush (University of Toronto, Toronto); Scott Walsh (Sunnybrook Health Sciences Centre - Division of Dermatology, Toronto)

A 51-year-old woman presented with a 1 week history of painful finger lesions 7 days after having a dental procedure, for which she received preprocedure amoxicillin. She had recently had a large meal including gluten. Past medical history included serodiscordant SLE manifested by malar rash and arthralgias, cold urticaria, DM2, and dermatitis herpetiformis. Usual medications included candestaran, alendronate, amitryptiline, domperidone, hydroxychloroquine, prednisone, omeprazole, sulfasalazine, and insulin glargine. She was started on prednisone and diphenhydramine. Her symptoms did not improve.
On physical exam, there were violaceous papules on the lateral aspects of both index fingers as well as smaller lesions scattered over her fingertips. These lesions were tender when palpated. The remainder of the physical exam was normal.
CBC, electrolytes, creatinine, and urinalysis were all normal. dsDNA was elevated at 32. ENA panel was otherwise negative. An echocardiogram was unremarkable.
On biopsy, the superficial dermis contains a mild, mixed, perivascular and interstitial, inflammatory infiltrate which is primarily lymphohistiocytic but with numerous admixed eosinophils and occasional neutrophils forming small abscesses in the papillary dermis. There is no vasculitis, but extravasation of red cells is noted. The mid to deep dermis is unremarkable. Hale's colloidal iron stain reveals no increase in dermal mucin, consistent with a diagnosis of purpuric variant of dermatitis herpetiformis.
She was started on dapsone and a gluten-free diet. Her symptoms resolved within 48 hours.

**108**

**Immunoglobulins Level and Risk of Infection in Systemic Lupus Erythematosus**

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**Objectives:** Infection is a major cause of mortality of SLE. We hypothesized that some patients with SLE have acquired immunoglobulin deficiency, which may put them at higher risk for infection. We aimed to examine the association and prediction of immunoglobulin levels and the risk for severe infections in lupus.
**Methods:** SLE patients are followed prospectively at 2-6 month intervals according to a standard protocol including recording of, infections and damage accrual. Severe infection was defined as either requiring parenteral antibiotics or having 3 infections within 2 years. Controls were patients followed for the same period who did not have infections. Immunoglobulin levels were recorded as low, normal, or high according to laboratory normal values. Persistently low immunoglobulins were defined as two or more consecutive low values. Logistic regression analysis was performed to determine first the factors associated with infection and then factors predisposing to severe infection.
**Results:** We identified 250 patients with severe infections and 381 patients without infection. Patients with severe infections had lower IgG and IgA levels, and were treated with higher doses of glucocorticosteroids (GCS). Logistic regression analysis revealed that age at SLE diagnosis (OR 1.019 95% CI 1.004,1035, P=0.014), low IgM levels (OR 2.175 95% CI 1.114, 4.245, p = 0.0228) and GCS dose (OR 1.079 95% CI 1.058, 1.101, p = <0.001) were associated with infection, adjusted for other demographic and clinical variables. We then examined 148 patients with persistently low immunoglobulins and no infection at first measurement and compared them to 430 controls for infection outcome. The low immunoglobulin group had more severe infections, higher SDI score, higher GCS and immunosuppressive use. Logistic regress ion analysis revealed low IgG levels (OR 3.546 95% CI 1.852, 6.787, p = 0.0001), low IgM levels (OR 2.209 95% CI 1.274, 3.83, p = 0.0048), female gender (OR 2.285 95% CI 1.019, 5.125, p = 0.045), SDI (OR 1.188 95% CI 1.029, 1.373 , p = 0.019) SLE duration (OR 1.056 95% CI 1.03, 1.084, p = <0.0001) to be predictors for severe infection and antimalarial treatment to be protective (OR 0.566 95% CI 0.355, 0.902, p = 0.0166) after adjustment for other demographic and clinical variables.
**Conclusion:** Our study shows consistent association between low immunoglobulin level and clinically significant infection in lupus patients. Furthermore, low IgG and IgM levels increase the risk of severe infection, while antimalarial treatment is protective. Thus immunoglobulin assessment should be performed routinely in patients with SLE.

**109**

**"Going Down a Different Path": A Qualitative Exploration of Costs Incurred by Patients with Systemic Lupus Erythematosus (SLE)**

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**Objectives:** While previous studies have investigated the economic costs of Systemic Lupus Erythematosus (SLE) among affected individuals in Canada, research has primarily been quantitative and focused only on direct costs. Given that SLE primarily impacts patients during their prime working years and symptoms can be complex, there is a need for contextualized understanding of the costs of this chronic disease. This research employs a qualitative approach to explore and contextualize the direct as well as indirect costs incurred by Canadian patients with SLE.
**Methods:** With input from the Lupus Society of Alberta, our interview guide focused on direct

and indirect costs as well as perceptions, experiences and coping mechanisms. Semi structured in-depth interviews were conducted with 8 key informants (3 expert physicians, 5 representatives from patient advocacy groups) and 28 adult SLE patients (26 women). Interviews were audio recorded with permission and transcribed verbatim. Transcripts were coded both inductively and deductively for recurring themes.
**Results:** Findings reveal that the early manifestations of the disease significantly rerouted the course of participants' economic livelihoods, often to part-time precarious employment and in some cases forced them to leave the workforce all together. These economic and health impacts were further compounded by a lack of health insurance benefits and poor Provincial health coverage for complementary care (e.g. massage therapy), leading to additional out-of-pocket expenses. Openness about diagnosis within the workplace varied greatly amongst participants, though all noted the challenges created by a general lack of information and public awareness about SLE. The use of workplace accommodations was met with mixed success and greatly depended on the work setting. While many participants reflected that there was little their employers could have done to further accommodate their needs, structural changes within Canadian policy could improve access to resources for promoting healthy lifestyles and disease management for those with SLE which, in turn, would serve to enhance economic security.
**Conclusion:** Through the use of a qualitative methodology, this research adds deeper understanding on the economic burden of chronic diseases by revealing the widespread and multifaceted costs associated with SLE. Elucidating the direct as well as the indirect costs incurred by patients provides a greater understanding of the long-term consequences of SLE and its implications for Canadian social policy. Supported by a CIORA grant.

**110**

**Predictors of Good Long-Term Renal Outcomes**

William Fung (University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Zahi Touma (University of Toronto, Toronto)

**Objectives:** Lupus nephritis (LN) manifests with proteinuria and/or active urine sediment. Renal composite indices include proteinuria, urinary active sediment (RBCs, casts) and serum creatinine. Complete proteinuria recovery is defined as <0.5 g/d but it is currently unclear which proteinuria cutoff best predicts good clinical outcomes. To determine: 1-the predictive ability of proteinuria, urinary sediment (uRBCs) and serum creatinine (Cr) at 1 year to predict good long-term outcomes, and 2- the best proteinuria cut-off at 1 year to predict good long-term outcomes.
**Methods:** Retrospective analysis on 1849 patients. Patients with lupus nephritis (LN) (24-hr proteinuria [24H-P] >0.5 g/d) with at least 7 years' follow-up were identified and baseline was defined as the onset of LN. Good renal outcome was defined as Cr <100 mmol/L and renal transplant/dialysis-free at 7 years. ROC curves examined the predictive power of Cr, 24H-P, and uRBCs at 1 year post-LN diagnosis with respect to good renal outcome. AUC were analyzed for: a) 24H-P at year 1, b) absolute change in 24H-P between year 1 and 7, and c) percent change in 24H-P between year 1 and 7. The proteinuria cutoff was identified by optimizing sensitivity/specificity.
**Results:** 101 LN patients were analyzed with baseline 24H-P of 2.36 ± 2.31 g/d. 24H-P of 0.6 g/d at 1 year after LN diagnosis best predicted good long-term renal outcome, with sensitivity 62%/specificity 70%. AUC analysis confirmed that 24H-P at 1 year, but not absolute/percent change, is a predictor of good long-term renal outcomes. uRBCs did not provide any predictive benefit while Cr at 1 year predicted long-term renal outcome with an AUC of 0.82. Additional sensitivity analyses were conducted for patients with baseline 24H-P of >2.5 g/d, >2.0 g/d, and

>1.5 g/d. This analysis was repeated for uRBCs and Cr.
**Conclusion:** Proteinuria of 0.6 g/d at 1 year and Cr at 1 year post-LN diagnosis best predicted good long-term renal outcome. Serum creatinine at 1 year was also a strong predictor of long-term renal outcome, whereas urinary RBCs did not offer any prognostic benefit.

**111**

**Accrual of Disease Comorbidities Over 8 Years in a Multicentre Inception SLE Cohort**

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**Objectives:** The annual accrual of comorbidities in patients with SLE is not well described. We report the annual occurrence of these features in an inception cohort of patients with SLE.
**Methods:** An international research network comprised of 33 centres from 11 countries has followed an inception cohort of SLE patients yearly according to a standardized protocol between 2000 and 2016. Of these, 717 patients followed for a minimum of 8 years constitute the study population. Comorbidities including atherosclerotic vascular events (AVEs), osteoporosis, osteonecrosis and diabetes are assessed using the SLICC/ACR Damage Index (SLICC/DI). AVEs are described and attributed on a specialized form. Diagnosis of an event is confirmed using standard clinical criteria, relevant laboratory data and imaging where appropriate. Attribution to atherosclerosis is made on the basis of lupus disease being inactive at the time of the event, and/or the presence of typical atherosclerosis (AS) changes on imaging or pathology and/or evidence of AS elsewhere. Diagnosis of osteoporosis is based on fracture or vertebral collapse demonstrated on X-ray and osteonecrosis was based abnormal imaging. Diabetes diagnosis is based on therapy, regardless of treatment type. Descriptive statistics were used.
**Results:** Of the 717 patients followed for at least 8 years, 90.2% were female, 47.3% were Caucasian, 13.8% were Black, 19.4% were Asian, 16.3% Hispanic and 3.2% other. Their mean age at enrolment was 34.2±13.1 years and SLEDAI-2K at enrolment was 4.17±4.49. The duration from diagnosis to enrolment was 5.9±4.4 months. Mean SDI gradually increases from 0.3±0.7 to 1.1±1.5 over 8 years. The accumulation of AVEs [4 (0.5%) to 25 (3.5%)]; osteoporosis [3 (0.4%) to 19 (2.7%)]; osteonecrosis [3 (0.4%) to 31 (4.3%)] and diabetes [13 (1.8%) to 25 (3.5%)] all increase progressively over an 8-year period. Caucasians accumulate AVEs (0.59% to 5.60%) and osteoporosis (0.00% to 4.14%) more frequently than all “other” ethnicities (AVEs: 0.53% to 1.59%; osteoporosis: 0.79% to 1.32%). In contrast, all “other” ethnicities accumulate osteonecrosis (0.26% to 5.82%) more frequently than Caucasians (0.59% to 2.66%). Both Caucasians (1.77% to 3.25%) and all "other" ethnicities (1.85% to 3.70%) accumulate diabetes at the same frequency over an 8 year period.
**Conclusion:** As expected disease damage and comorbidities in newly diagnosed patients increase over their first 8 years. Different ethnicities accumulate comorbidities at different rates.

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**Hospitalizations in Patients with Systemic Lupus Erythematosus**

Kaien Gu (University of Manitoba, Winnipeg); Dafna Gladman (University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto)

**Objectives:** Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease that predominantly affects women in their childbearing years, with a female-to-male ratio of approximately 9:1. Hospitalization occurs in approximately 10% of SLE patients each year and

accounts for the majority of the direct cost of SLE patient care. We aimed to determine the frequency of admission of SLE patients, describe causes and outcomes of hospital admission(s).
**Methods:** We reviewed all hospitalizations at University Health Network between 2011 and 2013 and isolated patients admitted with an ICD-10 code of M32 (SLE). A retrospective chart review of these patients categorized them based on SLE care provider (Lupus Clinic, non-Lupus Clinic, or non-rheumatologist) and cause of admission (active SLE, SLE damage, other SLE comorbidities, infection, or incidental). We recorded healthcare outcomes, including frequency of emergency room (ER) visits and duration of hospitalization. Descriptive statistics for patients' demographics, damage index, treatment, ER admissions and hospitalizations were summarized by mean ± std or N(%); Poisson and linear regressions were performed on the data to determine factors associated with frequency and duration of hospitalizations.
**Results:** We identified 247 unique SLE patients who were hospitalized a total of 491 times. The majority (87.4%) were female with an average age of 43.9 ± 17.9 years and disease duration of 13.7 ± 12.3 years. SLE admissions accounted for 0.6% of global UHN admissions. Incidental causes accounted for the largest proportion of admissions (35.6%). 21.4% and 22.4% of admissions were due to active SLE and infection, respectively. The SLE patients averaged 1.6 ± 1.1 hospitalizations with a mean duration of stay of 8.5 ± 8.9 days per hospitalization. 13% of admissions resulted in ICU admission, and 2.8% of hospitalizations resulted in death. Patient employment (Relative Risk 0.68 (95%CI: 0.53-0.87, p=0.002) was associated with fewer number of hospitalizations. Antimalarial use was associated with fewer hospitalizations as well as shorter length of stay. The presence of damage (p=0.024) correlated with increased hospitalizations. Higher educational level (p=0.003) and antimalarial use (p=0.022) correlated with shorter length of stay.
**Conclusion:** SLE patients are frequently admitted and often require readmission within two years. Hospitalization rates and duration were affected by factors such as presence of damage, which increased admission rate, and socioeconomic status and antimalarial use correlated with decreased number and shorter duration of hospitalizations.

**113**

**Oligoarthritis and Splenomegaly in a Patient with Primary Sclerosing Cholangitis**

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A 30-year-old male presented in November 2015 with diffuse pruritis, elevated total bilirubin (46 umol/L), AST (635 U/L), ALT (960 U/L) and GGT (1064 U/L). Imaging (MRI and endoscopic ultrasound) revealed evidence of distal biliary stricture and he required endoscopic retrograde cholangiopancreatography (ERCP) and stent placement. Although distal biliary strictures are atypical for primary sclerosing cholangitis (PSC), diagnosis was made on the basis of liver biopsy pathology findings (severe hepatocellular damage and mild cholestasis) and biochemistry (anti-mitochondrial antibody negative). He was treated with Prednisone between February 2016 and June 2016 with modest response of liver function tests.
He presented in August 2016 with oligoarthritis involving both wrists and both ankles. Although he had a long history of nodular, cystic scarring acne he also reported a worsening rash over his torso as well as intermittent non-painful ulcerations on his tongue and night sweats. There were features of splenomegaly on physical examination which were confirmed by MRI (15.7cm craniocaudally). Serum IgG4 was normal. ANA (titer 1:160 with homogeneous pattern) as well as anti-dsDNA (47 IU/mL) were positive with elevated inflammatory markers, ESR (74 m/hr)

and CRP (15.0 mg/L). There was persistent lymphopenia as of initial presentation in November. He presented two weeks later having failed a trial of NSAIDs and now reporting shortness of breath on exertion and pleuritic chest pain with further increases in inflammatory markers. Imaging did not reveal any evidence of pulmonary embolism or malignancy and this manifestation was deemed consistent with possible serositis. Patient was started on a course of Prednisone 40mg daily. Symptoms improved within days.
Given positive ANA/anti-dsDNA, lymphopenia, arthritis, serositis, rash and oral ulcerations the diagnosis of systemic lupus erythematosus (SLE) was made. He was shortly thereafter started on Hydroxychloroquine.
Some authors have reported the high frequency of autoimmune diseases in patients with PSC. For instance, the association of PSC with inflammatory bowel disease is well recognized. The coexistence, however, of PSC and SLE, the prototypic autoimmune disease par excellence, has rarely been reported. Further research into underlying common immune abnormalities is warranted.

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**Electrocardiogram Abnormalities Related to Anti-malarials in SLE**

Taneisha McGhie (University of Toronto, Toronto); Paula Harvey (Division of Cardiology, Women's College Hospital, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Nicole Anderson (Toronto Western Hospital, Toronto); George Tomlinson ( University of Toronto, Departments of Health Policy, Management, and Evaluation, and Medicine, Department of Medicine, Toronto); Zahi Touma (University of Toronto, Toronto)

**Objectives:** Anti-malarial drugs, hydroxychloroquine (HCQ) and chloroquine (CQ) are routinely used in the treatment of systemic lupus erythematosus (SLE) for a myriad of benefits. Cardiotoxicity is a rare but serious complication of anti-malarials with several case reports documenting potential conduction disturbances and chamber enlargement on electrocardiogram (ECG). Our objective was to study whether treatment with anti-malarials is associated with ECG abnormalities in patients with SLE.

**Methods:** We studied prospectively collected data from the University of Toronto Lupus Cohort. Patients' 1st routine 12-lead resting supine ECG was analyzed using the Minnesota Code by a single cardiologist blinded to identifying data. Demographics, disease activity, damage, medications and laboratory data were assessed. For the purpose of this study, structural ECG abnormalities were defined as: left ventricular hypertrophy (LVH) or atrial enlargement; conduction ECG abnormalities were defined as: arrhythmias including prolonged QTc, left bundle branch block (LBBB) and right bundle branch block (RBBB). First, normal and abnormal ECG patients were identified and described, associations between cumulative anti-malarial doses and ECG abnormalities (structural or conduction) were assessed using logistic regression analysis after adjusting for baseline patient characteristics. Second, a nested case control study (1:3 matching) based on gender, ECG testing years, SLE duration at ECG, and hypertension was conducted.

**Results:** For the 453 patients included in the analysis, 393 patients were treated with anti-malarial. Mean age at ECG was 49.2 ± 13.7 years, SLE duration at ECG was 19.7±10.4 years and the median cumulative anti-malarial dose was 1048 grams before ECG. 58 (12.8%) showed structural abnormalities, 71 (15.7%) conduction abnormalities and 118 (26.0%) structural or conduction abnormalities. The multivariable analysis found the following statistically significant ($p<0.05$) predictors of structural ECG abnormalities: SLE duration at ECG (OR: 1.04 95% CI: 1.01-1.07), hypertension before ECG (OR: 2.92 95% CI: 1.32-6.48); and cumulative anti-

malarial dose higher than median dose prior to ECG (OR: 2.08 95% CI: 1.12-3.87). SLE duration (OR: 1.04 95% CI: 1.01-1.08) and hypertension (OR: 9.17 95%CI: 1.16-72.29) predicted ECG conduction abnormalities. There was no association of anti-malarial dose with ECG conduction abnormalities (OR: 0.84 95% CI: 0.51-1.40). The nested case control analysis (58 cases:159 controls) confirmed the relationship between structural ECG abnormalities and a higher than median cumulative anti-malarial dose prior to ECG (OR: 2.14 95% CI: 1.07-4.29).
**Conclusion:** Higher cumulative anti-malarial doses are associated with structural ECG abnormalities.

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**Improving Assessment of Cognitive Function in SLE**

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**Objectives:** Cognitive Impairment (CI) is one of the most common manifestations of neuropsychiatric SLE. The wide variation in estimated prevalence rates of CI may relate to a dearth of validated metrics for CI in SLE. Objectives include: i) identify a sensitive and specific protocol that is cost- and time-efficient to screen for, diagnose and characterize CI over time, ii) study the role of biomarkers in screening and diagnosis of CI, and in predicting its change over time, iii) study demographic risk factors for CI in SLE, and iv) study the impact of CI on work productivity and health related quality of life (HRQoL).
**Methods:** A multidisciplinary team of rheumatologists, neuropsychologists, occupational therapists, neurologists, psychometrists, a registered nurse and a knowledge user have been assembled to study the assessment of CI in adult SLE patients attending the University of Toronto Lupus Clinic. Patients who fulfill at least ≥4 ACR (American College of Rheumatology) criteria aged 18-65 are invited to participate. Patients who are mentally or physically unwell (determined by treating physician) and unable to participate will be excluded. Patient assessment will be conducted at baseline, 6 and 12 months. Clinical and laboratory features of SLE are collected on a standardized protocol. Cognitive assessment includes the modified ACR battery, Automated Neuropsychological Assessment Metrics (ANAM), Hopkins Verbal Learning Test-Revised, amongst other tests. Patient reported outcomes (PROs) collected at each study visit include: the Perceived Deficits Questionnaire, Beck Depression and Anxiety Inventories, Fatigue Severity Scale, Personality Assessment Inventory, HRQoL questionnaires and the Work Productivity and Activity Impairment Questionnaire. Blood based biomarkers including classic SLE serology, other antibodies and cytokines will be collected at each study visit.
**Results:** To date, a total of 226 patients have been approached to participate; 137 patients consented and 89 declined. Reasons for consent refusal included the length of study visits and distance from the clinic. Six of the 137 patients consented withdrew due to length of study visits; 131 patients remain in the study. A total of 39 patients have completed and the remaining 92 are scheduled for baseline assessments. All patients completed the modified ACR battery, ANAM, and PROs.
**Conclusion:** Identification of the best screening, diagnostic and longitudinal evaluative protocol for patients with CI and better understanding of quality of life and productivity may help clinicians to identify CI earlier in SLE patients and to improve patient quality of care.

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**Development and Initial Validation of a Novel Lupus Disease Activity Index to Account for Glucocorticoids: Sledai-2K Glucocorticoids Index (SGI)**

Zahi Touma (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto)

**Objectives:** It is challenging to describe disease activity in SLE in the context of multiple levels of glucocorticoids (GCS) treatment. The objectives were to develop and validate a new index, SLEDAI-2K Glucocorticoids Index (SGI), to accurately describe disease activity while accounting for GCS doses.

**Methods:** Phase 1: Identification of patient scenarios followed in a longitudinal cohort. Phase 2: Equation's derivation explaining the association between SLEDAI-2K and GCS dose while using physician global assessment (Likert Scale: LS) as Gold Standard. Phase 3: Validation of SGI against SLEDAI-2K in active patients. Phase 1: Scenarios were identified using the top 13 organ involvement combinations, then patients were grouped into 7 categories based on GCS dose and 10 patients per category were selected. Scenario information included: SLEDAI-2K score, organ involvement combination and GCS dose. Phase 2: 3 rheumatologists ranked disease activity with LS. The sample size calculation was on the assumption of reliability with ICC $\geq$0.80 and required a minimum of 46 scenarios. Phase 3: An independent cohort was used for the validation. We hypothesized that in patients with improvement (SLEDAI-2K decrease $\geq$4), the change in SLEDAI-2K and SGI scores will follow the same direction but SGI scores will be at a higher level.

**Results:** Phase 1: 131 patients with different organ involvement on a range of GCS doses were identified. Phase 2: 131 scenarios were summarized and ranked by 3 rheumatologists leading to 393 records. An excellent agreement in LS was achieved ICC (2, k) of 0.89 (95% CI: 0.83, 0.89) among raters. A quadratic linear regression model relating GCS and SLEDAI-2K was structured in the following equation: SGI score =SLEDAI-2K score + [3.65 + 0.29 * GCS – 0.0027 (GCS * GCS)]. Then, the weight scores of different GCS doses were derived. Phase 3: Among the 158 patients studied, 109 patients improved, 38 remained unchanged and 11 patients worsened at 9-12 months of follow-up. In patients who improved SLEDAI-2K and SGI sores correlated highly (r=0.87), changed in the same direction but more importantly SGI scores were at a higher level.

**Conclusion:** We developed and validated a novel lupus disease activity index, SGI, that describes disease activity while accounting for GCS dose.

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**What is the Prevalence of Cognitive Impairment in Lupus and which Instruments are used to Measure It? A Systematic Review and Meta-Analysis**

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**Objectives:** To systematically review literature on: 1) the prevalence of Cognitive Impairment (CI) in SLE patients in the presence or absence of neuropsychiatric involvement (NPSLE), 2) the metrics of CI and 3) the relative risk (RR) for CI in SLE compared to Rheumatoid Arthritis (RA) and healthy individuals.

**Methods:** Literature search (1900-2016) in Ovid Medline, Embase and Psyc INFO for articles

on the prevalence of CI in adult SLE patients using a specified neuropsychological instrument of cognitive function (CF) was conducted. The prevalence of CI was studied for all instruments and whenever possible Pooled Prevalence (PP) was determined in the commonly used instruments [standardized batteries, Modified Mini–Mental State Exam (MMSE), Automated Neuropsychological Assessment Metric (ANAM) and Montreal Cognitive Assessment (MoCA)].
**Results:** Of 3422 references, 670 were selected for detailed review and 84 were included in the final analysis. Standardized batteries (including ACR battery) were utilized in 41 studies in 3338 patients and found a PP of CI of 34% (95% CI: 28-40%). CI was higher in NPSLE with PP of 41 (95% CI: 26-57%) (13 studies in 647 NPSLE patients). ANAM was utilized in 9 studies in 773 patients and yielded a PP of CI of 37% (95% CI: 20-55%). MMSE was utilized in 9 studies in 766 patients and yielded a PP of CI of 19% (95% CI: 10-30%). MoCA was utilized in 2 studies in 100 patients and yielded a PP of CI of 45% (95% CI: 14-77%). A large variability in the prevalence of CI and a high statistical heterogeneity (I2> 75%) among studies was identified. The RR for CI in SLE was 1.77 (95% CI: 1.19-2.64) compared to RA (data from 6 studies of 343 lupus and 193 RA patients. The RR for CI in SLE compared to healthy individuals was 2.57 (95% CI: 1.62-4.08) (data from 10 studies of 529 SLE patients and 328 healthy individuals).
**Conclusion:** Patients with lupus have a high prevalence of CI ranging from 2.7–80% and largely depending on the metrics and the presence or absence of NPSLE. There is a lack of a standardized approach on how to measure and define CI in SLE. ANAM and standardized batteries (including ACR) yielded similar CI prevalence, while MMSE carried the lowest prevalence. NPSLE patients are as well at a higher risk for CI compared to non-NPSE. Lupus patients are at a higher risk to develop CI compared to RA and healthy individuals.

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**Polyarteritis Nodosa Isolated to the Testes and Bladder in the Setting of Cryptorchidism. A Case Report and Review of the Literature**

Greg Marcotte (University of British Columbia, Vancouver); Natasha Dehghan (University of British Columbia, Vancouver); Michael Seidman (University of British Columbia, Vancouver)

A 54-year-old First Nations male, was well until he presented in April 2016 with a several month history of difficulty urinating and intermittent gross hematuria. In the course of his initial evaluation, he was found to have an enlarged prostate and was started on tamsulosin with improvement in his urinary symptoms. Further evaluation revealed the presence of an undescended testis on the right. He underwent cystoscopy in June 2016 which demonstrated evidence of a lesion concerning for a bladder tumor and an endoscopic resection was performed. An orchiectomy was also performed in June 2016. Pathologic examination revealed the presence of medium vessel vasculitis in both the urinary bladder and undescended testis. There was no evidence of malignancy. He was referred to rheumatology for evaluation. An extensive clinical review of systems revealed no evidence of systemic vasculitis. His investigations including basic blood work, CRP/ESR and ANCA were normal. ANA was positive (1:320). DsDNA and ENA were negative. A diagnosis of polyarteritis nodosa (PAN) was made. A repeat cystoscopy was performed in October 2016 which showed no evidence of ongoing inflammation. Given the lack of clinically apparent systemic vasculitis, no immunosuppressive therapy has been initiated and he will be followed at regular intervals. A CTA is pending to evaluate the possibility of occult vessel involvement elsewhere.

To our knowledge, this is the first case reported in the literature of PAN isolated to both the bladder and testes in the absence of more systemic involvement. Moreover, this is also the first case of PAN reported in the setting of an undescended testis. A literature review was undertaken.

The presence of isolated testicular vasculitis has been reported 37 times to date. The average age of presentation was 37 years (median 35 years) with pain and/or swelling as the presenting complaint in most. Of the 37 cases, 32 were pathologically consistent with PAN, 4 showed granulomatous small vessel vasculitis, and one showed "lymphocytic vasculitis". For patients in whom treatment information was available, most (22/32) were treated with surgical excision alone with no reported cases of emergent systemic disease over a mean follow-up of 25 months (median: 24 months). This case summarizes the current literature regarding the treatment of isolated testicular PAN. Our findings support withholding immunosuppressive therapy after surgical excision in these patients if there is no evidence of more systemic disease at onset. The risk of developing future extra-testicular involvement appears to be low.

**119**

**Shrinking Lung Syndrome in Systemic Lupus Erythematosus: A Single Centre Experience**

Kostantinos Tselios (University of Toronto, Toronto); Mery Deeb (University of Cork, Cork); Dafna Gladman (University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto)

**Objectives:** Shrinking lung syndrome (SLS) is a rare manifestation of systemic lupus erythematosus (SLE), characterized by decreased lung volumes and extra-pulmonary restriction. The aim of this study was to describe the characteristics of SLS patients in our lupus cohort with emphasis on prevalence, presentation, treatment and outcomes.

**Methods:** Patients attending the University of Toronto Lupus Clinic since 1980 (n=1439) and had pulmonary function tests (PFTs) during follow up (n=278) were enrolled. PFTs records were reviewed to characterize the pattern of pulmonary disease (obstructive, restrictive, mixed) according to the American Thoracic Society standardization. SLS definition was based on a restrictive ventilatory defect with normal corrected diffusing lung capacity for carbon monoxide (DLCO) in the presence of suggestive clinical (dyspnea, chest pain) and radiological (elevated diaphragm) manifestations. Chart data on clinical symptoms, functional abnormalities, imaging, treatment and outcomes were extracted in a data retrieval form. Descriptive statistics were used.

**Results:** Twenty-two patients (21 females) were identified with SLS for a prevalence of 1.53% (assuming that patients without PFTs did not have dyspnea at any time during follow-up or their dyspnea was attributed to other causes). Twenty patients were diagnosed based on PFTs; in two, diagnosis was established on the same criteria by a respirologist (no available PFTs and treatment information). Mean age was 29.9±13.1 years at SLE diagnosis and 37.8±14.5 years at SLS diagnosis. Main clinical manifestations included dyspnea in all patients and pleuritic chest pain (20/22, 91%). Sixteen patients (80%) had decreased maximal inspiratory (MIP) and/or expiratory pressure (MEP). Elevated hemidiaphragm was demonstrated in 12 patients (60%). Treatment with prednisone and/or immunosuppressives led to clinical improvement in 19/20 cases (95%), while spirometrical improvement was observed in 14/16 patients and was mostly partial (13/14, 93%). Radiological improvement was observed in 1/7 (14.3%) patient. During follow up, two patients (10%) relapsed (2 and 9 years after initial SLS diagnosis) and were successfully treated with corticosteroids and cyclophosphamide pulse therapy. One patient died due to respiratory failure one year after SLS diagnosis while another three patients died 7-11 years after SLS diagnosis from other causes.

**Conclusion:** SLS prevalence in SLE was 1.53%. Treatment with glucocorticoids and immunosuppressives was generally effective, although with a persistent chronic restrictive ventilatory defect.

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**Elevated Myoscardial Biomarkers in Asymptomatic Patients with Systemic Lupus Erythematosus**

Kostantinos Tselios (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Paula Harvey (Division of Cardiology, Women's College Hospital, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto)

**Objectives:** Antimalarial (AM)-induced cardiomyopathy is a rare complication of chronic AM therapy. We recently encountered such a patient who also had elevated muscle (creatine phosphokinase, CPK) and myocardial biomarkers (brain natriuretic peptide, BNP and cardiac troponin I, cTnI). Lupus patients are chronically treated with AM and some of them may be at risk for developing infiltrative heart disease. The aim of this study was to assess abnormal myocardial biomarkers in patients with systemic lupus erythematosus (SLE) and define associated factors.

**Methods:** One hundred seventy nine consecutive patients (162 females, 17 males) attending the University of Toronto Lupus Clinic were enrolled. BNP (assessing pressure and/or volume overload) and cTnI (assessing myocardial necrosis) were measured simultaneously. Upon evaluation, two patients had decompensated heart failure and three had exertional dyspnea; the remaining were asymptomatic (concerning cardio-respiratory system). None had ECG abnormalities suggestive of acute coronary syndrome. Analysis was performed with SAS 9.3; $p<0.05$ was considered significant.

**Results:** Twenty-seven patients (15.1%) had elevated BNP (n=24, 13.4%) and/or cTnI (n=10, 8.9%), (8 patients had both). Of note, 16 (8.9%) had no prior history of heart disease (congestive heart failure, coronary artery or valvular disease) or pulmonary arterial hypertension. Compared to 152 patients with normal biomarkers, they were older [54.7±15.1 vs. 47.8±12.2 years, p=0.037] and had longer disease duration [22.5±10.4 vs. 15.5±10.1 years, p=0.008]. Persistent CPK elevation (at least three abnormal CPK during the last two years) was more frequent in them [43.8 vs. 16.4%, p=0.008]. Their cumulative AM use duration was significantly longer [14.2±8.2 vs. 8.8±6 years for chloroquine (CQ), p=0.002 and 12.7±8.1 vs. 9.1±6 years for hydroxychloroquine (HCQ), p=0.033]. Cumulative dose was also higher [1509±690 vs. 933±601grams for CQ, p=0.062, 1251±883 vs. 1057±695grams for HCQ, p=0.335]. Multi-variable logistic regression revealed that persistent CPK elevation was associated with increased risk for elevated myocardial biomarkers [HR=4.62, 95%CI=1.22-17.51, p=0.024]. Two patients with myocardial biomarker elevation were diagnosed with AM-induced cardiomyopathy by endomyocardial biopsy after 13 and 22 years of AM use; both had persistent CPK elevation for 9 and 14 years before cardiomyopathy, respectively.

**Conclusion:** A considerable proportion of SLE patients (15%) had elevated myocardial biomarkers, most of them (9%) in the absence of prior cardiac disease. Age, disease duration and AM use were longer in these patients. Persistent CPK elevation was associated with increased risk for abnormal BNP and cTnI. Further assessment of these patients may reveal the cause of this subclinical heart damage.

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**Psoriasis in Systemic Lupus Erythematosus: A Single Centre Experience**

Kostantinos Tselios (University of Toronto, Toronto); Kristy Yap (University of Toronto, Toronto); Rattapol Pakchotonan (University of Toronto, Toronto Western Hospital, Toronto); Ari Polachek (University Health Network, University of Toronto, Toronto); Jiandong Su (Toronto Western Hospital, Toronto); Murray Urowitz (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

**Objectives:** The co-existence of psoriasis with systemic lupus erythematosus (SLE) has been reported in limited case series, raising hypotheses about shared pathogenetic mechanisms. Nevertheless, important differences regarding treatment do exist. The aim of the present study was to determine the prevalence and characteristics of psoriasis in a defined lupus cohort as well as the impact of psoriasis on disease activity, damage accrual, venous thromboembolic (VTEs) and cardiovascular events (CVEs).
**Methods:** Patients with psoriasis (diagnosis confirmed by a dermatologist) were retrieved from the University of Toronto Lupus Clinic database from its inception in 1970 up to 2015. Charts were hand-searched to collect psoriasis-related information (clinical and therapeutic variables) according to a pre-established data retrieval form. Patients with a minimum follow-up of two years after psoriasis diagnosis were matched with non-psoriasis patients to identify the impact of supervening psoriasis on lupus activity (clinical flares as defined by new development of a SLEDAI-2K component), damage accrual (as defined by the increase in SLICC Damage Index), VTEs and CVEs. Descriptive statistics were used for analysis.
**Results:** Psoriasis was diagnosed in 63 patients (49 females, 14 males) for a prevalence of 3.46% (63/1823). The male-to-female ratio was significantly higher in non-psoriasis patients (0.286 vs. 0.138, p=0.017). Plaque psoriasis was the most prominent type (55/63, 87.3%) whereas 3 patients had pustular disease; one had psoriatic arthritis. Nine patients (14.3%) were administered systemic treatment with methotrexate (n=5), azathioprine (n=1), ustekinumab (n=3) and etanercept (n=1). Psoriasis definitely deteriorated by hydroxychloroquine in one patient. The patient treated with etanercept developed serological (increased anti-dsDNA titers) and clinical (polyarthritis) flare after 12 months of treatment and was switched to ustekinumab. There was no significant impact of psoriasis on disease activity (clinical flares in the first two years 14.9% vs. 11.1%, p=0.095) or damage accrual (average increase in SLICC/DI after 2 years 0.22 vs. 0.13, p=0.635). The rate of new VTEs (4.3% vs. 3.7%, p=0.739) and CVEs (8.5% vs. 6.5%, p=0.593) did not differ between groups.
**Conclusion:** The prevalence of psoriasis was twice as high as that of the general Canadian population in this lupus cohort. Plaque psoriasis was the most prominent subtype and topical treatment was adequate in the majority of patients. Supervening psoriasis had no significant impact on lupus activity, damage accrual, thromboembolic and atherosclerotic cardiovascular events.

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**The Role of Immunosuppressive Therapy in Systemic Lupus Erythematosus Associated Pulmonary Arterial Hypertension**

Kostantinos Tselios (University of Toronto, Toronto)

**Objectives:** Pulmonary arterial hypertension (PAH) is detected in 0.5-17.5% of patients with systemic lupus erythematosus (SLE). Systemic inflammation plays a dominant role in its development, particularly in the early phases of PAH. The aim of this study was to describe the characteristics and assess the efficacy of immunosuppressive therapy in SLE-associated PAH (SLE-PAH).
**Methods:** Patients with PAH, defined as right ventricular systolic pressure (RVSP)>40mmHg on at least two separate transthoracic echocardiograms (TTE), were identified from our database of a long-term longitudinal prospective lupus cohort of 1876 patients. Patients' charts were hand-searched according to a pre-established data retrieval form with particular emphasis on the therapeutic approach and outcome. Demographic, clinical and immunological and therapeutic variables were retrieved from the database. Descriptive statistics were used for analysis.

**Results:** Fifty-one patients were diagnosed with PAH since clinic inception. SLE was the sole cause (SLE-PAH) in 32 (62.7%) whereas other causes were identified in 19 (37.3%). Mean age was 31.2±11.2 years at lupus onset and 38.7±12.3 years at PAH diagnosis. PAH was diagnosed within the first year of SLE in 13 (31%) cases. Mean initial RVSP was 59.2±17mmHg. Right heart catheterization (RHC) was performed in 15 patients [mean systolic pulmonary artery pressure (PAP)=62.7±24.7mmHg, diastolic PAP=25.4±9.4mmHg, mean PAP=39.4±14.8mmHg, pulmonary capillary wedge pressure=9.1±4.7mmHg, pulmonary vascular resistance=901±508 dynes-sec-cm-5]. Thirty-one patients (73.8%) had active involvement of other organs (4 central nervous system, 8 kidneys, 4 heart, 3 lung, 7 vasculitis, 8 musculoskeletal, 17 mucocutaneous and 1 catastrophic antiphospholipid syndrome) upon PAH diagnosis. Eleven patients (26.2%) had no other lupus clinical manifestation (8/11 had active serology which was concordant with PAH over time). SLE-targeted therapy (corticosteroids±immunosuppressives) was administered in 28 patients and was successful in 24 (85.7%) with a mean RVSP reduction of 17.7±7.3mmHg (from 63.7±19.1 to 44.1±14mmHg) in 6.1±3.1 months. Induction treatment consisted of prednisone (mean initial dose 41.6±16mg/d) in all patients, methylprednisolone pulses in 8 (500-1000mg/pulse for 1-3 days), cyclophosphamide pulses in 4 (500mg q2w) and other immunosuppressants in 12 (8 mycophenolate, 4 azathioprine). PAH-targeted therapy was administered to 9/28 patients (5 bosentan, 4 phosphodiesterase-5 inhibitors) and discontinued in two due to PAP normalization. Two-year and 5-year survival was 95.2% and 90.5% respectively.
**Conclusion:** SLE-PAH was usually diagnosed early in disease course and accompanied by other clinical and serological lupus manifestations. Aggressive immunosuppressive therapy was succesful in the majority of cases, occasionally diminishing the need for PAH-targeted therapy and leading to good survival.

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**The Toronto Risk Factor Study Revisited: Long-term Evolution of Risk Factors for Atherosclerotic Cardiovascular Events in Systemic Lupus Erythematosus**

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**Objectives:** Certain traditional and disease-related factors contribute to accelerated atherosclerosis in systemic lupus erythematosus (SLE). The aim of this long-term prospective study was the assessment of the evolution over time and relative importance of these parameters in the development of atherosclerotic cardiovascular events (CVEs) in lupus patients
**Methods:** The Toronto Risk Factor Study recruited 250 female lupus patients (mean age at enrollment 44.5±12 years, mean disease duration 13.7±9.7 years) and 250 age-matched healthy women (mean age 44.1±14 years) between 1998 and 2000. All subjects had similarly low (3.2%) 10-year risk for coronary artery disease (CAD) according to the Framingham Risk Score. Variables assessed at study entry included all traditional risk factors, as well as menstrual status, use of oral contraceptives or hormone replacement therapy, serum creatinine, homocysteine and C-reactive protein. For lupus patients, the 3-year adjusted mean SLEDAI (AMS) (1998-2000 and 2005-2007) was calculated to quantify global disease activity. Additional parameters included antiphospholipid antibodies and therapeutic variables. Subjects were followed for 15 years for the development of CVEs [angina, myocardial infarction (fatal, non-fatal), transient ischemic attack, stroke (fatal, non-fatal)]. Analysis was performed with SAS 9.3 software; $p<0.05$ was considered significant.
**Results:** SLE patients had consistently higher rates of CVEs, the difference becoming greater

with longer follow up (p=0.0001). CVEs occurred in 41/210 patients (19.5%) and 8/138 controls (5.8%), mostly in the second part (2008-2015) (24/41, 58.5% vs. 17/41, 41.5% in patients, 4 CVEs in each part in controls). Coronary artery disease was more common in SLE (32/210, 15.2% vs. 5/138, 3.6%, p=0.0041). There was no significant difference for cerebrovascular disease (10/210, 4.8% vs. 3/138, 2.2%, p=0.213). SLE, older age and triglycerides>2.8mmol/L were predictive of CAD in the early phase. In the late phase, hypertension, diabetes, dyslipidemia and higher BMI were more prominent in patients with CVEs. These patients had lower time-adjusted disease activity (AMS), however their cumulative prednisone dose between 2000-2007 was significantly higher. Of note, 60% of the new hypertension and all new diabetes cases were attributed to corticosteroids. Thirty-one deaths occurred in patients (10 due to CVEs) and 6 in controls (none due to CVEs); all CVE-related deaths occurred between 2008 and 2015.
**Conclusion:** SLE patients had 4-fold increased risk for CVEs and all-cause mortality as compared to healthy controls after 15 years. Disease-related factors dominate cardiovascular risk during the early stages while traditional factors, partially related to corticosteroid treatment, play a significant role later in disease course.

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**Disparate Outcomes in Indigenous and Ethnic Minority Lupus Nephritis Patients**

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**Objectives:** Lupus nephritis is a known predictor of mortality; we have previously shown an increased frequency of nephritis in Indigenous and Ethnic Minority lupus patients. Expanding on our previous work examining mortality risks in vulnerable populations, we examined the risks of end-stage renal disease (ESRD) and death among lupus patients with nephritis.
**Methods:** Patients from a single academic center were followed from 1990-2016 using a custom database. Records of all SLE patients were abstracted. Variables included birthdate, diagnosis date, ethnicity, ACR classification criteria (ACRc), SLICC Damage Index (SDI) including ESRD, treatment and date of death. For patients not seen within 2 years, updated vital status was obtained from provincial medical records. Ethnicity (by self-report) was categorized into Indigenous, Caucasian and all other (EM). In patients who had developed nephritis over their disease course, Kaplan Meier and Cox proportional hazard Models were used to compare ESRD and survival between ethnic groups.
**Results:** Nine hundred thirty-five SLE patients were identified: 237(25%) Indigenous, 574(62%) Caucasian, and 124(13%) EM; 89% female, mean disease duration 13.7 years. Fifty-seven percent of Indigenous (n=136; OR 2.1;95%CI 1.5-2.8), 39% of Caucasian (n= 225), and 73% of EM (n=91; OR 4.3;95%CI 2.8- 6.6) had had nephritis, p<0.001. Comparing nephritis patients (N=452), Indigenous (29years±15) and EM (29years±13) were younger at diagnosis; Caucasian (36years±16), p<0.001. Disease duration was similar in Indigenous and EM, both (11years±13); and longer in Caucasian (16years±11); p<0.001.There were no differences in additional ACRc met between ethnic groups. Damage in addition to ESRD was similar in Indigenous (SDI1.8±2.2) and Caucasian (SDI 2.0±2.5) and lower in EM(SDI1.2±1.4). ESRD developed in 11% of nephritis patients during follow-up: Indigenous 14%, EM18% and Caucasian 6%; p=0.003, and 17% died: Indigenous 24%, EM9%, Caucasian 16%; p=0.007. Mean age at death was Indigenous (47years±15); Caucasian (61years±19), and EM(41years±9) ; p<0.001.Adjusting

for age, SDI and ACRc, HR for ESRD was 4.1(95%CI 2.0-8.9) for Indigenous and 5.9(95%CI 2.7-12.9) for EM; HR for Death was 4.1(95%CI 2.4-6.8) for Indigenous and 1.7 (95%CI 0.8-3.8) for EM.

**Conclusion:** Compared to Caucasians, Indigenous and EM not only have a higher risk of nephritis, but among those with nephritis, risk of ESRD is fourfold higher in IND, and sixfold higher in EM. However, while adjusted risk of death was also fourfold higher in Indigenous, EM had a similar risk of death to Caucasians. Reasons for this may include renal pathology, care pathways, comorbid conditions and socioeconomic factors and need to be further explored.

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**Development of Lupus Nephritis in a Patient with Previous Scleroderma Renal Crisis**

Eilish McConville (University of Ottawa, Ottawa); Catherine Ivory (University of Ottawa, Department of Medicine, Division of Rheumatology, Ottawa); Douglas Smith (The Ottawa Hospital and University of Ottawa, Ottawa)

We present a rare case of a patient who initially presented with scleroderma complicated by renal crisis who then evolved into a classic systemic lupus erythematosus (SLE) phenotype with lupus nephritis in the setting of a severe Salmonella infection.

**Case:** Our patient was initially diagnosed with a connective tissue disorder in 1996 after presenting with Raynaud's phenomenon, polyarthritis, positive ANA and strongly positive RNP. In 2010, during her third pregnancy, she developed significant pre-eclampsia with rapid progression of nephropathy requiring dialysis. Serology at that time showed a strongly positive ANA and strongly positive anti-RNP with negative antibodies to Sm, Ro/SSA, La/SSB, Scl-70 and Jo-1. Antibodies to ds-DNA were negative and complements were normal. Kidney biopsy showed features of thrombotic microangiopathy consistent with scleroderma renal crisis. In May 2013 she was stable on hydroxychloroquine and perindopril. She was experiencing Raynaud's without digital ulcers. She had sclerodactyly with flexion contractures and skin thickening extending to the mid forearms and involving the face and feet. She had no proximal scleroderma. Serologies were unchanged from previous. In 2015 she developed symptoms suggestive of mononucleosis with positive IgM serology for EBV. Lupus serology was not repeated at that time as she was otherwise stable. She remained stable until Jan 2016, when she was admitted with Salmonella bacteremia, pneumonia and pleural effusion. She subsequently developed worsening renal failure, new nephrotic range proteinuria and microscopic hematuria. Serologies showed newly positive ds-DNA, anti-Sm and anti-Ro with low C3 and C4 complement. Renal biopsy showed chronic changes related to her previous thrombotic microangiopathy with new changes suggestive of lupus nephritis, Class III+V. She was subsequently treated with high dose steroids and mycophenolate mofetil. She is stable and is being worked up for possible renal transplant.

**Conclusions**: In reviewing the possible triggers for this patient's new positive serology and clinical manifestations, two interesting pathogens were identified: Salmonella and Epstein-Barr Virus (EBV). SLE triggers are complex and may involve genetics, environmental factors and various infections, most commonly EBV. Our patient clinically and serologically evolved from scleroderma/overlap syndrome into a classic SLE phenotype in the setting of severe Salmonella infection. Patients with SLE are prone to infections including Salmonella. Recent studies in mice suggest that proteins within bacterial biofilms may also cause immune activation and SLE antibody production. This case presents an intriguing evolution in a patient presentation, presumably in response to an infectious trigger.

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**Systemic Lupus Erythematosus in Immigrants to Canada: Results from the 1000 Canadian Faces of Lupus Study**

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**Objectives:** SLE is more prevalent in non-Caucasian ethnic groups in Canada. Rising migration rates of individuals potentially at high-risk for SLE to Canada raise the potential for increased SLE-specific healthcare needs. We aimed to describe immigrant patients with SLE.

**Methods:** The 1000 Faces of Lupus cohort is a multi-centre Canadian cohort of incident/prevalent SLE patients. Sociodemographics, ACR classification criteria, SLEDAI scores, SLICC/ACR damage index (SDI) scores, and treatment history are collected using standardized tools. Ethnicity was self-reported. Cross-sectional baseline data were used.

**Results:** 1243 of 2048 patients provided country of birth information and were included. Immigrants comprised 20% of participants (254/1243), which is similar (20.6%) to the general Canadian population. Immigrants were less often Caucasian (32% vs. 73%; OR 0.2, 95%CI 0.13-0.23), and more often Asian (35% vs. 13%; OR 3.5, 95%CI 2.6-4.9). Disease duration (10 vs. 9 years) and age at diagnosis (31 vs. 28 years) were similar, but more Canadian-born had disease onset in childhood (32% vs. 25%, OR 1.5, 95%CI 1.0-2.1). Mean ACR criteria (5.3 vs. 5.2) were similar, but immigrants had more lupus nephritis (42% vs. 27%; OR 2.0, 95% CI 1.5-2.7). Exposure to drug treatment for lupus and self-reported access to care were similar between groups. SLEDAI scores were similar, but patient-reported disease activity scores (SLAQ) were lower in immigrants (8.5 vs. 10.7, mean difference [MD] -2.2; 95%CI -3.0- -1.4), while damage was higher in immigrants (SDI scores 1.4 vs. 1.0; MD 0.4, 95%CI 0.1-0.6). Immigrants had higher physical health-associated quality of life (PCS) (41 vs. 37; MD 3.7, 95%CI 0.4-6.9) but similar mental health-associated quality of life (MCS). Comparing immigrant Asians (N=86) to Canadian-born Asians (N=118), disease duration was similar, but immigrants were older at diagnosis (25 vs. 15 years), with only 20% having childhood-onset (vs. 58%, OR 0.2, 95% CI 0.1-0.3). Number of ACR criteria, frequency of nephritis (50 vs. 52%), medications, SLEDAI, and SLAQ scores were similar. The groups reported similar PCS/MCS scores and access to care, but immigrants had lower incomes (32% vs. 17% low-income, OR 2.2, 95%CI 1.1-4.6). SDI scores were higher in immigrants (0.9 vs. 0.5; MD 0.4, 95%CI 0.04-0.80).

**Conclusion:** Our data suggest relatively severe disease with high frequencies of nephritis and damage in immigrant SLE patients. The low proportion of Asian immigrants with childhood-onset SLE may reflect barriers to immigration in children with SLE. Experts anticipate climbing immigration rates; monitoring lupus characteristics in immigrants is timely and relevant.

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**The Role of Laboratory Tests in Monitoring Systemic Lupus Erythematosus: A Systematic**

**Review**

Noura Al-Foraih (University of Alberta, Edmonton); Zahi Touma (University of Toronto, Toronto); Trish Chatterley (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton)

**Objectives:** Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease, often characterized by periods of flare and remission, with variable disease phenotypes and prognoses. Multiple laboratory studies (eg. complete blood count, creatinine, complement, C-reactive protein, anti-double-stranded DNA antibodies) are often used by clinicians to aid in monitoring SLE patients for disease flare and remission and adverse events related to medication. While some disease activity and damage instruments include certain laboratory tests as part of their descriptors, further evaluation is needed to identify which laboratory tests, independent of these instruments, are useful in predicting disease activity or damage. This systematic literature review was performed to identify which laboratory tests were associated with lupus outcomes including flare, mortality and damage.

**Methods:** MEDLINE, EMBASE, and the Cochrane Library databases were searched up to April 2016 for literature highlighting the PICO: population = SLE, intervention(s) = laboratory tests (eg. CBC, C3, C4, ds-DNA, creatinine), comparison = self, outcome(s) = flare, disease activity, damage, mortality. The quality of evidence was assessed by the Newcastle Ottawa scale.

**Results:** Our literature search yielded 12548 articles, out of which 305 articles were identified following title and abstracts screen. A total of 68 articles met the inclusion criteria. Thirty-seven studies (54%) demonstrated that anti-ds-DNA antibodies was predominately a marker of disease activity, and to a lesser extent, damage or morbidity. Thirty studies (44%) highlighted that low complements (C3 or C4) were associated with disease activity, specifically as a marker of renal involvement. C-reactive protein was associated with disease activity in 11 studies (16%). Cytopenias appeared to be associated with disease activity/flare in 8 studies (12%) for anemia, 7 studies (10%) for thrombocytopenia, and 6 studies (8%) for leukopenia. Renal indices associated with disease activity and renal flares included urinalysis in 4 studies (6%), 24hr urine protein in 3 studies (4%), and spot urine protein:creatinine ratio in 3 studies (4%).

**Conclusion:** The biomarkers anti-ds-DNA antibodies and complements correlated with the worsening disease activity and damage as evidenced by a large number of studies in this systematic review. In comparison, other lab parameters provided less clear evidence of their role in monitoring the lupus patient. Further study is needed to assess the utility of existing laboratory tests in monitoring lupus patients.

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**The Impact of Inflammatory Arthritis (Rheumatoid Arthritis, Spondyloarthritis, and Psoriatic Arthritis) on Maternal and Neonatal Outcomes: A Population-Level Analysis**

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**Objectives:** The impact of inflammatory arthritis (IA) including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and spondyloarthritis (SpA) on maternal, obstetrical and neonatal outcomes is not well described at a population-level. Accordingly, we compared maternal and neonatal outcomes of women with and without IA in a contemporary pregnancy-birth cohort in a defined geographic area (province of Alberta, Canada).

**Methods:** The patient population consisted of 312,081 women who delivered singleton, live babies between 01/01/05 and 12/31/2014. Previously established International Classification of Disease (ICD) version 9 or 10 were used to identify women with IA. Women with IA were

further categorized as RA and SpA. The "no IA", RA and SpA groups were compared with descriptive statistics. Multivariate regression analysis was used to evaluate for associations between RA and SpA with "small for gestational age".
**Results:** There were 633 women with RA; 2461 with SpA; and 308,989 with no IA. In addition to slightly older mothers (RA 30.4; SpA 30.5; no IA 29.3 years), more women with RA had aboriginal status (11.7%) compared to those with SpA (5.6%) and "no IA" (5.1%). Compared to the "no IA" group, women with RA and SpA had statistically greater number of women with hypertension, diabetes, and thyroid disease. In comparison to the "no IA" and "SpA" women, the RA group had statistically more cases of preterm delivery (RA 13.5%, SpA 7.4%, "no IA" 7.1%) and Caesarean sections (RA 33.9%, SpA 29.1%, "no IA" 28.4%) whereas maternal outcomes of maternal mortality, and gestational diabetes were similar across groups. Both RA and SpA women had statistically higher rates of pregnancy-induced hypertension/eclampsia compared to the "no IA" groups (RA 10.5%, SpA 7.3%, no IA 6.4%). Babies born to RA mothers were statistically smaller (lower birth weight/smaller for gestational age) than the SpA and "no IA" groups but no differences were seen for neonatal death/large for gestational age and congenital anomaly. The adjusted OR for small for gestational age was 1.51 (95% CI 1.21, 1.87) for RA and 0.97 (95% CI 0.85,1.10) for SpA.
**Conclusion:** Our study provides novel data on the prevalence of RA and SpA in a contemporary cohort of pregnant women. RA is associated with a higher likelihood of Caesarean section, preterm delivery, and small for gestational infants; however, "no IA' and "SpA" had less to no impact on maternal and neonatal outcomes. This study highlights the need for peri partum counseling of women with RA.

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**Which Criteria for Inflammatory Back Pain in Spondyloarthritis are Optimal? Data from the Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis Study (SASPIC)**

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**Objectives:** Criteria for inflammatory back pain (IBP) in spondyloarthritis (SpA) include the Calin, Berlin, and Assessments in SpA International Society (ASAS), although no studies have undertaken comparative validation to determine which are optimal versus the rheumatologist expert opinion gold standard assessment. We aimed to compare IBP criteria in unselected patients presenting with undiagnosed back pain to rheumatology practice.
**Methods:** The Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at the development and validation of a triage strategy for detection of axial SpA in patients presenting with undiagnosed back pain. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis, or colitis diagnosed by the relevant specialist undergo routine clinical evaluation by a rheumatologist for axial SpA. The rheumatologist first determines the presence or absence of IBP (defined as <5 or >5 on 0-10 scale, respectively) and then axial SpA (yes/no) after the clinical evaluation and review of labs (B27, CRP) and imaging (x-ray, MRI). Radiographs and MRI scans are also assessed centrally for diagnosis of axial SpA (yes/no). We assessed sensitivity and specificity of each of the IBP criteria for diagnosis of IBP according to the local rheumatologist, diagnosis of axial SpA by local rheumatologist, diagnosis of axial SpA by central assessment, and concordant

diagnosis of axial SpA by both local and central assessment.
**Results:** To date 167 patients (48.5% male, mean age 27.8 years, mean back pain duration 6.7 years) have been referred with iritis (29.9%), psoriasis (18.0%), Crohn's (38.3%) and ulcerative colitis (19.2%). IBP was considered present in 65.2% of all patients by the local rheumatologist and sensitivity/specificity of IBP criteria were 94.4%/38.6% (Calin), 84.1%/63.6% (ASAS), 88.8%/81.8% (Berlin). Axial SpA was considered present in 48.5% by the local rheumatologist and sensitivity/specificity of IBP criteria was 90.6%/19.1% (Calin), 85.9%/44.1% (ASAS), 85.9%/52.9% (Berlin). After central assessment axial SpA was considered present in 36.4% and sensitivity/specificity of IBP criteria was 93.8%/21.4% (Calin), 81.3%/33.9% (ASAS), 81.3%/42.9% (Berlin). Amongst patients with a concordant diagnosis by both local and central assessment 40.3% were considered axial SpA, and sensitivity/specificity of IBP criteria were 92.6%/22.5% (Calin), 85.2%/42.5% (ASAS), 85.2%/55.0% (Berlin).
**Conclusion:** All IBP criteria lack specificity for rheumatologist diagnosed IBP or axial SpA but the Berlin criteria have consistently better performance.

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**Interim Analysis of the Canadian Adalimumab Post-Marketing Observational Epidemiological Study Assessing Effectiveness in Ankylosing Spondylitis (Complete-AS): Baseline Characteristics of Adalimumab vs. Non-Biologic DMARD Treatment Groups**

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**Objectives:** COMPLETE-AS is an ongoing observational study expected to enroll 1120 AS patients from 60-80 sites across Canada. Eligible patients are anti-TNFα naïve adults, with active AS as per judgment of the treating physician, who require change in current AS treatment to either a subsequent non-biologic DMARD (nbDMARD), or to adalimumab (ADA). The goal of this analysis is to compare baseline demographic and disease parameters of nbDMARD and ADA treated patients enrolled thus far.
**Methods:** This was a pre-specified interim analysis of patients enrolled between June/2011 - October/2015. Patients are followed for up to two years as per routine care. Disease parameters collected include morning stiffness, extra articular manifestations (EAMs), disease activity (BASDAI), functional status (BASFI), quality of life (SF-36), mental health (BDI-II), health care utilization (HCU) and work limitations (WLQ). Between-group differences in baseline parameters were assessed with the Chi-square statistic for categorical variables, and the independent samples t-test or the Wilcoxon rank sum test for continuous variables, as appropriate.
**Results:** A total of 470 patients (nbDMARD n=148, ADA n=322) were included in the current analysis. No significant differences ($p<0.05$) in baseline demographics were observed across groups, with the exception of current employment (74.3% nbDMARD vs. 62.1% ADA, $p=0.010$). By nbDMARD and ADA groups, respectively: mean (SD) age was 41.6 (12.3) vs. 43.8 (13.8) years; the majority of patients were male (53.4% vs. 56.8%), Caucasian (89.2% vs. 85.1%), HLA B27+ (55.4% vs. 53.7%) and RF- (54.1% vs. 52.5%). Regarding baseline disease parameters, mean (SD) duration of morning stiffness was significantly longer in ADA patients [59.8 (37.6) vs. 75.8 (39.1) minutes, $p<0.001$], who also reported significantly higher ($p<0.001$) mean (SD) BASDAI [5.0 (1.9) vs. 6.4 (1.8)], BASFI [3.7 (2.3) vs. 5.6 (2.2)], and BDI-II [10.8 (7.3) vs. 15.2 (9.8)] total scores, and significantly lower ($p<0.001$) mean (SD) SF-36 scores

[MCS: 17.0 (1.6) vs. 16.1 (1.9); PCS: 27.6 (1.4) vs. 26.4 (1.5)]. Work limitation at baseline was higher in nbDMARD patients [WLQ mean (SD) score: 64.7 (11.9) vs. 56.6 (14.7); p<0.001]. No significant differences in baseline EAMs or HCU were found between groups.
**Conclusion:** AS patients initiating ADA in Canadian routine clinical care have significantly greater disease severity and impaired quality of life at baseline compared with those initiating traditional DMARDs.

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**Analysis of the Canadian Adalimumab Post-Marketing Observational Epidemiological Study Assessing Effectiveness in Ankylosing Spondylitis (Complete-AS): Association Between Baseline Extra Articular Manifestations and Patient-Reported Outcomes**

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**Objectives:** Ankylosing spondylitis (AS) is an immune mediated inflammatory disease. Although characterized by axial and peripheral joint manifestations, extra articular manifestations (EAMs) are a common clinical feature. EAMs have been found to negatively impact health outcomes including quality of life and work capacity. The aim of this analysis was to describe the prevalence of EAMs at baseline and assess their association with patient-reported outcomes (PROs) in a Canadian routine clinical care setting.
**Methods:** COMPLETE-AS is an ongoing observational study expected to enroll 1120 AS patients from 60-80 sites across Canada. All patients enrolled between June/2011 - October/2015 were included in this analysis. Eligible patients are anti-TNFα naïve adults, with active AS as per the judgment of the treating physician, who require change in current AS treatment. Baseline disease parameters assessed were EAMs (collected from medical chart, physician assessment or patient report), disease activity (BASDAI) and functional status (BASFI); baseline PROs assessed were related to mental health (BDI-II), work limitations (WLQ), and quality of life (QoL; SF-36 Physical (PCS) and Mental (MCS) component summaries). Multivariate linear regression models adjusting for baseline BASDAI and BASFI assessed the impact of EAMs on PROs.
**Results:** A total of 569 patients were included in the current analysis. Mean (SD) age and duration of disease was 43.3 (13.4) and 5.9 (9.8) years, respectively. The majority of patients enrolled were male (57.1%), Caucasian (86.1%), HLA B27+ (67.0%), and RF- (93.7%). The most common baseline EAM reported was enthesitis (15.3%), followed by psoriasis (13.0%), inflammatory bowel disease (IBD; 9.1%), and uveitis (3.2%). EAM combination 1 (EAM1: all EAMs) and EAM combination 2 (EAM2: excluding psoriasis), was reported by 33.2 %, and 23.7% of patients, respectfully. Regression analysis adjusting for baseline BASDAI and BASFI, found enthesitis, EAM1, and EAM2 to be significant negative predictors of SF-36 PCS scores (p<0.05). Individual EMAs were not found to impact PROs, except for uveitis, found to be a negative predictor of SF-36 PCS scores for which a statistical trend was identified (p<0.15). No association between EAMs and SF-36 MCS, BD-II or WLQ scores were found.
**Conclusion:** In a Canadian routine clinical care setting, a substantial proportion of AS patients requiring a change in treatment report EAMs. Patients with EAMs were found to have significant reduction in baseline QoL specifically related to physical functioning.

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**The Role of Conventional DMARDs Co-medication in TNF Inhibitor Drug Survival**

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**Objectives:** The aim of this research was to explore the effect of comedication with conventional synthetic disease modifying antirheumatic drugs (csDMARDs) on drug survival of tumour necrosis factor inhibitors (TNFi) in patients with ankylosing spondylitis (AS).
**Methods:** Patients with AS identified from a database of patients in a community rheumatology clinic in Ontario, Canada starting their first TNFi treatment between January 2001 and July 2016 were included. The median drug survival, age, concomitant csDMARDs treatment, and reasons for discontinuation were compared. The study comprised 149 AS patients treated with TNFi's for a minimum of three months with or without csDMARDs before July 2016; concurrent csDMARDs used include methotrexate (MTX), sulfasalazine, leflunomide, and azathioprine. Withdrawals from TNFi treatment were due to adverse events, lack of response, or lack of effectiveness after initial response.
**Results:** In our Cox regression analysis of the effect of concurrent csDMARDs on TNFi drug survival in biologic naïve patients, co-medication was found to increase the mean survival time for Etanercept (from 53 to 102 months; 23.5% on csDMARDs), but lower the mean survival time for Adalimumab (81 to 61 months; 32.5% on csDMARDs), Infliximab (116 to 106 months; 54.9% on csDMARDs), and Golimumab (24 to 23 months; 37.5% on csDMARDs). These differences were not statistically significant (p=0.465). Sixty-six patients of the 149 biologic naive patients were on concurrent csDMARD during the follow-up period. Additionally, as the majority of patients were on MTX, a separate analysis showed no statistically significant difference in biologic drug survival between MTX co-medicated and non-MTX co-medicated patients. Our secondary results showed that, in biologic naïve patients, Infliximab was associated with better drug survival compared with Etanercept, Adalimunab, and Golimumab, with a mean survival of 121 months compared with 77, 75, and 32 months respectively; this was not found to be statistically significant (p=0.273). However, in the subset of non-biologic naïve patients, Adaliumab, Infliximab, and Etanercept exhibited a statistically significant difference in their drug survival, of 61 months, 58 months, and 22 months respectively (p=0.04). This reduction of drug survival in non-biologic naïve patients, compared to their naïve counterparts, has been documented in literature.
**Conclusion:** In this study of patients with AS, our primary outcome showed that use of csDMARD co-medication was not associated with better TNFi drug survival. Our secondary outcome measures exhibited the highest mean drug retention for Adalimumab and Infliximab, when compared with Golimumab or Etanercept.

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## Comparison of the Imaging and Clinical Arms of ASAS Axial Spondyloarthritis Classification Criteria in Patients with Non-Radiographic Axial Spondyloarthritis

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**Objectives:** The ASAS classification criteria have provided new insights in the classification of axial spondyloarthropathy (axSpA). Some studies suggested different characteristics between the imaging and clinical arms of axial SpA particularly in response to biologics. However, available data is still limited and additional information is required. We present our results in a large group of patients with non-radiographic axSpA (nr-axSpA)
**Methods:** Patients were recruited from two centers with dedicated programs in SpA. Among the registries of these institutes patients coded as nr-axSpA were identified. Two rheumatologist from each center re-scored the X-rays and excluded those with diagnostic changes of AS. SIJ MRI readings were done according to ASAS recommendations. Clinical and laboratory characteristics were obtained and patients were stratified into imaging and clinical arms. The imaging arm was further stratified into B27- and B27+ groups.
**Results:** There were a total of 200 nr-axSpA patients. 147 (73.5%) and 53 (26.5%) of the patients were in the MRI-positive and clinical arms respectively. 28.6% of the patients have been treated with biologics. Comparison of imaging vs clinical arms of nr-axSpA demonstrated that age, sex, disease duration, BASDAI, BASFI and BASMI indices were similar between the groups. Uveitis and psoriasis were significantly increased in the clinical arm group. In contrast, increased acute phase reactants and good response to NSAIDs were more prevalent in the imaging arm. Other variables such non-response to biologics were distributed evenly between the groups. We also compared B27+ vs B27- imaging patients and clinical arm patients (all B27+ by definition). Age, sex distribution and disease durations were similar between these three groups. Increased acute phase reactants and good response to NSAIDs were higher in the both imaging groups compared to clinical arm patients. Biological utilization rates, family history and presence of uveitis were higher in all B27+ patients regardless of whether they were in the clinical or imaging arm. The remainder of the extra-articular features, BASDAI, BASFI and BASMI levels and non-response to biologics were comparable between the three subsets.
**Conclusion:** In this large cohort of nr-axSpA patients the clinical characteristics of nr-axSpA patients classified by the imaging vs clinical arms were comparable. It was of note that there was a comparable TNFi failure due to lack of response in both groups despite the higher CRP in the imaging arm. Our findings provide real world clinical support for the validity of the clinical arm for the classification of nr-axSpA.

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**Does the Physical Examination Reliably Reflect Spinal Damage in Ankylosing Spondylitis?**

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**Objectives:** One of the hallmark characteristics of the disease is new bone formation that manifests as syndesmophytes and spinal fusion. Spinal fusion results from bridging syndesmophytes extending across a discovertebral unit. The true impact of radiographic spinal fusion on function and spinal mobility is still debated. We studied the location and number of bridging syndesmophytes and their relation to spinal mobility measures.
**Methods:** The following patients were included from a longitudinal observational AS cohort: (i) patients who met the NY criteria for AS, (ii) who had complete sets of X-rays, and (iii) who had

available spinal mobility measures including cervical rotation, lateral lumbar flexion and Schober's test. Schober's test and lateral lumbar flexion reflects thoracolumbar spine mobility. Cervical rotation reflects cervical spine mobility. Trained rheumatologists did all spinal measurements. Bridging syndesmophytes were scored in the anterior corners of cervical and lumbar vertebrae. Two expert rheumatologists scored X-rays. A third expert reader settled discordant results. Demographics, clinical data and BASDAI were recorded. The independent effects of bridging syndesmophytes on mobility were assessed by multivariable regression after controlling for other clinical variables.

**Results:** From the cohort of 800 AS patients, 113 had bridging syndesmophytes in the cervical or lumbar or both vertebrae. Ninety-two patients had cervical and 47 had lumbar bridging syndesmophytes. The mean age and disease duration of the patients was 47±11.3 and 21.6±11.4 years respectively. 86.7% of the patients were male and B27 was present in 75%. The number of cervical bridging syndesmophytes showed moderate negative correlations with cervical rotation in patients with both active and inactive disease states (r=-0.56 and -0.59 respectively). Similarly lumbar bridging syndesmophytes had moderate inverse correlations with lateral flexion and Schober's measurements (r=-0.41 and -0.38 respectively). The total number of syndesmophytes and the degree of limitation of the spine both cervical and lumbar movements showed restrictions as the number increased. In regression models where age, sex, disease duration, increased acute phase response and B27 was included, the strongest predictor for the cervical rotation, lumbar lateral mobility and Schober's was the number of cervical (β=-0.59) or lumbar bridging syndesmophytes (β=-0.42 for lumbar side flexion and -0.37 for Schober's).

**Conclusion:** Bridging syndesmophytes independently influenced spinal mobility. The study also provides reference values regarding the location and number of syndesmophytes and their respective impact on spinal mobility.

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**The Effect of Cigarette Smoke on Bone Formation in Ankylosing Spondylitis**

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**Objectives:** Ankylosing spondylitis (AS) is characterized by inflammation and bone formation. It primarily affects the axial skeleton and disease progression leads to bony fusion and significant functional disability. The best-known marker of AS is HLA-B27, however, this gene does not predict the disease course. Smoking, on the other hand, has been identified as a predictor of AS severity, functional disability, as well as radiographic progression. Furthermore, our lab recently demonstrated a positive correlation between the rate of spinal fusion and increasing pack year history of smoking. In contrast, smoking has been shown to decrease bone density, increase fracture risk, and lead to poor bone healing. While the effect of smoking on new bone formation and spinal fusion in AS seems paradoxical, bone metabolism is a complex and dynamic process. The objective of this study was to examine the direct effects of cigarette smoking on osteoblasts.

**Methods:** Saos-2 cells from an osteosarcoma cell line were treated with varying concentrations of nicotine (0 to 1000 uM) to represent the solid phase component of cigarettes. As well, cells were treated with varying concentrations of cigarette smoke extract (CSE) to represent the gas phase component. CSE was obtained by bubbling the smoke of a single cigarette through 25 mL of PBS under constant pressure. The PBS was then filtered through a 0.2 um filter to remove particulate matter, before being diluted in culture media to make 10%, 5%, and 1% solutions.

Cells were treated with nicotine or CSE for 24 to 72 hours. RNA was isolated and real-time PCR was performed to assess the expression of genes (Alp, Bsp, Col1, Osx, and Runx2) involved in bone formation.
**Results:** CSE exposure led to a dose-dependent decrease in Alp, Bsp, Col1, Osx, and Runx2 compared to controls. Nicotine treatments did not result in any significant differences in gene expression compared to controls.
**Conclusion:** The gas phase component of cigarettes leads to suppression of genes involved in bone formation in our cell culture model. This is more in keeping with bone loss and does not support the link between smoking and increased bone formation in AS. In light of these findings, we are now analyzing our large patient dataset with bone density data and sequential x-rays on 500 patients to further analyze AS disease progression, smoking pack years, and bone mineral density.

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**Impact of HLA-B27 on Patient Profile and Treatment Response in AS Patients Treated with Anti-TNF in Canadian Real-World**

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**Objectives:** The aim of this analysis was to compare the profile of HLA- and HLA+ ankylosying spondylitis (AS) patients initiating anti-TNF treatment in Canadian routine clinical care.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab (IFX) or golimumab (GLM) for RA, AS, or PsA, or with ustekinumab for PsA. Patients eligible for this analysis included AS patients treated with IFX or GLM, enrolled since 2005 and 2010, respectively with available information on HLA B27 status. Descriptive statistics were used to assess patient and disease characteristics at Baseline and Month 12. Multivariate general linear models were used to assess the impact of HLA status on BASFI, BASDAI and ASDAS at Month 12 while adjusting for age, gender, disease duration, anti-TNF type, and baseline scores.
**Results:** A total of 147 HLA+ and 78 HLA- AS patients were included, of which 93 had available data at Month 12 (62 HLA+, 31 HLA-). HLA+ patients were significantly younger compared to HLA- patients both at diagnosis (32.2 vs. 46.8 years; P=0.001) and at anti-TNF initiation (42.1 vs. 48.2 years; P=0.002). HLA+ patients had significantly longer disease duration (7.7 vs. 3.9 years; P=0.002) and were more likely to be male (69.0% vs. 42.1%; P<0.001). Geographic distribution was comparable between HLA+ and HLA- groups (P=0.886). With respect to disease parameters, baseline BASDAI, BASFI and ASDAS were significantly higher in the HLA- group ($P < 0.05$), as was the proportion of HLA- patients reporting very high ASDAS disease activity (62.5% vs. 38.2%). Mean baseline CRP levels, although higher in HLA- patients compared to HLA+ patients (16.7 vs. 10.5 mg/L), were not found to be significantly different between groups (P=0.085). Upon adjusting for potential confounders, HLA+ patients experienced greater improvements from baseline to Month 12 in BASDAI (-2.13 vs. -0.24;

P=0.008), BASFI (-1.64 vs. 0.11; P=0.030), and ASDAS (-0.95 vs. -0.26; P=0.067). At Month 12, ASDAS DA categories were found to be statistically comparable across both groups (P=0.396), although a lower proportion of HLA- patients reported inactive-moderate disease (30.0% vs. 51.2%).
**Conclusion:** In this Canadian real-world cohort, HLA- AS patients were found to be demographically distinct from HLA+ patients and present with more advanced disease at baseline. Furthermore, HLA- was identified as an independent predictor of worse treatment outcomes, highlighting the importance of early diagnosis and management of HLA- AS patients.

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**Comparison of Clinical Profile of Geriatric and Non-Geriatric Ankylosing Spondylitis (AS) Patients**

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**Objectives:** Data on disease characteristics of geriatric patients (>=65 years) with AS are lacking. The objective of this study is to compare: 1) the clinical profile of geriatric and non-geriatric patients with AS and 2) geriatric AS patients with aged-matched non-AS comparators.
**Methods:** Data were extracted from a Toronto based longitudinal SpA cohort. Patients with AS were divided by current age into geriatric (age >= 65 years) and non-geriatric (age < 65 years) groups. Clinical and laboratory data were then compared. Data for the non-AS geriatric age-matched control group was obtained from a Toronto tertiary care orthopedics clinic.
**Results:** There were 48 geriatric AS patients out of 890 AS patients in the clinic. 322 knee OA patients were included for the non-AS geriatric comparison. Initial comparison (young vs geriatric AS), showed no differences in sex distribution. Age at time of diagnosis was higher in the geriatric AS patients ($p<0.001$). In terms of clinical activity, there was no difference in mean inflammatory markers or BASDAI scores. Extra-articular manifestations were similar. There was no significant difference between the 2 groups regarding the usage of NSAIDs, DMARDS, corticosteroids and biologics, nor in their side-effects. Only 1% of the geriatric group started biologic therapy at age >=65 yr. Infection frequency was similar between the two groups. Mobility (BASMI) and function (BASFI) scores were higher in the geriatric group ($p<0.001$ and 0.04 respectively). The geriatric group were more likely to have a history of physical trauma/ injury ($p=0.03$). The SF-36 mental component was also higher in the geriatric group. Quality of life scores were similar. Comparison of geriatric AS and geriatric OA patients revealed more males in the AS group. Non-AS patients are more likely to be smokers and have a history of diabetes ($p=0.04$). Functional disability scores were also higher.
**Conclusion:** We show that geriatric AS patients have reassuringly similar treatment and disease activity parameters, but differed in a select few functional components and comorbidities when compared to the younger population. The younger population was diagnosed earlier than the elder group, which may reflect better disease awareness among physicians over the last few years. When compared to geriatric non-AS controls, there was a higher prevalence of females, diabetes and smokers in the non-AS geriatric patients. Further research into the geriatric AS population is needed to better define and manage their specific needs, especially as this patient population will be substantial in the coming years.

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**Experience with Tofacitinib at the Institut de Rhumatologie de Montréal and the Centre d'Ostéoporose et de Rhumatologie de Québec. An Analysis from the Rhumadata® Clinical Database and Registry**

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**Objectives:** Tofacitinib, a new targeted synthetic DMARDS has recently appeared on the Canadian market. It is an oral agent, targeting two subunits of the Janus Kinase pathway, more precisely JAK 1 and JAK 3 indicated in the treatment of rheumatoid arthritis. We describe here the experience that we have accumulated in the last two years on 51 patients.

**Methods:** All patients exposed to tofacitinib at the Institut de Recherche en Rhumatologie de Montréal and the Centre d'Ostéoporose et de Rhumatologie de Québec either in monotherapy or combination with other csDMARDS was extracted from the database since its approval in Canada. All patients' data was obtained from the Rhumadata® clinical database and registry. Descriptive statistics include age, gender, diagnosis, previous and actual exposure to other CS DMARDS and biologic agent, CDAI at the initiation of tofacitinib, duration of treatment, response to treatment, and the reason for stopping.

**Results:** Of the 51 patients exposed to tofacitinib since its launch, 95% had a diagnosis of rheumatoid arthritis (RA), and 5% had spondyloarthropathies (SpA). The patients were mostly female (84%), and the mean age and disease duration at treatment initiation were respectively 58.6 (11.0) and 12.4 (11.9) years. For RA patients, 72 % were rheumatoid factor positive and 47% ACPA positive. At the time of the analysis, 59% were still on treatment. Reasons for stopping are inefficacy (48%), adverse events (19%), infection (5%) and other/unknown (24%). Of these patients, 31% had previously been treated with csDMARDS only. Prior biologic agent exposure ranges from 1 to 9 and 71% had been exposed to less than five biologic agents. The 6, 12 and 18 months' retention rates of RA patients treated with tofacitinib were respectively 64.5 % (SE=35.5), 58.7 (41.3) and 52.3 (47.7). Baseline CDAI for this subpopulation is 26.7 (SD=9.2) and improvement from baseline is on average 7.0 (SD=8.7). Percentage of patients with RA having reached remission is 9.5 %, low disease 16.7%, moderate 33.3% and high 40.5% at their last evaluation.

**Conclusion:** The majority of patients exposed to tofacitinib although they were severe patient with long disease duration and numerous exposure to other prior treatment, the majority being a biologic agent, show improvement in their disease activity score compared to baseline.

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**Injection Site Reaction (Pain) Associated with Subcutaneous (SC) Biologic Agents and Methotrexate. An Analysis from the Rhumadata® Clinical Database and Registry**

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**Objectives:** ISRs are associated with the SC route of administration of all biologic agents, and 3% to 30% of patients reports it. ISRs include pain, itching, redness, swelling or a combination of any of those. Rhumadata® has collected the intensity of pain associated with SC injection. We report here the results and compare levels of pain across agents.

**Methods:** As part of the PRO's, one question on pain intensity was asked to patients exposed to SC methotrexate or a biologic agent administered with a device or a syringe. The same question was asked at all visits making multiple answers available for the same patient. The intensity of pain was described using the following scale: 1- none, 2- negligible, 3- mild, 4- moderate, 5- severe, 6- extremely severe and 7- intolerable. Data comparing adalimumab (ADA), etanercept (ETA), certolizumab (CERTO), golimumab (GOLI) and methotrexate (MTX) is presented.

**Results:** A total of 7128 injection pain assessment were extracted. 4116, 1117 and 1895 were performed on patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) respectively. Women represented 75%, 39% and 47% of these cohorts. Mean ages at treatment initiation were 51.2(SD=12.1), 41.4(11.5) and 48.6(10.8). Severe, very severe or intolerable pain was reported among 3.26% of the RA, 10.47% of the AS and 7.60% of the PsA. RA (OR=0.407, 95% CI=[0.261, 0.635]) patients were less likely to report severe, very severe or intolerable pain than AS patients as were older patients (Age at treatment initiation OR=0.975, 95% CI=[0.961, 0.989]). Subjects treated with ADA (OR=5.70, 95% CI=[3.31, 9.799]), ETA (OR=3.396, 95% CI=[1.843, 6.255]) were more likely to report more pain than patients using MTX. Patients using ADA reported more severe, very severe and intolerable pain than ETA (OR=1.678, 95% CI=[1.018, 2.767]), CERTO (OR=8.269, 95% CI=[1.073, 63.733]), GOLI (OR=11.723, 95% CI=[3.285, 41.841). Stopping treatment for an ISR-pain is extremely rare. Among 359 patients stopping treatment with a first biologic, only one reported "Injection Problems" as the principal reason for cessation.

**Conclusion:** The intensity of pain associated with subcutaneous route of administration varies with age, diagnosis and administered medication.

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**Predictors of Treatment Retention among Patients with Rheumatoid Arthritis or Ankylosing Spondylitis Treated with Infliximab for Long-Term in Canadian Real-World**

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**Objectives:** Remission has become a target to achieve in rheumatic diseases and it also could be linked to treatment retention. The aim of this analysis was to identify independent predictors of retention in patients with rheumatoid arthritis (RA) or ankylosing spondylitis (AS) treated with infliximab (IFX).
**Methods:** BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients treated with IFX, golimumab, or ustekinumab. This analysis included RA and AS patients treated with IFX with at least 2 years of follow-up. Independent predictors of retention were assessed with multivariate cox regression. Receiver operator curve (ROC) analysis was used to determine the optimal cut-off points of CDAI and ASDAS for long-term retention.
**Results:** A total of 490 RA and 201 AS patients were included in the analysis. The mean (SD) disease duration since diagnosis was 9.4 (9.5) years for RA and 9.8 (10.0) years for AS. The mean CDAI score was 35.9 in RA patients and ASDAS was 3.8 in the AS group. In univariate analysis, among RA patients at baseline (BL): CDAI [HR (95% CI): 0.99 (0.99-1.00)], DMARD use [HR (95% CI): 0.70 (0.51-0.97)], steroid use [HR (95% CI): 1.23 (0.99-1.52)], at 24 months: CDAI [HR (95% CI): 1.02 (1.00-1.03)], and DMARD use [HR (95% CI): 0.82 (0.66-1.01)] were identified as potential predictors ($P<0.150$) of retention. No significant impact was observed for age, gender, disease duration, prior biologic experience, enrolment period, and steroid use at 24 months. In multivariate analysis, CDAI score at 24 months was the only significant ($P=0.013$) independent predictor of treatment retention [HR (95% CI): 1.02 (1.00-1.03)]. ROC analysis showed that the optimal 24-month CDAI cut-off score for downstream (non-) discontinuation was 11.7. In AS patients, ASDAS levels at 24 months were the only significant predictor of subsequent treatment discontinuation, with higher ASDAS score being associated with an increased hazard for discontinuation [HR (95% CI): 1.63 (1.12-2.38)]. Maintaining an ASDAS score of 2.7 or less at 24 months was associated with optimal retention on treatment long-term.
**Conclusion:** Results have shown that, among patients remaining on IFX after 2 years, disease activity at 2 years was the single determinant of subsequent long-term retention on IFX treatment both in RA and AS patients, highlighting the importance of the treat-to-target strategy to achieve remission but also maintaining it over time in order to ensure optimal treatment benefits.

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**Impact of E-Learning on Knowledge, Self-efficacy and Exercise Behaviours of Patients with Axial Spondyloarthritis: Results from a Longitudinal Randomized Control Trial**

Laura Passalent (Toronto Western Hospital, Toronto); Rita Kang (Toronto Western Hospital, Toronto); Daeria Lawson (Toronto Western Hospital, Toronto); Christopher Hawke (Toronto Western Hospital, Toronto); Ahmed Omar (Toronto Western Research Institute, University of Toronto, Toronto); Arane Thavaneswaran (Toronto Western Hospital, Toronto); Nigil Haroon (University Health Network, Toronto); Robert Inman (University Health Network, Toronto)

**Objectives:** There is a growing body of evidence to support education programs for patients with arthritis. Despite this, there has been little development or investigation into education strategies for patients with axial spondyloarthritis (axSpA). The Toronto Western Hospital Spondylitis Program recently developed an interactive web-based e-Learning education module for patients with axSpA with input from patients and an interdisciplinary team of health care professionals and consists of evidence-based topics including diagnosis, treatment and self-management for axSpA. The purpose of this study was to measure the effect of the axSpA e-Learning module with respect to: 1) knowledge of axSpA; 2) chronic disease self-efficacy, and 3) exercise behaviour.
**Methods:** Fifty-six adult patients with axSpA attending a tertiary academic spondylitis clinic

were randomly assigned to one of two groups: 1) e-Learning intervention, in addition to usual care, where patients were emailed a link to the online education module and asked to complete the module at their leisure; or, 2) usual care (i.e. control group). All patients completed outcome questionnaires at baseline, immediately after the completion of the e-Learning module and 6-12 months thereafter. Outcome measures included: the Ankylosing Spondylitis (AS): "what do you know" knowledge questionnaire; Stanford Chronic Disease Self-Efficacy Scale, and the Stanford questionnaire for Exercise Behaviours.
**Results:** Twenty-three patients with axSpA completed the e-Learning module, in addition to usual care, and 33 patients continued with usual care. Overall, mean (SD) age was 42.3 (12.9) years, 69.6% were male, mean (SD) disease duration was 12.9 (10.2) years and 75% had a post-secondary education. There were no statistically significant differences in the above outcome measures between the two groups at baseline or immediately following the completion of the e-Learning module. At the 6-12 month follow-up there was an increase in the number of minutes dedicated to all types of exercise the week prior to completing the outcome measures in the intervention group compared to controls, with a significant increase in the average minutes dedicated to bicycling as a form of exercise from a mean of 5.2 minutes to 34.6 minutes, p=0.02.
**Conclusion:** The results of this study demonstrate the addition of the axSpA e-Learning education module to usual care is equivalent to usual care provided at a tertiary academic spondylitis clinic and has potential to provide benefit to patients with axSpA who have limited access to specialty care. Long-term results suggest a significant impact on exercise behaviours in patients with axSpA who completed the e-Learning module. Supported by a CIORA grant.

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**Impact of E-Learning on Perceived Social Role Participation of Patients with Axial Spondyloarthritis: Results from a Longitudinal Randomized Control Trial**

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**Objectives:** People with arthritis identify social role participation (e.g. relationships, leisure activities, employment) as an important quality of life outcome. Evidence suggests that patient education programs are effective in improving function and quality of life. The Toronto Western Hospital (TWH) Spondyloarthritis Program recently developed an e-Learning education program for patients with axial Spondyloarthritis (axSpA) with input from patients and an interdisciplinary team of health care professionals. The purpose of this study was to measure the impact of the axSpA e-Learning education program on patients' perception of social role participation.
**Methods:** Fifty-six adult patients with axSpA attending the TWH Spondyloarthritis Program were randomly assigned to either: 1) e-Learning intervention, in addition to usual care, where patients were emailed a link to the online education module; or, 2) usual care (i.e. control group). All patients completed the Social Role and Participation Questionnaire (SRPQ) at baseline, immediately after completing the e-Learning module, and 6 to 12 months thereafter. The SRPQ includes 12 role domains with 3 dimensions: 1) role importance, 2) restriction to role participation, and 3) satisfaction with role performance. Univariate and bivariate analyses were conducted on SAS version 9.2.

**Results:** Twenty-three patients completed the e-Learning module and thirty-three patients continued with usual care. Overall, mean (SD) age was 42.3 (12.9) years, 69.6% were male, mean (SD) disease duration was 12.9 (10.2) years and 75% had a post-secondary education. Comparison by study group at baseline showed importance of family relationships was lower in the intervention group compared to controls ($p = 0.02$). There were otherwise no significant differences between groups at baseline. Immediate follow-up measures indicated lower perceived importance in the intervention group with respect to: "plan/attend social events" ($p = 0.007$); "having a paid job" ($p = 0.005$); "relationship with other family members" ($p = 0.02$); and "fully participating in all aspects of life" ($p = 0.02$) The intervention group reported lower satisfaction with "type of paid work" ($p = 0.03$). Otherwise, no significant differences were noted at immediate follow-up. At 6-12 months follow-up, the intervention group reported less physical difficulty "participating in hobbies" ($p = 0.04$) and "engaging in activities with children/grandchildren" ($p = 0.04$).

**Conclusion:** Although there are significant differences in the levels of importance of several social role subscales, the reported differences are relatively small. Long-term findings of less physical difficulty with some social role subscales indicate potential long-term benefits of the e-Learning module to patients with axSpA. Supported by a CIORA grant.

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**Adult Axial Spondyloarthritis Screening and Referral Practices amongst Primary Care Physicians, Physiotherapists, Chiropractors and Nurse Practitioners: Results from a Qualitative Study**

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**Objectives:** Early recognition of axial spondyloarthritis (SpA) is crucial in preventing major morbidity. Despite this, there is an average delay of 8 years between the onset of back pain and time when patients are diagnosed by a rheumatologist. Compounding this issue is the uncertainty regarding initial screening and referral practices amongst primary care practitioners for adults with suspected axial SpA. The purpose of this study was to explore the screening and referral practices for suspected axial SpA in adults with chronic back pain amongst primary care physicians (PCPs), physiotherapists (PTs), chiropractors (DCs) and nurse practitioners (NPs) working in community practice in the province of Ontario, Canada.

**Methods:** Semi-structured key informant (KI) interviews were conducted with PCPs, PTs, DCs and NPs working in community practice. Interviews addressed: 1) screening practices and 2) referral practices for adults with suspected axial SpA. Interviews were conducted in-person or over the telephone. Interviews were recorded and transcribed verbatim. Transcripts were analyzed using a compare and contrast methodology. This involved coding groups of words and identifying emergent themes that addressed the research objectives. These themes were organized into two main categories: Screening Practices; and Referral Practices. NVIVO V9 was used to assist with organization of codes.

**Results:** A total of 17 interviews were conducted: PCPs (5); PTs (3); DCs (6) and NPs (3). Practice locations for KIs were primarily urban (14 urban; 3 rural). Mean years of practice of key informants was 9.3 years (range, 1-22 years). Overall, 3 themes were identified related to

Screening Practices for axial SpA: 1) knowledge of axial SpA clinical manifestations; 2) uncertainty of role of investigations in early diagnosis, and 3) lack of awareness of assessment guidelines and screening tools. Themes related to Referral Practices included: 1) optimization of technology; 2) referral barriers, and 3) legislative hurdles.
**Conclusion:** Most primary care practitioners had a general understanding of clinical manifestations of axial SpA; however, knowledge deficits existed related to rare clinical presentations and the role of investigations in early identification of the disease. With respect to referral practices, there are opportunities to address system-level barriers, including more extensive use of technology (e.g. use electronic referral templates). Our research has identified opportunities for implementation of quality improvement initiatives and indication for collaboration with policy makers and other stakeholders. These results may be incorporated into a wider research initiative to gain better insight into primary care screening and referral practices for adults with suspected axial SpA. Supported by a CIORA grant.

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**Inter-professional Satisfaction and Perceptions of Collaborative Practice of an Innovative Model of Care for the Early Detection of Axial Spondyloarthritis**

Laura Passalent (Toronto Western Hospital, Toronto); Christopher Hawke (Toronto Western Hospital, Toronto); Andrew Bidos (University Health Network, Toronto); Nigil Haroon (University Health Network, Toronto); Robert Inman (University Health Network, Toronto); Raja Rampersaud (Toronto Western Hospital, Toronto)

**Objectives:** Emerging models of care in rheumatology integrate interdisciplinary approaches at different stages of the care pathway. Such models of have recently been implemented in the early identification of axial spondyloarthritis (SpA). The Toronto Western Hospital SpA Screening Clinic links with community-based primary care physicians (PCPs), physiotherapists (PTs), chiropractors (DCs) and nurse practitioners (NPs) to facilitate early detection of axial SpA and uses advanced practice physiotherapists and rheumatologists located at an academic tertiary care hospital to confirm diagnosis and initiate early treatment. The objective of this study was to examine the inter-professional satisfaction and perceptions of collaborative practice of an innovative model of care for the early detection of axial SpA in Toronto, Canada.
**Methods:** A cross-sectional survey was conducted of referring health care providers (HCPs) to the Toronto Western Hospital SpA Screening Clinic and included PCPs, PTs, DCs and NPs. HCPs were sent an electronic questionnaire with questions related to general satisfaction of the SpA Screening Clinic and perceptions and experience with the inter-professional collaborative process of the SpA Screening Clinic. An adapted version of the Modified Index of Interdisciplinary Collaboration was used to assess inter-professional collaboration. The survey was administered using Survey Monkey®. Data analyses consisted of descriptive statistics and were conducted using Microsoft Excel 2010.
**Results:** Thirty-two out of 59 (54%) referring HCPs participated in the survey. The majority of respondents were PCPs (65.6%), followed by PTs or DCs (21.9%). The majority of referring HCPs reported positive indicators of clinic satisfaction: receiving communication about their referred patients in a timely manner (53.1%); being informed regarding their referred patients' management plan (51.6%) and future re-referral rate for another patient with suspected axial SpA (83.9%). Overall perceptions of inter-collaborative practice with the SpA Screening Clinic were high: interdependence subscale mean score=2.04 (SD 0.41); newly created professional activities subscale mean score=2.19 (SD 0.2); flexibility subscale mean score=2.47 (SD 0.18) and collective ownership subscale mean score=2.25 (SD 0.21), with 1 representing the highest

possible perception of collaboration and 5 being the lowest possible perception.
**Conclusion:** These results suggest overall inter-professional satisfaction and high levels of perceived inter-professional collaboration with an innovative model of care aimed at the early detection of axial SpA. The results of this study may inform future research on the impact of inter-professional collaboration on outcomes for patients attending the Toronto Western Hospital SpA Screening Clinic.

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**A Systematic Review of Liver Fibrosis Using Transient Elastography in Patients with Inflammatory Arthritis**

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**Objectives:** Disease modifying anti-rheumatic drugs (DMARDs) such as, methotrexate (MTX) are commonly used in the treatments of inflammatory arthritis (IA) including rheumatoid arthritis (RA), psoriatic arthritis (PsA), and juvenile idiopathic arthritis (JIA). One of the adverse effects of DMARDs is hepatotoxicity, and current guidelines recommend frequent monitoring of liver function tests (LFTs) in DMARD treated patients. However, LFT monitoring may reveal mild to moderate abnormalities leading to potentially unnecessary discontinuation of therapy. Conversely, normal LFTs have been reported in cases of fibrosis/cirrhosis. An emerging technology for monitoring subclinical liver fibrosis is transient elastography (TE). A systematic review was conducted to assess the prevalence and predictors of liver fibrosis in IA detected by TE.
**Methods:** MEDLINE, EMBASE and Web of Science were searched from database inception to June 27th 2016 using search terms for IA or DMARDs and TE. Studies reporting on prevalence of liver fibrosis and/or risk factors as detected by TE in patients with IA were included. Two independent reviewers conducted the review and abstracted data in duplicate according to a registered study protocol. A meta-analysis was not conducted due to significant study design heterogeneity
**Results:** The search identified 345 studies, 28 underwent full text review and 10 published studies were included (Kappa 0.85). Seven studies were cross-sectional and 3 were case-control. The cut-off values to define liver fibrosis ranged from 5.3-8.6 kPa. The prevalence of RA patients with liver fibrosis as detected by TE varied from 3% to 23%, with higher prevalence found in Korean studies using a cutoff of 5.3kPa. Fibrosis was reported in 16-17% of PsA patients (n=2 studies). No studies were identified in JIA. Only 2 studies identified cumulative dose of DMARDs as independently associated with elevated liver stiffness (cumulative dose of MTX in one study and cumulative dose of leflunomide in the other). The most consistently reported independent predictor of fibrosis was obesity (either elevated body mass index, BMI, or waist circumference, n=3 studies). LFTs were found to be independently associated with elevated liver stiffness in only one study.
**Conclusion:** MTX or leflunomide cumulative dose were not consistently reported as independent predictors of liver fibrosis, whereas obesity was more consistently identified as a risk factor. Of note elevated LFTs were not consistently associated with TE measures. Further studies are needed to evaluate the prevalence and predictors of liver fibrosis and the utility of routine liver monitoring using TE in IA patients.

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**Secukinumab vs Adalimumab for the Treatment of Ankylosing Spondylitis: A Cost Per**

**Responder Analysis at 52 Weeks from a Canadian Perspective**

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**Objectives:** The cost per responder analysis attempts to quantify the relative value of the two comparator drugs by assessing how the two agents compare in terms of cost per treatment outcome. The objective of this analysis was to estimate and compare the long-term cost per responder based on the Assessment of Spondyloarthritis International Society (ASAS) outcomes following 52 weeks of treatment of ankylosing spondylitis (AS) with Secukinumab (anti-IL-17A antibody) relative to Adalimumab (anti-TNF antibody).

**Methods:** The cost per responder for each treatment namely Secukinumab and Adalimumab was estimated by dividing the drug acquisition cost for the course of treatment with its response rate. Drug costs were estimated on the basis of the Ontario drug acquisition costs (CAD$) and the number of doses required for 52 weeks. Long-term response rates were estimated using a matching-adjusted indirect comparison (MAIC) technique based on the data from MEASURE 2 and ATLAS clinical trials of Secukinumab and Adalimumab, respectively. MAIC analysis matched the age, gender distribution, Bath Ankylosing Spondylitis Functional Index (BASFI), C-reactive protein (CRP) and TNF-naive proportion at the baseline. A more stringent sensitivity analyses was also conducted by varying the choice of baseline characteristics (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)) used in MAIC analysis.

**Results:** MAIC analysis showed that ASAS (20, 40 and 5/6) response rates were significantly higher for Secukinumab compared to Adalimumab at 52 weeks. ASAS 20, ASAS 40 and ASAS 5/6 response rates were 81% vs 65%, 62% vs 47%, 74% vs 55% for Secukinumab vs Adalimumab, respectively. The cost per ASAS 20 responder was $15,307 vs $30,596, cost per ASAS40 responder was $19,899 vs $42,540, whereas, costs per ASAS 5/6 responder was $16,672 vs $36,201 for Secukinumab vs Adalimumab, respectively. The costs per ASAS (20, 40 and 5/6) responders were about 50%, 53% and 54% lower for Secukinumab compared to Adalimumab respectively at 52 weeks. Sensitivity analyses for ASAS response rates and cost per responder showed similar results, confirming the robustness of our main analysis.

**Conclusion:** The long-term cost per responder for all ASAS outcomes at 52 weeks were consistently lower for Secukinumab vs. Adalimumab. These findings indicate that it is more efficient to treat AS patients with Secukinumab vs Adalimumab. Therefore, more AS patients could be effectively treated in Canada versus Adalimumab with a given budget, due to the cost-offsets.

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**Work Instability Scores are Higher in Non-Radiographic Axial Spondyloarthritis than in Ankylosing Spondylitis and Psoriatic Arthritis**

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**Objectives:** Clinical subsets of spondyloarthitis (SpA), such as ankylosing spondylitis (AS) and psoriatic arthritis (PsA) may significantly impact work performance and attendance. Prior to becoming completely work disabled, patients will commonly experience a state of work instability (WI). Our purpose was to determine the characteristics of WI in a large population of patients with SpA.

**Methods:** Patients were recruited from two large, prospective longitudinal cohorts of AS and PsA. WI was evaluated using a validated questionnaire, the AS-WIS. AS-WIS scores WI on a 20 point scale (<11 low risk, 11-18 medium risk and 19-20 high risk of WI). Standard protocols were completed at the time of completion of the AS-WIS which included a detailed history, physical examination, physician-ascertained outcome measures and patient-reported outcomes.
**Results:** 718 respondents completed the questionnaire, 536 of which were employed and included in the analysis[D1] [SR2] . Mean age was 46.2 years (SD 12.1) and 66.7% were male. 60.9% had completed university. 66.0% were being treated with NSAIDs, 37.6% DMARDs and 56.0% TNF inhibitors. Mean swollen joint count was 0.06 (SD 0.28), tender joint count 0.84 (SD 2.60) and damaged joint count 3.44 (SD 8.45). Mean AS-WIS score was 7.55 (SD 6.1), corresponding to low risk of work instability. AS-WIS scores were equally low in PSA, ReA, and undifferentiated SpA (USpA). AS-WIS scores in nr-axSpA were significantly higher[IDR3] than in all the other diagnoses ($p<0.01$ for PSA and $p<0.05$ for AS, ReA, and USpA). AS-WIS scores in AS were also significantly higher than in PsA ($p<0.01$). Higher AS-WIS were significantly associated with female gender, an education level lower than university, higher tender joint count, higher tender and swollen joint count, higher damaged total joint count, current NSAID use, current biologic use, history of GI disease, history of CNS disease, and history of peripheral arthritis, enthesitis or dactylitis. Current NSAID use and current biologic use was not correlated. Multinomial logistic regression showed that the groups at the highest risk of WI were those with NSAID use[D4] and a history of peripheral arthritis[IDR5] , enthesitis and dactylitis.
**Conclusion:** In this cohort of SpA, WI was low overall. PsA was found to have significantly lower WI than any subset of ax-SpA, however, in this cohort, PsA was well controlled with low joint counts, which may have impacted the WIS scores. Presence of peripheral involvement (arthritis, dactylitis, enthesitis) increased WI. NSAID use was associated with higher WI, which may represent confounding by indication.

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**Comparative Effectiveness of Secukinumab and Adalimumab in Ankylosing Spondylitis as Assessed by Matching-Adjusted Indirect Comparison: An Analysis Based on Pivotal Phase 3 Clinical Trial Data**

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**Objectives:** Secukinumab (SEC) and adalimumab (ADA) are approved for the treatment of active AS. Although there are no head-to-head randomized controlled trials between SEC and ADA, matching-adjusted indirect comparison (MAIC) can be used to generate comparative effectiveness data. MAIC adjusts for differences in baseline characteristics by using individual patient data (IPD) from trials of one treatment to match the population of a different therapy arm of another trial. This MAIC aimed to assess the relative effectiveness of SEC and ADA in patients with active AS.
**Methods:** IPD from the pooled SEC 150 mg arms of MEASURE 1 (n=125) and MEASURE 2 (n=72) were weighted to match the baseline characteristics of the ADA 40 mg arm of ATLAS (n=208); placebo arms were also matched. Weights for age, sex, BASFI, CRP and previous anti-TNF therapy were determined. Recalculated SEC outcomes were compared with aggregated

ADA data at weeks 12, 16, 24 and 52. Comparisons up to week 12 were placebo adjusted because patients receiving placebo in ATLAS could switch to open label ADA after this time (placebo switchers). Imputation methods for missing data were matched between trials. NRI was available for all binary outcome data except ADA at week 52, which was LOCF only and included placebo switchers. This was matched by including placebo switchers for SEC at week 52.

**Results:** At week 12 there were no significant differences in placebo-adjusted ASAS response rates (responses) between SEC (effective sample size [ESS]=120; placebo ESS=120) and ADA. At week 16, there was a higher ASAS 20 non-placebo-adjusted response for SEC relative to ADA (OR [95% CI]: 1.60 [1.01–2.54], p=0.047). At week 24, there were higher ASAS 20 and 40 non-placebo-adjusted responses for SEC relative to ADA (OR: 1.76 [1.11–2.79], p=0.017 and OR: 1.79 [1.14–2.82], p=0.012, respectively). At week 52, there were higher ASAS 20 and 40 non-placebo-adjusted responses for SEC relative to ADA (OR: 1.48 [0.98–2.22], p=0.062 and OR: 1.54 [1.06–2.23], p=0.023, respectively). A sensitivity analysis that included BASDAI score in the baseline matching showed similar findings.

**Conclusion:** There were comparable placebo-adjusted ASAS responses at week 12 between treatments. Secukinumab was associated with higher (non-placebo-adjusted) ASAS 20 responses at weeks 16, 24 and 52 and ASAS 40 responses at weeks 24 and 52 relative to adalimumab. Substantial switching of placebo patients to adalimumab in ATLAS precluded placebo-adjusted analysis beyond week 12. This exploratory analysis requires confirmation by a head-to-head trial.

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## Association between Structural Lesions in the Sacroiliac Joints and Spinal Inflammatory Lesions in Patients with Non-radiographic Axial Spondyloarthritis

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**Objectives:** The relevance of structural lesions in non-radiographic axial SpA (nr-axSpA) is unclear, particularly without signs of MRI inflammation. In a post hoc analysis we evaluated the association between structural lesions in the sacroiliac joints (SIJ) and spinal inflammatory lesions on MRI in nr-axSpA. We hypothesized that, in nr-axSpA patients, structural lesions indicate a more dynamic disease phenotype that includes early spinal involvement visible on MRI.

**Methods:** EMBARK (ClinicalTrials.gov: NCT01258738) enrolled patients 18-49 years-old with axial SpA per ASAS criteria without meeting modified NY radiographic criteria, symptoms >3 months and <5 yrs, BASDAI score ≥4, and had failed ≥2 NSAIDs. Bone marrow edema (BME) in the SIJ and spine at baseline was assessed on short tau inversion recovery (STIR) scans by 2 independent readers using Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ and 23-discovertebral unit (DVU) scores, respectively. Baseline structural lesions were evaluated on T1 weighted scans blinded to STIR scans, using the SPARCC MRI SIJ structural score (SSS). Univariate analysis evaluated the relationship between spinal inflammation and these baseline characteristics: gender, presence/absence of any structural MRI lesions in the SIJ (SSS>0 or =0), presence/absence of specific MRI SIJ structural lesions, and SPARCC SIJ ≥2 or <2. Multivariate stepwise regression analysis evaluated the relationship between spinal inflammation and MRI

SIJ lesions after including age, gender, and symptom duration.
**Results:** MRI scans were available for 185 patients. Mean (SD) age was 32.0 (7.8) years, 60.5% were male, symptom duration was 2.4 (1.8) years, 133/182 (71.9%) patients were HLA B27+ and 152 (82.2%) met ASAS MRI imaging criteria. Mean (SD) SPARCC MRI 23-DVU spinal score was 4.0 (8.0); 128/183 (69.9%) patients had SPARCC SIJ BME scores ≥2 and 55/183 (30.1%) had scores <2. A total of 77/185 (41.6%) patients had ≥1 structural lesion on MRI: erosion (65/185, 35.1%), backfill (26/185, 14.1%), fat metaplasia (15/185, 8.1%) and ankylosis (4/185, 2.2%). Mean spine 23-DVU scores were higher in males vs females (5.5 vs 2.4, p=0.06); in the presence of SIJ inflammation (SPARCC SIJ ≥2 vs <2, 5.1 vs 2.4, p=0.01); and with SIJ structural lesions (lesions >0 vs =0, 6.3 vs 3.0, p=0.08). On multivariate analysis, erosion and backfill were independently associated with spinal inflammation; parameter estimates (SE): erosion: 2.9 (1.3), p=0.03; backfill: 3.9 (1.8), p=0.03.
**Conclusion:** MRI structural lesions in the SIJ occur in a substantial proportion of patients with nr-axSpA, suggesting a more dynamic phenotype of disease associated with early spinal involvement.

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**Prediction of Joint Damage Progression and Flare after Adalimumab Discontinuation**

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**Objectives:** The HONOR study was designed to investigate the possibility of patients discontinuing adalimumab (ADA) therapy for 1 year without flaring (DAS28-ESR ≥3.2). 14-3-3η is a mechanistic serum marker that is modifiable over the disease course, does not correlate with CRP and is a predictor of radiographic progression even in patients who achieve clinical remission. In this study, serum 14-3-3η was investigated as a predictor of joint damage and flares in the HONOR cohort
**Methods:** Serum 14-3-3η levels were measured in 62 Japanese patients, 51 of which were from the HONOR study at baseline, 1-year after treatment initiation, at discontinuation and at the time of flare. Of the 62 patients, 46 (74%) patients achieved sustained drug-free remission up to 1 year following ADA discontinuation. SHS scores were available at therapy initiation, discontinuation, and at 52 weeks. Relationships between continuous variables were assessed using uni- and multi-variable Gaussian linear regression models and logistic regression.
**Results:** At baseline and discontinuation, median (QR) 14-3-3η levels were 0.28 ng/ml (0.07-2.11) and 0.22 ng/ml (0.04-1.28) respectively, with 26 (59%) of 44 and 29 (54%) of 54 patients being positive (≥0.19 ng/ml) at the corresponding time-points. Paired t-test revealed that levels of 14-3-3η were significantly different between baseline and discontinuation, p=0.030. Level of 14-3-3η at baseline was positively associated with SHS at 12 months and at the time of flare, p=0.038. Bivariable modeling revealed that baseline 14-3-3η together with the change in 14-3-3η had a significant interacting effect on SHS at 12 months and the time of flare, p=0.02. Higher baseline 14-3-3η levels together with an increase in levels at the time of discontinuation was strongly associated with an increased SHS. Adding CRP, flare, sustained remission through 12 months, MTX dose at initiation and at ADA discontinuation did not improve predictive effects of 14-3-3η with SHS. Baseline 14-3-3η levels alone was not associated with flares at 12 months (p=0.15) however when combined with CRP, a significant interaction was present (p=0.03).

Specifically, patients with a low CRP, and a high 14-3-3η level had a higher likelihood of flaring versus those with a low 14-3-3η, 22% versus 12%.
**Conclusion:** Baseline 14-3-3η and increases in its levels are associated with worse radiographic outcomes in patients who achieve clinical remission and discontinue ADA. To reduce the risk of flare in patients who are candidates for discontinuation of ADA, CRP and 14-3-3η measurements should be considered in combination as markers of flare prediction.

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**Systemic Illness in a Patient with Palindromic Rheumatism**

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Occasional in rheumatology we encounter cases where an unfortunate patient is experiencing suffering and morbidity, or even multisystem failure, and the cause remains elusive even after exhaustive evaluation by numerous specialist services. We present the case of a 57-year-old Caucasian gentleman who presented to rheumatology with intermittent migratory arthritis and a positive ACPA in 2012. He was diagnosed as having classic palindromic rheumatism, and was managed with hydroxycholorquine with good effect. He subsequently developed weight loss, profound malaise, diffuse lymphadenopathy and progressive pedal edema. Echocardiography showed moderate to severe aortic, mitral and triscuspid regurgitation. He continued to lose lean body weight and decline in his functional status, and was recurrently hospitalized for heart failure. The etiology of his systemic disease remained obscure despite thorough assessments from multiple services, including our own. A cardiac valve specimen tested positive for Tropheryma whipplei. Appropriate antibiotics were initiated, and the patient began to improve. Whipple's disease has known systemic, cardiac, musculoskeletal, gastrointestinal and neurologic manifestations, several of which were present in this patient. Whipple's disease needs to be included in the differential diagnosis of patients with systemic disease with any of these manifestations, especially if the disease is chronic, severe and the diagnosis remains elusive.

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**An Unusual Case of Refractory, Seronegative, Rheumatoid Arthritis in a Gentleman with New Onset Gastrointestinal Symptoms**

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Herein we describe the case of a 69-year-old male with a recent history of resected thyroid cancer and a 10-year history of seronegative, refractory, rheumatoid arthritis affecting the neck, shoulders, wrists, MCPs, and ankles. He was maintained on methotrexate, hydroxychloroquine, low-dose prednisone, and intramuscular gold, having failed various mono and combination therapies previously. He presented to hospital with a 3-month history of odynophagia, abdominal pain, and unintentional weight loss. This was associated with subjective worsening of his small and large joint arthritis. Prior to presentation, he reported one episode of coffee ground emesis, however, he was found to be hemodynamically stable in the ER. His examination revealed a cachectic gentleman with lymphadenopathy in the axillae and clubbing of the fingers. He had mild ulnar deviation at the MCPs and decreased range of motion of the neck, wrists, and ankles. There was no evidence of active synovitis. He had evidence of

hyperpigmentation over the forehead and forearms. His investigations demonstrated a microcytic anemia, a creatinine of 116µmol/L, an INR of 1.4, and a CRP of 89mg/L. His immunologic profile was negative for RF, anti-CCP, and 14-3-3η, and ANA. Blood cultures, Hepatitis, and HIV testing were negative. Previous radiographs showed degenerative changes in the ankles, right midfoot and bilateral hands. A CT scan of the chest, abdomen and pelvis demonstrated mild mediastinal and mesenteric lymphadenopathy. A trans-thoracic echocardiogram was negative. He underwent an upper endoscopy which demonstrated upper and lower esophageal rings, active duodenitis, and foamy histiocytes. He was H. Pylori positive with PAS/D staining positive despite negative AFB staining. This was consistent with Tropheryma Whipplei, the pathogenic organism of Whipple's disease. Ultrasound-guided joint aspiration was unsuccessful. He was therefore initiated on intravenous ceftriaxone and transitioned to oral sulfamethoxazole and trimethoprim with complete resolution of his gastrointestinal, constitutional, and musculoskeletal complaints.
**Conclusion:** Whipple's disease is a rare but curable mimic of rheumatoid arthritis in which musculoskeletal complaints may predate the onset of gastrointestinal symptoms. This entity should be considered in the differential for atypical or refractory arthritis.

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**Characterization of Indigenous Community Engagement in Arthritis Studies: A Systematic Review of the Literature**

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**Objectives:** To characterize descriptions of Indigenous community engagement (CE) in rheumatology studies conducted in Canada, Australia, New Zealand and the USA.
**Methods:** We performed a large systematic review (MEDLINE, EMBASE, CINAHL and Indigenous-specific online indexes up to May 2016) to characterize the epidemiology, clinical outcomes, mortality and health services utilization for arthritis in Indigenous populations of the four countries (n=5,269 titles and abstracts). A total of 159 studies were ultimately identified to meet inclusion criteria for the relevant outcomes. These studies were then evaluated for descriptions of CE at inception of research, data collection, and interpretation of results. Extraction was performed in duplicate using a standardized checklist. Descriptions were subsequently mapped onto a CE spectrum, and ranked as having either informed, consulted, involved, collaborated or empowered the Indigenous population under study.
**Results:** Only 30.8% (n=49/159) of identified studies reported any description of CE. Specifically, 30.2% (n=48) demonstrated evidence for CE during the data collection stage, in contrast to only 6.3% (n=10) during inception of research and 6.3% (n=10) during interpretation of results. At inception of research, 5 studies informed and/or involved the community, and 5 collaborated with the population of interest. Thirty-two out of the 48 studies (66%) that described CE at the data collection stage reported informing and/or consulting the Indigenous community, and 16 (33%) reported involving and/or collaborating with the population. At the stage of interpretation of results, 2 studies were ranked as having informed and 3 studies were ranked as having involved the community, and 5 studies collaborated and/or empowered the Indigenous population. A temporal analysis showed a general increase in the frequency of CE reporting over time except for the data collection stage, which had a notable decline from 1996 onwards.
**Conclusion:** The reporting of CE in Indigenous arthritis studies in the specified countries is still

limited in frequency, and heavily skewed towards the lower end of the CE spectrum (i.e. informing and consulting the community). CE was most frequently reported during the data collection stage and is mostly described at the consultation level of the CE spectrum, which can be reached by merely obtaining individual informed consent, reflecting more of the researchers' adherence to ethical guidelines than collective engagement. The decline in CE reporting during the data collection stage is likely reflective of a recent emphasis on database-derived epidemiological studies, for which CE has not been reported or required.

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**The Association between Sonographic Enthesitis and Radiographic Joint Damage in Psoriatic Arthritis**

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**Objectives:** Enthesitis is a common clinical finding and a key pathogenic feature in psoriatic arthritis (PsA). Ultrasound is emerging as a preferred method to assess enthesitis. Little is known about the relation between the presence of enthesitis and the severity of joint damage in patients with PsA. Our objective was to examine the association between sonographic enthesitis and the severity of radiographic features of damage in the peripheral and axial joints in PsA.

**Methods:** A cross-sectional study was conducted in consecutive patients with PsA. The MAdrid Sonography Enthesitis Index (MASEI) scoring system was used to quantify the extent of sonographic entheseal abnormalities in 12 entheseal sites. Total MASEI was further categorized into: bone scores (enthesophytes, erosions) and soft tissue scores (structural changes, vascularization, bursitis). Radiographic joint damage in the peripheral joints and spine was assessed independently of the ultrasound results using the modified Steinbrocker score, Modified New York Criteria for sacroiliitis and the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). Additionally, the presence of ankylosis, arthritis mutilans and periostitis in the hands or feet was determined. Linear and logistic regression models were used to assess the association between MASEI score and the radiographic features of joint damage after controlling for age, sex, BMI, PsA duration and the use of DMARDs and biologic medications.

**Results:** 222 patients were included (58% men) with mean (s.d.) age of 55.9 (12.9) years and PsA duration of 16.7 (12.4) years. The mean MASEI score was 15.6 (12.6). The mean modified Steinbrocker score was 18.1 (32.3), mSASSS was 1.7 (7.3) and 37% had sacroiliitis. Multivariate regression analyses found an association between higher MASEI scores and peripheral joint damage: modified Steinbrocker score (β 9.26, $p<0.0001$), joint ankylosis (Odds Ration (OR) 2.09, $p=0.0001$) and arthritis mutilans (OR 1.73, $p=0.005$). The association between MASEI scores and periostitis was of borderline statistical significance (OR 1.29, $p=0.06$). Similarly, an association was found in multivariate analyses between higher MASEI scores and axial damage as measured by mSASSS (β 1.55, $p=<0.0001$) and sacroiliitis (OR 1.36, $p=0.02$). Sub-analysis showed that the MASEI bone score were more strongly associated with radiographic damage outcomes than the MASEI soft tissue score.

**Conclusion:** The severity of sonographic enthesitis is a marker of radiographic peripheral and axial joint damage in PsA. The association was found with both erosive and bone formation lesions. These findings highlight the potential role of enthesitis in the pathogenesis of articular damage in PsA.

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**Real-World Efficacy of Anti-TNF in Psoriatic Arthritis Patients with Enthesitis and Correlation of Enthesitis with Tender / Swollen Joints**

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**Objectives:** Previous studies have shown that psoriatic arthritis (PsA) patients with enthesitis present with increased disease activity compared to patients without. The aims of this analysis were (1) to evaluate the effectiveness of anti-TNF agents in PsA patients with enthesitis at baseline treated in a Canadian routine clinical practice setting, (2) to explore the relative localization of enthesitis and joint swelling/tenderness, and (3) to determine which of these conditions (swollen joints or enthesites) is more taken into account by physicians in a routine practice.

**Methods:** BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab (IFX), golimumab (GLM), or ustekinumab (UST). In this analysis, PsA patients treated with IFX between 2005-2016 or GLM between 2010-2016, who had available enthesitis information at baseline were included. For the comparison of the co-localization of enthesitis and joint involvement in the shoulders, elbows and knees the independent-samples t-test was used. Improvements over time in continuous variables were assessed for statistical significance with the paired t-test. Correlation between swollen joints, enthesitis count and physician global was assessed with Spearman's coefficient (rs).

**Results:** A total of 202 PsA patients were included with a mean (SD) age of 50.6 (11.8) years and disease duration of 5.6 (7.4) years. At baseline, mean (SD) DAS28 was 4.4 (1.4), HAQ was 1.1 (0.66) and 28-swollen joint count (SJC28) was 5.2 (4.5). Enthesitis was present in 52.5% of patients while 8.9% had enthesitis and one swollen joint count or fewer. Joint tenderness and swelling was significantly ($P<0.05$) higher in all anatomical sites (shoulders, elbows, and knees) with enthesitis with the exception of the right knee and the right shoulder where joint involvement was higher without achieving statistical significance. In correlation analysis, SJC28 showed a strong correlation (rs=0.643) with physician global (MDGA) compared to enthesitis count where a moderate correlation (rs=0.406) was observed with MDGA. Among those patients with baseline enthesitis statistically significant and clinically meaningful improvements were observed in DAS28 ($P=0.014$), SJC28 ($P=0.001$), TJC28 ($P<0.001$), physician global ($P<0.001$), and enthesitis count ($P<0.001$).

**Conclusion:** A high prevalence of enthesitis was observed at anti-TNF treatment initiation (52.5%). Joint tenderness and swelling coincided with the entheseal points suggesting localized inflammation. However, physicians were found to take swollen joints more into account than the presence of enthesitis in routine practice. Treatment with IFX or GLM for 6 months was associated with a significant reduction in both enthesitis and clinical and patient outcomes.

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**Gene Expression in Cellular Subsets in Psoriatic Disease**

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Toronto)

**Objectives:** Psoriatic arthritis is an inflammatory musculoskeletal disease which develops in 30% of patients with psoriasis. Our previous peripheral blood microarray study identified CXCL10, NOTCH2NL, HAT1, and SETD2 as differentially expressed between PsA and psoriasis patients without arthritis (PsC). This study aimed to determine gene expression in leukocyte subsets to elucidate their functions in psoriatic disease.

**Methods:** Peripheral blood mononuclear cells were isolated using Ficoll paque separation from PsA and PsC patients not receiving biologic therapy and healthy controls (HC). T cells (CD3+), monocytes (CD14+), and NK cells (CD56+) were separated by positive selection. mRNA was extracted using RNeasy miniprep kits and qPCR performed with 75ng mRNA to determine CXCL10, CXCR3, NOTCH2NL, IL-17A, HAT1, and SETD2 gene expression. A two-way ANOVA with Bonferroni's post-hoc test was used to determine significant differences ($p<0.05$).

**Results:** Gene expression was measured in 15 PsA (mean age 59, 60% males), 15 PsC (mean age 57, 67% males), and HC (mean age 54, 60% males). Expression of IL-17A in monocytes was 18.42-fold greater in PsA patients than PsC ($p<0.0001$) and 31.36-fold greater in PsA than HCs ($p<0.0001$). There were no other significant differences in gene expression between disease groups in each given cell type. However, in T cells, CXCL10 was elevated in PsA compared to PsC (1.42-fold) and HC (2.47-fold). A similar trend was found for the receptor, CXCR3, where expression was higher in PsA than PsC (1.18-fold) and HC (1.13-fold). Finally, SETD2 expression in PsA was higher than PsC (1.65-fold) and HC (1.28-fold) in T cells. CXCL10 expression in monocytes ($p<0.0001$; 11.1-fold) and NK cells ($p<0.0001$; 2.04-fold) was higher than in T cells. Expression of CXCR3 was higher in T cells compared to monocytes ($p<0.0001$; 208.17-fold) and NK-cells ($p<0.0001$; 1.3-fold). HAT1 was more highly expressed in T cells as compared to monocytes ($p=0.0003$; 3.41-fold) and NK cells ($p=0.0274$; 1.48-fold). Expression of SETD2 was elevated in T cells compared to monocytes ($p=0.0007$; 3.2-fold) and NK cells ($p=0.0082$; 1.22-fold). NOTCH2NL expression was elevated in T cells compared to monocytes ($p=0.0154$; 2.43-fold).

**Conclusion:** Genes of interest were differentially expressed in leukocyte subsets. The higher expression of these genes in PsA compared to PsC and HCs could provide insight into their role in driving the development of PsA. Knowing which cell types are predominantly involved with expression of certain biomarkers will aid in developing targeted treatments.

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**Depression Increases the Risk of Psoriatic Arthritis among Patients with Psoriasis: A Population-based Study**

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**Objectives:** The factors that contribute to the development of psoriatic arthritis (PsA) among patients with psoriasis are not well known; however, systemic inflammation is believed to play a role in disease severity. Major depressive disorder (MDD), has recently been associated with increased systemic inflammation, independent of underlying inflammatory disease, and it is well known that both psoriasis and PsA are associated with an increased risk of developing MDD. Our objective was to determine if MDD confers an independent risk towards the development of

PsA among patients with psoriasis.
**Methods:** We conducted a population-based cohort study from 1987 to 2012 with up to 25 year follow-up using The Health Improvement Network (THIN), a primary care medical records database representing 5% of the United Kingdom's population. Individuals with incident psoriasis were identified in THIN. Only those age 20-90 and without history of MDD or PsA were included, yielding a sample of 73,447 patients with psoriasis. Covariates identified at the time of psoriasis diagnosis included age, sex, medical comorbidities, socioeconomic status, obesity, smoking status and alcohol use. Psoriasis severity was also determined for each patient, with moderate-severe psoriasis defined by use of systemic therapy. The primary exposure was development of incident MDD. The primary outcome was development of PsA.
**Results:** Of the 73,447 cases of psoriasis identified, 5216 (7.1%) developed MDD. Among all psoriasis patients, 1466 (2.0%) developed PsA. Cox proportional-hazards models were used to estimate the hazard ratio (HR) for the development of PsA, accounting for all covariates. There was no evidence for effect modification by any of the covariates using a likelihood ratio test (p=0.387). MDD significantly increased the risk of developing PsA among patients with psoriasis when adjustments were made for all covariates (HR 1.37, 95%CI 1.05 to 1.80, p=0.021). This finding remained significant through numerous sensitivity analyses.
**Conclusion:** Among individuals with psoriasis, MDD significantly increased the risk of developing PsA. Heightened screening for and management of MDD among psoriasis patients seems warranted. MDD should be explored further in the context of inflammation and its role in instigating systemic inflammatory disorders.

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**The Relationship between the Patient Acceptable Symptom State (PASS) and Disease Activity in Patients with Psoriatic Arthritis (PsA)**

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**Objectives:** PASS is the highest level of symptoms beyond which patients consider themselves well. Psoriatic Arthritis Disease Activity Score (PASDAS) is a recently developed composite disease activity measure that summarizes a patient's disease in a single 0-10 score. In this study, we aimed to identify the PASDAS cut-off points for PASS, and to examine the agreement between PASS and the PASDAS thresholds for low (<3.2), moderate (3.2-5.4), and high disease activity (>5.4).
**Methods:** Patients were prospectively recruited from the University of Toronto PsA clinic. A standard protocol including physician assessment and patient-reported outcomes was used to record variables required to calculate PASDAS. In addition, each patient was asked to "think about all the ways your PsA has affected you during the last 48 hours. If you were to remain in the next few months as you were during the last 48 hours, would this be acceptable to you?" to assess PASS. For analysis, the PASDAS threshold for PASS was identified with the ROC analysis to maximize specificity and sensitivity. Furthermore, the agreement between PASS and low, moderate, and high PASDAS disease activity cut-offs were evaluated.
**Results:** 169 patients [61% male, mean age 56.1, mean disease duration 16.9 years, mean (SD) PASDAS 3.25 (1.1)] were recruited. The PASDAS threshold for the patient acceptable symptoms state (PASS+) was identified to be 3.84 (AUC – 0.88, sensitivity 0.82, specificity 0.94) using ROC analysis. 91% of patients with low disease activity (PASDAS <3.2) considered

their symptoms state acceptable (PASS+), and 100% of the patients with high disease activity (PASDAS >5.4) considered their symptom state as unacceptable (PASS-). Furthermore, the mean (SD) PASDAS was 4.5 (1.0) in the PASS- group and 2.8 (1.1) in the PASS+ group.
**Conclusion:** The PASDAS threshold for patient acceptable symptoms state is 3.84, which is within the moderate disease activity range. This means, with a PASDAS of 3.84 or lower, PsA patients consider their symptom state acceptable. This cut-off should be considered for shared decision making regarding treatments in PsA patients.

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**Comparison of Baseline Characteristics of Psoriatic Arthritis Patients Initiating Therapy with Subcutaneous Golimumab or Ustekinumab: An Analysis from a Prospective, Observational Registry**

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**Objectives:** The selection of initial biologic therapy in psoriatic arthritis (PsA) patients is based on baseline patient demographics and disease parameters, though physician and patient preference may further impact this choice. Health Canada's approval of ustekinumab (UST) in 2014 increased the armamentarium of biologic therapies for the treatment of active PsA in Canada. The aim of this analysis was to compare baseline characteristics of PsA patients initiating subcutaneous golimumab (GLM) and UST.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or GLM for PsA, rheumatoid arthritis or ankylosing spondylitis, or with UST for PsA. PsA patients enrolled between June 2014 and April 2016 were included in the analysis. Differences in continuous variables were assessed for statistical significance with the Wilcoxon Rank Sum test, and differences in categorical variables with the chi-square test.
**Results:** A total of 121 PsA patients were included in the analysis, of whom 81 (66.9%) were treated with GLM and 40 (33.1%) with UST all of whom were bio-naive. At baseline, the mean (SD) age was 52.1 (12.7), disease duration was 6.1 (8.3) years, and the majority of patients (61.9%) were female, without any significant differences between treatments. A significantly higher proportion of patients who initiated UST resided in Western Canadian provinces as compared to other territories (GLM: 10.0%, UST: 33.3%; p=0.007). Higher disease activity was generally observed among GLM patients, as illustrated by significantly higher mean (SD) swollen joint count [GLM: 5.8 (4.4), UST: 4.1 (4.0); p=0.034] and DAS28 [4.4 (1.3) vs. 3.8 (1.1); P=0.040], as well as statistical trends in regard to mean (SD) tender joint count [7.6 (6.4) vs. 5.8 (5.4); P=0.146] and MDGA [5.60 (1.93) vs. 4.73 (2.35); P=0.059]. However, patients initiating UST had significantly higher mean (SD) PASI scores [GLM: 2.79 (5.24), UST: 5.53 (7.73); p=0.003] and a marginally higher proportion of UST patients presented with distal interphalangeal joint arthritis (GLM: 27.6%, UST: 44.1%; p=0.116) at baseline.
**Conclusion:** The results of this analysis show that differences exist in the baseline profile of PsA patients initiating different biologic agents suggesting channeling bias. Further analyses with larger patient populations are necessary to further validate this.

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**Do Specific Entheseal Points in SpA Patients Impact Patient Reported Outcomes? Implications for Clinical Practice**

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**Objectives:** To describe the impact of enthesitis count and enthesitis profile on functional status (HAQ) and patient global assessment of disease activity (PtGA) among SpA patients treated with anti-TNFs under Canadian routine clinical care.

**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab (IFX) or golimumab (GLM) for RA, AS, or PsA, or with ustekinumab (UST) for PsA. In this analysis, AS and PsA patients treated with IFX between 2005-2016 or GLM between 2010-2016, and PsA patients treated with UST between 2014-2016, were included. Based on enthesitis location 8 groups were created: supraspsinatus, medial epicondyle humerus, lateral epinondyle humerus, greater trochanter, quadriceps patella, Achilles, plantar fascia, and patellar-tibia. The impact of specific entheseal points on HAQ, PtGA, and pain (only for PsA) was assessed with the independent-samples t-test; general linear models were used to assess the relative impact of each location on these outcomes.

**Results:** 503 AS patients and 330 PsA patients with 1669 and 1126 assessments, respectively, were included. At baseline, mean (SD) age was 45.4 (13.0) and 51.0 (12.3) years for AS and PsA patients, respectively, and disease duration was 6.6 (9.6) and 5.4 (7.1) years. In terms of disease activity, mean (SD) ASDAS and BASDAI were 3.5 (1.0) and 6.1 (2.2), respectively, whereas, among PsA patients, DAS28 was 4.3 (1.4). Overall, a weak correlation ($r<0.4$) was observed between enthesitis count and HAQ, PtGA and pain in both AS and PsA patients. Presence of enthesitis at all sites, however, was associated with significantly ($P<0.05$) higher HAQ and PtGA irrespective of SpA type. Upon adjusting for age and gender, among AS patients, enthesitis at supraspinatus, greater trochanter, and Achilles were the main predictors of higher HAQ and PtGA whereas enthesitis at plantar fascia was associated with higher HAQ only. Among PsA patients, medial or lateral epicondyle humerus and greater trochanter were the main predictors of increased HAQ and PtGA, while patellar/tibia was associated with significantly HAQ only.

**Conclusion:** Although enthesitis at all sites was associated with significantly higher HAQ and PtGA, individual sites were differentially associated with these outcomes. In AS, supraspinatus, greater trochanter, and Achilles were identified as the main predictors of poor patient outcomes, while, among PsA patients, medial/lateral epicondyle humerus and greater trochanter were the most important sites. These results suggest that, in addition to the presence of enthesitis, location of enthesitis may have an impact on patient reported outcomes.

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**Disease Progression Among Non-Achievers of Minimal Disease Activity in PsA Patients Treated with Infliximab or Golimumab**

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**Objectives:** Early achievement of minimal disease activity (MDA) is recommended as a valid treat-to-target approach in psoriatic arthritis (PsA). The purpose of the current analysis was to evaluate disease progression in PsA patients among non-achievers of MDA treated with anti-TNF agents under Canadian routine practice.

**Methods:** Biologic Treatment Registry Across Canada (BioTRAC) is an ongoing, prospective registry of patients initiating treatment for rheumatoid arthritis, ankylosing spondylitis, or PsA with Infliximab (IFX) or Golimumab (GLM), or with ustekinumab (UST) for PsA. Eligible people for this analysis included PsA patients treated with IFX who were enrolled since 2005 or with GLM enrolled since 2010 or with UST enrolled since 2014 and with available MDA information at 6 and 12 months of treatment. MDA was defined as the fulfillment of ≥5 of the following criteria: TJC28≤1, SJC28≤1, PASI≤1 or BSA≤3, Pain (VAS)≤15mm, PtGA (VAS)≤20mm, HAQ ≤0.5, tender entheseal points ≤1. Pairwise comparisons in disease parameters were assessed with the non-parametric Wilcoxon test. Variables associated with improved DAS28 and MDA achievement were examined using general linear models and logistic regression, respectively, wherein variables showing a statistical trend (P<0.150) in univariate analysis were considered in multivariate analysis to identify predictors.

**Results:** A total of 106 patients (55.2% male and 88.7% bio-naïve) were included with a mean (SD) age and disease duration of 49.6 (11.4) and 5.6 (6.9) years, respectively. The proportion of patients who achieved MDA at 6 months was 49.1% (n=52) while 50.9% (n=54) did not achieve MDA. Among patients with MDA at 6 months, 75.0% had sustained MDA at 12 months and among the non-achievers, 14.8% achieved MDA at 12 months of treatment. No statistically significant changes were observed between 6 and 12 months in disease parameters among the non-MDA achievers. Multivariate logistic regression analysis showed MDA achievement at 6 months was associated with higher odds (OR=12.604; P<0.001) of MDA achievement at 12 months of treatment and a trend for lower baseline HAQ (OR=0.459, P=0.071). Multivariate general linear models showed that MDA achievement at 6 months (B=-0.770, P=0.042) and being bio-naïve (B=-2.296, P=0.001) were significant predictors of DAS28 improvement at 12 months of treatment.

**Conclusion:** The results of the current analysis have shown that achievement of MDA at 6 months is critical for MDA achievement/maintenance at 12 months highlighting the importance of intensive treatment early on. Furthermore, these results highlight the importance of treatment optimization in cases where MDA is not achieved.

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## Articular and Axial Involvement Differences in Psoriatic Arthritis Patients Treated with Golimumab in Canadian Real-World Practice

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Toronto); Cathy Tkaczyk (Janssen Inc, Toronto); Brendan Osborne (Janssen Inc, Toronto)
**Objectives:** Psoriatic arthritis (PsA) is a complex rheumatic disease with severity that ranges from mild to severe. The mild form of PsA can be referred to as oligoarticular (OLIGO), whereas more severe cases are considered polyarticular (POLY) form. Furthermore, peripheral joint and axial involvement are also recognized in PsA. This analysis examined OLIGO vs. POLY differences and presence of axial involvement at initiation of golimumab (GLM) for the treatment of PsA in a Canadian routine clinical practice setting.
**Methods:** Biologic Treatment Registry Across Canada (BioTRAC) is an ongoing, prospective registry of patients initiating treatment for inflammatory arthritis with Infliximab, GLM, or ustekinumab. PsA patients treated with GLM who were enrolled since 2010 were eligible for the analysis. OLIGO involvement was defined as (≤2 SJC) and POLY (>2 SJC), while axial involvement included spinal symptoms or spondylitis with peripheral arthritis. Minimal disease activity (MDA) was defined as the fulfillment of ≥5 of the following criteria: TJC28≤1, SJC28≤1, PASI≤1 or BSA≤3, Pain (VAS)≤15mm, PtGA (VAS)≤20mm, HAQ ≤0.5, tender entheseal points ≤1.
**Results:** A total of 201 PsA patients were included in this analysis; 30.8% had oligoarthritis, 68.0% had polyarthritis, while 26.0% had axial involvement at baseline. Increased baseline disease activity was observed among patients with axial involvement for MDGA, PtGA, pain, and presence of enthesitis ($p<0.05$). Patients with polyarthritis were older, less likely to have been previously treated with a biologic, and had significantly ($p<0.05$) higher SJC28, TJC28, morning stiffness, MDGA, PtGA, pain, DAS28, HAQ, and enthesitis at GLM initiation. At 6 months, statistically significant between group differences were observed for MDA achievement. There were significantly lower proportions of patients achieving MDA among patients with axial involvement (26.7% vs. 61.8%, $p=0.020$) and polyarthritis (35.9% vs. 80.0%, $p<0.001$). Multivariate logistic regression analysis showed that patients with oligoarticular involvement (OR=3.92; $p=0.035$), younger age (OR=0.96; $p=0.051$), and lower baseline HAQ (OR=0.32; $p=0.007$) were associated with higher odds of MDA achievement at 6 months of treatment while axial involvement did not have a significant impact.
**Conclusion:** The results of the current analysis highlight that differences exist in the baseline patient profile based on the presence or absence of axial involvement and POLY involvement among PsA patients treated with GLM. Furthermore, OLIGO disease was identified as a significant independent predictor of MDA achievement with almost a four-fold higher likelihood of achieving target relative to patients with polyarthritis.

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**Impact of Concomitant Methotrexate Administration on the Risk of Infections among Rheumatoid Arthritis Patients Treated with Anti-TNF in Real-World**

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**Objectives:** Methotrexate (MTX) is routinely used among rheumatoid arthritis (RA) patients treated with anti-TNF agents to enhance treatment efficacy and minimize the dose of biologic therapy. The aim of this analysis was to evaluate the risk of infections among patients treated

with infliximab (IFX) or golimumab (GLM) in combination with MTX in the first 12 months following the start of biologic therapy.
**Methods:** BioTRAC is an ongoing, prospective registry of patients initiating treatment with infliximab or GLM for RA, ankylosing spondylitis, or psoriatic arthritis (PsA), or with ustekinumab for PsA. Eligible participants for this analysis included RA patients treated with IFX or GLM enrolled since 2002 and 2010, respectively, in combination or in monotherapy with MTX. Patients were excluded from the analysis if concomitant corticosteroids were used during any time point from baseline to 12 months of treatment. Serious and non-serious infections were assessed with the incidence density rate (IDR) as events /100 patient-years (PY). Poisson regression was used to compare the IDRs of infections between treatments while controlling for baseline disease activity and length of exposure to biologic treatment.
**Results:** A total of 526 RA patients were included in the analysis. At baseline, 71 (13.5%) were on anti-TNF monotherapy, while 109 (20.7%) were on combination therapy with MTX ≤15mg (low-moderate dose), and 346 (65.8%) with MTX>15mg (high dose). The vast majority (93.3%) of patients were bio-naïve, 73.4% were female, mean (SD) age was 55.7 (13.4) years and disease duration since diagnosis was 7.5 (8.3) years. A total of 163 (37.4 events/100 PY) infections were reported by 104 (19.8%) patients and a total of 10 (2.8 events/100 PY) serious infections. Specifically, the mean (95% CI) adjusted IDR was 23.9 (14.4-39.8) events/100 PY for monotherapy, 30.2 (21.4-42.7) events/100 PY for MTX low-moderate dose, and 30.5 (24.9-37.4) events/100 PY for MTX high dose. Furthermore, among patients treated with MTX, no association between use of other concomitant DMARDs in the treatment regimen and risk of infection was observed while adjusting for MTX dose with mean (95% CI) IDR of 33.6 (25.6-44.1) events/100 PY for DMARDs vs. 33.8 (25.2-45.3) events/100 PY for no DMARDs.
**Conclusion:** The results of this real-world observational study have shown that, overall, a low incidence of serious infections is observed with anti-TNF treatment. Concomitant use of MTX with anti-TNFs may be associated with a lower incidence of infections, possibly due to potentiation of lower dosing.

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## The HAQ Reversible and Irreversible Components Measuring Function in Rheumatoid Arthritis

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**Objectives:** To assess the reversible and irreversible components of RA physical function as measured by the HAQ in Canadian routine clinical practice.
**Methods:** BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab (IFX), golimumab (GLM), or ustekinumab. Eligible participants included RA patients treated with IFX since 2002 or with GLM since 2010, who had a baseline HAQ>0 and at least one follow-up assessment at SDAI, CDAI or DAS28 remission or low disease activity (LDA). HAQ scores at the time of remission or LDA represented the irreversible component of the disease functional limitation (residual HAQ score). The

reversibility of HAQ score was determined as the relative improvement in baseline HAQ at remission or LDA achievement; the fraction of HAQ irreversibility was calculated as the residual HAQ score divided by the maximum possible score. The correlation of disease duration with the HAQ irreversible component was described with the Pearson's r. Multivariate linear regressions adjusted for age, gender, anti-TNF, and baseline disease duration and HAQ score were performed to assess the impact of coverage type (private, public).
**Results:** 753 patients were included in this analysis (499 on IFX, 254 on GLM) with a baseline mean (SD) age of 56.4 (13.4) years, disease duration of 8.7 (9.3) years and HAQ score of 1.5 (0.7). 74.8% of patients were females. At treatment initiation, 356 (47.8%) and 289 (38.8%) patients were on public and private drug coverage, respectively. Variation in the reversibility of HAQ score was observed depending on target outcome used, with 44.8% reversibility reported based on DAS28 remission to 57.6% with SDAI remission and, from 33.1% based on CDAI-LDA to 36.4% with SDAI-LDA. Weak correlations between disease duration and HAQ irreversible component were observed for all target outcomes, varying from r=0.105 based on derived definition of remission to r=0.270 with CDAI remission and, from r=0.119 based on SDAI-LDA to r=0.202 with DAS28-LDA. Upon adjustment for potential confounders, patients on private insurance had significantly greater HAQ reversibility when assessed with SDAI remission (β= -27.39; P=0.029) and derived definition of remission (β= -17.94; P=0.036) than patients on public coverage. Coverage type did not impact the fraction of HAQ irreversibility and the irreversible component.
**Conclusion:** Patients on private insurance at treatment initiation have a greater reversibility of RA functional impairment than patients on public coverage. However, the type of coverage did not have an impact on irreversible components of the disease.

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**Predictors of Golimumab Retention among Patients with Rheumatoid Arthritis on Stable Treatment in Canadian Real-World Setting**

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**Objectives:** Previous studies have shown inherent differences between patients remaining on anti-TNF for long-term as opposed to short-term. The aim of this analysis was to identify independent predictors of retention in patients with rheumatoid arthritis (RA) that have been on stable treatment with golimumab (GLM) under Canadian routine practice.
**Methods:** BioTRAC is an ongoing, prospective registry of inflammatory arthritis patients initiating treatment with infliximab, GLM, GLM IV or ustekinumab. Eligible participants included RA patients enrolled since 2010 who were on stable treatment with GLM defined as a minimum follow-up of 2 years. Independent predictors of retention were assessed with multivariate cox regression. Receiver operator curve (ROC) analysis was used to determine the

optimal cut-off point of DAS28 for long-term retention.
**Results:** 118 RA patients were included with a mean (SD) follow-up of 36.4 (12.0) months. Mean (SD) age was 58.0 (14.9) years and disease duration was 8.2 (8.2) years. The majority of patients were biologic naïve (90.7%) and female (71%),. Mean (SD) CDAI score was 26.3 (16.6), SJC28 was 8.3 (6.6), and HAQ-DI was 1.24 (0.72). A total of 84% and 74% of patients were retained following 12 and 24 months, respectively. Only 24 patients were discontinued, the most common reason for discontinuation being loss of response (5.9%), loss to follow-up (4.2%), adverse event (4.2%), and consent withdrawal (3.5%). In univariate analysis, DAS28 at 24 months [HR (95% CI): 1.02 (0.98-1.06)] and DMARD use at 24 months [HR (95% CI): 0.21 (0.10-0.47)] were identified as potential predictors of retention on GLM. No significant impact or statistical trend ($P<0.150$) was observed for patient age, gender, disease duration at baseline, prior biologic experience, enrolment period, baseline DAS28, baseline DMARD and steroid use, and steroid use at 24 months. In multivariate analysis, DAS28 score at 24 months was the only significant ($P=0.049$) independent predictor of treatment retention [HR (95% CI): 1.43 (1.00-2.04)]. ROC analysis showed that maintaining a DAS28 score of 3.7 or less at 24 months was associated with optimal retention on treatment long-term.
**Conclusion:** Among RA patients on stable GLM treatment for 2 years, disease activity at 2 years is the single determinant of subsequent long-term retention, highlighting the importance of not only achieving disease targets as early as possible but also maintaining them over time. DMARD use at 24 months was also identified as a predictor of future retention on treatment, however, its effect was dependent on DAS28 levels.

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**Ultrasonographic Identification of Entheseal Findings in Psoriatic Arthritis Patients: Pilot Study**

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**Objectives:** Enthesitis frequently occurs in psoriatic arthritis (PsA) and can often be considered the earliest site of inflammation. Clinical examination of enthesitis can be challenging. Ultrasound could improve detection of enthesitis. However, there is no accepted score for assessment of ultrasonographic enthesitis in PsA. The objective of this study is to identify characteristics of entheseal sites among PsA individuals which will be used for subsequent development of ultrasound score for PsA patients.
**Methods:** The selection of entheseal sites for the study was based on: 1) Expert opinion of two rheumatologists experienced in musculoskeletal ultrasound in PsA (LE, GK); 2) Systematic literature review. A total of 28 entheseal sites in the upper and lower extremeties were assessed. Based on OMERACT definition for ultrasonographic enthesitis, the following features were assessed: structural changes (hypoechogenicity), thickness, bone erosion, enthesophytes, calcification, power Doppler signal, bursitis, tendon sheath widening and bone irregularities. Patients were recruited at Toronto Western Hospital PsA clinic during clinic visit. Ultrasound was conducted using MyLab 70XVG scanner equipped with a 6-18 MHz linear transducer. Scans were conducted by an expert rheumatologist (LE) and a rheumatology trainee (ST) and scored concurrently (LE and ST). The frequency of sonographic entheseal changes in each site was computed.
**Results:** In total, 11 PsA patients were scanned. Mean age was 62.2±8 years, 82% were males and mean disease duration was 23.2±8.5 years. The most commonly affected sites were quadriceps insertion (86%), plantar fascia (77%) and tibial tuberosity (73%). Soft tissue

abnormalities (structure and thickness) were most commonly found in the tibial tuberosity (72%), supraspinatus (67%) and MCL (50%). Power Doppler signal was most frequently found at the triceps (20%) and tibialis posterior (18%). Bony enthesophytes most frequently affected the quadriceps (86%) and the plantar fascia (72%) while bone erosions tended to affect the MCL (50%) and supraspinatus (67%).
**Conclusion:** We identified ultrasonographic abnormalities among PsA patients using previously studied and new entheseal sites. We will use these results to select fewer sites for scanning in our next phase of the study that will compare PsA and healthy controls to identify potential disease-specific findings.

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**Syndesmophytes in Axial Psoriatic Arthritis- Where Should we Start at Looking at?**

Sibel Aydin (University of Ottawa, Ottawa); Sibel Ureyen (University of Ottawa, Ottawa); Umut Kalyoncu (Hacettepe University, Ankara); PsART (Ottawa)

**Objectives:** We aimed to investigate the prevalence of syndesmophytes in cervical and lumbar spine in Psoriatic Arthritis (PsA) in comparison to sacroiliitis to provide a recommendation on where and how to start screening.
**Methods:** PsART (PsA Registry of Turkey) is a multicenter web-based registry where patients with PsA are consecutively recruited. Within 1195 PsA patients that were recruited between 2014-2016, 399 had radiographs of the spine (377 lumbar, 217 cervical spine and 195 had both) and were included. The sacroiliac joint radiographs could be compared to 113 patients for lumbar, 46 for cervical spine and in 115 patients for any of those. All radiographs were scored by one investigator, blinded to the clinical data. The sacroiliac joint and spine radiographs were scored independently. The comparisons were based on having at least one syndesmophyte in the spine and sacroiliitis fulfilling the modified New York (mNY) criteria.
**Results:** The percentage of patients having syndesmophyte was similar for cervical and lumbar spine (62/377 (16.4%) for lumbar and 38/217 for cervical spine (17.5%)). The presence of syndesmosphytes at both sites were significantly linked to each other: 29/195 patients (14.9%) were positive and 144/195 (73.9%) were negative for both sites. 22 patients (11.3%) had only syndesmophytes either at the cervical or lumbar spine, meaning asking for radiographs of both sites had value in these patients. Patients that fulfilled the mNY criteria had more frequent syndesmophytes in lumbar and cervical spine compared to patients that don't fulfil (Lumbar: 9/46 vs 3/67; cervical 9/24 vs 1/22; p=0.01 for both). Within patients that didn't fulfill the criteria, 4/69 (5.8 %) had syndesmophytes on the spine whereas 11/46 (23.9%) had syndesmophytes if they had sacroiliitis (p=0.009). Therefore only 4 in 115 patients had syndesmophytes despite not having significant sacroiliitis.216 of the patients were classified as having axial disease (54.1%). 57/71 (80.3%) of patients with syndesmophytes were classified as axial disease on the basis of clinical assessment, misclassifying 19.7 % of patients. This was higher in women as 12/39 (30.8%) had syndesmophytes and being classified as non–axial disease whereas 2/32 (4.3%) of men had silent disease.
**Conclusion:** Syndesmophytes are frequent in PsA. Axial disease can be underdiagnosed based on clinical assessments only, especially in women. Screening only the lumbar or cervical spine leads to underdiagnosing 11.3% of patients. Patients that has sacroiliitis fulfilling the mNY criteria significantly have more syndesmophytes, suggesting the role of spine imaging especially in these patients.

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**The Significance of Syndesmophytes in Psoriatic Arthritis and Risk Factors**

Sibel Aydin (University of Ottawa, Ottawa); Sibel Ureyen (University of Ottawa, Ottawa); Umut Kalyoncu (Hacettepe University, Ankara); PsART (Ottawa)
**Objectives:** Most of the knowledge on spine involvement in Psoriatic Arthritis (PsA) has been explorated from the ankylosing spondylitis data. In this study, we aimed to investigate the significance of syndesmophytes in PsA and associated risk factors. Since gender is an important prognostic factor in spine involvement, the analysis was also performed separately for women and men.
**Methods:** PsART is a multicenter web based registry where patients with PsA are consecutively recruited with the aim of investigating the real life data. Within the period of June 2014 and May 2016, 399 cases had radiographs of the spine and were included in this study (377 lumbar and 217 cervical spine radiographs and 195 patients had both). All radiographs were scored by one investigator, blinded to the clinical data. Patients with or without syndesmophytes were compared for demographics and disease features. Factors that were significant different in both groups were tested in multivariate analysis. Further comparisons were made to understand gender differences.
**Results:** Patients with syndesmophytes were older ($p<0.001$), had longer duration of PsA ($p=0.05$) and psoriasis ($p=0.007$), higher Leeds enthesitis index ($p=0.04$) and had higher BMIs ($p=0.03$). The presence of syndesmophytes was not associated with worse PROs as well as physician global assessment despite higher CRP values ($p=0.01$). Men tended to have more syndesmophytes than women (32/140 (22.9% vs 39/259 (15.1%); $p=0.056$). Patients that were using anti-TNF medications also had more syndesmophytes (27% vs 13.9%, $p=0.005$) Multivariate analysis showed that increased age ($p<0.001$), anti TNF exposure ($p=0.02$), Leeds enthesitis index ($p=0.001$), smoking (pack/years, $p=0.04$) and male sex ($p=0.002$) were linked to having syndesmophytes whereas CRP and BMI were not associated. Then analysis was done separately for women and men. For women, by using the same model, only age and Leeds enthesitis index were significantly contributing to the presence of syndesmophytes ($p=0.001$) and all the other parameters were found insignificant. In men age ($p=0.007$) and smoking ($p=0.03$) were the only contributors.
**Conclusion:** The risk factors for having syndesmophytes in PsA seem to differ in women and men such as enthesitis being more important in women and smoking in men, suggesting gender driven differences in pathogenesis. As this was a cross sectional study, it's not possible to provide a causative link with the parameters and syndesmophytes, such as anti-TNF exposure or high CRP.

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## Psoriasis Symptom Inventory (PSI) as a Patient-Reported Outcome in Mild Psoriasis: Real Life Data from a Large Psoriatic Arthritis Registry

Sibel Aydin (University of Ottawa, Ottawa); Sibel Ureyen (University of Ottawa, Ottawa); Umut Kalyoncu (Hacettepe University, Ankara); PsART (Ottawa)
**Objectives:** Psoriatic arthritis (PsA) is a heterogeneous disease affecting not only the joints but also the skin, nail as well as the tendon and its insertions. The skin assessment has been recognized as an important outcome measure in PsA, but still not frequently measured by the rheumatologists. Psoriasis Symptom inventory (PSI) is a relatively new patient reported outcome measure consisting of 8 items assessing skin symptoms. Response options 5-point Likert-type rating scale including itching, redness, scaling, burning, stinging, cracking, flaking, and pain. The validity of PSI has previously been demonstrated in severe psoriasis in drug trials, mostly patients with a body surface area $\geq 10$. However in clinical practice, most of the patients with

psoriasis have a BSA <3 and the most important limitation of the PASI is being insufficient to measure and discriminate these patients. We aimed to understand whether PSI is a valid tool in a) real life, b) in patients with mild psoriasis.
**Methods:** PsART is a multicenter, web based registry giving information about real life data, including a detailed clinical assessment, patient and physician reported outcomes. Within the period of June 2014 and May 2016, more than 1200 patients were recruited to the registry, however only patients that had the PSI data were analyzed in this study.
**Results:** Four hundred and forty six patients had PSI data (270 female, 176 male). The mean (SD) age was 46 (12.5) with a disease duration of 172.5 (128.7) months for psoriasis and 55.5 (65) months for PsA. The mean (SD) PSI was found to be 7.8 (7.3) and 17.7 % had a PSI of 0. There was a significant correlation between PSI and patient reported outcomes (patient global assessment, fatigue, pain and HAQ) and physician global assessment (r: 0.271-0.376; $p<0.001$ for all). There was a moderate correlation between BSA and PSI (r: 0.466; $p<0.001$). Interestingly, the best correlation was observed in patients with very mild skin disease (BSA<3) (r:0.529, $p<0.001$).
**Conclusion:** PSI is feasible, patient reported outcome for assessing psoriasis activity. This study shows that PSI can replace the other more complex tools or physician reported outcomes in the rheumatology practice where most of the patients have mild psoriasis.

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**Vascularity of Nail Bed by Ultrasound to Discriminate Psoriasis, Psoriatic Arthritis and Healthy Controls**

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**Objectives:** Ultrasonography (US) has been increasingly used in the field of psoriasis and psoriatic arthritis (PsA) for improving diagnosis, follow up and therapy guidance. PsA is a complex disease affecting the skin, nail, joints, tendons and enthesis and US has been demonstrated to have a role to visualize all of these structures. For the nail, the grey scale changes by US are loss of trilaminar appearance and pitting and these findings agree with clinical assessment in 76.3% of nails. Although PD changes on the nail have been described in psoriasis, the nail bed is an extremely vascular site, which raises the question of whether nail bed and matrix PD changes may necessarily reflect pathology. We aimed to find the frequency and severity of PD signals in psoriatic nail disease compared to healthy controls (HC) to understand whether PD signals are associated with disease.
**Methods:** The PD of the nail bed was scored on 86 patients with psoriasis (169 nails) and 19 healthy controls (HC) (38 nails) using a semiquantitative scoring between 0-3, by a sonographer blinded to the clinical findings.
**Results:** Forty two (48.8%) psoriasis patients had PsA and 52 (60.5%) had any clinical nail disease. In psoriasis patients' nails 26/169 (15.4 %) had no PD signals, similar to 7/38 (18.4%) of

nails of HC. The PD grade 3 signals were more frequent in HC (65.8% vs 38.5%; p=0.005). For psoriasis, when nails with clinical findings (n=83) were compared with clinically normal nails (n=86), there were no significant differences for the percentage of grade 3 PD (35 (42.2%) vs 30 (34.9%); p=0.4). To understand the contribution of psoriasis in the absence of any nail findings, the psoriasis group that had no clinical nail disease was compared with HC showing HC had more grade 3 PD signals (25/38 (65.8%)) than patients with psoriasis (30/86 (34.9); p=0.002). Then psoriasis patients with or without PsA were compared. Focusing only on healthy nails, the frequency of grade 3 PD signals were similar in both groups. However for nails that had an abnormality, there were less grade 3 PD signals if they also had arthritis (PsA: 10/38 (26.3%) vs psoriasis 25/45 (55.6%); p=0.008).

**Conclusion:** Nail bed is a vascularized tissue and Doppler signals can be detected in normal nail bed with paradoxical lower signals in psoriasis and psoriatic arthritis. Caution needs to be paid before concluding as PD as a prognostic marker in psoriatic nail disease.

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**Differential Serum Protein Expression in Groups of Psoriatic Arthritis Patients Characterised by Specific HLA Genotypes and Clinical Feature**

Musaab Elmamoun (St. Vincent's University Hospital, University College Dublin, Dublin); Angela Mc Ardle (University College Dublin, Dublin); Muhammad Haroon (St. Vincent's University Hospital, Dublin); Robert Winchester (Columbia University, New York); Stephen Pennington (University College Dublin, Dublin); Oliver FitzGerald (St Vincent's University Hospital and University College Dublin, Dublin)

**Objectives:** Psoriatic arthritis (PsA) is a heterogeneous disease with diverse clinical and radiographic manifestations. A number of human leukocyte antigen (HLA) alleles have been found to be associated with PsA.1,2 HLA-C*06:02 is associated with severe skin disease and a late onset, milder musculoskeletal phenotype; HLA-B*27:05 with entheseal based disease, severe musculoskeletal disease, enthesitis, symmetric sacroiliitis (SI) and mild psoriasis; HLA-B*08:01 with synovial based disease, asymmetric SI, joint deformity, joint fusion and dactylitis while HLA-B*38:01/39:01 is associated with more axial involvement and joint damage progression.3 Our hypothesis is that in each of these distinct genetic groups and perhaps as a consequence of the inflammatory events that occur following MHC-peptide interaction, a different pattern of inflammation involving diverse systemic molecules and mediators may be unleashed which in turn determines clinical phenotype and possibly therapeutic response. Our objective is to identify whether there are differences in serum protein expression between groups of patients with specific combinations of HLA genotypes and clinical features.

**Methods:** Patients with a diagnosis of PsA, fulfilling the CASPAR criteria, aged >18 years were included, 10 patients from each of the 4 defined HLA groups. We included a fifth distinct clinical group, Arthritis Mutilans, which as yet has no defined genotype. All patients had a full clinical assessment and serum samples were obtained. Proteomics Strategy: Serum samples from patients in each of the 5 groups were pooled. Serum pools were depleted of high-abundant proteins. The protein concentration of the remaining low abundant protein fractions was digested. Finally, samples were purified prior to LC-MS/MS analysis.

**Results:** Replicate LC-MS/MS analysis of each the 5 pools (n=3) revealed that a total of 437 proteins could be identified. Of these proteins, 219 were found to be significantly differentially expressed across the different groups (FDR: 0.01, $p \leq 0.05$). 43, 28, 91, 37, and 20 proteins were differentially expressed when comparing one PsA subgroup to the other 4 combined groups. Unforced hierarchical clustering analysis of the significantly differentially expressed proteins

revealed stark differences in the protein expression levels across the different PsA subgroups.
**Conclusion:** In this study it was possible to identify proteins that were significantly differentially expressed across the 5 PsA phenotypes. Validation strategies are in progress to measure all differentially expressed proteins in individual patient samples using a targeted proteomics approach. This work is an important first step toward the development of a protein biomarker panel that can be used to distinguish between different PsA subgroups.

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**Cytokine Expression in Groups of Psoriatic Arthritis Patients Characterised by Specific HLA Genotypes and Clinical Features**

Musaab Elmamoun (St. Vincent's University Hospital, University College Dublin, Dublin); Sytze de Roock (University Medical Centre, Utrecht); Wilco de Jager (University Medical Centre, Utrecht); Muhammad Haroon (St. Vincent's University Hospital, Dublin); Robert Winchester (Columbia University, New York); Stephen Pennington (University College Dublin, Dublin); Oliver FitzGerald (St Vincent's University Hospital and University College Dublin, Dublin)

**Objectives:** Psoriatic arthritis (PsA) is a heterogeneous disease with diverse clinical and radiographic manifestations. A number of human leukocyte antigen (HLA) alleles have been found to be associated with PsA.1 HLA-C*06:02 is associated with severe skin disease and a late onset, milder musculoskeletal phenotype; HLA-B*27:05 with entheseal-based disease, severe musculoskeletal disease, enthesitis, symmetric sacroiliitis (SI) and mild psoriasis; HLA-B*08:01 with synovial-based disease, asymmetric SI, joint deformity, joint fusion and dactylitis while HLA-B*38:01/39:01 is associated with more axial involvement and joint damage progression.2 Our hypothesis is that in each of these distinct genetic groups and perhaps as a consequence of the inflammatory events that occur following MHC-peptide interaction, a different pattern of inflammation involving diverse systemic molecules and mediators may be unleashed which in turn determines clinical phenotype and possibly therapeutic response. Our objective is to identify whether there are differences in cytokine expression between groups of patients with specific combinations of HLA genotypes and clinical features.
**Methods:** Patients with a diagnosis of PsA, fulfilling the CASPAR criteria, aged >18 years were clinically assessed, 10 patients from each of the 4 defined HLA groups. We included a fifth distinct clinical group, Arthritis Mutilans (AM), which as yet has no defined genotype. Serum samples were obtained. Cytokine Strategy: 50 individual patient samples (10 per group) and 5 reference pools (each pool consists of 50 samples) were subjected to in-house developed and validated multiplexed immunoassays to measure 47 cytokines using the Luminex xMAP. Analysis was performed in the Laboratory for Translational Immunology, UMC, Utrecht, The Netherlands. Data were analysed by 5-parametric curve fitting using BIO-Plex Manager software version 6.1.1.
**Results:** Forty-seven cytokines were analysed in each individual sample (n=50). Four samples were excluded because of cross reaction. Fourteen cytokines were excluded because they were out of reference range (either above or below). Twelve cytokines were excluded as their coefficient of variation (CV) was > 20%. On analysis of the remaining 21, only 1 cytokines (IL18) was differentially expressed among the 5 groups, Figure1. IL18 was elevated in the HLA-B*27 group, with statistically significant difference between B*27 and AM (P<0.256, CI-135.6 to-9.982) and between B*27 and B*38/39 (P<0.0320, CI-129.3 to-6.524).
**Conclusion:** IL 18 was significantly increased in the HLA-B*27 group compared to both AM and HLA-B*38/39 grous.

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## Does Combination of Conventional Synthetic Disease Modifying Antirheumatic Drug with AntiTNF Influence the Long Term Retention Compared to AntiTNF Monotherapy in Psoriatic Arthritis? An Analysis from Rhumadata® over 12 Years

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**Objectives:** In rheumatoid arthritis, it has been shown that antiTNF therapy (TNFi) in combination with a conventional synthetic diseasemodifying antirheumatic drug (csDMARD), often methotrexate (MTX), is more effective than antiTNF monotherapy to improve clinical outcomes and TNFi retention. We assessed the longterm retention of TNFi with and without csDMARDs in the firstline treatment of psoriatic arthritis (PsA) in the real world Rhumadata® clinical database.

**Methods:** The data of all PsA patients treated with a first biological agent was extracted from Rhumadata®. The data included age, gender, clinical variables, patient and physician specific assessments, and laboratory measures. Composite assessment of disease activity including the DAS28CRP and the simplified and clinical disease activity indices (SDAI and CDAI) were calculated using readily available formulas. Concomitant use of csDMARDs (MTX, hydroxychloroquine, leflunomide, and sulfasalazine) was collected. Patients were classified into four groups: TNFi alone, TNFi+MTX alone, TNFi+nonMTX csDNMARDs and TNFi+MTX+other csDMARDs. KaplanMeier methods were used to compute the cumulative incidence of biologic agent discontinuation in those groups and differences in discontinuation rates were tested using the logrank tests. Potential predictors of biologic retention were entered in univariate and multivariate proportional hazard regression models. Statistical analysis was performed using SAS version 9.4.

**Results:** Our cohort included 398 patients, 102 receiving antiTNF monotherapy, 165 concomitant MTX only, 90 MTX + other csDMARDs and 41 concomitant nonMTX csDMARDs .. Mean baseline disease activity measured using DAS28ESR or CRP are respectively, 4.1 and 4.0. Drugs survival analysis showed no significant difference between groups: AntiTNF monotherapy versus combination with MTX only, or with MTX + other csDMARDs or with a nonMTX csDMARDs (p=0.09). Drugs survival analysis for each of the antiTNF (adalimumab, etanercept or golimumab) did not demonstrate a significant difference when adding MTX +/ other csDMARDs. As for infliximab (IFX) used in combination with MTX +/ other csDMARDs showed a trend towards better retention (p=0.07). Multivariate analysis showed that antiTNF in combination with MTX and at least one other csDMARDs was a predictor of improved retention (HR 0.49, 95% CI 0.310.78, p=0.003). Smoking, female gender and higher DAS28 (CRP) were associated with increased drug discontinuation. Main reason for treatment discontinuation in all groups was lack of efficacy.

**Conclusion:** In this real world analysis, antiTNF therapy in combination with csDMARDs vs monotherapy, did not significantly influence the biologic longterm retention, except for IFX, where a tendency was observed. Combination therapy with MTX and at least another csDMARDs is a predictor of better retention.

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**Secukinumab vs Adalimumab for the Treatment of Psoriatic Arthritis: A Cost per Responder Analysis at 48 Weeks from a Canadian Perspective**

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**Objectives:** The cost per responder analysis attempts to quantify the relative value of two comparator drugs by assessing how the two agents compare in terms of cost per treatment outcome. The objective of this analysis was to estimate and compare the long-term cost per responder based on the American College of Rheumatology outcomes (ACR 20/50/70) following 48 weeks of psoriatic arthritis (PsA) treatment with Secukinumab (anti-IL-17A antibody) relative Adalimumab (anti-TNF).

**Methods:** The cost per responder for each treatment was estimated by dividing the drug acquisition cost for the course of treatment with its response rate. Drug costs were estimated using the Ontario drug acquisition costs (CAD$) and the number of doses required for 48 weeks. The long-term response rates were estimated using a matching-adjusted indirect comparison (MAIC) technique based on the data from FUTURE 2 and ADEPT clinical trials of Secukinumab and Adalimumab, respectively. MAIC analysis matched the age, weight, race and gender distribution, PASI score, HAQ-DI score, and proportions of patients using methotrexate, with psoriasis ≥3% BSA, presence of dactylitis, enthesitis, and TNF-naive at baseline. A more stringent sensitivity analysis was also conducted by varying the choice of baseline characteristics (added variables PsA duration (years), swollen joint count, and CRP) used in the MAIC analysis.

**Results:** The MAIC analysis showed that ACR (20/50/70) response rates were higher for Secukinumab 150mg and 300mg compared to Adalimumab at 48 weeks. ACR 20 response rates were 80%, 74% and 56% ACR 50 response rates were 57%, 61% and 44%, whereas the ACR 70 response rates were 32%, 43% and 30% for Secukinumab 150mg, Secukinumab 300 mg and Adalimumab respectively. Among PsA patients, costs per ACR20 responder were $14,459, $31,313 and $32,828, the costs per ACR50 responder were $20,149, $37,489 and $42,278, and the costs per ACR70 responder were $35,576, $53,673 and $62,008 for Secukinumab 150mg, Secukinumab 300mg and Adalimumab respectively. The sensitivity analysis confirmed and produced more favorable results for Secukinumab.

**Conclusion:** ACR 20/50/70 response rates were higher for Secukinumab 150mg and 300mg compared to Adalimumab at 48 weeks. The long term cost per responder for all ACR outcomes at 48 weeks were consistently lower for secukinumab (150,300mg) vs. adalimumab. These findings indicate that it is more efficient to treat PsA patients with Secukinumab vs Adalimumab. In addition, with a given budget, more PsA patients could be effectively treated in Canada versus adalimumab, due to the cost-offsets especially in biologic-naïve patients treated with Secukinumab 150mg.

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**Ixekizumab Provides Improvements through 52 Weeks in Physical Function, Quality of Life, and Work Productivity in Biologic Disease-Modifying Antirheumatic Drug-Naive**

**Patients with Active Psoriatic Arthritis**

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**Objectives:** To evaluate whether the monoclonal antibody ixekizumab (IXE), a high-affinity interleukin-17A antagonist, improves patient-reported outcomes (PROs) over 52 weeks in biologic disease-modifying antirheumatic drug (bDMARD)-naive patients with active psoriatic arthritis (PsA) in a phase 3 study (SPIRIT-P1). Previously reported results of this study showed that IXE significantly improved (versus placebo), at Week 24, PRO measures of the Health Assessment Questionnaire-Disability Index (HAQ-DI), Short Form-36 Health Survey Physical Component Summary (SF-36 PCS), European Quality of Life 5 Dimensions Visual Analog Scale (EQ-5D VAS), and Work Productivity and Activity Impairment-Specific Health Problem (WPAI-SHP; presenteeism, work productivity, and activity impairment).

**Methods:** 417 bDMARD-naive patients with active PsA were randomly assigned 1:1:1:1 to subcutaneous IXE 80mg every 4 weeks (Q4W) or 2 weeks (Q2W), each with a 160mg starting dose; adalimumab 40mg Q2W (active reference); or placebo in the double-blind treatment period (Weeks 0 to 24). Of these patients, 381 continued into the extension period (EP; Weeks 24 to 52). Placebo- and adalimumab-treated patients were randomly re-assigned (1:1) to 80mg IXEQ4W or IXEQ2W at Week 16 (inadequate responders) or Week 24. Analyses for the EP were conducted on the EP population (patients who received at least 1 dose of study drug during the EP). Missing values were imputed by nonresponder imputation for categorical data and modified baseline observation carried forward for continuous data.

**Results:** Baseline demographics and clinical characteristics were generally similar between treatment groups; population mean baseline (Week 0) scores for HAQ-DI, SF-36 PCS, and EQ-5D VAS indicated impaired physical function and quality of life. Physician-assessed American College of Rheumatology (ACR) 20 response was achieved by 69% of patients treated with IXE for 52 weeks. Patients receiving IXEQ4W or IXEQ2W for 52 weeks reported similar improvements from baseline in HAQ-DI (IXEQ4W: -0.53, IXEQ2W: -0.55), SF-36 PCS (9.5, 9.2) EQ-5D VAS (14.7, 14.4), and WPAI-SHP (presenteeism [-23.6, -25.4], work productivity [-25.3, -24.9], and activity impairment [-26.2, -29.1]) as reported at Week 24. The percentage of patients receiving IXE for 52 weeks with improvement from baseline HAQ-DI score ≥0.35 who achieved a minimally clinically important difference for HAQ-DI was sustained at Week 52 (57.1%) compared with Week 24. At Week 52, patients receiving adalimumab/IXE showed similar improvements in ACR20 response and most PRO measures to those observed at Week 24.

**Conclusion:** IXE provided sustained improvement over 52 weeks in physical function, quality of life, and work productivity in bDMARD-naive patients with active PsA.

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**52-Week Efficacy and Safety Results from SPIRIT-P1: A Phase 3 Study of Ixekizumab in Patients with Active Psoriatic Arthritis**

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Company, Indianapolis); Chin Lee (Eli Lilly and Company, Indianapolis); Dafna Gladman (University of Toronto, Toronto)

**Objectives:** To evaluate efficacy and safety of ixekizumab (IXE) over 52 weeks in biologic disease-modifying antirheumatic drug (bDMARD)-naive patients with active psoriatic arthritis (PsA) in a phase 3 study (SPIRIT-P1). IXE is a high-affinity monoclonal antibody that selectively targets interleukin-17A; IXE was superior to placebo (PBO) for improving joint and skin measures at Week 24 in this study.

**Methods:** A total of 417 bDMARD-naive patients with active PsA were randomized 1:1:1:1 to IXE 80 mg once every 4 weeks (Q4W) or 2 weeks (Q2W) including a 160 mg starting dose; to 40 mg adalimumab; or to PBO (all subcutaneous dosing) during the double-blind treatment period (DBTP: Weeks 0 to 24). Of these, 381 patients completed the DBTP and entered the extension period (EP: Weeks 24 to 52) where patients not already assigned to IXE were re-randomized 1:1 at Week 24 to 80 mg IXEQ4W or IXEQ2W. Efficacy and safety data are presented for patients in the EP population who were assigned to IXEQ4W or IXEQ2W at baseline and therefore remained assigned to these treatments during the EP. Missing values were imputed by nonresponder imputation for categorical data and modified baseline observation carried forward for continuous data.

**Results:** A total of 304 patients completed the EP. At Week 52 for the IXEQ4W/IXEQ4W and IXEQ2W/IXEQ2W groups who were treated with IXE for 52 weeks, the respective response rates for American College of Rheumatology 20/50/70 were 69.1/54.6/39.2% and 68.8/53.1/39.6%, Psoriasis Area and Severity Index 75/90/100 were 78.8/66.7/56.1% and 81.8/78.2/67.3%, and static Physician Global Assessment score of (0 or 1)/(0) were 81.3/60.4% and 78.4/62.2%. For the IXEQ4W/IXEQ4W and IXEQ2W/IXEQ2W groups, the respective changes from baseline to Week 52 for percent Body Surface Area involvement of psoriasis were -13.5 and -9.3 and for Nail Psoriasis Severity Index were -16.5 and -21.6. The frequency of treatment-emergent adverse events (AEs) in the EP was consistent with that observed in the DBTP; the majority were mild or moderate in severity. In the EP, serious AEs occurred in 4 patients treated with IXE for 52 weeks, and no deaths occurred.

**Conclusion:** At Week 52, IXE demonstrated clinically significant improvements in signs and symptoms of PsA, including nail and skin symptoms in patients treated with IXE since baseline. The safety profile of IXE observed in the EP was consistent with that observed in the DBTP and other phase 3 studies of IXE in patients with plaque psoriasis (UNCOVER studies).

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**Apremilast, an Oral Phosphodiesterase 4 Inhibitor, is Associated with Long-term (52-Week) Improvements in BASDAI in Patients with Psoriatic Arthritis: Pooled Results from 3 Phase III, Randomized, Controlled Trials**

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**Objectives:** Bath Ankylosing Spondylitis Disease Activity Index scores (BASDAI) were obtained as an exploratory measure in patients in the PALACE 1-3 trials considered to have axial involvement; psoriatic arthritis (PsA) spondylitis was not confirmed by imaging. We assessed

the impact of apremilast 30 mg BID (APR) on BASDAI over 52 weeks using PALACE 1-3 pooled data of patients with active PsA despite prior conventional disease-modifying anti-rheumatic drugs (DMARDs) and/or biologics.
**Methods:** APR treatment outcomes are reported for a subset of patients with baseline BASDAI ≥4 ("subset") over 16, 24, and 52 weeks.
**Results:** Baseline BASDAI ≥4 was reported in 454/1493 (30%) patients. Mean PsA duration was similar between the subset and rest of the PALACE 1-3 population (n=1039). Slightly more of the subset had history of palmoplantar, nail, scalp, or plaque psoriasis; mean baseline psoriasis body surface area (BSA) and proportion with BSA involvement ≥3% were slightly higher. The subset had higher mean baseline CRP, pain visual analog scale (VAS) scores, and patient's global disease assessment (PGA)/physician's global disease assessment (PhGA) ratings and markedly worse mean HAQ-DI, SF-36v2 Physical Functioning (PF), and FACIT-F scores. Tender joint count was higher; swollen joint count (SJC) and DAS-28 were less differentiated. Despite disease activity differences, baseline concomitant oral DMARD use was similar between groups; methotrexate was the most common DMARD. The subset was slightly higher in baseline NSAID and analgesic use and 73.6% had only been treated with oral DMARDs prestudy; 44.9% were treated with only 1 DMARD. Some patients (25.1%) had prior biologic use; 9% had prior biologic failure. Mean baseline BASDAI was 6.6 (APR) and 6.4 (placebo). APR resulted in a greater mean decrease in BASDAI vs. placebo at Weeks 16 (−1.53 vs. −0.91; P=0.0173) and 24 (−1.64 vs. −0.74; P=0.0002); other disease measures improved at Week 24, including marked HAQ-DI (−0.301 vs. −0.117; P=0.0067), PhGA (−22.1 vs. −7.4; P<0.0001), and FACIT-F (4.38 vs. 1.29; P=0.0082) changes. Long-term mean improvements were seen across measures at Week 52 in BASDAI (−2.18), HAQ-DI (−0.464), SJC (−8.5), SF-36v2 PF (7.06), pain VAS (−22.1), FACIT-F (6.77), PGA (−19.8), and PhGA (−34.3).
**Conclusion:** In this post-hoc analysis, patients reporting BASDAI ≥4 appear to have greater disease burden; this may not be captured by some disease activity measures, and effective treatment strategies may not have been available. APR resulted in long-term improvements in BASDAI and other measures in patients with clinically suspected axial disease.

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**Abatacept in the Treatment of Active Psoriatic Arthritis: 24-Week Results from a Phase III Study**

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**Objectives:** Abatacept (ABA), a selective T-cell co-stimulation modulator, showed promise for the treatment of PsA in a Phase II trial.1 This prompted the conduct of the Phase III Active pSoriaTic aRthritis rAndomizEd triAl (ASTRAEA; NCT01860976); key results are presented here.
**Methods:** In this international, double-blind, multicenter study, patients with PsA were randomized (1:1) to SC ABA 125 mg wkly or placebo for 24 wks, and then treated with open-label SC ABA up to 24 mths. Patients had active disease (≥3 tender and ≥3 swollen joints), ≥2 cm target lesion of plaque psoriasis and inadequate response or intolerance to ≥1 non-biologic DMARD. Randomization was stratified by MTX use, prior TNFi use and skin involvement ≥3%

of body surface area (BSA). Patients not achieving ≥20% improvement in SJC and TJC at Day 113 were switched to open-label ABA (early escape). Primary endpoint: ACR20 response at Wk 24. Key secondary endpoints at Wk 24: HAQ response (change from baseline ≥0.35); ACR20 response in the TNFi-naïve and -exposed subgroups; radiographic non-progression (PsA-modified total Sharp/van der Heijde score; change from baseline ≤0). Other secondary/exploratory endpoints included: ≥50% improvement in Psoriasis Area and Severity Index score (PASI50) in patients with ≥3% BSA; change in HAQ score; safety. Comparisons were performed using a 2-sided Cochran–Mantel–Haenszel chi-square test, adjusted for stratification criteria. Patients designated as early escape or with missing data were imputed as non-responders/radiographic progressors. Change in HAQ score was analyzed using a longitudinal repeated measures model (early escape patients set to missing at Days 141 and 169).
**Results:** Of 424 patients enrolled, 213 received ABA and 211 placebo; 76 were early escape patients in ABA and 89 in placebo; 12 patients discontinued in ABA and 24 in placebo. Baseline characteristics were comparable between the groups. Most (>60%) patients had prior exposure to TNFis. ABA significantly improved the proportion of patients achieving an ACR20 response at Wk 24 ($p<0.001$). The proportion of HAQ responses was numerically higher with ABA vs placebo ($p=0.097$). Higher proportions of patients receiving ABA vs placebo had an ACR20 response in the TNFi-naïve and -exposed subgroups, and radiographic non-progression (nominal $p<0.05$), with modest numerical improvement in PASI50. Efficacy was maintained at 1 year. The safety profile of ABA was similar to placebo, with no new safety signals.
**Conclusion:** Abatacept improved disease and was well tolerated in patients with active PsA, regardless of prior exposure to TNFis. Mease P, et al. Arthritis Rheum 2011;63:939–48.

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**The Association between Occupational-related Mechanical Stress and Radiographic Damage in Psoriatic Arthritis**

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**Objectives:** Physical trauma and mechanical stress have been associated with a higher risk of developing psoriatic arthritis (PsA). We aimed to assess the association between occupational-related mechanical factors and the severity of radiographic peripheral and axial joint damage in patients with longstanding Psoriatic Arthritis (PsA).
**Methods:** A retrospective cohort study, using prospective collected data, was conducted involving patients of the University of Toronto Psoriatic Arthritis Cohort. Eligible patients included those with a PsA disease duration of 10 years or more, have had paid occupations since the age of 18 and those with radiographic data. Using an occupation history questionnaire, patients were asked to report all paid employment since the age of 18. The key predictor variables included various occupational-related mechanical exposures. For each job, the Occupational Information Network (O*NET), which is a job classification database, was used to rate the level of exposure to various occupational physical activities. The outcomes of interest were the extent of radiographic damage in the peripheral and axial joints, as measured by the modified Steinbrocker score (mSS), and the modified Stokes Ankylosing Spondylitis Spine Score (mSASSS). The association between the predictor and outcome variables was assessed by linear multivariable regression models after adjusting for age, sex, PsA duration, medications and lifestyle habits.
**Results:** A total of 307 eligible patients were analyzed. In the multivariable regression analysis

prolonged repetitive hand movements was associated with a higher peripheral joint damage score (by mSS, β 29, 95% CI 7, 50, p=0.008), while prolonged time spent sitting was associated with a lower mSS (β -12.7, 95% CI -26.1, 0.1, p=0.06). Additionally, occupations that required higher level of finger dexterity were associated with higher mSS. For axial joints, occupations that required static strength were associated with a higher mSASSS score (β 0.58, 95% CI 0.01, 1.17, p=0.047). PsA duration was found to have a positive independent association with both peripheral and axial joint damage (p<0.001).

**Conclusion:** High level of occupation-related mechanical stress in associated with increased radiographic peripheral and axial joint damage. This finding support the potential role of micro-trauma in the pathogenesis of PsA.

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**Peripartum Issues in the Inflammatory Arthritis (IA) Patient: A Survey of the RAPPORT Registry**

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**Objectives:** Multiple issues surround the peripartum period for IA patients including medication use, risk of disease flare and potential impact on neonatal outcomes. We aimed to better understand these issues by surveying patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA) in childbearing age.

**Methods:** We performed a retrospective evaluation of the peripartum period in female patients of less than 50 years of age with RA or PsA who consented to participate in the RAPPORT registry and agreed to receive emails for associated studies. An anonymous electronic-based RedCAp survey was sent to 440 females and survey information evaluated using descriptive statistics and Fisher's exact test.

**Results:** 162 patients (133 RA/29 PsA) completed the survey, with 103 patients having 234 pregnancies, 164 (out of 234) pregnancies occurring prior to the IA diagnosis and 70 (out of 234) pregnancies occurring after the diagnosis. Pregnancy outcomes from 103 patients included: 96% live births, 1.9% stillbirths, 23% miscarriages, and 15% therapeutic abortions. A third of patients had fewer children than desired due to IA disease activity, medications and other reasons. In the 63 pregnancies after the IA diagnosis (excluding those with therapeutic abortions): (1) pre-conception counseling was obtained in 49% of pregnancies; (2) most described good IA disease activity control during pregnancy but flared in the first 3 months postpartum; (3) IA medication was discontinued during 79% of pregnancies; (4) 35% of pregnancies occurred while on biologic therapy at the time of or prior to conception and continued for all or part of the pregnancies in 5 of cases (3/5 with complications including ectopic, intrauterine growth retardation, multiple pregnancy, flare). For patients planning conception (46/63 post-IA, 107/153 pre-IA diagnosis pregnancies) time to pregnancy was 0-2 months in 41% post-IA vs 46% pre-IA diagnosis pregnancies. Gestational age at time of delivery was 37-40 weeks in 58% (33/57) post-IA vs 66% (83/126) pre-IA diagnosis pregnancies. There were no statistically significant differences in pregnancies that occurred before or after IA diagnosis regarding pregnancy planning, fertility treatment, labor and delivery complications, delivery methods, birth defect frequency or neonatal complications. Pregnancy complications (including disease flare) and neonatal ICU admissions were significantly lower in pre-IA diagnosis pregnancies compared to post-IA diagnosis pregnancies. No pregnancy complications were noted in 24/54 pregnancies on medications compared to 6/9 pregnancies not on medications (not statistically different).

**Conclusion:** This study demonstrates the increased peripartum issues for women with IA and importance of informed decision-making before, during and after pregnancy.

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**A Systematic Review and Appraisal of the 'Pragmaticism' of Randomized Trials of Biologic Therapy in Combination with Methotrexate for Rheumatoid Arthritis**

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**Objectives:** Randomized controlled trials (RCTs) can vary widely in their design, which may affect the generalizability of the results. Pragmatic trials are designed to reflect how treatment is applied in daily clinical practice, whereas explanatory trials are undertaken in idealized circumstances to maximize the ability to detect an effect. Our objective was to rate RCTs for methotrexate and methotrexate-based DMARD combinations of traditional and biologic DMARDs along an explanatory-pragmatic continuum.

**Methods:** RCTs from a recently published Cochrane review comparing approved biologic or targeted synthetic therapy in combination with methotrexate to placebo or any other DMARD(s) in RA were included. Trials were rated on an explanatory-pragmatic continuum, using the PRECIS-2 (PRagmatic Explanatory Continuum Indicator Summary-2) tool. PRECIS-2 assesses 9 domains (eligibility, recruitment, setting, organization, flexibility of delivery, flexibility of adherence, follow-up, primary outcome, and primary analysis), each rated from 1 (very explanatory) to 5 (very pragmatic). Two raters assessed RCTs independently using PRECIS-2 and mean (SD) scores for domains across RCTs were calculated.

**Results:** 77 trials were included from 2000-2016, 57% had a placebo comparator. The mean (SD) age of patients in the trials was 52 (3) years and mean disease duration was 6 (4) years. The domains 'eligibility' and 'follow-up' were rated as the most explanatory with mean (SD) PRECIS-2 scores of 1.8 (0.5) and 1.8 (1.3) respectively. The eligibility criteria typically had strict restrictions on the disease severity and prior use of DMARDs and corticosteroids allowed. Patient follow-up usually required frequent follow-up assessments and extensive data collection. The 'organization' and 'delivery' domains were also rated as explanatory (mean 2.0, SD 0.6 for both) as extra resources were often employed and protocols for medication adjustments were restrictive with limited allowance for dosing changes or concomitant medications. 'Primary outcome' was rated at a mean of 3.0 (SD 1.0) as many trials used criteria such ACR response that were less relevant to clinical practice. Studies were more pragmatic in the domains of 'setting' (mean 3.8, SD 1.3), as many studies were international, multi-center trials and 'primary analysis' (mean 4.6, SD 0.9) as most studies used intention-to-treat analyses. There was insufficient information on adherence and recruitment to be rated.

**Conclusion:** RCTs of biologic and targeted synthetic DMARD treatment in combination with methotrexate for RA were rated as explanatory in most domains of the PRECIS-2 tool, which may affect the generalizability of trial results to clinical practice.

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**Anti-Dense Fine Speckled (DFS) Autoantibodies in Autoinflammatory Vasculopathies**

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**Objectives:** One of the challenges in anti-neutrophil cytoplasmic antibody (ANCA) testing is the

interference with subsets of anti-nuclear antibodies (ANA) that can generate "false" positive indirect immunofluorescence (IIF) ANCA tests. We hypothesize that one of these subsets may be autoantibodies to dense fine speckles 70 (DFS70), which is now recognized to be more common among apparently healthy individuals compared to patients with ANA-related rheumatic disease (AARD). The purpose of this study was to determine the frequency of anti-DFS70 in a spectrum of autoinflammatory vasculopathies (AV) and whether anti-DFS70 positive sera produced a positive ANCA IIF test on neutrophil substrates.
**Methods:** Patients diagnosed with AV by a rheumatologist (AF-M) in Calgary, Alberta, were enrolled in the Southern Alberta Vasculitis Patient Registry. IIF ANCA was performed using ethanol and formalin fixed neutrophil substrates and fluorescein (FITC) conjugated to anti-human IgG. Antibodies to proteinase 3 (PR3), myeloperoxidase (MPO), and DFS70 were detected by a chemiluminescence immunoassay. ANA were detected by IIF on HEp-2 cell substrate and SLE-related autoantibodies by laser bead immunoassay. The association between anti-DFS70, ANA, and demographic and autoantibody profiles was assessed using univariate logistic regression analysis.
**Results:** 55 AV patients included 74.5% females, 36.4% ANA positive, 1.8% anti-DFS70 positive, 12.7% anti-PR3 positive, and 5.5% anti-MPO positive. The mean age was 56.8 +/- 15.7 years (SD). There were 9 leukocytoclastic vasculitis, 8 Takayasu's arteritis, 8 giant cell arteritis, 7 granulomatosis with polyangitis, 6 polyarteritis nodosa, 5 Sjögren's syndrome vasculitis, 3 Behcet's disease, 2 microscopic polyangiitis, 1 eosinophilic granulomatosis with polyangiitis, and 6 other vasculopathies. The single anti-DFS70 positive patient and two others from another cohort were negative on ethanol and formalin fixed cells. Patients testing positive for anti-PR3 were younger (39.3 vs. 59.2, p=0.001), while patients who were positive for ANA (63.6 vs. 52.8, p=0.01) or anti-MPO were older (73.3 vs. 56.4, p=0.06) than their negative counterparts.
**Conclusion:** This is the first report that anti-DFS70 autoantibodies are not associated with IIF staining of either formalin or ethanol fixed ANCA substrates. Hence, even when present, they do not present confusing IIF ANCA patterns that might be associated with a positive ANCA. The prevalence of anti-DFS70 autoantibodies in AV was rare (1.8%), similar to the frequency seen in other AARDs. The frequencies of ANA, PR3 and MPO was associated with age of patients, however due to small sample size, further multi-centre studies are required for a more definitive study of anti-DFS70 clinical correlations.

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**ANA Negative SLE: Re-evaluation in an International Inception Cohort**

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**Objectives:** The prevalence of ANA-negative SLE is reportedly 5-20%. Cytoplasmic or mitotic cell indirect immunofluorescence (IIF) patterns are usually reported as ANA-negative. This study examined the prevalence of ANA-negativity (no intracellular IIF pattern) and pure cytoplasmic and/or mitotic IIF patterns (CMP) in a large international, SLE inception cohort and examined demographic, clinical and autoantibody associations.
**Methods:** Patients fulfilling ACR Classification Criteria were enrolled in the Systemic Lupus International Collaborating Clinics (SLICC) inception cohort within 15 months of diagnosis and

data and serum samples were collected at enrollment. ANA were detected by IIF on HEp-2000 substrate (ImmunoConcepts), SLE-related autoantibodies by laser bead immunoassay (TheraDiag), and anti-dsDNA and anti-dense fine speckles 70 (DFS70) by chemiluminescence immunoassay (Inova). Three groups were examined: 1) ANA-positive (presence of nuclear IIF pattern), 2) ANA-negative (no IIF pattern), and 3) pure CMP. The association between ANA-negativity or CMP (versus ANA-positivity) and baseline demographic, clinical, and autoantibody profiles was assessed using univariate and multivariate logistic regressions.
**Results:** 1137 patients were included; 89.9% were female. 92.3% were ANA-positive, 6.2% were ANA-negative, and 1.5% had a CMP. In the ANA-positive versus the ANA-negative and CMP groups, the mean age was 34.7 versus 39.9 years, 23.2% versus 5.7% were of Asian descent, 29.3% versus 43.2% resided in Canada, 43.6% versus 30.7% had used immunosuppressants, 40.5% versus 21.7% had anti-dsDNA, 47.3% versus 23.9% had anti-SSA/Ro60, and 32.4% versus 11.4% had anti-U1-RNP. The mean global SLEDAI-2K-score was higher in the ANA-positive (5.4) than in the ANA-negative (4.1), but did not differ from the CMP (5.4). In the multivariate analysis, patients from Canada (Odds Ratio (OR) 2.07 [95% CI: 1.28, 3.36]) or with anti-DFS70 (OR 4.45 [95% CI: 1.37, 14.39]) were more likely to be ANA-negative or have CMP. Patients of Asian descent (OR 0.34 [95% CI: 0.13, 0.86]) or with anti-dsDNA (OR 0.53 [95% CI: 0.30, 0.94]), anti-SSA/Ro60 (OR 0.51 [95% CI: 0.30, 0.87]), or anti-UI-RNP (OR 0.35 [95% CI: 0.17, 0.70]) were less likely to be ANA-negative or CMP.
**Conclusion:** In newly diagnosed SLE, the prevalence of ANA-negativity was at the lower end (6.2%) of the range previously published. An additional 1.5% had a CMP pattern. In contrast to previous reports, we did not find a positive association between ANA-negativity and anti-SSA/Ro60 as our HEp-2000 substrate overexpresses SSA/Ro60 antigen. The prevalence of true ANA-negativity will likely decrease as future guidelines are expected to recommend that non-nuclear patterns, such as CMP, are also reported.

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**Is Rheumatoid Arthritis a Risk Factor for Fractures: A Systematic Review of Observational Studies**

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**Objectives:** Rheumatoid Arthritis (RA) is a risk factor for osteoporosis. There are many factors that contribute to this increased risk, including the use of glucocorticoids, systemic inflammation due to the disease and relative physical inactivity. Only a few studies have assessed the risk of fractures in RA. The objective of this systematic review was to assess the risk of fractures in adults with RA compared with controls from the general population.
**Methods:** Two authors screened citations from the following electronic databases: MEDLINE, EMBASE, Cochrane Database of Systematic Reviews and CINAHL. Included citations were written in English, included patients greater than or equal to 18 years of age and compared fracture incidence/prevalence between RA patients and a control group. Case control, cohort and cross-sectional studies were included. Abstracts and conference proceedings were not searched. The primary outcome was fracture incidence and/or prevalence. Two authors extracted data using a standardized data extraction form. The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS).
**Results:** The searches resulted in 3451 citations, and after applying the inclusion criteria, we selected seventeen observational studies. The risk of fracture was elevated in RA compared to

controls in 14 of the 17 studies. Thirteen studies adjusted for glucocorticoid use and there was an increased risk of fracture with glucocorticoid use in 4/13 of these studies. Seven studies analyzed RA severity or functional impairment as a risk factor for fracture and the risk of fracture was elevated in 2/7 of these studies. Fracture ascertainment was performed by searching medical records in seven studies, analyzing spine radiographs in six studies, self-reported history in two studies and by multiple methods in two studies. Eight studies evaluated fractures at multiple sites, whereas nine studies evaluated fractures only at a single site. Only two studies reported specific data on fragility fractures, whereas in the remaining studies, the fracture mechanisms were not defined. Assessment using the NOS revealed that the studies were of high quality. Limitations of the studies included: studies enrolled a diverse range of patient and control group populations, and generally included all types of fractures determined by various methods and involving multiple sites. These differences between the studies made it difficult to directly compare them. Due to the marked study heterogeneity, a meta-analysis was not performed.
**Conclusion:** The risk of fracture in RA is elevated compared to the general population.

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**Site Variation in Early Treatment Strategies and DAS28 Remission at 6 Months in the Canadian Early Arthritis Cohort (CATCH)**

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**Objectives:** Compare clinical practice variations across Canadian early rheumatoid arthritis clinics and associations with achieving DAS28 remission at 6 months.

**Methods:** Data were analyzed from participating centers in the Canadian Early Arthritis Cohort (CATCH) study that had enrolled at least 40 patients. Simple and multivariable logistic regression with clustered standard errors by center were used to estimate associations between early treatment strategies (conventional (csDMARD), biologic DMARD (bDMARD) and steroids at baseline or within 3 months of CATCH enrolment), participant characteristics (age, gender, income, education, comorbidities, smoking status, ethnicity, seropositive status, body mass index, symptom duration and baseline DAS28), site characteristics (site size) and DAS28 remission at 6 months.

**Results:** The analysis included 1,929 participants and 16 centers. Baseline mean (sd) age for all cohort participants was 54 (15) years, 1397 (73%) were female, and mean DAS28 was 4.9 (1.5). There were significant differences between centers in participant characteristics (gender, age, symptom duration, body mass index, comorbidities, smoking status, education, ethnicity, marital status, seropositive status, erosions), baseline disease activity measures and early treatment strategies. The csDMARD and bDMARD strategies in order of frequency of use were: methotrexate-based combination therapy in 36% (site range 11%-67%), methotrexate monotherapy in 33% (oral 17% (site range 4%-61%), subcutaneous 16% (site range 0%-49%)), non-methotrexate csDMARDs in 15% (site range 0%-33%), triple therapy in 13% (range 0%-64%), and bDMARD in 3% (site range 0%-21%). Overall 61% of participants were exposed to steroids (intra-articular, intramuscular, or oral) in the first 6 months of treatment (site range 22%-

78%). At 6 months, 37% of patients across all sites had achieved DAS28 remission (site range 13%-65%). In multivariable analysis, relative to methotrexate oral monotherapy, methotrexate combination therapy (OR 2.2, 95%CI 1.4-3.3), subcutaneous methotrexate (OR 2.0, 95%CI 1.2-3.4), non-methotrexate csDMARD combination therapy (OR 2.4, 95%CI 1.5-3.8) and bDMARD therapy (OR 2.7, 95%CI 1.0-7.1) were all associated with higher odds of DAS28 remission. Household income >$50,000 per annum (OR 1.5, 95%CI 1.2-1.9) was also associated with higher odds of DAS28 remission. Steroid exposure (OR 0.6, 95%CI 0.4-0.7), female gender (OR 0.6, 95%CI 0.4-0.9), number of comorbidities (OR 0.6, 95%CI 0.5-0.7), non-Caucasian ethnicity (OR 0.6, 95%CI 0.4-0.8), increasing age, longer symptom duration and higher baseline DAS28 score were associated with lower odds of DAS28 remission.

**Conclusion:** Treatment strategy and patient characteristics vary across CATCH sites and contribute to variable remission rates achieved at 6 months.

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**A Systematic Review of Rheumatic Disease Epidemiology in the Indigenous Populations of Canada, the United States, Australia and New Zealand**

Cairistin McDougall (University of Calgary, Calgary); Kelle Hurd (University of Calgary, Calgary); Cheryl Barnabe (University of Calgary, Calgary)

**Objectives:** Our objective of this study was to perform a systematic search to identify all relevant papers describing the epidemiology of rheumatic diseases in Indigenous populations in Canada, the United States of America, New Zealand and Australia.

**Methods:** A systematic search was performed using search terms for Indigenous populations combined with search terms for inflammatory arthritis conditions (rheumatoid arthritis, spondyloarthropathies, juvenile idiopathic arthritis), connective tissue disorders (systemic lupus erythematosus, scleroderma, myositis, sjogren's), crystal arthritis and osteoarthritis. Studies were included if they reported epidemiologic data for the conditions of interest.

**Results:** Prevalence rates of RA in Alaskan Native populations were similar to that of the general population but ranged from 2.15 to 6.8% in the Blackfeet, Chippewa and Pima American Indians. Reported rates in Canadian First Nations ranged from 1.0 to 7.1%. While Australian Indigenous rates and New Zealand prevalence was as high as 2.7% and 3.30% respectively. More contemporary studies of SLE found prevalence rates to be higher in Alaskan Natives (149 to 159 per 100,000) and Native American populations (138 to 263 per 100,000) than in earlier studies of the same populations. Studies of Canadian and Australian Indigenous populations observed SLE prevalence rates to be at least double that of non-indigenous populations. AS prevalence in various Alaskan Native, Native American and Canadian populations ranged from 0.1 to 0.4%, 0.0 to 3.0% and 0.36 to 2.3% respectively. Only one case finding study examined prevalence of AS in the New Zealand Maori and reported a rate of 0.0%. Crystal arthropathies have been reported to occur in Alaskan Native and Canadian First Nations populations at rates of 0.30% and 0.44% respectively while the prevalence of gout reported in more recent studies on the New Zealand Maori ranged from 6.40 to 11.10%. The rates in the Maori were significantly higher than non-Maori or European populations which ranged from 2.3 to 4.12%.

**Conclusion:** The burden of rheumatic disease in North American, Australian and New Zealand indigenous populations is high and in many instances, significantly higher than that of non-indigenous populations. Knowledge of the epidemiologic landscape of rheumatic conditions in these populations should sharpen clinicians' vigilance when caring for individuals from these backgrounds, hopefully leading to earlier recognition and diagnosis of disease. In addition, this

knowledge should help to focus distribution medical services and ultimately improve outcomes in these populations that tend to suffer from greater socio-economic and health disparities while also experiencing these diseases at higher rates.

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**Mortality in Indigenous Populations of Canada, the United States, Australia, and New Zealand with Rheumatic Disease: a Systematic Review**

Kelle Hurd (University of Calgary, Calgary); Cheryl Barnabe (University of Calgary, Calgary)

**Objectives:** Background/Purpose: Indigenous populations of Canada, America, Australia, and New Zealand share similar experiences of colonization impacting their rheumatic disease clinical outcomes. The objective of our systematic review was to describe mortality in Indigenous populations with rheumatic conditions.

**Methods:** Methods: A systematic search was performed in medical (Medline, EMBASE, CINAHL), Indigenous and conference abstract databases (to June 2015). Search terms for Indigenous populations were combined with terms for inflammatory arthritis conditions, connective tissue disorders, crystal arthritis, and osteoarthritis. Studies were selected for data extraction if they reported measures of mortality (e.g. mortality rate, survival rates, potential years of life lost). Given the heterogeneity in the reporting of measures in each study, a narrative summary was prepared.

**Results:** Results: A total of 5,269 titles and abstracts were reviewed, 504 underwent full-text review and 12 (n=5 Canadian First Nations with SLE; n=2 Native Americans with SLE; n=3 Australian Indigenous with SLE; n=1 Native Americans with RA; n=1 Native Americans with scleroderma) were included for data extraction. First Nations ethnicity was associated with higher mortality compared to Caucasians in all Canadian SLE studies, reflected by a higher crude proportion of deaths (n=3 studies), increased risk of death after adjustment for covariates (hazard ratios 2-3, relative to Caucasians, n=2 studies), higher odds of death (n=1 study) and increased potential years of life lost (n=2 studies). Risk of death was 43% higher in Native Americans with SLE compared to Caucasians in age and sex adjusted models, and in models with expanded covariates, with the highest risk reported in women ages 45-65 years. Crude death rates and causes of death were reported in Australian Indigenous people with SLE (n=3). In these cohorts, Aborigines had higher death rates than Caucasians, mostly related to SLE complications. The RA study in Pima Indians included a comparison of mortality rates between RA and non-RA subjects, with an age and sex-adjusted mortality rate ratio of 1.28 (95%CI 1.01 to 1.62) and a death rate 1.74X higher in those with RA compared to those without RA. The one study in Native Americans with scleroderma reported a crude death rate, with nearly all deaths related to progressive disease.

**Conclusion:** Conclusions: In Canada, America and Australia, Indigenous populations with rheumatic diseases have higher mortality rates. Several studies identified rheumatic disease as contributing to the deaths. We did not identify any studies disentangling the proportional attribution of rheumatic disease severity from higher mortality rates in Indigenous populations.

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**Outcomes of Aboriginal Patients with Early Inflammatory Arthritis: A CATCH Study Analysis**

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**Objectives:** Health inequities exist across many chronic diseases for Aboriginal patients. Our study compares Aboriginal and Caucasian patients with early inflammatory arthritis in disease presentation, treatment strategy, and outcomes over five years.
**Methods:** Participants were enrolled in the CATCH Study, a longitudinal multi-center cohort study of patients with <1 year inflammatory arthritis symptom duration followed prospectively in rheumatology practices across Canada. Demographics, clinical characteristics, therapeutic strategy and frequency of remission were contrasted by self-identified ethnicity (Aboriginal or Caucasian). Linear mixed-model repeated measures (for DAS28, HAQ, and patient-reported outcomes) and Poisson regression analysis (for tender and swollen joint counts) were used to determine rates of change over five years, with adjustment for baseline demographics and disease activity.
**Results:** Aboriginal (n=100) and Caucasian (n=2073) participants (70% female, mean 54(SD 15) years) had similar symptom duration (mean 179(SD 91) days), baseline DAS28 (mean 4.87(SD 1.48)) and baseline HAQ scores (mean 0.88(SD 0.68). Socioeconomic and demographic prognostic factors (smoking status, body mass index, education, household income) disfavoured Aboriginal patient outcomes (all p<0.02). The frequency of use of therapeutic strategies and escalation was not different between groups. In mixed effects logistic regression models adjusting for smoking status, education, income, seropositive status, erosions, and baseline HAQ and DAS28 scores, Aboriginal participants were not more likely to receive oral steroid therapy (adjusted OR 1.24, 95%CI 0.54 to 2.85;p=0.62), biologic therapy (OR 0.63, 95%CI 0.19 to 2.11;p=0.46), or DMARD combination therapy (adjusted OR 1.66, 95%CI 0.66 to 4.14;p=0.28). However, DAS28 remission occurred less frequently in Aboriginal participants at visits up to 36 months (3 months 16% vs 30%; 6 months 17% vs 41%; 12 months 16% vs 50%; 18 months 24% vs 53%; 24 months 29% vs 58%; 36 months 40% vs 59%, p<0.01). Higher DAS28 scores in Aboriginal participants were driven by a slower improvement in swollen joint counts (slope difference between groups p=0.034), and the lack of significant improvement in patient global scores (p=0.115). Although HAQ and pain scores improved in both groups, fatigue did not improve in Aboriginal participants.
**Conclusion:** We observed differences in disease phenotype in Aboriginal patients, and worse disease outcomes. Standard treatment escalation strategies failed to achieve the same frequency of remission as seen for the Caucasian population. Our results may reflect disparities in socioeconomic status and differences in environmental exposures associated with worse disease outcomes, or alternatively speak to the need for re-evaluation of the appropriateness of current treatment strategies applied in different population contexts.
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## The Perspectives of Patients, their First Degree Relatives, and Rheumatologists Around Preventative Treatments for Rheumatoid Arthritis

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Columbia, Vancouver)

**Objectives:** To identify relevant attributes for a discrete choice experiment (DCE) representing the factors that influence the preferences of patients, first-degree relatives (FDRs) of patients, and rheumatologists about a preventative treatment for rheumatoid arthritis (RA).

**Methods:** Semi-structured focus groups were conducted with 1) RA patients in British Columbia, 2) FDRs of people with RA in British Columbia, and 3) rheumatologists from across Canada. Participants were recruited through a combination of convenience and homogenous sampling. Focus group guides were adapted from a previous study in which we developed a DCE representing an RA treatment decision. In the first round of focus groups, moderated discussions with RA patients, FDRs, and rheumatologists elicited open-ended responses to the interview guide questions. Findings from analysis of these discussions were reduced to a list of potential attributes for the DCE. In the second round, RA patients and FDRs provided feedback to improve the validity and representation of the potential attributes. All focus groups were audio recorded, transcribed, and analyzed using Framework Analysis.

**Results:** Five focus groups were conducted with 13 RA patients, 5 FDRs, and 7 rheumatologists from four Canadian provinces. Analysis of the focus group discussions revealed that all groups considered competing risks when considering a preventative treatment decision: risks of developing RA and when it might occur; accuracy of predictive tests and the risk of a false positive; and the risks of treatment itself. For rheumatologists, the empirical evidence supporting preventative tests and preventative treatments for RA, as well as treatment side effects were of significant importance. Interestingly, some rheumatologists did not consider prevention to be part of their role. FDRs frequently mentioned the impact that a preventative treatment would have on their lifestyle, the accuracy of predictive test, and weighing the potential benefits against the possible side effects of treatment as key factors in considering whether to take a preventative treatment for RA. The health care provider's (nurse/family physician/rheumatologist) knowledge of RA and perceived trustworthiness was also important to FDRs to whether they would consider a heath care provider's recommendation for preventative treatment. Our Framework Analysis highlighted key themes in this discussion which informed the attributes to be included in a DCE

**Conclusion:** Through qualitative analysis, we obtained attributes to be included in a DCE. Our findings suggest there are important differences in how uncertainties surrounding the potential benefits of a preventative treatment for RA are valued from the perspectives of patients, FDRs and rheumatologists. Supported by a CIORA grant.

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**Patterns of Methotrexate Use in Least Developed African Countries: Preliminary Results of Semi-Structured Interviews**

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**Objectives:** Methotrexate (MTX) is the standard of care and first-line therapy for rheumatoid arthritis (RA) patients. European and American guidelines for RA treatment and MTX use did not contemplate the specific realities of resource limited countries.

**Methods:** Medical doctors self-identified as MTX prescribers from different African countries participated in individual conference calls (45 minutes) with semi-structured interviews on the patterns of MTX use. We report key aspects discussed and recorded on the interviewer's notes.

**Results:** 25 physicians from 23 African countries were interviewed. Among these, 10 interviews represented 'least developed countries' (LDCs) according to the United Nations Committee (2016). Those 10 LDCs are home to a population of 293.78 million people. Eight of the physicians interviewed were rheumatologists with a mean (SD) number of years in practice of 9.1 (6.2, min 2- max 22). Most them (9/10) practiced at University Affiliated Hospitals in major cities serving predominantly adults patients (8/10 also provided pediatric care). The number of rheumatologists per LDCs ranged between 0 (2/10 countries) and 10 (2/10). In 7/10 countries physicians other than rheumatologists (i.e. internists and orthopedic surgeons) were reported as MTX prescribers. Oral MTX was the only available formulation in 5/10 countries. The main indications for MTX prescription were RA (100%), connective tissue diseases (67%) and psoriatic arthritis (33%). Most physicians (9/10) evaluated patients for pulmonary, hepatic and renal dysfunction and excluded cytopenias prior to prescribing MTX. Baseline chest X-rays were requested by 6/10 physicians, whereas HIV test by 4/10 and Hepatitis B and C serologies by 3/10. Pregnancy screening was largely based on patient self-report (9/10). Discussing alcohol consumption was only considered pertinent to the local consumption by 3/10 MD's interviewed. Most physicians (9/10) reported that MTX was not consistently available throughout the year, and only 3/10 reported that MTX was provided by the hospital pharmacy. The monthly cost of MTX (10-15mg/week) was 15.4±9.0 US dollars. The starting dose of MTX was 10.5±2.6 mg/week. Routine prescription of folic acid with MTX was reported by 8/10 physicians. Major barriers to MTX adherence included costs (9/10), drug availability/access to care (4/10) and patient's belief/education (2/10).
**Conclusion:** The challenges of treating RA patients in African LDCs differ from those in other regions. Costs of medical care, drug availability, limited manpower and patient specific beliefs are key factors limiting the use of MTX. A better understanding of the African LDCs reality would allow the development of policies to bridge the gap in RA care.

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**A Qualitative Study Exploring Participants' Perception of the Making it Work Program, an Online Program to Help People with Inflammatory Arthritis Maintain Employment**

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**Objectives:** Health services addressing employment needs for people with arthritis are lacking. To address this, we developed the Making it Work (MiW) program, an on-line self-management program aimed at helping people with inflammatory arthritis (IA) deal with employment issues. MiW consists of e-learning modules and on-line group meetings facilitated by a vocational rehabilitation counselor (VRC); followed by individual assessments (ergonomics and VRC). As part of a RCT evaluating program effectiveness, this study aimed to explore participants' experiences and to obtain insight on perceived benefits and drawbacks of participating in MiW.
**Methods:** Participants were recruited from rheumatologist practices in BC, Alberta and Ontario. Inclusion criteria included: IA; currently employed; age 18-59 years; concerned about ability to work; and access to a computer. All participants who attended the final group meeting between 01/2015 and 04/2016 were included. Semi-structured debriefing group discussions were

conducted by the facilitator on the last online group meeting, which was recorded and transcribed. Using content analysis, transcripts were coded and concepts grouped into meaningful clusters to identify emerging themes.
**Results:** The sample included 62 participants [87% female; mean(SD) age: 46(9.9) years; disease duration: 9(9.1) years; RA:51%, AS:13%; PsA:18%; SLE:18%]. Helpful strategies learnt highlighted by participants included those to manage fatigue and stress, and problem solving/goal setting. Not all module content was relevant for everyone, as job situation (e.g. self-employed) or disease characteristics (e.g. those without fatigue) meant some content (e.g. disclosure, job accommodations, or dealing with fatigue) was not applicable to some workers. Perceived benefits/drawbacks of participation clustered around four themes: 1) Heightened awareness of: how arthritis affected their work; their rights; and available resources. 2) Empowerment vs. Frustration: most participants felt empowered by their increased awareness, but a few felt frustrated because they were unable to make changes to their work situation. 3) Improved self-efficacy: many described feeling more confident about dealing with the challenges at work due to arthritis as a result of strategies and skills learnt. Many described it changed their world view. 4) Validation from participating in group meetings: recognizing that symptoms and struggles at work were shared by others provided support, others served as role models; confirmation of usefulness of their strategies prior to MiW encouraged them to "keep at it".
**Conclusion:** This study provides insight into what participants found helpful about the MiW program. These findings are informative to health professionals assisting clients in dealing with employment issues and researchers designing arthritis programs dealing with employment.

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**Improving Preventative Care in Patients with Rheumatologic Diseases**

Faranak Esmaeilbeigi (University of Western Ontario, London Health Sciences Centre, London); Janet Pope (Western University, London); Andrew Thompson (UWO, Arva)

**Objectives:** Comorbidities are common in rheumatologic disease including but not limited to cardiovascular disease, osteoporosis/osteopenia, and malignancies. Previous research has shown that rheumatologists do not routinely communicate some of these risks to family physicians despite most feeling that family physicians may not be aware of these possible preventable comorbidities. Our objective was to create easily accessible information tables for family physicians and statements that can be embedded into EMR systems to assist in translation of knowledge and improve quality of care for patients with rheumatologic diseases.
**Methods:** A review of the literature was completed investigating current preventative care recommendations in cardiovascular disease, osteoporosis prevention, and malignancy screening for various rheumatologic disorders including ankylosing spondylitis, lupus, rheumatoid arthritis, psoriatic arthritis, polymyalgia rheumatica, scleroderma, and giant cell arteritis. A table and a set of EMR statements were created using this information. Canadian guidelines were used where possible. This information was sent electronically to family medicine residents and they were surveyed regarding their preferences and opinions on whether a similar tool would be of assistance in preventative care strategies in family practice.
**Results:** Preliminary data suggests that family medicine residents would appreciate guidance from subspecialists on preventative care strategies in special populations such as in rheumatologic practice. Preference would be to incorporate these statements into EMR systems for simplification and learning.
**Conclusion:** An EMR based system of information translation may be beneficial, particularly if congruent among diseases. This strategy would be especially helpful if it included alerts for

complex patient populations such as patients with rheumatologic diseases. This type of system may improve adherence to guidelines and quality of care. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Virtual Interactive Cases to Teach and Assess Clinical Competencies and Resource Stewardship in Rheumatology**

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**Objectives:** Clinical competencies, such as the ability to assess a patient in a cost-conscious manner, are difficult to teach by traditional medical education approaches alone. Digital case-based training modules can simulate real patient encounters and assess costs of care.

**Methods:** Rheumatology Virtual Interactive Case (VIC) modules were developed to allow trainees to practice diagnosing and managing rheumatology patients through virtual history-taking, physical exam, laboratory investigations and consultation requests. Cases include gout, septic arthritis, psoriatic arthritis, rheumatoid arthritis, polymyalgia rheumatica and ankylosing spondylitis. Costs associated with each action were derived from the Ontario Health Insurance (OHIP) Schedule of Benefits and Fees. These modules, distributed to medical trainees at the University of Ottawa and the University of Toronto, were evaluated based on anonymously tracked responses and qualitative feedback.

**Results:** Between June 2015 and September 2016, twenty medical trainees (7 medical students, 13 residents) completed 30 VIC modules. On average, trainees spent $227.52 and 9 minutes, translating into 68 virtual minutes, per patient. The average number of essential actions performed was 36 (31%). The diagnostic accuracy was 100% and the management accuracy was 58.3%. Qualitative feedback was largely positive – learners liked the case-based learning style, particularly praising the “life-like scenarios” and “the vast amount of choices, including questions to ask and investigations to order, that helped me become more confident in my decision-making skills”. At case-end, evidence-based feedback for each action along with feedback on in correct choices, cost of care, and time taken was provided. This was positive for trainees, and one trainee remarked that “seeing the associated time and cost per action helped me become more aware of how time-consuming and costly unnecessary investigations can add up to be”. In addition to qualitative feedback, 85.7% said they felt more comfortable working-up similar cases, going forward.

**Conclusion:** Interactive virtual rheumatology modules simulate real-world rheumatology clinic patient scenarios. They can enhance trainees learning of rheumatology cases and cost-conscious care, and demonstrate problem solving ability, resource stewardship, and knowledge of the work-up of common rheumatic diseases. Further case development and evaluation will improve these for wider dissemination and utilization. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Human Resources Committee's Subgroup-interpretation of Student Recruitment Activities**

Alfred Cividino (McMaster University, Hamilton); Kimberly Legault (McMaster University, Hamilton); Caroline Barry (Dalhousie, Halifax); Jane Purvis (Peterborough); Diane Crawshaw (McMaster University, Hamilton)

**Objectives:** Canada faces a critical shortage of rheumatologists overall and more so in rural

isolated communities. To address this problem the Canadian Rheumatology Association (CRA) has supported various initiatives over time. The Human Resources Committee in 2016 endeavored to interpret the results and benefits of some of these programs. The findings of this review are reported.
**Methods:** Data and reports were requested from the following areas: Summer Studentship program - reviewed the number of students who participated in the program between 2001 and 2012, and determined how many of those former participants chose rheumatology as a specialty as indicated in a post-summer studentship follow-up survey. Training the Rheumatologists of Tomorrow/#MakeRheum program - elicited feedback from postgraduate (PG) rheumatology programs and undergraduate (UG) medical students through surveys completed at the Ontario Medical Students Weekend (OMSW) in 2015 and 2016. Survey of 2016 Rheumatology Graduates and Residents - conducted by the CRA in the spring of 2016 to determine how rheumatology graduates and residents chose rheumatology as a specialty.
**Results:** Summer Studentship Program Eleven percent of students who participated in the summer studentship program from 2001 to 2012 went on to become rheumatologists. A recent CRA 2016 survey revealed the program was influential to some of the participants. Training the Rheumatologists of Tomorrow Since 2012, 11 rheumatology programs across the country have participated in identifying ways to increase recruitment to rheumatology. This resulted in material that formed a campaign titled #MakeRheum, to encourage trainees to "make room" for an experience in Rheumatology. All programs have been sent the #MakeRheum materials and are being encouraged to utilize them. The Facebook page and twitter campaigns are active targeting undergraduate and post graduate students. 2016 Survey of Rheumatology Graduates and Residents A survey of both rheumatology graduates and residents asked several questions to determine how these individuals chose this specialty. There were many enlightening responses particularly that the single most important factor in their choice to pursue rheumatology was an encounter with a rheumatologist and the interesting diseases that are seen in the subspecialty.
**Conclusion:** The Human Resources Committee will continue to strive to support programming to address the shortage of rheumatologists in Canada. Addressing the unequal distribution of service can only be done with multiple coordinated, collaborative and sustained national efforts informed by research such the projects described here. Rheumatology programs need to join into the efforts towards increasing recruitment.

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**Rheumatic Disease in Pregnancy: Closing the Information Gap**

Maeve Gamble (Western University, London); Andrew Thompson (UWO, Arva)

**Objectives:** Rheumatologists are increasingly involved in the care of pregnant women. Many rheumatic diseases affect women of child bearing age. In the age of biologic therapy, women are achieving better disease activity and there are increasing numbers of women with rheumatic diseases attempting pregnancy. Previous surveys have shown that patients feel that there are information gaps in their understanding of pregnancy and parenting with arthritis. Rheumatologists are an important resource for their patients and it's becoming increasingly important for them to have the proper resources to hold a reliable dialogue with their patients. We conducted a nationwide needs assessment to determine the level of comfort rheumatologists experience when discussing pregnancy issues with patients.
**Methods:** A survey monkey survey was distributed to rheumatologists and rheumatology fellows across Canada. The survey was open from 3/13/2016 - 9/12/2016.
**Results:** One hundred and twenty six rheumatologists and rheumatology fellows participated in

the study. Ninety four percent (115/122) of participants felt that having tangible resources available to them would make it easier to counsel their patients on the safety of using rheumatic medications in pregnancy. Although 86% (107/124) of rheumatologists felt generally comfortable discussing the safety of medications with a pregnant patient, only 23% (28/124) felt completely comfortable with their knowledge. Despite feeling comfortable, 64% (79/124) would refer to resources just to be certain. About one quarter (27%, 34/124) of participants were only in practice for 0-5 years.

**Conclusion:** Although a large portion of rheumatologists and rheumatology fellows across Canada are comfortable managing their pregnant patients with rheumatic disease, almost all felt having more resources would be beneficial. It's interesting to note that the survey included rheumatologists who had only been in practice 0-5 years. This category includes rheumatology fellows and those new to practice. Despite this, 64% of all participants were generally comfortable counselling patients on medications in their pregnant patients. This may indicate that the newer trainees have more training in rheumatic disease in pregnancy especially in the biologic era. Based on this survey, we created pamphlets to help guide discussions with patients and for patients to have information to review at home. This fits well with recent European League Against Rheumatism (EULAR) recommendations about the importance of needs-based patient education that can be accessed over the disease course and at different life stages. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Development of a Curriculum on Patient Safety and Quality Improvement for Rheumatology Residents**

Ines Midzic (The Ottawa Hospital/University of Ottawa, Ottawa)

**Objectives:** At the present time, our rheumatology residency training program is in the early stages of incorporation of the concepts of safety culture. This led to the need for the development of a formal curriculum on quality improvement (QI) and patient safety. The objectives of this curriculum are to: i) enhance the awareness of rheumatology residents of the safety culture; ii) increase the recognition and reporting of adverse events with the application of human and system factors; and iii) apply quality improvement, patient safety, and/or resource stewardship principles through a QI project.

**Methods:** Tools acquired at the ASPIRE (Advancing Safety of Patients in Residency Education) workshop organized by the Royal College of Physicians and Surgeons of Canada were used to develop the curriculum. Prior to the design of the curriculum, a needs assessment was performed through a planning committee with faculty and resident representation. Prior to the start of the curriculum, further needs assessment is done using a survey and an interview of residents on aspects of QI and patient safety. CanMeds 2015 roles were used to develop the objectives for the curriculum pertaining to patient safety, QI and resource stewardship.

**Results:** The curriculum has four components. The first component includes reading material and exposes the residents to the Canadian Medical Protective Association (CMPA) Good Practices Guide. The second component is a 3-hour academic half day. The teaching methods comprise an interactive lecture, a case-based discussion, a video debrief, a demonstration, and a role play. The third component represents a structured presentation of mortality and morbidity (M&M) rounds including a facilitator for the session, and dissemination of conclusions. The fourth component includes a longitudinal QI project. The assessment methods of the curriculum include questions on a formative exam, direct observation and feedback during M&M rounds

and the QI project, as well as an oral and poster presentations of the QI project. The evaluation of the curriculum will be done through the residents' evaluation the academic half day, a survey of the residents' appreciation of the entire curriculum, and the residents' use of the hospital's patient safety incident reporting system from the start to the end of their training.
**Conclusion:** This curriculum presents a novel approach to teaching QI and patient safety in a rheumatology training program given its development through consultation of faculty and residents, the objectives matching CanMeds roles, and the application of various teaching methods. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**The National Written Rheumatology In-Training Examination (NWRITE): A Survey Based Evaluation**

Ceri Richards (University of Manitoba, Winnipeg); Raheem Kherani (University of British Columbia, Division of Rheumatology, Department of Medicine, Richmond ); Steven Katz (University of Alberta, Edmonton); Heather McDonald-Blumer (University of Toronto, Toronto); David Robinson (University of Manitoba, Winnipeg)

**Objectives:** In sub-specialties, comprising 1-2 residents, development of formative in-training examinations is challenging and standardized assessment impossible. A low-cost national in-training examination (NWRITE) for adult rheumatology subspecialty residents that resembles the Royal College format and provides national comparisons between residents was created in 2010. NWRITE is written by rheumatology residents in Canada. We sought to determine the perceived utility of this examination from the perspective of both program directors (PDs) and residents.
**Methods:** An online survey was disseminated to all Canadian Rheumatology Association (CRA) members via the CRA email in September 2016. Current and past program directors were surveyed via an author's email address. Responses were included if respondents indicated they had written the NWRITE, the date of residency training was consistent with this, and they responded to >1 question.
**Results:** The survey was completed by 138 CRA members, including 15 PDs (response rate 34%; 65%). 42 of the CRA members met inclusion criteria for having written the NWRITE. Both PDs and residents indicated the NWRITE exam was worthwhile (PDs 100%; residents 77%). Face-to-face review of the exam was found to be of more value (PDs 100%; residents 82%) than review of the national ranking scores (PDs 69%; residents 64%). PDs were more likely to find the NWRITE more useful than the Rheumatology American Board of Internal Medicine (ABIM) exam (PDs 90%; residents 47%). Only half of PDs (47%) felt there was good agreement with In Training Evaluation Report (ITER) performance. Most PDs felt residents performed the same or worse than expected (73%; 27%), compared to residents who had a more varied response (same 53%; worse 28%; better 20%). Both PDs and residents felt there was improvement on subsequent writings (73%; 80%). PDs agreed that they used the results to advise residents and to change curricula (80%; 57%). Some residents changed the nature or the quantity of studying (43%; 30%).
**Conclusion:** The examination was found overall to be worthwhile by both PDs and residents, and was noted to be of similar or more utility than the Rheumatology ABIM examination. Poor correlation with ITER performance, and some residents performing worse than expected suggests new information was gained by PDs. Modified forms of NWRITE may play a future role as a competency-based evaluation tool in Rheumatology fellowship training. We have

developed a formative in-training examination that is low-cost, may reduce the burden on PDs and provides national-level comparisons.

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**The National Written Rheumatology In-Training Examination (NWRITE): A Low-Cost Formative Examination**

Ceri Richards (University of Manitoba, Winnipeg); Raheem Kherani (University of British Columbia, Division of Rheumatology, Department of Medicine, Richmond ); Steven Katz (University of Alberta, Edmonton); Heather McDonald-Blumer (University of Toronto, Toronto); David Robinson (University of Manitoba, Winnipeg)

**Objectives:** Formative in-training examinations are highly useful to assess residents' progress through residency. In small sub-specialties, comprising 1-2 residents, development of formative in-training examinations is challenging and standardized evaluation impossible. The American Board of Internal Medicine in Rheumatology is multiple choice, and does not reflect the short answer format of the Canadian Royal College Examination. A low-cost national in-training examination that mimics the Royal College format, and provides national comparisons between residents was needed.

**Methods:** The NWRITE, a Canadian formative in-training examination was created and has been continually modified since 2010. The development and administration of this examination is described below.

**Results:** Each year, 4th year (PGY4) and 5th year (PGY5) Rheumatology residents in Canada write a common NWRITE examination. The examination occurs on a fixed date in June at the local centres and is administered in both French and English. Using an online document, all adult Rheumatology program directors (PDs) in Canada are asked to submit two questions on one of the topics reflective of the Canadian Royal College 'Objectives of Training' including: systemic lupus erythematosus, crystal arthropathy, soft tissue disease, psoriatic arthritis, pregnancy in rheumatic diseases, rheumatoid arthritis, ankylosing spondylitis, vasculitis, anatomy, immunology, and osteoarthritis. One editor compiles the questions, the answer key, and, with a second editor, performs quality control. The content of the examination varies year to year. Questions are stored in a question bank and may be re-used. Each resident's exam is scored by his or her own PD using a common grading rubric. All scores are compiled nationally and shared with PDs. PDs are encouraged to review both the exam and national ranking results with residents. However, PDs are encouraged not to provide the questions to the students so they may be used in future years. The number of residents with reported scores by year are: 33 (2010), 32 (2011), 31 (2012), 38 (2013), 45 (2014), 45 (2015) and 51 (2016). Mean yearly proportion of PGY4=52%, PGY5=45% and not reported=3%.

**Conclusion:** We have developed a low-cost formative in-training examination that enables PDs in a small subspecialty to provide residents with national level comparisons. This model may work well for other small specialties and subspecialties. Modified forms of NWRITE may play a future role as a competency-based evaluation tool in Rheumatology fellowship training.

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**Rheumatology Residents' Approach to Reading the Literature**

Sarah Troster (University of Alberta, Edmonton); Laura Fullerton (Ontario Best Practices Research Institute, University Health Network, Toronto); Earl Silverman (The Hospital for Sick Children, Toronto); Heather McDonald-Blumer (University of Toronto, Toronto)

**Objectives:** Peer reviewed journals play a crucial role in disseminating up-to-date research and innovation, and guiding evidence-based clinical practice. Although it is important for

rheumatology resident trainees to regularly engage with peer-reviewed literature, residents face challenges in keeping up with the growing body of medical literature, selecting high-yield articles for reading, understanding content with limited background knowledge, and applying new knowledge to clinical practice. This research explores how rheumatology residents read the literature, facilitators and challenges of engaging with the literature, and opportunities for the development of literary resources to enhance reading and understanding.

**Methods:** A total of 13 Canadian rheumatology residents participated in one of two semi-structured focus group discussions. In each session, residents were asked to describe their rheumatology journal reading habits, facilitators/barriers to their reading, and recommendations for the development of a literary resource to improve reading and understanding of peer-reviewed literature. Focus group discussions were audio-recorded and transcribed verbatim. Transcripts were analyzed by two independent investigators using standard qualitative description. Themes were identified using constant comparative technique, and data were tabulated by theme to identify key trends.

**Results:** Rheumatology resident's reported the following motivators for reading peer reviewed literature: 1) improved patient care through evidence-informed practice, 2) enhanced knowledge on topics relevant to clinical or academic work, and 3) scholarly purposes, such as keeping up to date or conducting research. Residents reported reading peer reviewed literature daily or weekly, and rely primarily on electronic updates to direct their reading. Key challenges to reading included: 1) gaining access to articles of interest, 2) understanding basic science and other concepts with a minimal background knowledge, and 3) identifying key papers of interest when not guided in what to read. Facilitators to reading included: 1) improved access to articles, 2) article features such as illustrations, summary boxes or clinical pearls to facilitate understanding, 3) suggested reading for trainees, and 4) increased exposure to journals in their academic training. Residents provided ideas for literary resources, however, emphasized the need for expert guidance and expressed concern regarding the influence of bias on such a tool.

**Conclusion:** Rheumatology literature is not being used in a manner that meets current educational needs for residents. Improved tools, especially electronic resources, would facilitate reading and optimal understanding. Such resources exist in the Internal Medicine and other subspecialty literature, but are not yet available in rheumatology journals.

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**Evaluating the Confidence Level of Residents in Different Areas of Rheumatology-Differentiating Perceived Strengths and Weaknesses: A Longitudinal Observational Study**

Stephanie Yang (University of Toronto, Toronto); Dharini Mahendira (St. Michael's Hospital, University of Toronto, Toronto)

**Objectives:** Rheumatic diseases contribute to a significant disease burden within society. Despite this, rheumatology is often overlooked in medical education, compared to other bodily systems. Rheumatology has been cited as an area in which residents feel less confident, compared to other internal medicine subspecialties. However, the confidence levels in different areas of rheumatology knowledge (eg. history-taking, physical exam etc.) is unknown. This study aims to assess the confidence level of residents at St. Michael's Hospital at the University of Toronto, in different areas of rheumatology. It also aims to assess how confidence levels change after completion of a rheumatology rotation. This knowledge will be used to better refine our rheumatology training program for postgraduate trainees.

**Methods:** Residents completing a rheumatology rotation at St. Michael's Hospital will be invited to participate in this study. An online questionnaire with a 5 point Likert scale will be

used to measure the confidence levels in performing a rheumatologic history, describing an approach to rheumatologic conditions, performing joint examinations, recognizing the correct use and interpretation of serology, performing knee arthrocentesis, and interpreting synovial fluid results. The questionnaire will be distributed at the start and end of the rotation. Confidence levels will be assessed and pre-rotation and post-rotation levels compared.
**Results:** Since study initiation in November 2016, a total of three residents have participated. On a Likert scale from 1 (not at all confident) to 5 (very confident), residents were most confident in obtaining a monoarthritis history (4/5) and least confident in obtaining a polyarthritis and chronic low back pain history (3/5). Residents were most confident in describing an approach to polymyalgia rheumatica (4/5) and least confident in systemic sclerosis (2/5). Residents were most confident in examining the back and knee (4.33/5), and least confident in examining the neck, wrist, hand, ankle and foot (3.67/5). Residents were most and least confident in recognizing the correct use and interpretation of ANA (4.33/5) and ENA (3.67/5) respectively. Residents' confidence levels in performing a knee arthrocentesis and interpreting synovial fluid results were 2.33/5 and 3/5 respectively. Inadequate data was available at the time of abstract submission to compare pre and post-rotation data. However, we anticipate having larger response numbers and comparative data by early next year.
**Conclusion:** Residents at the University of Toronto have varying levels of confidence in different areas of rheumatology knowledge. Ongoing assessment of confidence levels before and after completion of a rheumatology rotation may help target future teaching interventions.

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**Remote Assessment via Video Evaluation (RAVVE): Video-based Peer Assessment to Support Rheumatology Continuing Professional Development**

Raheem Kherani (University of British Columbia, Division of Rheumatology, Department of Medicine, Richmond ); Christopher Yao (University of British Columbia, Vancouver); David Collins (University of British Columbia, Vancouver); Kevin Eva (University of British Columbia, Vancouver); Shahin Jamal (University of British Columbia, Vancouver); Barry Koehler (University of British Columbia, Richmond); Graydon Meneilly (University of British Columbia, Vancouver); Helen Novak-Lauscher (University of British Columbia, Vancouver); Kamran Shojania (University of British Columbia Faculty of Medicine; Arthritis Research Canada, Vancouver); Kendall Ho (University of British Columbia, Vancouver)

**Objectives:** Video review processes for evaluation and coaching are often incorporated into medical education. Video-based peer evaluations can potentially overcome logistical challenges and accurately capture physician-patient interactions compared to direct observation. However, the literature in this domain is limited. This study aims to explore the acceptability and feasibility of video-based peer consultations to support professional development and quality improvement in patient care.
**Methods:** Five rheumatologists, with a camera placed in their exam rooms, each provided four videos of patient consultations. Peers assessed the videos by using a questionnaire based on a five-point scale, providing annotations in the video recordings, and offering recommendations. The rheumatologists reviewed the videos of their own four patient interactions along with the feedback. They were asked to document if they would make practice changes based on the feedback. Focus groups were conducted and analysed to explore the effectiveness of video-based peer assessment in assisting physicians on improving clinical practice.
**Results:** Participants felt the video-based consultation provided accurate and detailed information in a more convenient, less intrusive manner than direct observation. Peer review

enabled participants to evaluate more detailed information than a chart review alone. They suggested that reviewing the recorded consultations allowed them to reflect on their practice and gain insight into other potentially valuable communication methods. Three of five participants felt the feedback would help them make practice changes.
**Conclusion:** Video-based peer consultation, along with clinicians' ability to view their own performance, is an acceptable and feasible approach to support professional development and improve clinical care among rheumatologists. Further investigation into the effectiveness of this approach is needed. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**"Conversion Rates of Abstracts Presented at the Canadian Rheumatology Association Annual Meetings into Full-text Journal Articles"**

Laura Soong (University of Alberta, Edmonton); Elaine Yacyshyn (Division of Rheumatology, University of Alberta, Edmonton)

**Objectives:** Dissemination of research studies is important for research ideas to be transformed from initial abstracts to full publications. Publication of research as full text journal articles is a key step for providing access of research findings to the greater clinical and scientific community and is an indicator of higher quality research. It is essential that important research is submitted through peer review and publication to add to the body of evidence for clinical and other topics, as individual or pooled research can have important implications to change or influence clinical practice. Analyses of the scientific impact and publication record of the Canadian Rheumatology Association (CRA) Annual meetings have not been previously described. This study determines the publication rate of abstracts presented at the CRA Annual Meetings 2005-2013 to full-text journal articles and the factors associated with publication.
**Methods:** Program records of previous CRA meetings from 2005-2013 were obtained. Abstracts were searched for corresponding full text publication in Google Scholar and PubMed using a search algorithm. Abstracts and subsequent published articles were evaluated for type of abstract, time to publication, study type, publishing journal, and journal impact factor.
**Results:** A total of 1401 abstracts were included in the study, 567 of which were converted to full-publications. The publication rate over 9 years was 40.5%, with the highest rate of publication in 2011 at 49.6%, and lowest in 2013 at 29.9% The average time to publication was 19.7 months, with 89% of abstracts published within 3 years of being presented. Eighty three percent of abstracts were clinical in nature, and 58% of published studies were observational in design. Articles were published in a wide range of journals, with the top publisher being the Journal of Rheumatology (31%). Eighty six percent of articles had a Journal Impact Factor >2.
**Conclusion:** Overall, 40.5% of abstracts presented at the CRA Annual Meetings 2005-2013 were published. This publication rate is within the range of other medical specialties. Further research is needed to determine barriers and limitations to publication of abstracts to full text journal articles and to determine ways to ensure important research is disseminated to the clinical community as higher quality journal articles that have been subject to peer review and are available through indexing.

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**Management of Inflammatory Arthritis in Pregnancy: A National Survey of Canadian Rheumatologists**

Mary De Vera (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver); Corisande Baldwin (University of Calgary Faculty of Medicine,

Calgary); Nicole Tsao (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver); Alyssa Howren (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver); Stephanie Ensworth (University of British Columbia Faculty of Medicine, Vancouver)
**Objectives:** To survey rheumatologists across Canada about their current practice when treating inflammatory arthritis in pregnant patients, or those planning pregnancy, and to determine areas of consensus and discrepancy.
**Methods:** An online survey was developed consisting of 23 multiple-choice questions on the use of inflammatory arthritis therapies during management of planned and unplanned pregnancies in patients with various disease severities. Email invitations were sent to 450 members of the Canadian Rheumatology Association, including rheumatologists and rheumatology trainees, with data collected from March 8th to 28th, 2016. Responses were summarized with descriptive statistics.
**Results:** A total of 90 members responded to the survey (20% response rate), of which 58% were female and 69% worked in an academic/teaching hospital setting. There was representation from 9 provinces. The majority of respondents agreed that non-steroidal anti-inflammatory drugs (NSAIDs) are safe only during certain trimesters (72%), but 59% would not recommend discontinuing them in patients planning pregnancy. Most respondents (79%) agreed that azathioprine, sulfasalazine, and antimalarials were safe and can be used throughout pregnancy. Most also agreed (93%) that methotrexate, leflunomide, cyclophosphamide, and mycophenolate mofetil are not safe at all during pregnancy, and 96% would recommend discontinuation when planning pregnancy. In the event that a patient became pregnant on these latter four medications, 60% would discontinue the drug and counsel the patient regarding termination. Discrepancies were seen in responses about biologics, as 39% felt that tumour necrosis factor (TNF) alpha inhibitors are safe throughout pregnancy while 29% felt they are only safe during certain trimesters. Although the majority of respondents (78%) would not discontinue TNF alpha inhibitors in patients planning pregnancy, up to 27% would recommend discontinuation if a patient became pregnant while using a TNF alpha inhibitor. In general, there was little consensus in responses about the safety and practices of using cyclosporine, non-TNF alpha inhibitor biologics, small molecule inhibitors, mino/doxycycline, and gold salts in patients planning pregnancy, or during pregnancy. In open-ended comments, respondents wanted more guidance on medication compatibility with lactation, leflunomide washout, and disease specific recommendations.
**Conclusion:** Despite recently published international guidelines, much uncertainty still exists on prescribing medications in pregnant patients with inflammatory arthritis. Rheumatologists are currently divided regarding the safety of cyclosporine, non-TNF alpha inhibitor biologics, small molecule inhibitors, mino/doxycycline, and gold salts before and during pregnancy. Future research should focus on these specific treatments in order to inform evidence-based guidelines for medications use during pregnancy and lactation.

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## eHealth Supported Collaborative Care for Gout Involving Rheumatology, Pharmacy, and Dietetics: Mid-Term Outcomes

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(University of British Columbia Faculty of Medicine, Vancouver); Russell Friesen (Providence Health, Vancouver ); Mary De Vera (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver)
**Objectives:** Our objective was to evaluate the feasibility of the "Virtual Gout Clinic Study" (VGCS) a collaborative approach to gout management involving rheumatology, pharmacy, and dietetics that take advantage of shared access of electronic medical records (EMRs) to support this unique, decentralized model of care.
**Methods:** We conducted a proof-of-concept, longitudinal observational study beginning in February 2015. Patients with gout were eligible if they were: 1) seen in 1 of 4 participating rheumatology practices across BC; 2) experienced ≥1 flare in the past year; and 3) have a serum uric acid (SUA) level ≥ 360 µmol/L within the previous 2 months. Within the VGCS, patients receive follow-up with their rheumatologist on an as needed-basis, monthly telephone consults from the study pharmacist, one telephone consult with the dietician. All health care professionals have access to the shared EMR to facilitate remote communication and collaboration. Prospective data was collected at baseline, 3, 6, and 12 months. The primary outcome measure was SUA at 12-months, specifically below recommended target level of 360 µmol/L. Patient-reported outcome measures included the Compliance-Questionnaire-Rheumatology 5-item (CQR5) to assess medication adherence.
**Results:** 29 individuals with gout (86% male; mean age 59.2 ± 14.2 years) are enrolled in the VGCS. 27 patients have completed their 6-month follow-up. At baseline 20 (69%) patients were prescribed urate lowering therapy (ULT). Specifically, 19 patients were prescribed allopurinol (six at 100mg; five at 200mg; seven at 300 mg; and one at 600 mg) and one patient was prescribed febuxostat at 80 mg. The remaining 9 patients initiated ULT during the study period and allopurinol dosage was up-titrated for 12 patients between baseline and 6 months. A total of 117 pharmacist and 21 dietician consults have been provided. Mean SUA decreased over baseline, 3 months, and 6 months from 449 µmol/L, to 375 µmol/L, and lastly 357 µmol/L, respectively. 27 patients fully completed the CQR5 at baseline and 50% of patients were classified as adherent. By 6 months (n=15) 71% of patients were considered adherent.
**Conclusion:** These interim findings provide preliminary evidence for the feasibility and effectiveness of the VGCS. With respect to feasibility, we successfully established the shared EMR framework between rheumatologists and study pharmacist and dietitian and demonstrated utility with respect to facilitating communication and collaborative care between health care providers and providing outcomes data. With respect to effectiveness, interim findings show declining SUA over follow-up to 6 months and improved adherence. Supported by a CIORA grant. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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**Exploring how Individuals with Gout Experience an eHealth Supported Collaborative Care Model: Preliminary Results from a Qualitative Study**

Alyssa Howren (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver); Mary De Vera (University of British Columbia Faculty of Pharmaceutical Sciences; Arthritis Research Canada, Vancouver)
**Objectives:** To explore how individuals with gout experience and perceive the Virtual Gout Clinic (VGC), in an effort substantially expand understanding of the complexity of the context and circumstances under which participants experience an electronic health (eHealth) supported inter-professional care model for gout.

**Methods:** Qualitative interviews are the second stage in the overarching explanatory sequential mixed-methods evaluation of the VGC, a longitudinal study of a collaborative care model for gout involving rheumatology, pharmacy, and dietetics. Quantitative findings of the VGC integrate with the qualitative exploration through informing and directing the interview guide. The qualitative study will be applying the constructivist grounded theory design. Interviews are ongoing and participants are purposively sampled from the VGC to participate in a one-on-one semi-structured telephone interview. Eligible participants are those with 1) a rheumatologist diagnosis of gout, 2) completed at least 6 months in the VGC, and 3) can speak and comprehend English. Interviews are audio-recorded, transcribed verbatim, and imported to NVivo 11 for analysis. Data analysis utilizes the inductive, constant comparative method and applies the grounded theory concepts of theoretical sampling and memo-writing. Further, the qualitative design follows an emergent framework and engages in reflexivity.
**Results:** We sent 14 invitations to individuals with gout meeting the eligibility criteria. Preliminary qualitative analysis has resulted in the construction of three emergent themes. The first theme explores perceived benefits to the VGC, namely: a) convenience in terms of time and location; b) clarification and/or validation of medication concerns; c) understanding dietary "triggers"; and d) receiving personalized care. The second emerging theme encompasses logistical considerations such as coordination of telephone consults. Participants also expressed enrolment to the VGC would be optimal at the onset of a diagnosis of gout, specifically either when initiating medication therapy or before referral to a rheumatologist. The third theme centers on indifference among participants with regards to the communication or collaboration between health professionals, indicating no direct knowledge of this phenomenon.
**Conclusion:** The preliminary findings offer insight into the complexity of receiving care through an eHealth supported inter-professional care model for gout. Patients were receptive to the specialized support offered from health professionals, but knowledge of collaboration did not seem to significantly impact their overall experience. Initial results suggest the introduction of a care model for gout, such as the VGC, should take into account an individual's stage of diagnosis and disease status. Supported by a CIORA grant. Recognized by the CRA Optimal Care Committee for Quality Improvements and Choosing Wisely.

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## Experiences of Patients with Inflammatory Arthritis Negotiating Power on their Healthcare Team

Laura Nimmon (University of British Columbia, Vancouver); Catherine Backman (Arthritis Research Canada, Vancouver); Wendy Hartford (University of British Columbia, Vancouver); Raheem Kherani (University of British Columbia, Division of Rheumatology, Department of Medicine, Richmond ); Joyce Ma (Arthritis Research Canada, Richmond); Annette McKinnon (Arthritis Research Canada, Richmond); Shanon McQuitty (Arthritis Research Canada, Vancouver); Linda Li (University of British Columbia (Department of Physical Therapy)/Arthritis Research Canada, Richmond)

**Objectives:** It is known that a multidisciplinary team approach is the preferred mode of care delivery for chronic disease management, and patient-centered care is the ideal type of care. However, patients' active role participating in their own care is often hindered by the power dynamics of patient care negotiation that characterizes some healthcare team interactions. This ethnographic observational study examines the problematic context in which patients with inflammatory arthritis (IA) are expected to manage their care and to assert themselves in the decision-making process on their healthcare team.

**Methods:** We are purposefully sampling IA patients who have been diagnosed in the past five years. At the time of diagnosis, there are great demands on patients with IA where intensive symptom control is required to prevent disease complications supported by a multidisciplinary team. Patients are recruited through our research team`s social media outlets and health professional networks. They participated in 1-hour face-to-face in-depth interviews, and completed demographic, social network surveys and patient journals. Ethnographic field notes and patient health education documents were also collected. We use a qualitative approach with a three tiered analytic strategy that involves compiling items together at the specific level and then creating more abstract statements about patterns of relationships in the data.
**Results:** Data collection is ongoing. Seven participants (5 women; 2 men) aged between 25-70 have been recruited thus far. Four emerging themes have been identified in our preliminary analysis: (1) patients` preference for shared decision-making evolves as they learn more about their disease and take charge of their care, (2) patients` describe a variety of mechanisms they use to gain power on their healthcare team (referencing the opinion of a more influential team member; going silent; switching providers; ignoring treatment recommendations), (3) patients` sense of empowerment shifts depending on the healthcare team member they interact with, (4) patients experience burden having to "transfer" and "relay" information amongst team members about their treatment plan.
**Conclusion:** Findings illuminate the complex ways that patients with IA experience team-based care and how they negotiate power on their healthcare team. We are building on these preliminary findings by interviewing all healthcare team members (health professionals, informal caregivers) about their perception negotiating power in the decision making process around the patient's care. Mapping and describing team interactions around care may lead to further reflective practices around power negotiation to ensure patient empowerment and the enactment of patient-centered care philosophy.

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**Canadian Study of Outcomes in Adalimumab Patients with Support for Adherence: Results from the COMPANION Study**

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**Objectives:** Adalimumab (ADA) is a TNF-alpha inhibitor indicated for use in various inflammatory autoimmune diseases including rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Patients receiving ADA in Canada are eligible to enroll in a patient support program (PSP) providing personalized services including tailored interventions. This retrospective cohort study assessed the impact of specific factors, including PSP services and patient characteristics, on persistence and adherence to ADA.
**Methods:** An algorithm based on probabilistic matching was developed to link patients in the ADA PSP database to the IMS Health longitudinal pharmacy transaction database. Patients who started ADA therapy between July 2010 and August 2014 were selected and their prescriptions were evaluated for a period of 12 months after the index date to calculate days until end of

persistence (defined by a gap in therapy of ≥90 days), censored for patients who remained on therapy through month 12. Cox proportional hazards modelling provided hazard ratios (HR) for the association between persistence and patient characteristics and PSP services. Adherence, measured by medication possession ratio (MPR), was calculated and multivariable logistic regression provided adjusted odds ratios (OR) for the relationship between high adherence (MPR >= 80%) and patient characteristics and PSP services.
**Results:** The linkage algorithm yielded a final sample of 10,857 patients (2,067 RA, 2,499 AS or PsA). Statistically significant differences in the hazard rate of discontinuation and the odds of high adherence were identified across multiple variables. Male patients demonstrated 20% less likelihood of discontinuation (HR = 0.801, $p<0.0001$) and had a significantly greater odds of adherence (OR = 1.118, $p<0.015$). Relative to the 30-39 year category, older age groups had significantly greater odds of adherence (40-49, 50-59, 60-69, 70+; OR = 1.247, 1.234, 1.323, 1.411, $p<0.01$ for all comparisons). Patients receiving ongoing care coach calls were 72% less likely to cease therapy when compared to those who did not receive the interventions (HR = 0.282, $p<0.0001$) and were also more adherent (OR = 1.483, $p<0.0001$). Treatment abandonment (failure to initiate therapy after enrolment in the PSP) was >80% more frequent in patients who did not receive an initial care coach call ($p<0.0001$).
**Conclusion:** Ongoing care coach calls, as provided by the ADA PSP, were found to have a large and statistically significant association to greater patient persistence and adherence over 12 months. These results may help refine interventions aiming at improving treatment adherence.

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**Erectile Dysfunction in Men with Rheumatic Diseases: A Systematic Review**

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**Objectives:** Given the obvious female predominance of rheumatic diseases, significant attention has already been drawn to the impact of these conditions on female sexual function. Nevertheless, rheumatic diseases can also present with challenges that are unique to male sexual function and thus, we aimed to systematically review the prevalence of erectile dysfunction in rheumatic diseases.
**Methods:** Using Medline, EMBASE, and Web of Science electronic databases, we performed a systematic review to identify original articles evaluating the prevalence of erectile dysfunction, assessed using the validated international index of erectile function (IIEF-5) questionnaire, in men with rheumatic diseases, including systemic sclerosis (SSc), systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and ankylosing spondylitis (AS). The search was restricted to English articles and performed in May 2016. We hand-searched reference lists, review articles, and grey literature for relevant articles not captured by the electronic searches.
**Results:** Our literature search identified 54 studies of which 34 were selected for full-text review. Of the potentially relevant studies retrieved, 12 studies were included in the final analysis. Five studies (n=219) focused on patients with SSc and reported ED prevalence ranging from 81-88%. In these studies, ED was found to correlate with disease severity and was associated with ultrasonographic evidence of penile vascular impairment. Comparatively, in RA (3 studies, n=138) and AS subjects (4 studies, n=272), ED prevalence ranged respectively from 46-54% and 12-42%. In AS, increased Bath Ankylosing Spondylitis Disease Activity Index scores, duration of morning stiffness, and disease duration were associated with ED. In the aforementioned studies, the age-matched healthy control population had ED rates ranging from

11-27%. Of note, only 2 studies (n=35) examined SLE and/or antiphospholipid-antibodies-positive subjects but standardized questionnaires were not used to evaluate ED and thus, these studies were excluded.
**Conclusion:** Men with SSc, RA, and AS have a substantially higher prevalence of ED compared to age-matched healthy controls. Given the importance of normal erectile function in sexual health and quality of life, clinicians should be aware of the increased prevalence of ED in men with rheumatic diseases and offer preventative, as well as therapeutic strategies to minimize its impact.

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**Are there Genetic Predispositions to Diffuse Large B-cell Lymphoma (DLBCL) in Systemic Lupus (SLE)?**

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**Objectives:** The determinants of the increased risk of non-Hodgkin Lymphoma (NHL) in systemic lupus (SLE) are unclear. The most common type of NHL in SLE (as in the general population) is the Diffuse Large B-Cell lymphoma (DLBCL) subtype. Our purpose was to identify if known susceptibility loci for DLBCL occur more frequently in SLE.
**Methods:** We used data from a recent GWAS of SLE conducted in a North American case-control sample of European ancestry Our study comprised 7,219 SLE cases and 15,991 non-SLE controls, genotyped on Affymetrix Genome-Wide Human SNP Array 6.0. We studied 4 loci that have been associated with DLBCL in recent GWAS studies, to determine if these DLBCL-associated SNPs occur more frequently in SLE versus the general population.
**Results:** For the DLBCL SNP of interest rs2621416 on 6p21.32 (associated with HLA-DOB 1), while the G (versus A) risk allele is a risk factor for DLBCL, the same allele is protective for SLE (odds ratio, OR for the G allele in SLE versus the general population was 0.78, 95% confidence interval, CI 0.63, 0.97, p value 0.023). For the DLBCL SNP of interest rs4530903 on 6p21.32 (associated with HLA-DQA1), while the T (versus C) risk allele is a risk factor for DLBCL, the A allele was possibly protective for SLE (OR for the A allele in SLE versus the general population was 0.72, 95% CI 0.50, 1.02, p value 0.066). For the other two DLBCL SNPs of interest, the SLE OR was close to 1 with a wide confidence interval.
**Conclusion:** We did not identify an increased occurrence of known susceptibility loci for DLBCL in SLE in these analyses.

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**Comparative Effectiveness of Tofacitinib, Biologic Drugs and Traditional Disease-Modifying Antirheumatic Drugs in Rheumatoid Arthritis**

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**Objectives:** Tofacitinib is the first oral Janus kinase (JAK) inhibitor approved in the USA for the treatment of rheumatoid arthritis (RA). Our aim was to compare the effectiveness of traditional disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs and tofacitinib for RA

patients with inadequate response to methotrexate.
**Methods:** We performed a retrospective cohort study using MarketScan® Databases (2010-2014). We studied RA individuals, 18 years or older, previously treated with methotrexate (oral or SQ, at any time) and newly prescribed one of the medications under study (DMARDs, biologics or tofacitinib), between January 2011 and December 2013. The date of first filled prescription or infusion drug was defined as the cohort entry and individuals must have had no prior use of biologics or tofacitinib at any point before cohort entry. We required subjects to be continuously enrolled in the medical and pharmacy plan for 12 months before and 12 months after the cohort entry. A patient's therapy was defined as effective if none of the following occurred during the first year of follow-up: 1) non-adherence, defined as medication possession ratio (MPR) lower than 80% or the number of infusions lower than the minimum expected for each biologic. 2) Switching or adding a new biologic agent or tofacitinib. 3) Switching or adding a new DMARD. 4) Having at least one glucocorticoid joint injection between the months 4 and 12 of follow-up. We presented descriptive analysis of baseline characteristics and the proportion of patients achieving therapy effectiveness and the individual criteria by exposure groups.
**Results:** 16,305 RA patients were included; 2,879 began therapy with DMARD, 13,345 with biologics and 81 with tofacitinib. Among all patients, 77.5% were female and the mean age was 56.2 years (standard deviation 12.6). The rate of therapy effectiveness was 16.3% for DMARD, 17.9% for biologics, and 18.5% for tofacitinib. The rates for the individual criteria differed among groups. Fewer patients using biologic agents were non-adherent (54.5%) compared to DMARD (75.1%) and tofacitinib (69.1%), while more patients using biologic agents switched to or added a new biologic agent or tofacitinib (34.6%) compared to DMARD (16.1%) and tofacitinib (18.5%).
**Conclusion:** The results suggest that tofacitinib are not usually prescribed as a therapy option after inadequate response to methotrexate. At least through the end of 2014, patients initiating tofacitinib before biologics appear quite dissimilar to initiators of first time biologics. Further analysis should focus on outcomes of tofacitinib as second and third therapy options for RA patients.

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**Prevalence of Rheumatoid Arthritis Patients followed by a Rheumatologist in Edmonton & Northern Alberta**

Jason Soo (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

**Objectives:** While previous data has estimated the prevalence of rheumatoid arthritis (RA) in Alberta similar to the often cited prevalence of 1%, it is unknown how many patients actively follow with a rheumatologist. The aim of this study is to estimate the prevalence of RA patients in Edmonton and northern Alberta followed by a rheumatologist.
**Methods:** Cases of RA were identified from provincial billing data of all rheumatologists north of Red Deer from 2013-2014. All diagnoses were based on ICD-9 coding of rheumatoid arthritis (714.X) by a rheumatologist based on at least 1 clinic visit. Geographic location of each patient was mapped to the Alberta Health Services zone/subzone in which they live to further determine overall and zone population prevalence. Only AHS zones north of Red Deer were included in the analysis as it would be expected a majority of patients south of Red Deer would follow with a southern Alberta rheumatologist. Overall group demographics were also reported (sex, gender).
**Results:** 7647 patients with rheumatoid arthritis had at least 1 visit with a rheumatologist during the two-year period (average visits = 3.94). This represents an overall population prevalence of 0.379%. The majority of patients are women, with most patients between the ages of 56-

65. The prevalence of each health subzone varied significantly, from 0.212%-0.511%.
**Conclusion:** The prevalence of rheumatoid arthritis based on our data is significantly lower than the expected prevalence of 1%. This could suggest that many RA patients in Edmonton and northern Alberta are not receiving ongoing care from a rheumatologist. Further analysis is necessary to determine if this represents a gap in care or an artifact of improper coding of billing data by non-rheumatologists.

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**Risk of Lung Cancer from HRCT Scans in Systemic Sclerosis**

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**Objectives:** High-resolution computed tomographic (HRCT) scans are the gold standard for the diagnosis and follow-up of systemic sclerosis (SSc)-associated interstitial lung disease (ILD). However, there is concern that repeated radiation exposure might increase the risk of lung cancer. We undertook this study to determine if exposure to lung HRCTs is associated with lung cancer in SSc.

**Methods:** We designed a case-control study using data from the Canadian Scleroderma Research Group. We identified incident lung cancer cases recorded by study physicians. Cases were confirmed by pathology reports and/or death report forms. Visits at which the lung cancer diagnosis was recorded was identified as the index visit. Four controls, matched on time from cohort entry to index visit, were identified for each case. The exposure of interest was lung HRCTs, modeled as ever/never and, alternatively, as number of scans. We performed univariate and multivariate analyses to determine if exposure to HRCT was associated with lung cancer. Multivariate models were adjusted for age, sex, smoking exposure and presence of ILD. To minimize detection bias, we performed a sensitivity analysis excluding HRCT scans performed in the year prior to index visit.

**Results:** We identified 18 cases and 72 controls. Mean age (cases: 47.3, controls: 43.7 years) and disease duration (cases: 19.6, controls: 17.8 years) were similar in both groups. Cases were more likely to have diffuse cutaneous disease (50% vs 31%) and be male (67% vs 94%) compared to controls. Cases had a mean of 1.2 HRCT, compared to 0.7 for controls. In univariate analyses, ever HRCT (odds ratio (OR) 5.0, 95% confidence interval (CI) 1.3, 19.0) and number of HRCT (OR 2.3, 95% CI 1.2, 4.6) were significantly associated with lung cancer, although the estimates lacked precision. In multivariate analysis, there was a trend towards an association between HRCT and lung cancer (ever HRCT OR 9.3, 95% CI 0.9, 101.4; number of HRCT OR 2.1, 95% CI 0.9, 4.6). The results of the sensitivity analysis excluding HRCT done in the year prior to the index date were consistent with this (ever HRCT OR 4.6, 95% CI 0.8, 27.6; number of HRCT OR 1.3, 95% CI 0.7, 2.3).

**Conclusion:** Our results suggest that HRCT may be a risk factor for lung cancer in SSc. However, there was considerable uncertainty around the magnitude of the risk. A well-powered study would be required to confirm these findings and improve the precision of the magnitude of the risk.

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**Correlation between Antibodies to the Phosphotidylserine/Prothrombin Complex and Conventional Antiphospholipid Antibodies**

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**Objectives:** Autoantibodies to the phosphotidylserine/prothrombin (aPS/PT) complex are purported to be a surrogate for the lupus anticoagulant (LAC) and an independent risk factor for arterial/venous thrombotic events (TE) and pregnancy loss. This study examined the correlation between aPS/PT and the laboratory criteria for antiphospholipid antibody syndrome (APS): LAC, anticardiolipin (aCL), and anti-β2glycoprotein-1 (anti-β2GP1) and their associations with TE.
**Methods:** Patients fulfilling the American College of Rheumatology (ACR) or Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for SLE were enrolled in the University of Calgary Lupus Cohort. A single serum sample from each patient was analysed for aPS/PT (IgG/IgM) by ELISA (QUANTA Lite, Inova Diagnostics), LAC (tissue thromboplastin inhibition test and dRVVT with confirmation), and aCL (IgG) and anti-β2GP1 (IgG) by ELISA. The Spearman correlation between aPS/PT and the other autoantibodies and between each autoantibody and TE (defined as current usage of an anticoagulant) was calculated. The association between number of autoantibodies (IgG/IgM aPS/PT, LAC, aCL, and anti-β2GP1) and TE was assessed using univariate logistic regression.
**Results:** 183 patients were included; 91.3% were female with a mean age at diagnosis of 34.2 years (SD 15.1) and mean disease duration of 13.8 years (SD 11.6). 32.2% of patients were aPS/PT-positive, 9.9% LAC-positive, 13.3% aCL-positive, and 14.1% anti-β2GP1-positive. 11.6% were on anticoagulants. The aPS/PT was positive in 100% of patients who were LAC-positive and 24.5% of those who were LAC-negative. Among the IgG aPS/PT-positive, 64.0% were LAC-positive, 64.0% aCL-positive, and 66.7% anti-β2GP1-positive. Among the IgM aPS/PT-positive, 27.3% were LAC-positive, 29.5% aCL-positive, and 34.1% anti-β2GP1-positive. The correlation between IgG aPS/PT and LAC, aCL, and anti-β2GP1 was 0.72 (95% CI 0.64, 0.79), 0.60 (95% CI 0.49, 0.68), and 0.60 (95% CI 0.49, 0.68), respectively, and the correlation between IgM aPS/PT and LAC, aCL, and anti-β2GP1 was 0.33 (95% CI 0.19, 0.45), 0.27 (95% CI 0.12, 0.40), and 0.33 (95% CI 0.19, 0.45), respectively. The correlation between IgG aPS/PT, IgM aPS/PT, LAC, aCL, and anti-β2GP1 and TE was 0.27 (0.12, 0.40), 0.13 (-0.02, 0.27), 0.23 (95% CI 0.08, 0.36), 0.21 (95% CI 0.07, 0.35), and 0.25 (95% CI 0.11, 0.39), respectively. The odds of TE increased incrementally by 70% for each additional autoantibody (Odds Ratio 1.70, 95% CI 1.25, 2.31).
**Conclusion:** IgG aPS/PT is highly correlated with other antiphospholipid antibodies, particularly LAC. IgG aPS/PT and the accepted laboratory criteria of APS are all similarly correlated with TE. IgG aPS/PT should be considered as a criterion for APS.

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**Does she or doesn't she? A Case of an Atypical Autoantibody Profile in a Patient with SLE**

Samuel Pike (McGill University, Montreal); May Choi (University of Calgary, Calgary); Ann Clarke (University of Calgary, Calgary); Marvin Fritzler (University of Calgary, Calgary)

Autoantibodies directed against nuclear autoantigens (ANA) are a serological hallmark of and a classification criterion for SLE. However, 5-20% of SLE patients are reported to be ANA-negative. We report a 46-year-old female presenting with clinical features of SLE, including diffuse alopecia, oral ulcers, polyarthritis, pleuritis, myalgias, sicca symptoms, fatigue, and low-grade fever. Conventional ANA testing on HEp-2 (human epithelial) cells in a large regional laboratory was repeatedly negative. However, testing at a specialty laboratory revealed multiple

autoantibodies directed to non-nuclear HEp-2 cell components, including centrosomes, the midbody of telophase cells, and other cytoplasmic components at a titre of 1/320. Although the lupus anticoagulant was negative by routine tests, the patient had IgM autoantibodies to the phosphatidylserine/prothombin (PS/PT) complex, a purported surrogate for the lupus anticoagulant. All other autoantibodies were negative, including dense fine speckles (DFS70), double-stranded DNA, Sm, Ro52/TRIM21, SSA/Ro60, SSB/La, RNP, PCNA, Ku, ribosomal P, C1q, chromatin, cardiolipin, and β2-glycoprotein 1. Her CBC, ESR, C-reactive protein, C3, C4, creatinine, urinalysis, and urine protein/creatinine ratio were normal; Coombs' test was negative. A CT angiogram revealed no pulmonary emboli. She was treated with moderate dose prednisone with rapid improvement.

This case describes a patient with clinical, but not classifiable SLE as she fulfilled only three of the required four American College of Rheumatology (ACR) Classification Criteria. Although she fulfilled four of the Systemic Lupus International Collaborating Clinics Classification Criteria, these were all clinical and she did not meet at least one immunological criterion. Many laboratories will only report a positive ANA when nuclear staining is observed and, as in this case, cytoplasmic staining goes unreported. A negative ANA in SLE may reflect: 1) presence of autoantibodies directed to cytoplasmic or antigen targets uniquely expressed during mitosis (as in this case), 2) conventional HEp-2 antigenic substrate(s) that typically do not detect certain autoantibodies (e.g. SSA/Ro60, Ro52/TRIM21, ribosomal P, 3) inactive disease or immunosuppression in a patient with a previously positive ANA, or 4) persistent profound proteinuria. As illustrated by this case, autoantibodies other than ANA should be reported as they may provide serological evidence for B cell dysregulation and a diagnosis of SLE, facilitating early initiation of therapy and avoidance of unnecessary consultations and diagnostic procedures. Despite the ACR proclaiming the ANA as the "gold standard" screening test for SLE, clinicians should be aware of its limitations and informed of how their laboratory reports ANA and if cytoplasmic staining is included.

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## The Relationship between Comorbidity and Non-Surgical Treatment of Knee Osteoarthritis

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**Objectives:** Knee osteoarthritis (OA) is associated with significant morbidity and mortality, yet remains under-diagnosed and under-treated. A potential barrier to OA care is the high prevalence of comorbidity in people with OA, which may preclude safe use of recommended therapies. Our aim was to examine the relationship between comorbidity and non-surgical treatment of knee OA.

**Methods:** In consecutive patients with primary knee OA referred to orthopaedic surgery for total knee arthroplasty, a standardized questionnaire assessed socio-demographics, knee OA severity (WOMAC pain, KOOS-PF), medical comorbidities, and ever and current use of recommended non-surgical OA therapies (exercise, weight loss, acetaminophen, NSAIDs, opioids, intraarticular injections, physical therapy, walking aids, and biomechanical devices (insoles, braces, etc.)). Comprehensive treatment was defined as use of exercise and analgesia, plus weight loss if BMI ≥ 25 kg/m2. Multivariate logistic regression assessed the relationship between number of comorbidities (0, 1, 2 and ≥3) and OA treatment, adjusting for socio-demographics, BMI and OA severity.

**Results:** 1,448 participants were included: mean age 65.4 years (SD 9.1), 58% female, mean BMI 32.5 kg/m2 (SD 6.8), mean WOMAC pain 11.6/20 (SD 3.7) and mean KOOS-PF 56.2/100 (SD 17.9). 72% self-reported ≥ 1 comorbidity (1: 35.7%, 2: 23.3%, ≥3: 12.9%). Overall, 54.3% and 24.1% of participants self-reported ever and current receipt of comprehensive treatment, respectively. In multivariate analysis, only the following specific treatments were related to level of comorbidity (adjusted ORs [95% CIs] compared to 0 comorbidities): exercise ever (1: 0.61 [0.46–0.88], 2: 0.65 [0.44–0.95], ≥3: 0.72 [0.45–1.14]) and current (1: 0.65 [0.49–0.86], 2: 0.73 [0.53–1.00], ≥3: 0.66 [0.45–0.97]); NSAIDs ever (1: 0.79 [0.55–1.14], 2: 0.55 [0.38–0.81], ≥3: 0.52 [0.33–0.82]); and current (1: 0.90 [0.67–1.20], 2: 0.71 [0.51–0.97], ≥3: 0.66 [0.45–0.97]); opioids ever (1: 1.22 [0.91–1.63], 2: 1.44 [1.04–1.99], ≥3: 2.15 [1.45–3.18]) and current (1.38 [0.99–1.90], 2: 1.56 [1.09–2.22], ≥3: 2.41 [1.60–3.62]); and walking aid ever (1: 0.97 [0.71–1.33], 2: 1.31 [0.93–1.84], ≥3: 2.13 [1.42–3.19]) and current (1: 1.22 [0.86–1.72], 2: 1.33 [0.91–1.93], ≥3: 2.21 [1.45–3.37]).
**Conclusion:** At surgical referral, the proportion of patients self-reporting prior and current comprehensive treatment for knee OA is low. We found an association between burden of comorbidity and several therapies, including exercise. Clinical trials are needed to identify safe and effective approaches to management of OA in people with comorbidities.

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**Predictors of Patient Reported Decision to Discontinue Anti-Rheumatic Medication in Rheumatoid Arthritis Patients: Data from a Rheumatoid Arthritis Cohort**

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**Objectives:** Despite the availability of safe and effective treatments and the establishment of treatment guidelines, real-world effectiveness remains suboptimal largely due to low patient adherence with prescribed treatment. The purpose of this study was to systematically evaluate sociodemographic, health insurance, and disease-related factors associated with patient reported decision for discontinuation of anti-rheumatic medications (ARM) in a large observational cohort of RA patients followed in Canadian routine clinical care.
**Methods:** RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) clinical registry and had at least two years of follow-up were included in the analysis. Treatment discontinuation due to patient reported decision was defined as ARM discontinuation. Independent predictors of ARM discontinuation were evaluated with multivariate cox-regression using both time-fixed and time-dependent variables. Factors considered included patient sociodemographics (age, gender, race, education status, annual income, smoking history), health insurance information (private vs. non-private, % coverage), disease parameters (RA duration, presence of erosion, RF positivity, DAS28, physician global, HAQ-DI, number of comorbidities), types of medications used, and physician characteristics (gender, academic position, urban vs. rural, distance from patient's residence).
**Results:** A total of 1,762 patients were included in the analysis with a mean (SD) age of 57.4 (13.0) years and disease duration of 8.5 (9.3) at the time of enrolment to the registry (baseline). The majorities of patients were female (77.7%), had post-secondary education (55.3%), and had

private insurance (67.2%). In terms of disease severity, 54.5% had prior erosion, 69.5% were RF positive, and mean (SD) DAS28 was 4.5 (1.5). In a multivariate analysis, married status (HR, 0.73 ; 95% CI 0.56-0.96), RF positivity (HR, 0.73 ; 95% CI 0.56-0.96), and higher number of comorbidities (HR, 0.92 ; 95% CI 0.85-0.99) were identified as significant predictors of ARM continuation while higher physician global score (HR, 1.10 ; 95% CI 1.04-1.15), NSAID use (HR, 1.75 ; 95% CI 1.29-2.38), and polypharmacy (HR, 1.23 ; 95% CI 1.07-1.40) were associated with ARM discontinuation due to patient reported decision. In a subset analysis, multivariate analysis showed that higher HAQ and use of bDMARDs over time were significantly associated with a lower hazard for discontinuation of csDMARDs and/or bDMARDs.

**Conclusion:** In this systematic approach a variety of factors encompassing sociodemographics, disease, and medication characteristics, were identified as significant independent predictors of ARM discontinuation due to patient reported decision. These results should be taken into consideration when developing patient adherence support programs and in the choice of treatment regimens.

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**Psychometric Evaluation of a Modified Measure of Presenteeism in Inflammatory Arthritis**

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**Objectives:** Recent employment studies in arthritis have drawn attention to the importance of decreased productivity at work, or presenteeism. Yet, how to best measure presenteeism remains challenging. The Work Limitations Questionnaire (WLQ) is frequently used. A drawback is that it measures the amount of time when people are limited in performing their job, rather than the extent to which they are limited. In contrast, the Workplace Activity Limitations Scale (WALS), measures the extent of limitation but not time. To evaluate the need for both concepts, items from each tool were offered both time and difficulty response scales (dual scales). The objective of our study was to evaluate the psychometric properties of the instruments; specifically internal consistency, criterion and construct validity.

**Methods:** Baseline data from the RCT of an employment intervention, the Making It Work Program, were used. Participants were recruited from BC, Alberta and Ontario. Inclusion criteria included: diagnosis of inflammatory arthritis, currently employed, age 19-59, and having concerns about arthritis affecting ability to work. The sample includes 364 participants (195 with RA, 54:PsA, 46:Lupus, 69: AS; 77% female; mean(SD) age: 45.9(9.8) years, 84% Caucasian). Degree of difficulty was correlated to amount of time for each item, using polychoric correlations. Internal consistency of each scale/subscale was evaluated using polychoric alphas, separately, for difficulty and time. Criterion, and construct, validity were evaluated by measuring correlation (Pearson and Spearman coefficients) between WALS or WLQ and other presenteeism measures (WPAI and WIS); and, other constructs expected to influence limitations at work, such as disease measures and job characteristics, respectively.

**Results:** High correlation ($\geq 0.8$) between difficulty and time was only found in 2/12 items (WALS) and 11/25 (WLQ), justifying the need for dual answer scales. High internal consistency was found for WALS and all WLQ subscales for both answer scales (alphas 0.690-0.926), with higher consistency for difficulty than time. Moderate correlations were found between WALS or WLQ and WPAI and WIS (0.41-0.77), with higher correlations for difficulty than time. For

almost all disease and job measures, correlations in the expected direction, varying from mild to moderate, were found with WALS and WLQ time and difficulty scales.
**Conclusion:** Our results confirm the value of evaluating both degree of difficulty and amount of time, because they seem to measure different constructs. Our study demonstrated initial indicators of reliability and validity for both components of the dual scaled versions of the WALS and WLQ.

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## Collection of Anti-Rheumatic Medication Data from Both Patients and Rheumatologists Shows Strong Agreement in a Real World Clinical Cohort: The Ontario Best Practices Research Initiative (OBRI) a Rheumatoid Arthritis Cohort

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**Objectives:** Collection of Anti-Rheumatic Medication (ARM) information from both patients and rheumatologists is considered a strength for Rheumatoid Arthritis (RA) registries and cohorts. However, it is important to assess the agreement between these two data sources. We aimed to examine the agreement of ARM reporting between patients and rheumatologists in the Ontario Best Practices Research Initiative (OBRI).
**Methods:** Adult Patients enrolled in the OBRI who consented to both patient interviews and rheumatologist evaluations were included. Patients in the OBRI are interviewed every six months, while rheumatologist assessments are conducted as per routine care. For this analysis, we compared reports where rheumatologist visits and interviews occurred within 60 days of each other. ARM included conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs) and biologic DMARDs (bDMARDs). Sensitivity and Positive Predictive Value (PPV) of rheumatologist reports were calculated using the patient's report as gold standard. Kappa statistics of agreement between the two data sources were calculated. To examine factors associated with agreement, logistic regression was used to model the odds of agreement.
**Results:** 2,862 patients (78.1% female) were included with a mean (SD) age at OBRI enrolment of 57.5 (12.8) year. Mean (SD) disease parameters were: DAS28: 4.3 (1.6); SJC: 5.5 (4.9); TJC: 6.0 (6.2); physician global: 4.2 (2.5); patient global: 4.8 (2.8), and HAQ disability Index: 1.2 (0.8). The prevalence of csDMARDs and bDMARDs was 69.6% and 19.5% in patient reports, respectively, whereas in rheumatologist reports, the prevalence was 73.3% and 20.6%, respectively. The sensitivity of rheumatologist reports was 96.4% for csDMARDs and 93.7% for bDMARDs. Overall agreement for ARM reports between the two data sources was interpreted as good (Kappa: 0.72; 95%CI: 0.71-0.73, p=0.01). In a multivariate logistic regression, higher DAS28 was significantly associated with the lower agreement (OR: 0.91; 95%CI: 0.87-0.96, p=0.0002). By contrast, older age (OR: 1.01; 95%CI: 1.01-1.02, p<0.0001), higher annual household income (>50,000 vs ≤ 50,000 CD) (OR: 1.41; 95%CI: 1.27-1.57, p<0.0001), female rheumatologist (OR: 1.16; 95%CI: 1.05-1.29, p=0.01) and academic rheumatologist (OR: 1.30; 95%CI: 1.17-1.44, p<0.0001) were significantly associated with higher agreement between the data sources.
**Conclusion:** The results of this analysis suggest that ARM reports from the two data sources have strong agreement in the OBRI. This agreement is even better for patients who are older, have higher income and are being treated by a female, academic rheumatologist. Further analysis is proposed to assess agreement between patient and rheumatologist reported ARM start and stop

dates.

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**Mortality Trends in Systemic Sclerosis: A Population-based Study**

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**Objectives:** Systemic Sclerosis (SSc) is associated with significant morbidity and mortality. Improvement in mortality has been demonstrated for some rheumatic diseases (e.g. rheumatoid arthritis). Mortality trends in SSc are largely unknown. To address this knowledge gap, we evaluated mortality trends in patients with SSc in the context of a general population, from January 1, 1997 to December 31, 2012.

**Methods:** Using an administrative health database from the province of British Columbia, Canada (population 4.5 million), we identified all incident cases of SSc and up to 10 non-SSc controls matched on age, gender, and year of entering the study. The cohort was then divided into two sub-cohorts based on the year of SSc diagnosis to evaluate trends in mortality. Cox proportional hazard model was used to calculate hazard ratios (HR). We calculated the rate difference using as additive hazard model, while adjusting for possible confounders (i.e. healthcare utilization, comorbidities, medications at baseline).

**Results:** Overall mortality in SSc patients continues to remain higher in comparison to the general population, with a hazard ratio of 2.74 (95%CI 2.22-3.33). This trend is seen across all age groups in the study. Furthermore, comparison of overall mortality between early and late cohorts remains elevated with HR of 3.44 (95% CI 2.30-5.13) and HR of 2.20 (95% CI 1.66-2.97), respectively amongst patients suffering from SSc.

**Conclusion:** Our population-based study shows that patients with SSc have an increased risk of premature death. Unlike other rheumatic diseases no improvement on survival has occurred. This gap warrants further research to better elucidate the pathogenesis of systemic sclerosis and to develop novel therapies to improve overall survival and quality of life in those afflicted with the disease.

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**Methotrexate Therapy Associated with Radiographic Improvement in Osseous Sarcoidosis**

Nicolas Richard (McGill University, Jewish General Hospital, Montreal); Ines Colmegna (McGill University Hospital Centre, McGill University, Montreal); Pantellis Panopalis (McGill University, Montreal)

Sarcoidosis is a multisystem inflammatory disorder characterized by noncaseating granuloma formation[1]. Rheumatologic manifestations are among the most common extra-pulmonary manifestations of this disease[2].

A 37-year-old man with a known diagnosis of pulmonary, cutaneous and ocular sarcoidosis, presented with new-onset of pain and swelling in several joints and phalanges of both hands. Synovitis of the 2nd and 4th right proximal interphalangeal joints was confirmed by ultrasound. Radiographs showed a lace-like permeative pattern involving the proximal phalanx of the second digit bilaterally and the middle phalanx of the right fourth and fifth digits; as well as acro-osteolysis of the left fifth digit (figures 1A and 2A).

The patient’s history and radiographic findings supported the diagnosis of sarcoid arthropathy with osseous involvement. Oral methotrexate 20 mg weekly was added to his previous treatment

[azathioprine (150 mg daily) and prednisone (10 mg daily)]. At a 3-month follow-up visit, clinical improvement was noted and the prednisone was tapered to 2.5 mg daily. Radiographs done 6 months following the start of methotrexate therapy showed significant bone repairing and reduction in soft tissue swelling (figures 1B and 2B).
Corticosteroids are considered a first-line therapy in sarcoidosis, and can decrease pain and inflammatory changes at sites of bone involvement[3, 4]. However, they do not normalize the bone abnormalities[4]. In cases of corticosteroid therapy failure, the use of methotrexate in sarcoid arthropathy is supported by limited data from case series[2, 5]. To our knowledge, this is the first report of radiographic regression of bone abnormalities with methotrexate.
[FIGURES 1 AND 2 TO BE INCLUDED ON POSTER]
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**Severe Gastrointestinal Disease in Early Systemic Sclerosis is Associated with an Increased Risk of Mortality**
Nicolas Richard (McGill University, Jewish General Hospital, Montreal); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal); Mianbo Wang (Lady Davis Institute for Medical Research, Montreal); Murray Baron (McGill University, Jewish General Hospital, Montreal); Canadian Scleroderma Research Group (Montreal); Genevieve Gyger (McGill University, Jewish General Hospital, Montreal)
**Objectives:** Studies of severe gastrointestinal(GI) disease in systemic sclerosis(SSc) are limited by small, selected samples composed largely of subjects with prevalent disease. We undertook this study to examine the morbidity and mortality associated with severe GI disease in SSc in a large, unselected inception cohort.
**Methods:** A retrospective cohort of subjects with <3 years of disease duration and without severe GI disease at baseline study visit was identified from the Canadian Scleroderma Research Group registry. Severe GI disease was defined using a previously published definition(Steen and Medsger, A and R 2000) as follows:malabsorption, hyperalimentation, pseudo-obstruction, or either antibiotics for bacterial overgrowth or esophageal stricture requiring dilatation with ≥10% associated weight loss. Subjects who developed severe GI disease during follow-up were compared to those who did not using descriptive statistics. Morbidity was assessed with the Medical Trust Short Form 36(SF-36) physical(PCS) and mental(MCS) component summary scores. Mortality rates between subjects with and without severe GI disease were compared by dividing the number of deaths per person-years of observation in each group.
**Results:** Data was available for 306 subjects with <3 years of disease duration; of these, 21(7%) had severe GI disease at baseline study visit. Severe GI disease over a mean follow-up time of 3.8 years developed in an additional 18%(50/285) of subjects: 84% female, mean age 53 years,

mean disease duration at baseline 1.6 years and proportion with limited/diffuse cutaneous SSc 54%/46%. Subjects who developed severe GI disease were more likely to have digital ulcers(52.0% vs 35.7%,p=0.03) and worse skin scores(15.7±12.0 vs 12.1±10.9,p=0.003) at baseline study visit. Physical health status was more impaired at baseline in subjects with compared to without severe GI disease(SF-36 PCS 35.4±11.3 vs 39.0±10.9,p=0.05). There were no difference in mental health status between the 2 groups at baseline(SF-35 MCS 47.1±11.3 vs 48.6±12.2,p=0.30). There were 10 deaths in 137 person-years of observation among those with, compared to 21 in 1040 person-years of observation among those without severe GI disease, for a mortality rate of 3.7.

**Conclusion:** Severe GI disease was common in this inception cohort, affecting approximately 25% of subjects within the first 5 years of disease. It was associated with considerable impairment in physical health status and a striking increase in the risk of mortality. Baseline predictors of severe GI disease included markers of vasculopathy and fibrosis. These findings provide compelling evidence to identify interventions that target selected pathophysiological pathways to reduce the burden of severe GI disease in SSc.

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**Immunosuppression Does Not Prevent Severe Gastrointestinal Disease in Systemic Sclerosis**

Nicolas Richard (McGill University, Jewish General Hospital, Montreal); Marie Hudson (McGill University, Jewish General Hospital, Lady Davis Institute for Medical Research, Montreal); Mianbo Wang (Lady Davis Institute for Medical Research, Montreal); Murray Baron (McGill University, Jewish General Hospital, Montreal); Canadian Scleroderma Research Group (Montreal); Genevieve Gyger (McGill University, Jewish General Hospital, Montreal)

**Objectives:** Severe gastrointestinal (GI) disease is associated with considerable morbidity and high mortality in systemic sclerosis (SSc). There are no known preventative treatments. We wished to test the hypothesis that exposure to immunosuppression (for skin, lung, joint or muscle condition) in early disease could modify the risk of severe GI disease in SSc.

**Methods:** Subjects with < 3 years of disease duration (since the onset of the first non-Raynaud's disease manifestation) and without severe GI disease at baseline study visit were identified from the Canadian Scleroderma Research Group registry. Severe GI disease was defined using a previously published definition (Steen and Medsger, A and R 2000) as follows: malabsorption, hyperalimentation, pseudo-obstruction, or either antibiotics for bacterial overgrowth or esophageal stricture requiring dilatation with ≥10% associated weight loss. A retrospective cohort study was performed with immunosuppression to methotrexate, azathioprine, mycophenolate and/or cyclophosphamide as the exposure of interest and severe GI disease as the outcome. Descriptive statistics were used to compare the baseline characteristics of the subjects, according to exposure status. The risk of severe GI disease in exposed versus unexposed subjects was estimated using a Cox proportional hazard model, with exposure to immunosuppression modeled as a time-dependent variable and including inverse probability of treatment weights (IPTW) to account for confounding. The model was adjusted for potential demographic and disease-related confounders.

**Results:** This study included 285 subjects, 84% female, mean age 53 years old, mean disease duration at baseline 1.6 years, proportion limited/diffuse cutaneous SSc 54%/46%. During a mean follow-up time of 3.8 years, 152 (53%) subjects were exposed to immunosuppression and 133 (47%) were not. In univariate analyses, subjects exposed to immunosuppression were more likely to have diffuse disease (62.5% vs 26.3%, p<0.001), interstitial lung disease (37.8% vs

18.9, p<0.001%), inflammatory myositis (14.6% vs. 1%, p<0.001) and worse skin scores (16.5 ± 11.2 vs 8.4±9.5, p<0.001) at baseline study visit. In a multivariate Cox proportional hazard analysis modeling immunosuppression as a time-dependent variable and incorporating IPTW, exposure to immunosuppression did not modify the risk of developing severe GI disease: hazard ratio 0.71, 95% confidence interval 0.32, 1.58.
**Conclusion:** Contrary to our hypothesis, exposure to immunosuppression did not prevent severe GI disease. Further research is required to identify effective prevention and treatment interventions for severe GI disease in SSc.

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**H-Indices of Two University Medical Departments: An Evaluation of Academic Rank, Gender, Number of Reviews and Salary**

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**Objectives:** Research productivity, as measured by the H-index, is an important factor in determining promotion, tenure and grant support at certain academic institutions. However, the H-index may vary by specialty across institutions, and may also be biased towards researchers who frequently publish highly-cited review articles. The aim of this study was to examine the influence of academic rank, gender, and number of reviews on H-index score, as well as determine any relationship in between H-index scores and salaries received by a researcher within a medical faculty.
**Methods:** A public information search was conducted to obtain faculty member lists from two academic medical institutions in Canada. Academic ranking, specialty and gender identifiers were obtained for all members of the Faculty of Medicine at each respective school. H-indices as of July 2016 were calculated using Scopus. Publicly available information about Government compensation was found on the salary and severance disclosure page through the Government of Alberta, although not available for comparison from the other institution.
**Results:** 1977 faculty of medicine employees were identified from 2 Canadian universities (822 assistant professors, 561 associate professors, and 594 full professors). There was a significant difference in H-indices between all academic ranks (p<0.0001). Median (IQR) H-indices were 2 (0-6), 9 (4.5-15) and 23 (14-34) for assistant, associate and full professors, respectively. H-index comparison between males and female was significantly different in favour of male academic professors (males 10 (3-21); females 5 (2-14)). When examining faculty with an H-index greater than 30, it was found that 81.4% of this group experienced a decrease in H-index when their review articles were excluded from H-index calculation. A positive correlation was noted between H-index and level of public compensation within a select group.
**Conclusion:** The results provide some guidance as to expected H-indices within medical faculties in Canada. These results may also provide evidence suggesting that faculty members with higher academic productivity may have a larger amount of public compensation. A significant difference exists between the H-indices of male and female faculty at both institutions. Furthermore, these results demonstrate the need to develop institution based guidelines for H-index, as there was a significant difference between the two institutions in regards to H-indices.

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**Evaluating the Associations between Motivation and Physical Activity Participation in People with Knee Osteoarthritis**

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Richmond); Johannes Rebane (University of British Columbia, Vancouver); Lynne Feehan (Arthritis Research Centre, Vancouver); Alison Hoens (University of British Columbia, Vancouver); John Esdaile (University of British Columbia (Division of Rheumatology)/Arthritis Research Canada, Richmond); Linda Li (University of British Columbia (Department of Physical Therapy)/Arthritis Research Canada, Richmond)
**Objectives:** Physical activity is a key component of successful osteoarthritis (OA) management. Theory of Planned Behaviour states that adoption of a health behaviour (e.g., being active) is driven by a set of constructs comprising Perceived Behavioural Control (PBC), Attitude, and Subjective norm. This cross-sectional pilot study aimed to explore associations between these motivational constructs and physical activity participation in knee OA patients.
**Methods:** 51 participants from Vancouver, BC (mean age 62.5 [SD 9.0] years; 82.4% female) with knee OA and no contraindication to physical activity were assessed using the Knee Injury and OA Outcome Score (KOOS) questionnaire. Participants' motivation for physical activity was measured using Rhode's Theory of Planned Behaviour questionnaire. The SenseWear accelerometer (7-days continuous wear) was used to derive time during all hours spent performing moderate-to-vigorous physical activity (MVPA) at >3 METs (easy walking) and >4 METs (gardening or higher level activity). Associations of these (in minutes/day) with KOOS and Theory of Planned Behaviour questionnaire results were tested using Spearman's correlation. Independent variables significantly associated with MVPA ($p < 0.05$) were further tested using linear regression models, adjusting for confounders.
**Results:** In correlation analysis, MVPA at >3 METs and at >4 METs had significant positive correlation with Attitude (>3 METs [rs=0.39, p=0.005]; >4 METs [rs=0.37, p=0.008]). MVPA at >4 METs also had a significant positive correlation with PBC (rs=0.28, p=0.047) and the KOOS Activities of Daily Living subscale (rs=0.32, p=0.024). MVPA participation was analysed by several linear regressions, using Theory of Planned Behaviour constructs as predictors. Linear regression analysis showed a significant association between Theory of Planned Behaviour constructs and MVPA at >4 METs (R2adj=11.5%; F(4, 46)=2.6, p=0.047), but not at >3METs (R2Adj=8.4%; F(3,47)=1.4, p=0.242).
**Conclusion:** Results from this pilot study suggest weak but significant correlations between Theory of Planned Behaviour constructs and MVPA. While linear regressions showed a significant association between these constructs and >4 METs MVPA, the model fit was poor, suggesting that other factors may play additional roles in MVPA participation.

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**Systematic Review of Non-Surgical Therapies for Osteoarthritis of the Hand: An Update**

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**Objectives:** To systematically review published randomized controlled trials (RCTs) evaluating pharmacological and non-pharmacological therapies in patients with hand osteoarthritis (OA), updating our earlier 2005 and 2009 systematic reviews. Surgical therapies were not evaluated.
**Methods:** Published RCTs between 1966 and December 2015 were identified by searching electronic data sources, as well as reference lists. A total of 1755 non-duplicate citations were screened and 173 RCTs were reviewed in full text. Of these, 94 RCTs met inclusion criteria. Details of study demographics, methodology, quality, and outcomes were analyzed.
**Results:** When compared with hip and knee OA, there were surprisingly few published RCTs in hand OA. There were 8 RCTs that studied systemic NSAIDs, 8 studied dietary supplements, 8

studied other systemic agents, 11 studied intra-articular therapies, and 10 studied topical pharmacologic therapies. Amongst RCTs evaluating non-pharmacologic therapies, 14 examined the efficacy of gloves/splints, 8 used exercise as the intervention, and 27 miscellaneous studies used other non-pharmacologic therapies, including therapies with leeches, paraffin baths, and low level lasers. Overall, there was evidence that systemic NSAIDs, chondroitin supplements, topical trolamine salicylate, and topical capsaicin were more efficacious than placebo. The remainder of the therapies had mixed or negative results, or efficacy was only demonstrated in a single study. There was an increase in published RCTs in hand OA with each decade (2 RCTs published between 1970-1979, 5 between 1980-1989, 14 between 1990-1999, 34 between 2000-2009, and 39 between 2010-2016). Generally, these RCTs were of low quality with an average Jadad score of 2.98 (with a range of 0 to 5, with a higher score reflecting higher quality). RCTs were weakened by lack of consistent case definitions and standardized outcome assessments prior to 2006, with improvements noticed after publication of the OARSI Consensus Recommendations for the Conduct of RCTs in Hand OA. The methods used for randomization, blinding, and allocation concealment were often not described. The number and location of symptomatic and evaluated hand joints per treatment group were usually not stated.
**Conclusion:** It is apparent that hand OA is a more complex area in which to study the efficacy of therapies when compared to hip and knee OA. There have been some improvements in RCT quality over time, with increasing Jadad scores over each decade since the 1990s. Additional RCTs of high quality are needed to evaluate the diverse therapeutic options available for patients with hand OA.

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**Systematic Review of Randomized Controlled Trials Evaluating Bisphosphonates for the Prevention and Treatment of Glucocorticoid- Induced Osteoporosis**

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**Objectives:** Glucocorticoid therapy is a major risk factor for osteoporosis related fractures. A meta-analysis conducted by Homik et al reported bisphosphonate therapy increased BMD in glucocorticoid- induced osteoporosis (GIO) when compared to placebo, whereas results for incident vertebral fracture did not reach statistical significance. The objective of this systematic review was to evaluate the efficacy of bisphosphonates in GIO based on randomized controlled trials (RCTs). Both placebo-controlled and active comparator trials were analyzed.
**Methods:** Two authors screened citations from Medline (1998-2015), EMBASE (1998-2015), and Cochrane Library (1998-2015). A manual search was completed for conference proceedings from the ACR (2010-2015), CRA (2009-2015), and ASBMR (2009-2014). We used the study by Homik et al to identify RCTs published prior to 1998. Only RCTs with a minimum prednisone dosage of 5 mg/day or equivalent and treatment duration of at least 3 months were included. Primary outcomes were changes in BMD and incident fractures. Two authors abstracted data using a standardized data abstraction form. We used the Cochrane Risk of Bias Tool to evaluate the quality of selected RCTs and devised a quality score ranging from 0 to 6, where 6 represents the highest quality.
**Results:** A total of 466 citations were identified (239 Medline, 217 EMBASE, 10 Cochrane Library). Fourteen RCTs met the inclusion criteria. An additional two RCTs were identified from conference proceedings. Eleven RCTs compared bisphosphonate to placebo, three RCTs compared bisphosphonate to a vitamin D derivative, one RCT compared alendronate to

teriparatide, and one RCT compared zoledronic acid to risedronate. RCTs were of reasonably good quality with a mean quality score of 4. Overall, of the 11 RCTs that compared bisphosphonate to a placebo, all found bisphosphonate was superior. Nine RCTs were pooled for mean percentage change in lumbar spine mean BMD (bisphosphonates n=667, placebo n=654). The pooled mean percentage change was in favor of bisphosphonates compared to placebo [weighted mean difference(WMD) of 4.03%, 95% CI (1.59-6.47), p=0.001]. Six RCTs were pooled for mean percentage change in femoral neck BMD (bisphosphonates n=486, placebo n=481) and the results favored bisphosphonates compared to placebo [WMD of 2.95%, 95% CI (0.09 -5.82), P=0.04]. Seven RCTs were pooled for outcome of incident fractures (bisphosphonates n=613, placebo n=469) and the results favored bisphosphonates compared to placebo [RR of 0.65, 95% CI (0.48-0.88), P= 0.006]. Results were pooled using RevMan (version 5.3).

**Conclusion:** Bisphosphonates mitigate adverse changes in BMD and lower fracture risk in patients treated with glucocorticoids.

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**The Rationale for Using a Composite Score when Designing Future Randomized Controlled Trials in the Post-menopausal Osteoporisis Population: A Systematic Review**

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**Objectives:** The cost required to complete a randomized controlled trial is continuously increasing. The most common primary outcome selected in trials aiming to assess the efficacy of treatments of post-menopausal osteoporosis is incident vertebral fractures. However, the incident rate of vertebral fractures is relatively low. Utilizing a composite outcome, where multiple end points are combined allows for greater statistical efficiency by increasing event rates, therefore allowing for smaller sample sizes or shorter follow-up duration (or both). The purpose of this review is to summarize the available literature on the use of a composite fracture outcome in the current literature in the field of post-menopausal osteoporosis treatment and to assess if it would be a reasonable practice.

**Methods:** A systematic review was conducted to identify all RCTs in patients with post-menopausal osteoporosis where fracture was an outcome of interest. The Ovid MEDLINE and Embase databases were searched on March 4, 2016. All records were screened at the title and abstract level. The full texts of the included studies were obtained. The eligibility assessments were done independently by two reviewers (AL, XZ). Each full text was reviewed to identify the number of studies which utilized a composite as its primary outcome, the primary outcome utilized, and the other fracture outcomes reported that could be included in a composite score.

**Results:** In total, 29 studies met our inclusion and exclusion criteria after full text review. A composite outcome was used in 2 studies, where the outcome was new clinical fracture at any site. The most common primary outcome was incident vertebral fracture, which was utilized in 19 studies. New or worsening vertebral fractures were the primary outcome in 6 studies. All 25 studies that used vertebral fracture as a primary outcome utilized new morphometric vertebral fractures as the event. Incident hip fracture was the primary outcome in 1 study.

**Conclusion:** This systematic review reveals the use of composite outcomes is not a common practice in the field of osteoporosis research. Certainly, future trials should consider the use of a composite primary outcome as it can provide a great degree of trial efficiency, although careful

consideration must be taken in its formulation, as a poor choice in the components included in the composite can lead to difficulty in the interpretation of the results.

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**A Giant Headache: A Giant Cell Imposter**

Hafsah Al-Azem (University of Ottawa, Ottawa); John Thomson (University of Ottawa, Ottawa); Nataliya Milman (The University of Ottawa, Ottawa)

A Giant Headache: A Giant Cell Imposter

A 64 year old woman of Haitian decent presented to hospital with excruciating right sided headache which was refractory to analgesics, and an elevated ESR. She described pain radiating down her jaw and tenderness to palpation over the entire right side of her head as well as right sided visual disturbances. She had a history of biopsy-proven temporal arteritis diagnosed 5 years prior when she had presented with similar symptoms. Over the course of her illness, she had been admitted to hospital many times with recurrent headache and was treated with high dose prednisone.

Her other comorbidities included long-standing type 2 diabetes with microvascular complications (retinopathy, neuropathy) and gastroparesis, mild cognitive impairment, GERD, hypertension, and bilateral glaucoma and cataracts. She was on a long list of medications which included prednisone, leflunomide, and risedronate. She had recently undergone a dental procedure in relation to a possible dental abscess.

Her headache was refractory to high dose steroids and persisted in spite of analgesics. Upon further investigation, she was found to have osteonecrosis of the jaw and referred urgently to ENT.

Osteonecrosis of the jaw is a rare but well-described adverse event associated with the use of bisphosphonate therapy. Exposure of the mandible to the external environment has been linked as an additional risk factor for patients on oral bisphosphonate therapy. Often, this is seen in relation to periodontal disease or trauma, and more specifically, tooth extraction. The patient's history of diabetes and glucocorticoid use also confers an increased risk for the development of osteonecrosis of the jaw.

This case highlights the importance of identifying osteonecrosis of the jaw and maintaining a thorough assessment and broad differential diagnosis in the management of patients with established rheumatologic conditions.

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**Low-Dose Methotrexate in the First Trimester is Associated with Increased Risk Fetal Death: A Systematic Review**

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**Objectives:** Methotrexate is the cornerstone of treatment for Rheumatoid Arthritis which commonly manifests in young females. However, methotrexate is a known teratogen that results in spontaneous abortion and birth deformities. Data on methotrexate's effect when exposed pre-conception is unclear; few studies analyze the effect of low-dose methotrexate prescribed for rheumatic diseases on pregnancy outcomes. Our objective is to examine the aggregate risk of low-dose methotrexate on pregnancy outcomes based on exposure in the pre-conception period or in the first trimester.

**Methods:** A literature search strategy was created from the PICO question "what is the risk and type of teratogenicity based on timing and dose of methotrexate use should a patient become pregnant" with the aid of a librarian. The search strategy was run on the following databases: CINAHL, EMBASE, Global Health, MEDLINE, and Web of Sci for all types of references. Data of interest was extracted into standardized forms to be reported or compared using risk ratios.
**Results:** We obtained 1313 references through our search strategy. Using specific criteria, references were excluded at the title/abstract and full text levels. We excluded 979 references from title/abstract, and 208 after reviewing the full texts. Furthermore, we encountered difficulty retrieving 107 references and obtained one reference through a manual search. A final 20 studies reporting low dose methotrexate were included for analysis. There were 26 pregnancies (first trimester N=22) in which the malformations in liver births and aborted fetuses were described in sufficient detail to categorize by general system, including: heart (11/26), GI (9/26), skeletal defects (9/26), facial (8/26), cranial ossification (6/26), GU (6/26), lung (4/26), CNS (2/26), and reproductive organs (2/26). We found a reduced risk of spontaneous abortions/fetal death associated with receipt of MTX during the pre-conception period versus first trimester with a risk ratio 0.55 (95% CI, 0.35, 0.86) though there was substantial heterogeneity among the 5 studies (I2=69%). We found a higher risk of birth defects associated with pre-conception exposure with a risk ratio of 1.43 (95% CI, 0.54, 3.77). We did not find significant heterogeneity with I2=9% for the 3 studies.
**Conclusion:** Pre-conception methotrexate exposure is associated with decreased risk of fetal death but a higher incidence of birth defects possibly due to an increase in nonviable fetuses with first trimester exposure. These data provide support for current recommendations to avoid even low dose methotrexate in pregnancy and the preconception period.

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**Geographic Distribution of Pediatric Rheumatology Referrals in Southwestern Ontario: The Association of Travel Distance with Visit Frequency in Juvenile Idiopathic Arthritis**

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**Objectives:** Although greater geographic distances have been associated with reduced access to care in adult rheumatoid arthritis, there are currently no studies linking geography to access of care in pediatric rheumatology patients. Canadian recommendations suggest follow-up visits at intervals of 3 to 4 months in patients with controlled disease and more often in those with uncontrolled disease. The catchment area in southwestern Ontario covers a large geographic area of over 33,675 square km. This study seeks to identify the current utilization of pediatric rheumatology services and explore the possible association between where patients with juvenile idiopathic arthritis (JIA) reside and their attendance to scheduled outpatient appointments.
**Methods:** We performed a retrospective, cross-sectional study of pediatric patients that were seen in the pediatric rheumatology clinic at Children's Hospital in London, Ontario between January 2010 to July 2015. Patient and medication data was obtained from the hospital administrative database. Patient diagnoses were categorized according to OHIP diagnostic codes. Demographic variables investigated were distance from place of residence to the tertiary care centre and median household income. ESRI 2014 ArcGIS software version 10.3 was used to map patient diagnoses to a dissemination area unit containing a minimum of three patients according to their area of residence. For the medical records of patients with JIA, the number of patient

visits was examined. The use of biologics and prednisone were examined as a surrogate for more severe disease. Multivariate logistic regression analysis was used to examine a possible association between travel distance to disease severity and to the frequency of scheduled patient visits.

**Results:** The diagnoses of the 1083 patients included were categorized as follows: non-inflammatory musculoskeletal conditions 32.1%, JIA or chronic arthritis 19.5%, systemic autoimmune rheumatic disease 12.4 %, and autoinflammatory diseases 7.0%. The mean travel distance for all patients was 73.4 km. For patients with JIA, the mean travel distance was 84.3 km, and the frequency of scheduled visits decreased by a factor of 1.25 after a threshold distance of 44.3 km ($p = 0.04$).

**Conclusion:** Travel distances greater than 44.3 km were associated with decreased frequency of scheduled visits for patients with JIA. Further studies are needed to explore alternative strategies that may allow facilitate patient attendance to appointments, such as telemedicine or additional training for primary care providers.

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**Celiac Disease in Children Diagnosed with Juvenile Idiopathic Arthritis – A Case Series**

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**Objectives:** Celiac disease (CD) is a systemic autoimmune disease triggered by gluten. A higher incidence of CD in rheumatology conditions is reported. Joint pain and arthritis are also manifestations of celiac disease. Therefore the aim of this study is to characterize the presentation of Celiac disease in children with juvenile idiopathic arthritis (JIA).

**Methods:** Celiac screening for children with JIA has become routine practice in our clinic over the last several years. Patients with JIA and celiac disease who initially presented to the rheumatology clinic were identified via an existing research database and clinic charts. Charts were reviewed to characterize the presentation of joint and celiac disease.

**Results:** A total of 10 children with JIA had confirmed celiac disease. All 10 had a positive anti-tissue transglutaminase antibody with 9 having greater than detectable levels. In 9 patients the diagnosis were confirmed via biopsy and 1via genetic testing. Median age at JIA diagnosis was 8 years (3-16). The time interval between JIA diagnosis and subsequent celiac diagnosis ranged from 0-12 years (median 0.5). Median number of joints involved at celiac diagnosis was 2.5 (1-40), with greater than half being polyarticular pattern. 9 patients had no gastrointestinal complaints and were detected on routine screening (although after celiac diagnosis 4 retrospectively reported mild abdominal pain which was not severe enough to seek medical care). 1 patient was tested due to chronic abdominal pain and family history. None had a classic presentation of celiac disease with diarrhea and poor weight gain. 6 of 10 patients were ANA positive. None were RF positive. 8 of 10 patients were tested for HLA-B27, 1 was positive. 4 patients were treated with disease-modifying anti-rheumatic drugs (DMARDs), while the remainder were treated with steroid joint injections and NSAIDs. 6 of 10 patients had joint symptoms improvement with initiation of a gluten free diet. Of these, only 1 was treated with

DMARDs.
**Conclusion:** The presentation of celiac disease in children with JIA is varied. It can present at any age and with any number of joints. Importantly, there may be minimal or no gastrointestinal symptoms. Furthermore, our results suggest that for children with celiac disease and arthritis, initiation of a gluten-free diet may result in improved joint control. As untreated celiac disease can lead to significant morbidity, and treatment of celiac disease may improve joint disease, we recommend providers consider celiac screening in any child presenting with JIA.

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**Confidence in Performing Pediatric Musculoskeletal Examinations in Canadian Pediatric Residents**

Jennifer Lee (University of Toronto, Toronto); Karen Duffy (Children's Hospital of Eastern Ontario, Ottawa); Roman Jurencak (University of Ottawa, Ottawa); Marg Bisch (Children's Hospital of Eastern Ontario, Ottawa); Mercedes Chan (University of Alberta, Edmonton)

**Objectives:** Pediatric musculoskeletal (pMSK) complaints are common, but international studies suggest that pediatric health providers (residents and consultants) are not confident in their musculoskeletal assessments. Our study evaluates the confidence of Canadian pediatric residents in performing pMSK examinations. In a subgroup of residents, we assessed changes in confidence after targeted pMSK training.

**Methods:** All pediatric residents enrolled in an accredited Canadian pediatric residency during the 2015-2016 academic year were invited to participate in an anonymous nationwide questionnaire. Survey respondents rated their confidence in performing pMSK examinations alone and compared to other body systems using a 10-point Likert scale. Pediatric residents enrolled in two Canadian centers (University of Ottawa and University of Alberta) participated in a one-day standardized pMSK examination workshop to learn the pediatric Gait, Arms, Legs, and Spine (pGALS) exam, a validated screening tool to facilitate pediatric joint examination; focused regional joint examinations were also reviewed. A follow-up confidence questionnaire was distributed immediately and six months' after the intervention.

**Results:** 143 of 616 pediatric residents (23% response rate) from 14 Canadian residency programs responded to the nationwide survey. Of the respondents, 56% (n=80) were previously taught the musculoskeletal examination in children yet only 14% (n=20) reported routinely examining a child's musculoskeletal system as part of a complete physical examination. The vast majority of respondents were "somewhat confident" with their pMSK examination, with an average confidence level of 4.6 (95%CI 4.3-4.9; 1=No confidence, 10=Very confident). Confidence in pMSK examination was lower in comparison to cardiovascular, respiratory, and abdominal exams, but higher in comparison to peripheral nervous system and ophthalmologic examinations. In our subgroup analyses (n=50), we found an average increase in confidence by 2.1 points immediately after the workshop intervention, from an initial confidence level of 4.9 (95% CI 4.5-5.4) to 7.1 (95% CI 6.6-7.5). This increase in confidence was sustained with a mean confidence rating of 6.9 (95% CI 6.1-7.7) six months post-workshop. The most frequently reported barriers to musculoskeletal examination confidence were limited practice (n=34, 68%) and limited training opportunities (n=19, 38%).

**Conclusion:** Few Canadian pediatric trainees perform a pMSK examination as part of a complete physical examination, and self-rated confidence in pMSK examination was evaluated as "average" by the majority. We demonstrate that a standardized educational intervention can lead to increased confidence in performing pMSK examinations, but a decline in confidence is observed with time and without consistent practice.

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**Developing a Novel Technique for Visualizing In Vivo Inflammation and Matrix Metalloproteinase Activity in a Murine Model of Kawasaki Disease**

Eugene Krustev (Memorial University of Newfoundland, St. John's); Alicia Fisch (The Hospital for Sick Children, Toronto); Rae Yeung (The Hospital for Sick Children, Toronto)

**Objectives:** Kawasaki disease (KD) is a systemic vasculitis that was first described by Tomisaku Kawasaki in 1967. Over the past 50 years, significant progress has been made into understanding KD; however, significant gaps in our knowledge of the disease still exist. Animal models have proven extremely useful in understanding the pathogenesis of this disease. Coronary artery inflammation and subsequent matrix metalloproteinase (MMP) upregulation have been linked to aneurysm formation in animal models. The aim of this study was to investigate whether novel in vivo fluorescent imaging could be used to visualize inflammation and MMP activity in the Lactobacillus casei cell wall extract (LCWE)-induced murine model of KD.

**Methods:** Male and Female C57Bl/6 mice received a single i.p. injection of either LCWE (0.5mg) or PBS (control). Fluorescent molecular tomography (VisEn FMT2500) was used to visualize systemic ProSense 750 FAST activity (fluorescent marker of inflammation; 4nmol; i.v.) and MMPSense 645 FAST activity (fluorescent marker of matrix metalloproteinase activity; 4nmol; i.v.) on days 3 and 7 post treatment.

**Results:** When ProSense 750 FAST activity was measured on day 3, female LCWE treated mice showed a slight increase in activity when compared to female controls. Furthermore, this difference was least pronounced when ProSense activity was assessed systemically, and most pronounced when only the mediastinum was assessed. Surprisingly, there was no observable difference in male mice. When ProSense 750 FAST activity was assessed 7d after LCWE treatment, there was a visible difference when compared to controls in both the female and male groups. Interestingly ProSense 750 FAST activity appeared to be much higher in female LCWE treated mice when compared to male mice. When mice were injected with both ProSense 750 FAST and MMPSense 645 FAST, and fluorophore activity was assessed on days 3 and 7 post LCWE treatment, there was no observable difference in ProSense 750 FAST activity between LCWE treated and PBS groups; however, MMPSense 750 FAST activity was increased on day 3 in female LCWE treated mice.

**Conclusion:** The results presented here show that in vivo imaging of systemic and localized inflammation is possible in the LCWE-induced murine model of KD. Furthermore, these results suggest that this inflammatory response increases between days 3 and 7, and that signal intensity is greatest in female mice. Future studies are needed to understand the cause of this sex difference in signal intensity, and to improve our double labelling technique.

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**Renal Outcomes in Pediatric Anti-neutrophil Cytoplasmic Antibody Associated Vasculitis – A Pediatric Vasculitis Initiative (PedVas) Study**

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**Objectives:** Renal disease is the most common complication affecting pediatric patients with ANCA-associated vasculitis (AAV). However, renal outcomes have not been well described in children with AAV. Our objectives were to describe the early renal disease course and 12-month outcomes in pediatric AAV.

**Methods:** From an international registry (ARCHiVE) consisting of patients from 40 sites,

patients diagnosed with AAV <18 years of age with pauci-immune glomerulonephritis on renal biopsy or a decrease in renal function requiring dialysis were included. Patients' renal findings and investigations were examined at presentation and at 12 months following presentation. Glomerular filtration rate (GFR) based outcomes included the proportion of children with normal GFR (>90 ml/min/1.73m2), moderately reduced (MR) GFR (30-60 ml/min/1.73m2), severely reduced (SR) GFR (15-30 ml/min/1.73m2) and renal failure (<15 ml/min/1.73m2). GFR was estimated using the Schwartz equation.

**Results:** Of the 71 patients who met inclusion criteria, 69% were female, 57% were Caucasian, and 82% had GPA (granulomatosis with polyangiitis). Initial GFR of the 63 patients with creatinine data at presentation were as follows: renal failure (32%, n=20), SR-GFR (14%, n=9), MR-GFR (22%, n=14) and normal GFR (32%, n=20). Renal findings of the 71 patients on presentation include hypertension (37%), oliguria (23%) and nephrotic syndrome (17%). 27% of patients required dialysis at presentation. At 12 months, 64% of those requiring dialysis at presentation either remained on dialysis (n=7) or received a kidney transplant (n=2). Only 38% of patients at 12 months had a normal GFR while 41% and 3% had MR- and SR-GFR respectively.

**Conclusion:** Early renal disease in pediatric AAV is often severe with over two thirds of patients presenting with a GFR<60 ml/min/1.73m2 and one quarter of patients requiring acute dialysis. Even though a number of patients improved after induction therapy, only 38% of patients have a normal GFR at 12-months. Future analysis from the ARCHIVE registry will allow us to better explore longer term outcomes as well as predictors of outcomes.

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**The Performance of the Kobayashi and Egami Scores in Detecting IVIG Resistance in Kawasaki Disease in a Large Single Centre Canadian Cohort Treated with IVIG and Low Dose Aspirin**

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**Objectives:** Patients with Kawasaki disease (KD) resistant to IVIG are at risk for the development of coronary artery abnormalities (CAA) and remain a challenge. Prediction of IVIG resistance in Japanese patients has been successful with the Kobayashi and Egami scores. We aim to evaluate IVIG resistance, assess if it is a risk factor for CAA, and calculate the sensitivity and specificity of both scoring systems in predicting IVIG resistance in this single centre Canadian cohort.

**Methods:** A retrospective chart review was performed for patients with KD and treated with at least one dose of IVIG (2 g/kg) and low dose ASA (< 10 mg/kg/day) between 01/2004 and 12/2014. Patients were excluded if they were transferred from another centre or if they had a significant structural cardiac defect not related to KD at baseline. IVIG resistance was defined as the requirement for further treatment after the first dose of IVIG. Coronary arteries were considered abnormal if the dimension adjusted for BSA and expressed in SD units had a z score > or equal to 2.5 at the 6-8 week echocardiogram. Sensitivity and specificity calculations were performed. P-values for categorical variables were calculated with the Chi-square test; Wilcoxon rank sum test for continuous variables.

**Results:** Of the 308 patients identified, 269 met inclusion criteria. There were 150 (55.8%)

males; 119 (44.2%) females. The mean age was 3.7 years. Criteria for complete KD were met by 206 (76.6%); 63 (23.4%) had incomplete KD. IVIG resistance was seen in 31.6% (85/269). For the Kobayashi and Egami scores, analysis was carried out in complete KD with full laboratory data sets (Kobayashi=130; Egami=160). The sensitivity of the Kobayashi and Egami scores was low at 47.7% and 28.3% respectively but specificity was high at 83.7% and 86%. From the total cohort, 15 (5.6%) had CAA. There was a significant increase in CAA in IVIG resistant patients (10/85; 11.8%) compared to IVIG responders (5/184; 2.7%) (p=0.003). IVIG resistant patients did not differ statistically from IVIG responders in regards to age, gender or duration of fever at diagnosis.

**Conclusion:** To our knowledge, this is the largest non-Asian cohort that assesses the performance of both scores. In this cohort, both failed to predict IVIG resistance. Patients with IVIG resistance had a higher incidence of CAA. These results highlight the need for the development of a new risk assessment tool for the prediction of IVIG resistance in North American children with KD.

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**Single-arm Study of Etanercept (ETN) in Adult Patients with Moderate to Severe Rheumatoid Arthritis (RA) who Failed Adalimumab (ADA) Treatment**

Majed Khraishi (Memorial University of Newfoundland, St. John's); Louis Bessette (Laval University, Quebec); Alan Kivitz (Altoona Arthritis and Osteoporosis Center, Altoona); Arunan Kaliyaperumal (Amgen Inc., Thousand Oaks); Rana Grantab (Amgen Inc., Mississauga); Melanie Poulin-Costello (Amgen Canada Inc., Mississauga); David Collier (Amgen Inc., Thousand Oaks)

**Objectives:** EULAR guidelines for RA recommend adding a biologic disease-modifying antirheumatic drug (bDMARD) to conventional synthetic DMARD (csDMARD) like methotrexate (MTX) if poor prognostic factors are present or response to csDMARD is insufficient. Upon first bDMARD failure, another should be used, eg, switching from one tumor necrosis factor inhibitor (TNFi) to another. It is unknown whether antibodies to one TNFi influence the effectiveness of another. This phase 4, single-arm study evaluated the efficacy and safety of ETN in patients with RA who failed ADA.

**Methods:** Adults (≥18 years) with moderate to severe RA (disease activity score using 28-joint count and C-reactive protein [DAS28-CRP] ≥3.2) who failed to respond (primary ADA failure) or lost satisfactory response (secondary ADA failure) to ADA+MTX were enrolled. After ≥2 weeks without ADA, ETN 50 mg once weekly for 24 weeks was added to ongoing MTX. Visits occurred at weeks 0, 4, 8, 12, 18, and 24. Assessments included American College of Rheumatology 20% (ACR20), 50% (ACR50), and 70% (ACR70) improvement criteria, and DAS28-CRP. The primary efficacy endpoint was ACR20 at week 12.

**Results:** Eighty-five patients received ETN: 80% women and mean age 56.6 years. Overall, 28% had anti-ADA antibodies (42% neutralizing, 58% non-neutralizing), including 7/33 with primary ADA failure and 17/52 with secondary ADA failure. Median duration of prior ADA therapy was 46 weeks (range 12–466 weeks). Of 84 evaluable patients, 36% achieved ACR20 at week 12 (95% confidence interval [CI]: 26%-47%) and 35%  at week 24. The rates for ACR50 and ACR70 with ETN were 11% and 2%, respectively, at week 12, and 16% and 4% at week 24. Among anti-ADA antibody-positive/negative and primary/secondary ADA failure subgroups, patients with antibodies and secondary failure were most likely to achieve ACR20 at week 12 (65%; odds ratio vs antibody-negative 5.2; 95% CI: 2.0-13.5; P <0.001). DAS28-CRP improved by a mean of 0.8–2.0 in each subgroup at week 12, with the greatest improvement in patients

with antibodies and secondary failure: 82% had DAS28-CRP improvement ≥1.2 at week 12. ACR20 responses at week 12 in patients with antibodies were 40% (4/10) for neutralizing and 57% (8/14) for non-neutralizing. Safety results—≥1 adverse event in 73% of patients and no fatal adverse events—were consistent with the known safety profile of ETN.
**Conclusion:** Patients who fail ADA could consider ETN as a therapeutic option. Presence of anti-ADA antibodies with secondary ADA failure may guide treatment decisions.

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**Patient-Reported Outcomes for Etanercept Therapy in Adult Patients with Moderate to Severe Rheumatoid Arthritis who Failed Adalimumab Treatment**

Majed Khraishi (Memorial University of Newfoundland, St. John's); Louis Bessette (Laval University, Quebec); Alan Kivitz (Altoona Arthritis and Osteoporosis Center, Altoona); Arunan Kaliyaperumal (Amgen Inc., Thousand Oaks); Rana Grantab (Amgen Inc., Mississauga); Melanie Poulin-Costello (Amgen Canada Inc., Mississauga); Maya Isaila (Amgen Inc., Mississauga); David Collier (Amgen Inc., Thousand Oaks)

**Objectives:** When a tumor necrosis factor inhibitor (TNFi) fails in a patient with moderate to severe rheumatoid arthritis (RA), new American College of Rheumatology (ACR) guidelines recommend a switch to either another TNFi or a non-TNFi biologic. This study evaluated disease activity and patient-reported outcomes (PROs) in patients with RA who switched to etanercept after adalimumab failure.
**Methods:** Adults (age ≥18 years) with moderate to severe RA (disease activity score using 28-joint count and C-reactive protein ≥3.2) who failed to respond (primary failure) or lost a satisfactory response (secondary failure) to adalimumab treatment, based on ACR 20% improvement criteria (ACR20) or investigator judgment, were enrolled in an open-label, multicenter, single-arm study. After ≥2 weeks of washout, etanercept 50 mg once weekly for 24 weeks was added to ongoing methotrexate treatment. Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire (HAQ) disability index (DI), and pain visual analog scale (VAS) were evaluated at weeks 0, 4, 8, 12, 18, and 24. Other PROs, including Medical Outcomes Short Form 36 (SF-36) and Work Productivity and Activity Impairment (WPAI), were assessed at weeks 0, 12, and 24. The primary efficacy endpoint (ACR20 at week 12) and safety data from this study were presented previously; this analysis focused on PROs at each visit.
**Results:** Of 85 patients studied (80% women; mean age 56.6 years), 84 were evaluable for efficacy. After switching from adalimumab to etanercept, clinical outcomes and PROs improved from baseline at each study visit. Improvement in mean HAQ DI (–0.31 points from baseline to week 24) exceeded the minimal clinically important difference of 0.22 points. Mean improvement in HAQ DI from baseline to week 24 by adalimumab failure and anti-adalimumab antibodies was –0.05 (primary failure, antibodies; n = 7), –0.65 (secondary failure, antibodies; n = 17), –0.15 (primary failure, no antibodies; n = 22), and –0.37 (secondary failure, no antibodies; n = 33). Improvements in other PROs (HAQ pain VAS, SF-36 physical function, and WPAI absenteeism/presenteeism) also were greatest for patients with secondary failure and antibodies. Adverse events were consistent with the known safety profile of etanercept.
**Conclusion:** Clinical outcomes and PROs improved from baseline at every visit when patients with RA switched to etanercept after adalimumab failure, particularly among those with anti-adalimumab antibodies and secondary failure to adalimumab. Limitations were small subgroup sample sizes, analysis of secondary endpoints, and lack of long-term outcomes after 24 weeks.

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**Canadian Humira Post-Marketing Observational Epidemiological Study Assessing**

**Effectiveness in Psoriatic Arthritis (COMPLETE-PsA): Interim Analysis**

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**Objectives:** COMPLETE-PsA is an observational study planning to enroll 670 PSA patients (pts). The objectives of this analysis are to describe the demographics and baseline disease parameters and to report preliminary real-life effectiveness of ADA in PsA.

**Methods:** This was a pre-specified interim analysis of pts enrolled between 8/2011−8/2015. Pts have active PsA with ≥3 tender and swollen joints, active psoriatic skin lesions/history of psoriasis, are anti-TNF naïve and require a change in treatment. Data include disease activity (tender [TJC28] and swollen [SJC28] joints, HAQ, physician [PGA] and patient [PtGA] global assessment, morning stiffness, psoriasis body surface area [BSA], PASQ, and DLQI), quality of life (SF-36, BDI-II), and work limitations (WLQ).

**Results:** Of the 319 pts (ADA n=181, DMARD n=138), 236 (74%) had 6-month data. Mean age was 51.0 yrs (SD 12.3), 51.7% were female, and mean disease duration was 4.2 yrs (SD 6.5). There were no significant differences between treatment groups. At baseline, ADA pts had significantly higher DAS28 (4.9 vs. 4.5; P=0.017), SJC28 (8.5 vs. 6.0; P<0.001), morning stiffness (88.5 vs. 58.7 min; P=0.008), PtGA (56.6 vs. 44.6; P<0.001), HAQ (1.1 vs. 0.9; P<0.001), and lower SF-36 score (26.6 vs. 27.4; P=0.003), but comparable CRP, ESR, TJC28, BSA, PGA, PASQ, and DLQI. Productivity loss was higher in DMARD pts (17.8% vs. 16.4%; P=0.021). By 6 months, 8% of DMARD pts vs. 2.8% ADA pts (P=0.035) were discontinued. Significant improvements were observed in almost all disease parameters. Adjusting for baseline values, ADA pts had significantly lower DAS28 (2.6 vs. 3.7; P<0.001), TJC28 (3.0 vs. 5.8; P=0.001), SJC28 (1.4 vs. 4.2; P<0.001), PGA (16.9 vs. 34.5; P<0.001), PtGA (29.3 vs. 39.9; P=0.030), HAQ (0.64 vs. 0.93; P<0.001), PASQ (9.5 vs. 10.7; P=0.015) and DLQI (2.2 vs. 4.1; P=0.015) vs. DMARD pts.

**Conclusion:** PsA pts initiating ADA in Canadian routine clinical care have more severe disease compared with those initiating traditional DMARDs. However, over 6 months, ADA treatment had better retention, and was more effective in reducing symptom severity and improving outcomes.

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**20 Years of Experience with Methotrexate in Psoriatic Arthritis. An Analysis from the Rhumadata® Clinical Database and Registry**

Valerie Nadon (Institut de Rhumatologie de Montréal, Montreal); Louis Coupal (Institut de Rhumatologie de Montréal, Montréal); Louis Bessette (Laval University, Quebec); Boulos Haraoui (Institut de Rhumatologie de Montreal, Montréal); Frederic Massicotte (Institut de Rhumatologie de Montréal, Montréal); Jean-Pierre Pelletier (Institut de Rhumatologie de Montréal, Montréal); Jean-Pierre Raynauld (Institut de Rhumatologie de Montréal, Montréal); Marie-Anaïs Remillard (Institut de Rhumatologie de Montréal, Montréal); Diane Sauvageau (Institut de Rhumatologie de Montréal, Montreal); Angèle Turcotte (Centre d'ostéoporose et de rhumatologie de Québec, Québec); Edith Villeneuve (Institut de Rhumatologie de Montréal, Montréal); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal)

**Objectives:** Methotrexate has become the anchor drug for the treatment of psoriatic arthritis (PsA) since the end of the eighties. It has been associated with the development of all biologic agents, apremilast, and JAK inhibitors. Worldwide registries have devoted the majority of their

publications to these new agents mostly in rheumatoid arthritis. Very few has dedicated their attention to methotrexate in PsA.
**Methods:** Data from PsA patients exposed to methotrexate at the Institut de Recherche en Rhumatologie de Montréal and the Centre d'Ostéoporose et de Rhumatologie de Québec either in mono or combination therapy were extracted from the database. Three periods were identified: before December 31st, 1999, from January 1st, 2000 to December 31st, 2009, and from January 1st, 2010 to September 2nd, 2016. Extracted data include age, gender, diagnosis date and duration, comorbidities, disease activity score, methotrexate dose, duration, and route of administration, adverse events profile and the reason for stopping. Comparative effectiveness using Kaplan-Meier survival analysis and safety profile of the different cohorts are also tabulated.
**Results:** For each period, there are respectively 173 patients, 638 patients, and 767 patients, and the ratio female/male is maintained 1:1 throughout the different eras. The median age at treatment initiation, for each era, is respectively 42.1 years, 46.7 years and 49.1 years. Median S/C and PO MTX dose increase over time. Median initial doses of S/C methotrexate (25 mg) are higher than the PO dose (20 mg). Adverse events explain near 25% of methotrexate arrest, while inefficacy reason decreases significantly throughout the observation periods. GI and hepatic events are the main reported adverse events. Methotrexate retention, when used in monotherapy, were higher in the first era as biologic agents were unavailable during that period.
**Conclusion:** This study describes the use of methotrexate in PsA patients through the years. Dosages and S/C usage have significantly increased over time. S/C MTX usage has gained more adepts in recent years. The age increase over time reflects both the natural aging of our patient population and the MTX usage knowledge improvement associated with the biologic agent development era. It's retention over time reflects alternative treatment availability and a new appreciation for its therapeutic usefulness even in older patients. MTX in monotherapy and combination with other agents is still the preferred anchor medication in PsA.

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**20 Years of Experience with Methotrexate in Rheumatoid Arthritis. An Analysis from the Rhumadata® Clinical Database and Registry**

Valerie Nadon (Institut de Rhumatologie de Montréal, Montreal); Louis Coupal (Institut de Rhumatologie de Montréal, Montréal); Louis Bessette (Laval University, Quebec); Boulos Haraoui (Institut de Rhumatologie de Montreal, Montréal); Frederic Massicotte (Institut de Rhumatologie de Montréal, Montréal); Jean-Pierre Pelletier (Institut de Rhumatologie de Montréal, Montréal); Jean-Pierre Raynauld (Institut de Rhumatologie de Montréal, Montréal); Marie-Anaïs Remillard (Institut de Rhumatologie de Montréal, Montréal); Diane Sauvageau (Institut de Rhumatologie de Montréal, Montreal); Angèle Turcotte (Centre d'ostéoporose et de rhumatologie de Québec, Québec); Edith Villeneuve (Institut de Rhumatologie de Montréal, Montréal); Denis Choquette (Institut de Rhumatologie de Montréal, Montréal)

**Objectives:** Methotrexate has become the anchor drug for the treatment of rheumatoid arthritis since the end of the eighties. It has been associated with the development of biologic agents, apremilast, and the JAK antagonists. Worldwide registries have devoted the majority of their publications to these different agents, very few have focused on methotrexate.
**Methods:** The data from RA patients ever exposed to methotrexate at the Institut de Recherche en Rhumatologie de Montréal and the Centre d'Ostéoporose et de Rhumatologie de Québec either in monotherapy or combination with other medication were extracted from the database. Three periods were identified: before December 31st, 1999, from January 1st, 2000 to December

31st, 2009, and from January 1st, 2010 to September 2nd, 2016. Extracted data include age, gender, diagnosis date and duration, comorbidities, rheumatoid factor and anti-CCP status, disease activity score, methotrexate, dose, duration, and route of administration, adverse events profile and the reason for stopping. Comparative effectiveness using Kaplan-Meier survival analysis and safety profile of the different cohorts are tabulated.
**Results:** The data from 1074, 2434, and 1868 patients was extracted for each of the three treatment periods. The median age at treatment initiation, for each group, is respectively 47.3 years, 52.6 years and 55.7 years, and the female/male ratio is maintained at 3:1 throughout the different eras. Median initial doses of s/c methotrexate are higher than the PO route. S/C doses used increased through the different periods. Adverse events explain near 50% of methotrexate arrest, while inefficacy reason decreases significantly throughout years. GI and hepatic events are the primary adverse reactions reported (about 50% of the time). Methotrexate retention, when used in monotherapy or with a biologic agent, were higher in the first era.
**Conclusion:** This study describes the use of methotrexate in RA patients through the years. The increased age of the exposed population coincides with the aging of the population and the used of MTX in that population. Mean MTX dose usage also increases over time. This could be attributed to the better understanding of MTX usage through the biologic agent development era. The growing popularity of MTX s/c administration parallels the improved knowledge about its better bioavailability and efficacy and the reduction of some side effects. It's retention over time reflects alternative treatment availability and a new appreciation for its therapeutic usefulness. Methotrexate remains a preferred anchor drug for the treatment of rheumatoid arthritis.

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**Prediction of Non-adherence in Patients with Rheumatoid Arthritis (RA) – Comparison of Baseline and Six Months' Data**

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**Objectives:** Medication adherence in patients with RA is estimated to lie between 60-70%. This fact led us to investigate medication adherence (csDMARD and biologic) in patients with rheumatoid arthritis and to evaluate the usefulness of the French version of the «Compliance Questionnaire on Rheumatology» (CQR) as an adherence screening tool. Our first abstract showed a correlation between the CQR and the preceding 6 month adherence rate (assessed by medical possession ratio). We present here the prospective data collected six months later. Our principal objective is to confirm the validity of the French version of the CQR through time. Moreover, these data allow us to assess whether this questionnaire as well as the associated patient education helps in improving adherence.
**Methods:** We conducted a longitudinal study of RA patients seen at the IRM. Selected patients had to be French, 18 years of age or older, a diagnosis of RA for at least a year, and been treated for RA for at least the last six months (csDMARD and biologic agent). Patients completed the French version of the CQR questionnaire during a routine medical visit held between November 11th and December 17th, 2013 and, a second time, during a follow-up medical visit six months later. The pharmaceutical profiles of all patients for the six-month periods preceding each of the two medical visits were obtained from their pharmacist. The medical possession ratio (MPR) was then calculated for each patient and compared to the result of the CQR questionnaire at baseline and six months.
**Results:** One hundred and twenty-three of the initially selected 160 patients (76.9%) completed

the six-month CQR questionnaire. The adherence rate measured at six months is similar to the initial rate (73% vs. 75%). This result suggests that having responded to the CQR does not influence adherence. As previously shown, participants were more adherent to P.O. than sc methotrexate (79.3% vs. 50.0%), and to biologic agents rather than csDMARDs (92.6% vs. 74.1%). Adherence, as assessed using the MPR, show a small positive correlation with CQR result as it did at baseline.
**Conclusion:** This follow-up study confirms that the French version of the CQR questionnaire could become a helpful tool to evaluate adherence in RA patients. However, its use has no impact on future adherence.

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**Initial Use of Subcutaneous Methotrexate in Early Rheumatoid Arthritis is Associated with Decreased Time to Biologic Use: Results from the CATCH Cohort**

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**Objectives:** Treatment for moderate-severe early rheumatoid arthritis (RA) often involves using a methotrexate (MTX)-based, treat-to-target strategy aiming for remission. Optimizing initial MTX therapy may reduce the need for more expensive biologic therapy. The objective of this study was to compare effects of different initial MTX-based strategies (monotherapy, combination therapy and route) on time to first biologic use in patients with early RA.
**Methods:** Data were analyzed from the Canadian Early Arthritis Cohort (CATCH). The present study included patients who met 1987 or 2010 ACR/EULAR RA criteria, had <12 months symptom duration, moderate or high disease activity based on the DAS28 at baseline and were treated with MTX. Patients ever treated with a biologic were excluded. Patients were followed until they started a biologic or they were censored due to loss to follow up or the end of the 3-year study period. Cox proportional hazards survival analysis was used to estimate adjusted effects of different initial MTX-based treatment strategies on time to first use of a biologic, controlling for age, gender, education level, symptom duration, pain, baseline erosions, baseline DAS28, and corticosteroid use.
**Results:** 1189 patients were included and 207 first events of biologic use occurred in the 3-year followup period. Median time to biologic start was 9 months. At baseline, 865 (71%) patients were female with a mean (sd) age of 54 (15) years, symptom duration of 6 (3) months, and DAS28 of 5.5 (1.2). MTX monotherapy was used as initial treatment in 40% of patients (oral (20%), subcutaneous (sc) (20%)) and MTX combination therapy in 60% (MTX + HCQ (42%), MTX + HCQ + SSZ (13%), other combinations <1%). In fully adjusted Cox proportional hazards models, there were no overall differences between MTX monotherapy and MTX combination therapy. However, relative to patients started on oral MTX monotherapy patients treated with subcutaneous MTX monotherapy had a significantly reduced biologic start (HR = 0.53, CI 0.31-0.98)
**Conclusion:** Treatment with sc MTX monotherapy was associated with less initiation of biologic

therapy relative to oral methotrexate monotherapy. This may be due to increased treatment efficacy compared to oral MTX. MTX combination therapy was not associated with longer time to biologic initiation, potentially due to provincial regulations requiring a trial of combination DMARD therapy before initiating biologics. This study suggests that early use of sc MTX can potentially delay the need for more expensive biologic therapies.

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**Pulseless in Periphery: A Case of AL Amyloidosis Mimicking Large Vessel Vasculitis**

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Amyloidosis is a plasma cell dyscrasia causing deposition of proteins derived from immunoglobulin light chain fragments. It is a multiorgan disease that has many varied clinical presentations.

This case is a 48-year-old lady who presented to a tertiary care hospital with retrosternal chest pain. Over the prior 18 months she reported a significant decline in her health with chronic headaches, jaw claudication, recurrent fevers and a 15 pound weight loss. During that time she had an episode of amaurosis fugax, a myocardial infarction and a stroke that left her with residual right arm weakness. On exam she was cachectic. Her peripheral pulses were not palpable and she has bilateral beaded and hardened temporal arteries. She had positive troponins and an EKG showed anterolateral ST depressions. Echocardiography revealed severe global hypokinesis, with a left ventricular ejection fraction of 20-25% and a small pericardial effusion. Her NT-pro BNP was elevated at 21,363 ng/L. An angiogram revealed normal coronary arteries with a decreased left ventricular function that suggested non-ischemic cardiomyopathy. Infectious workup including testing for Chagas disease was negative. She was found to have a normocytic anemia with hemoglobin ranging from 70-90 g/L and an elevated ESR and CRP of 35 mm/h and 15.3 mg/L, respectively. Given these results and her physical exam findings she was started on empiric therapy for large vessel vasculitis with prednisone at 1 mg/kg. In further investigations, an SPEP showed a monoclonal peak with elevated free lambda light chains and a free kappa/lambda ratio of less than 0.01. A diagnosis of multiple myeloma complicated by amyloid light (AL) chain amyloidosis was considered. A skeletal survey shows lytic lesions in the spine at C6 and T10 and a bone marrow biopsy shows 70% plasma cell burden. A cardiac MRI showed diffuse enhancement reflecting protein deposition, in keeping with amyloidosis. Temporal artery and abdominal fat pad biopsies confirmed multiple myeloma complicated by AL amyloidosis. Hematology started VMP (bortezomib, melphalan and prednisone) chemotherapy. Her clinical status has improved after 5 months of therapy.

This case illustrates amyloidosis as an important mimicker of large vessel vasculitis. Amyloidosis should be considered in the differential diagnosis of large vessel vasculitis especially if there are atypical features.

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**Speaking Up: Vocal Cord Nodules in ANCA Vasculitis**

Steven Thomson (University of Calgary, Calgary); Douglas Bosch (University of Calgary, Calgary); Paul MacMullan (University of Calgary, Calgary)

The literature contains only rare cases of sup-epithelial deposits or “bamboo nodes,” associated with autoimmune disease. The most common reports are of vocal cord deposits associated with rheumatoid arthritis, but connective tissue diseases have also been implicated. In this case we reviewed a 69-year old woman who presented with polyarthritis (wrists, elbows, knees, and

MCPs) and finger-tip blood blisters that appeared intermittently. She also has a history of sinus congestion. Her arthritis was treated with depot steroid injection and intermittent oral prednisone. Initial ANCA, RF and ACPA testing were negative.
She complained of five months of progressive dysphonia, for which she was referred to otolaryngology. She was found to have deposits on the vocal cords termed bamboo nodes. Shortly after this time, she developed mild hemoptysis and bibasilar infiltrates on CT of the chest. At this point she was started on Methotrexate and oral Prednisone at 5mg, then referred to Pulmonology. Repeat ANCA testing revealed MPO positive vasculitis. DMARD and steroid therapy improved her vasculitis and arthritis. She was seen again in follow-up by otolaryngology after treatment with DMARDS, and the nodes had resolved.
Cases of ANCA associated vasculitis with bamboo nodes are rare in the literature. Some previous authors have treated the nodes surgically, but have noted recurrence. In this case we see that the nodules resolved with medical treatment.
Bamboo nodes are an under-appreciated manifestation of various autoimmune diseases, but little has been published in the area. The next step in this line of inquiry is to retrospectively identify patients at our institution who have bamboo nodes to determine the prevalence and to look for concurrent autoimmune diseases. With that information, we can see how often they are an early feature of autoimmune disease and also, if they consistently resolve with treatment of the underlying autoimmune disease. This case series project is underway.

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**Inflammation as an Under-Recognized Cause of Ascending Aortic Aneurysms: A Single-Center Clinical and Pathological Study of 53 Cases Over 6 Years**

Tariq Al Araimi (University of Toronto, Toronto); Arthur Bookman (University of Toronto, Toronto)

**Objectives:** This study is aimed at estimating the prevalence of inflammatory ascending aneurysms, describing clinical and histopathological findings, and assessing whether appropriate follow-up was arranged.

**Methods:** Data from Enterprise Data Warehouse was retrieved for all cases of ascending aortic aneurysms from Jan 2009-Dec 2015 requiring surgery at the University Health Network for the following diagnostic codes: thoracic aortic aneurysm, ruptured (I71.1) or without rupture (I71.2); aortic aneurysm of unspecified site, ruptured (I71.8) or without rupture (I71.9). After eliminating duplicates, 743 had their ascending aorta resected. Of these, 730 had aneurysmal dilatation (≥40mm measured by pre-operative echo or cardiac CT/MRI). All cases with ascending non-infectious inflammatory aneurysms were reviewed.

**Results:** Among the 730 cases studied, 53 (7.3%) were of a non-atherosclerotic, non-infectious inflammatory pathogenesis. Mean age was 67 years (18-68), with 50.9% women. Asymptomatic presentation occurred in 52.9%, 7.8% had constitutional symptoms and 43.1% had symptoms that could be attributed to an aneurysm. Isolated aortitis with no other evidence of arterial involvement presented in 41 (77.3%), and 12 had underlying rheumatic disease: Rheumatoid Arthritis (4), Polymyalgia Rheumatica (3), Giant Cell Artertitis (3), Systemic Lupus Erythematosus (1) and Cogan's Syndrome (1). Echocardiographic findings demonstrated a maximum mean aneurysm diameter of 54.7± 6.8mm, aortic insufficiency (AI) in 73.5%, stenosis (AS) in 9.4% and mixed AS & AI in 3.8%. A bicuspid aortic valve was found in 15.1%. Ten patients had changes of calcification or atherosclerosis seen on CT (10) or intraoperatively (12). Histopathology revealed Giant Cell Aortitis in 35.8% (19), Takayasu's Arteritis in 5.7% (3), Lymphoplasmacytic Aortitis in 22.6% (12), Mixed Lymphoplasmacytic with Giant Cells in

15.1% (8) and unclassified in 20.8% (11). No lymphoplasmacytic cases were stained for IgG4. Only 1 had aortitis mentioned in the discharge summary. Of the 53, 24 had a follow-up visit, 8 of which had aortitis diagnosis in the follow-up notes. Rheumatologist referrals status for the remaining 45 (84.9%) patients after discharge is unknown.
**Conclusion:** Ascending Aortitis is under-recognized as a cause of ascending aortic aneurysms. Most patients are asymptomatic. The presence of an aortic bicuspid valve , aortic stenosis, changes of atherosclerosis on imaging or in the intraoperative period do not rule out an inflammatory aortic aneurysm. IgG4 staining should be routine practice for all patients with lymphoplasmacytic aortitis. This retrospective review is suggestive of poorly standardized follow-up and many patients may never know that there was inflammatory pathology. The consequences of this have yet to be determined.

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**Refractory GCA on Prednisone and Tocilizumab: Improvement with Subsequent Tuberculosis Reactivation**

Carson Chin (University of British Columbia, Division of Rheumatology, Department of Medicine, Vancouver); Irfan Kherani (University of Ottawa, Department of Ophthalmology, Ottawa); Femida Kherani (University of British Columbia, Department of Ophthalmology, Vancouver); Raheem Kherani (University of British Columbia, Division of Rheumatology, Department of Medicine, Richmond )

**Objective:** To review a challenging case of refractory GCA and to discuss the role of tocilizumab including risk of tuberculosis reactivation.
**Background:** Giant cell arteritis (GCA) is a large vessel vasculitis and one of the most common forms of vasculitis to occur in adults. Symptoms typically include headaches, joint pain, fever and occasionally permanent vision loss. GCA classically responds to high dose steroids.
**Case Description:** We report a case of steroid refractory GCA with bilateral vision loss who was initially treated with tocilizumab 8mg/kg IV monthly. Although there was improvement in her vision documented with fundoscopy and fluorescein angiography, she developed constitutional symptoms and cough and was found to have reactivation pulmonary tuberculosis (TB) despite negative TB skin test (TBST) prior to biologic therapy. The patient had a long and protracted course with treatment for active TB with numerous complications and eventually passed away.
**Discussion:** While rarely reported in the literature, tocilizumab has been associated with TB reactivation. Screening for latent TB is mandatory but false negative TBST is common when patients are on concurrent glucocorticoids and are immunosuppressed. Tocilizumab is a promising treatment for GCA. Adverse effects including opportunistic infections are a concern especially when combined with high dose glucocorticoids.

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**Granulomatosis with Polyangiitis Associated with Immune Checkpoint Blockade: Case Report and Literature Review**

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**Objectives**: Granulomatosis with polyangiitis (GPA) is an anti-neutrophil cytoplasmic anti-body-associated small vessel vasculitides, characterized by granulomatous inflammation and necrotizing vasculitis of small to medium-sized blood vessels. We will describe a patient with GPA induced by immune checkpoint inhibition used as treatment for malignant melanoma and

perform literature review of GPA associated with immune checkpoint blockade in patients with cancer.
**Case description**: A 66 year female with a prior history of malignant melanoma was treated with a combination of ipilimumab and nivolumab. Three weeks later she developed symptoms of sudden onset left temporal headache, generalized arthralgia, documented fever, palpable purpuric rash on lower limbs, and worsening sinusitis with decreased left side hearing. Shortly after, she developed hemoptysis and hematuria.
Renal biopsy was completed and biopsy was compatible with focal proliferative glomerulonephritis. Laboratory results showed a positive c-ANCA anti-PR3 with a titre of 1501 MFU. She received methylprednisolone 1 g IV for 3 days, followed by prednisone 60 mg daily. Treatment was consolidated with rituximab. Retrospectively she reported a 3 year history of chronic sinusitis, not responsive to antibiotic or Budesonide use.
Literature review revealed the presence of one similar case of GPA induced by checkpoint immune blockade in a patient with stable pulmonary nodules. The patient in this study was retrospectively weakly c-ANCA positive.
**Conclusion**: The time course of symptoms in this patient, and a literature review of case reports, is suggestive that immune checkpoint blockade therapy used in melanoma treatment may be a causative trigger for vasculitis. There have also been possible triggers for other systemic autoimmune diseases. Our case would be a second case of potentially sinus limited GPA that developed into systemic GPA after chemotherapy. We would recommend both careful history and biochemical analysis in patients who may receive immune checkpoint blockade, as the potential for a trigger for systemic disease.

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**Prospective Cohort of Surgically-Diagnosed Aortitis at the Ottawa Hospital**

Kyle Walker (University of Ottawa, Ottawa); Munir Boodhwani (University of Ottawa Heart Institute, Ottawa); Nataliya Milman (The University of Ottawa, Ottawa)

**Objectives:** Idiopathic Aortitis (IA) is a poorly defined entity characterized by the presence of aortic inflammation and absence of clinical features of another systemic condition. We aim to establish a prospective cohort of patients with surgically diagnosed aortitis and compare disease features in patients with IA and aortitis secondary to a systemic inflammatory condition (SA).
**Methods:** Patients are recruited following identification of aortitis on surgical specimen. Following a detailed clinical assessment, laboratory investigations and full imaging of the aorta and its branches, patients are classified as either IA or SA. Patients are followed prospectively with at least yearly clinical assessments and measurements of ESR/CRP, and imaging every 1-2 years. Primary outcome is radiographic progression of aortitis (new aortic/branch lesions or progression of existing lesions). Secondary outcomes include need for delayed immunosuppressive therapy, need for aortitis-related surgeries, or a change in diagnosis (from IA to SA).
**Results:** Fourteen patients have been enrolled to date, 8 IA, 6 SA (5 giant cell arteritis (GCA), 1 rheumatoid arthritis (RA)). Majority of patients are female (7/8 IA, 6/6 SA); average age 74 and 75 years in IA and SA respectively. Four of eight patients with IA and 2/6 with SA had aortic branch lesions at baseline. Mean follow-up is 2.3 and 1.8 years in IA and SA groups, respectively. One patient (with SA) was found to have worsening aortic dilatation 15.4 months post-biopsy (PB); new aortic branch involvement was observed in 3/8 patients with IA (identified at mean 9.3 months PB) and in 3/6 SA (identified at mean 13.3 months PB). Surgical re-intervention was required in 2 patients with IA (mean 6.5 months PB). Two patients with IA

received a combination of prednisone and methotrexate starting at 36.0 months and 38.2 months PB respectively for worsening aortitis. Two patients with SA received prednisone for worsening of their underlying condition, not related to diagnosis of aortitis: one was finishing a course of prednisone initiated for a flare of RA prior to diagnosis of aortitis and the other was treated for symptomatic GCA 3.2 months PB. Diagnosis was not changed in any patients. One patient with IA died due to a cause unrelated to aortitis 17.5 months PB.
**Conclusion:** Preliminary data suggest patients with IA and SA may experience a significant rate of radiographic vascular progression, particularly in terms of development of branch vessel abnormalities. Further enrollment and a longer duration of follow-up are needed to draw more definitive conclusions.

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**Cerebral Artery Aneurysm, Bladder Mass, and Jejunal Ulceration in a 46 Year Old Male with Pyoderma Gangrenosum**

Shannon Fong (University of Alberta, Edmonton); Jason Soo (University of Alberta, Edmonton)

**Objectives:** Granulomatosis with polyangiitis is a small vessel vasculitis that can involve multiple organ systems. There are a number of reports of rare manifestations of the disease involving the gastrointestinal tract, central nervous system, and urogenital tract. However, there are none reported of these symptoms presenting simultaneously in a single patient. We report a case of GPA where a patient presented with bladder mass, cerebral artery aneurysm and jejunal ulceration.
**Methods:** The records of the patient were reviewed including hospital admissions; relevant investigations; and outpatient clinic visits. A review of the literature was performed to determine whether any similar presentations had been reported. While we were unable to find any previous cases involving all the rare manifestations of our patient, we utilized the literature to determine the frequency of these manifestations in isolation.
**Results:** A 46 year old male initially presented with intermittent hematuria and urinary retention. He was found to have a bladder mass, and biopsies of the mass were nondiagnostic. While admitted he developed a ruptured cerebral aneurysm of unclear etiology. Meanwhile, imaging for staging of suspected malignancy had revealed cavitary lung lesions. The patient went on to develop gastrointestinal bleeding from ulcerated mucosa in the jejunum, in addition to small volume hemoptysis and renal failure. When laboratory results and pathology from the aneurysm, lung, jejunum, and kidney were reviewed, a diagnosis of GPA was established. Despite his complicated presentation, the patient responded well to treatment with rituximab and is currently in clinical remission.
**Conclusion:** Urogenital involvement occurs in less than 1% of males with GPA and most commonly presents as prostatitis, but can affect the penis, urethra, bladder, ureter, and testicles (1). Gastrointestinal manifestations are also rare, estimated to occur in 5-11% of patients and associated with high morbidity and mortality (2). Although neurological involvement is more common, occurring in up to 54% of patients, it usually manifests as peripheral neuropathy. In a recent retrospective review of central nervous system manifestations of GPA, only 2 out of 35 patients developed cerebral hemorrhage (3). This case serves as a reminder that GPA is a multisystem disease. The presentation can be atypical or, as in this case, a combination of atypical and typical manifestations. The diagnosis requires a high level of suspicion and should be considered when multiple organs are involved without a clear unifying etiology. *References available upon request.

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**Assessing Canadian Practice Patterns Regarding Idiopathic Aortitis**

Marissa Keenan (Ottawa University, Ottawa); Nataliya Milman (The University of Ottawa, Ottawa); CanVasc (Toronto)

**Objectives:** Idiopathic Aortitis (IA) and its subset, Isolated Aortitis (IsA), are presently poorly defined entities. The purpose of this study is to determine the current practice patterns of Canadian rheumatologists with respect to these conditions.

**Methods:** An online survey was administered to members of the Canadian Rheumatology Association using FluidSurveys (www.fluidsurveys.com) in June 2016. The survey was developed by the investigators in consultation with core members of the Canadian Vasculitis Network (CanVasc).

**Results:** Seventy-four of the 420(18%) members of the CRA responded, 68(16%) took the survey and 60/68(88%) completed it. Twelve of 64 participants (19%) were core members of CanVasc, 44(69%) worked at an academic centre and 20(31%) were in a community practice. Fifteen participants (23%) had never seen a patient with IA; out of 47 respondents, who saw at least one IA patient, 37(79%) saw 0-1 patient per year, 9(19%) saw 2-5, and one saw 6-10. Only 12/47(26%) participants reported making a distinction between IA and IsA; 9/12 (75%) considered exclusion of radiographic abnormalities in aortic branch vessels to be important for the definition of IsA, consistent with our definition of IsA. The majority of respondents performed thorough clinical, biochemical, and radiographic assessment of their patients. Still, only 42% consistently performed testing to exclude tuberculosis, 78% consistently tested for syphilis, and 38% performed full imaging of chest and abdominal aortic branches. Great variability exists with respect to managing of these conditions. When branch vessel abnormalities were present, respondents were more likely to treat aortitis diagnosed on pathology compared to radiographic aortitis, with 26% and 61% respectively reporting treating their asymptomatic IA patients with normal inflammatory markers in the 2 scenarios. Treatment rates were lower for IsA, with 23%-26% of respondents treating their asymptomatic cases of IsA with normal inflammatory markers. The greatest variability in practice exists for IA where the involved area was completely surgically removed, with 18% of respondents reporting always using corticosteroids, 21% did sometimes and 34% never. More than 70% of participants reported monitoring their patients with IA or IsA every three months. Thirty-six of 37 participants (97%) reported they felt the development of recommendations for the management of patients with IA and/or IsA would be beneficial.

**Conclusion:** IA is a rare condition. A significant proportion of Canadian rheumatologists are not familiar with IA and IsA. Great variability exists with respect to their definitions, workup, treatment, and monitoring, highlighting the need for systematic studies and management recommendations.

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**Management of Venous Thromboembolism in ANCA-Associated Vasculitis: Case Series and Review of the Literature**

Norman Madsen (University of Alberta, Edmonton); Elaine Yacyshyn (Division of Rheumatology, University of Alberta, Edmonton)

**Objectives:** ANCA-associated vasculitides (AAV) are a group of small vessel vasculitides associated with serum positivity for anti-neutrophil cytoplasmic antibodies (ANCA). Disease course in AAV ranges in severity from minor airway or cutaneous symptoms to organ and life-threatening disease due to pulmonary hemorrhage and glomerulonephritis. Autoimmune and inflammatory conditions are known to increase risk of venous thromboembolism (VTE) and the

AAV are without exception. There are a few case reports, case series and randomized controlled trials describing high rates of venous thromboembolism in this cohort of patients. However, given the potential for catastrophic complication of anticoagulation in active vasculitis, anticoagulation for treatment of VTE remains controversial during active flares. AAV have also been associated with higher than usual rates of VTE. In algorithms for treatment of AAV, preventive therapy for possible VTE has not been addressed[EY1] .

**Methods**: Two recent cases of AAV complicated by venous thromboembolism were identified at the University of Alberta Division of Rheumatology. A literature search was completed using PubMed and the keywords "ANCA" or "ANCA vasculitis" and "thrombosis" or "venous thromboembolism".

**Results:** No prospective trials on the management of thrombotic complications of ANCA-associated vasculitis were identified. Several case reports were identified in both the adult and paediatric population. There was no consensus on optimal treatment of AAV-related VTE with anticoagulation, systemic therapy or devices such as IVC filters during the active phase or in remission.

**Conclusion:** ANCA-associated vasculitis is a significant risk factor for venous thromboembolism. Management of thrombotic complications in patients with active vasculitis and related hemorrhage is a challenging clinical conundrum. There is currently no prospective published data on the management of thrombosis in the setting of vasculitis. Thrombotic complications of ANCA-associated vasculitis should be tailored to the individual clinical scenarios with consideration for risk of bleeding complications. More research into the treatment and prevention of venous thromboembolism in the setting of ANCA-associated vasculitis is needed.

[EY1] Norm check the CanVASC guidelines and EULAR.

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**A Single Centre Cohort Description of 225 Granulomatosis with Polyangiitis Patients**

Bailey Russell (University of Toronto, Toronto); Rach Chahal (Mount Sinai Hospital, Toronto); Simon Carette (University of Toronto, Toronto); Christian Pagnoux (University of Toronto, Toronto)

**Objectives:** Several cohorts of adult patients with granulomatosis with polyangiitis (GPA) have been reported worldwide, but not yet from Canada. The objective of this study was to describe the characteristics at diagnosis, treatments, and outcomes of the cohort of 225 adults with GPA followed in the vasculitis clinic in Toronto, using the newly-created CanVasc database, and to compare with previously published series.

**Methods:** The following information were collected from patient charts and entered into the CanVasc database for subsequent analysis: demographics, comorbidities, main clinical manifestations of vasculitis, biologic results including serum creatinine level and ANCA reactivity, initial induction and maintenance treatments, and outcomes (global relapse and survival rates, and according to year of diagnosis [before vs. ≥2005]).

**Results:** 225 patients diagnosed with GPA between 1970 and 2016 have been followed in the clinic, with an average follow-up of 100.0 (± 135.5) months from diagnosis. Mean age at diagnosis was 42.7 ± 18.7 years, and female:male sex ratio was 1.45. The most common clinical findings at diagnosis were ENT manifestations (76.4%), renal involvement (53.8%), arthralgias, myalgias and/or arthritis (51.1%). Pulmonary nodules were observed in 40% of patients, alveolar hemorrhage in 30.2%, and subglottic and/or bronchial stenosis in 8.9% of patients at diagnosis. The mean BVAS was 15.2 ± 7.4; 81.6% of patients tested positive for cANCA and 8.6% for

pANCA by IF; 76.6% were PR3-ANCA+ and 6.5% were MPO-ANCA+ by ELISA. In addition to prednisone, cyclophosphamide was most often used for induction at diagnosis (64.2%), followed by methotrexate (22.6%), mainly for limited forms, or rituximab (3.9%). Azathioprine and methotrexate were used for maintenance in 49.8% and 38.7% of patients, respectively. Death occurred in 6 (2.7%) patients, with one death attributed to active vasculitis. Relapses occurred in 64.4% of patients, with an average time to first relapse of 87.3 ± 7.3 months. Those diagnosed in or after 2005 were more likely to relapse than those diagnosed earlier, with an HR adjusted for age and use of cyclophosphamide of 2.33 (95%CI 1.56-3.49, $p<0.01$)

**Conclusion:** Clinical manifestations, treatments and outcomes of this cohort are similar to those reported in non-Canadian cohorts. The use of rituximab for induction has been low until now, but will likely expand. The possible reasons for the observed, unexpected higher relapse rate in patients diagnosed after 2005 are multiple and may include referral center bias over time, changing disease patterns or treatment approaches leading to reduced cyclophosphamide exposure.

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**Long-term Damage in the 225 Patients with Granulomatosis with Polyangiitis from the Toronto-CanVasc Cohort**

Rach Chahal (Mount Sinai Hospital, Toronto); Bailey Russell (University of Toronto, Toronto); Simon Carette (University of Toronto, Toronto); Christian Pagnoux (University of Toronto, Toronto)

**Objectives:** Damage due to granulomatosis with polyangiitis (GPA) and its treatments is common, but there has been no recent study in Canada in adult patients regarding this aspect.

**Methods:** A selected dataset from patients with GPA followed at the vasculitis clinic in Toronto was extracted from the CanVasc database and included age at diagnosis, sex, use of cyclophosphamide (CYC) at any time during the course of the disease, duration of follow-up, relapses (none, 1 or ≥2), deaths and all items of the vascular damage index (VDI) and the final VDI score at last follow-up. VDI is a validated, cumulative score for damage in patients with vasculitis, and includes 64 items, grouped by organ or system and each scoring 1 point (range, 0-64). We analyzed the VDI scores and items, and studied whether age, sex, use of CYC or relapses were associated with more damage.

**Results:** 225 patients diagnosed with GPA between 1970 and 2016 have been followed for an average of 100.0 (± 135.5) months in the clinic. Mean age at diagnosis was 42.7 ± 18.7 years, and female:male sex ratio was 1.45. CYC was used at some point during the course of the disease in 171 (76%) patients. A total, 47 patients (20.9%) experienced one relapse, 98 (43.5%) had ≥2 relapses; 6 (2.7%) patients died. A minority (n=48, 21%) of patients had no recorded damage (VDI=0) at last follow-up, while 59 (28%) had a VDI=1, 48 (21%) a VDI=2, 30 (28%) a VDI between 3 and 6, and 6 (3%) a VDI ≥7. Most common damage items recorded in the VDI at last visit included nasal blockade (n=44, 19.6%), sinusitis (n=42, 18.7%), nasal perforation/collapse (n=39, 17.3%), hearing loss (n=33, 14.7%), subglottic stenosis (n=28, 12.4%), peripheral neuropathy (n=24, 10.7%), decreased GFR <50% (n=25, 11.1%), dyspnea (n=20, 8.9%),osteoporotic fracture (n=18, 8%), diabetes (n=13, 5.8%), cataract (n=12, 5.3%), and myocardial infarction (n=5, 2.2%). In univariate (and multivariate; Poisson regression with sex, age at diagnosis, use of CYC and number of relapse) analysis, only a greatest number of relapses was significantly associated with a higher VDI at last follow-up ($P<0.01$, with an expected increase of 23% in VDI for every additional relapse).

**Conclusion:** More than three-quarters of patients with GPA suffer damage, mainly ENT but also

neurological and/or renal. Strategies and sustained, long-term efforts to limit damage are important aspects of the management of these patients, and include the prevention of relapse.