1
Breast, Ovarian and Endometrial Cancers in Women Diagnosed with SLE before Age 40

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Objectives: Various studies have confirmed an overall increase in cancers in systemic lupus, SLE. This increased incidence is largely driven by haematological malignancies, while for some cancers there may be a decreased incidence in SLE (breast, endometrial and ovary). Although 90% of SLE patients are female, only a few studies in the past have focussed on breast, endometrial, and ovarian cancer. To date, no study so far has looked at the incidence of these female reproductive cancers specifically in young females diagnosed with SLE, despite the fact that SLE is mostly diagnosed in female patients in child bearing years. Our objective was to determine the incidence of breast, ovarian and endometrial cancer in females diagnosed with SLE prior to age 40.

Methods: Data were obtained from a multicentre cohort study of SLE patients from 23 centres. The SLE diagnosis was established by American College of Rheumatology Criteria or clinical criteria. Patients were followed up in outpatient clinics and cancer cases were ascertained through linkage with regional tumor registries. Standardized incidence ratios (SIR) were calculated for breast, ovarian and endometrial cancer by dividing the observed number events for a given cancer by the expected number of the respective cancer. Expected numbers of cancers were determined by multiplying the person years at risk in the cohort by age and sex matched general population cancer rates.

Results: 5,406 females diagnosed with SLE under age 40 (mean age at diagnosis 26.8 years, standard deviation, SD, 7.4) were observed for a total of 44,073 patient-years (average follow up 8 years). A total of 121 cancers were diagnosed in this population during the observation period, 1/4 of these cancers accounted for breast (29), ovarian (1) and endometrial cancer (3). Data suggested a decrease in breast (SIR 0.38, 95% confidence interval, CI 0.26-0.55) and endometrial cancer (SIR 0.33, 95% CI 0.07-0.96). There was a trend towards a decrease in ovarian cancer (SIR 0.25, 95% CI 0.01-1.41) in female patients who were diagnosed with SLE under age 40.

Conclusion: In the present cohort study, data suggested a decreased risk of breast and endometrial cancer in females who developed SLE prior to age 40. The data on ovarian cancer incidence are inconclusive. Limitations of the current analyses include that the general population cancer rates were not perfectly matched for geography, race/ethnicity and calendar year of cancer diagnosis.

2

Systematic Review of Therapeutic Plasma Exchange for the Treatment of Catastrophic Antiphospholipid Antibody Syndrome

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Objectives: Catastrophic antiphospholipid antibody syndrome (CAPS) is a rare life-threatening variant of the antiphospholipid antibody syndrome manifesting with rapidly progressive thrombosis leading to multiorgan failure. The objective of this project was to systematically evaluate the benefit of therapeutic plasma exchange (TPE) on complete recovery, death, permanent organ dysfunction, dialysis, amputation, chronic symptomatic lung disease, or permanent neurologic deficit in patients with definite or probable CAPS.

Methods: Data sources for this systematic review were MEDLINE (1946 to July 2013), and EMBASE databases, the Cochrane library and reference lists. Studies reporting the effect of TPE on outcomes for patients with definite or probable CAPS were included. There was no language restriction. Studies were excluded if they contained duplicate data. Study characteristics, outcomes and quality assessment were extracted in duplicate. Quality assessment was performed using the GRADE system.

Results: Data Synthesis: Only 1 study met selection criteria. Despite fulfilling the systematic review criteria, an estimate of the treatment effect of TPE on any of the prespecified outcomes could not be obtained from the included study due to study methodology. The quality of evidence was rated very low.

Conclusion: Conclusion: Data from the only included publication was insufficient to determine the effect of TPE on patient-important outcomes in CAPS, and furthermore, the quality of the included studies was graded as very low, thus any resultant estimate of the effect of TPE in CAPS based on the existing literature would be very uncertain. This review highlights the difficulty in synthesizing evidence for the treatment of rare diseases. It is difficult to find high-quality published data due to the difficulty in performing randomized controlled trials in these populations, and much of the evidence is based on lower-quality case reports or case series with inherent potential for biases in design. Well-designed patient registries could enhance our understanding of optimal therapeutic interventions in rare diseases, such as CAPS.

3

Systemic Sclerosis in Canada's Black and Asian Population: Clinical and Serological Manifestations

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Objectives: The purpose of this study is to compare the clinical features of SSc in Black and Asian patients with Whites enrolled in the Canadian Scleroderma Research Group (CSRG) registry

Methods: This was a cross-sectional, multicenter study of patients included in the CSRG registry whose baseline visit was between September 2004 and January 2013. Patients were evaluated with standardized medical histories, physical exams, and self-administered questionnaires. Ethnicity was self-reported. Descriptive statistics were used to summarize and compare clinical and serological characteristics.

Results: Among 1285 SSc patients, 1101 (81%) were White, 14 (1%) were Black, 38 (3%) were Asian, and 132 (10%) were other ethnicity. Compared to Whites, Black patients had distinct clinical and serological features, including younger age at disease onset, higher rates of diffuse cutaneous disease, more severe Raynaud's phenomenon (RP) and digital ulcers, more inflammatory polyarthritis and inflammatory myositis, more gastrointestinal involvement, and higher frequency of anti-topoisomerase I antibodies. None of the Black patients had anti-centromere antibodies, compared to 1/3 of the White patients. Compared with Whites, Asians also had distinct clinical and serological manifestations, including higher rates of diffuse cutaneous disease, lower rates of digital ulcers and fewer gastrointestinal symptoms, including esophageal dysmotility. There was at trend towards higher seropositivity for anti-topoisomerase I and lower seropositivity for anti-RNA polymerase III antibodies in Asians compared to White patients.

Conclusion: Ethnic differences exist in the clinical and serological manifestations of SSc. This study provides rationale to pursue further research into genetic and environmental determinants of SSc.

4

Durability of First Biologic is not Influenced by Initial/Early DAS28

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Objectives: The Ontario Best Practices Research Initiative (OBRI) collects data on RA treatment in the real world. Patients are enrolled and prospectively followed to assess response to biologic and DMARD therapy as well as to collect data on other factors. The objective of this study is to look at a real-world population and determine if initial disease activity influences the durability of the first used biologic in RA treatment.

Methods: Biologic-naïve RA patients were included if they started a biologic at baseline or at any time after entry into OBRI. For initial DAS, we used the DAS28 value when it was measured between 6 months before and 3 months after the start of the first biologic, whichever was closer to the date of biologic use. This was done so as the initial DAS28 would best reflect the patient's DAS at start of biologic. Patients were censored at treatment stop date or discontinuation date, date of death, or up to 18 months after initiation of biologic, whichever occurred first. Persistence was defined as the length of time the patients continued to receive the drug, irrespective of change in dose, route, or addition of any other DMARD, steroids, etc. If the drug was stopped for <60 days after which the patient restarted the same medication, it was considered a continuation and the duration was calculated accordingly. Survival was first compared using KM curves and then again using Cox-regression analysis. Analysis was performed for all years and also censored at 1.5 years.

Results: 471 patients were included. At 1 year, the survival probability was 0.76 (95% CI 0.68-0.81). Median survival was 5.005 years (95% CI 3.466-8.337). Patients who were on biologic monotherapy, with no concomitant DMARD use, have worse persistence of their initial biologic. Patients were divided into three groups for analysis based on initial DAS28 score. Despite the initial trend towards better survival associated with lower initial DAS, this was not statistically significant. Similarly, type of insurance (public/private) did not impact survival. As seen in other studies, the only significant factor to impact survival on initial biologic was use of DMARD with the biologic.

Conclusion: Early/initial DAS28 score did not impact persistence on their initial biologic, nor did insurance type. This suggests that initial DAS28 score does not influence the durability of the initial biologic Combination of DMARD and biologic was more durable than biologic monotherapy.

5

Delivering Preoperative Rehabilitation Exercise Program to Patients with Severe Functional Limitations Awaiting Total Knee Arthoplasty: Experiences of Patients and Physical Therapists

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Objectives: To learn about benefits and challenges of delivering a home-based pre-operative exercise program (PREP) to patients with severe disability (WOMAC scores 50+) awaiting total knee arthroplasty (TKA). The PREP program was comprised of exercise and education delivered by physical therapists in participants' homes. Therapists 1) visited participants in their home at baseline, week4 and week 8, with weekly telephone calls to adjust exercise and answer questions.

Methods: Within a randomized control trial comparing PREP with usual care, a qualitative study was conducted in PREP recipients and study physical therapists. A purposive sample of ten patients and five physical therapists who participated in PREP. Semi-structured interviews with patients after TKA and a focus group with the physical therapists were completed. Interviews and the focus group were audio-recorded and transcribed verbatim. Content analysis was used for identifying, coding and categorizing the primary patterns in the data. The basic demographic information from all the participants and the medical and surgical information from the patients were collected and used to describe the sample.

Results: Of the 10 patients, 8 were female and 2 male with ages ranging from 60 to 85 years. All except one had 3 or more comorbidities. The experiences of PREP and TKA were defined in biomedical, personal and social contexts, and were intertwined with the complexity of patients' life events, other competing health issues and the natural aging process. Patients described PREP as a range of interventions that were catered to their specific individual needs and delivered in their homes. While the experiences of pain and mobility among the patients varied, they reported being physically and emotionally better prepared for the surgery. Physical therapists were female and had 4 to 50 years of experience. They reported that patients were receptive to having a therapist come to their homes and adherent to their exercise routines. Physical therapists perceived positive changes in patients over time PREP was delivered, including improved range of motion, progress in mobility and improved emotional health.

Conclusion: Delivering a pre-operative program for TKA was well-received by patients and physical therapists. Participants who did not understand the purpose of the pre-operative program also had difficulty with adherence. Overall, participants felt they were better prepared for their surgery although preparation was compounded by personal factors individual to the patients.

6

Intensity of Physical Activity in Arthritis: Canadian Community Health Survey

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Objectives: While there is strong evidence to support the benefits of structured exercise to improve cardiovascular fitness and reduce musculoskeletal complaints in people with arthritis, factors that explain physical activity engagement are not clear. The primary objective of this study was to determine what factors explain the intensity of physical activity among Canadians who report having with arthritis.

Methods: In a national cross sectional survey, the Canadian Community Health Survey, 16.3% of 120,838 respondents who were 18 years or older and had arthritis. Physical activity was derived from the self-reported amount of total energy expenditure to obtain metabolic equivalent of task (METs), Absolute METs were classified into four activity levels (sedentary, light, moderate and vigorous), stratified by age, as defined the US Surgeon General. Adjacent category logistic regression was used to determine the factors associated with intensity of physical activity. Because a complex sampling frame was used, sampling design weights were used to account for unequal probabilities selection for sample estimates to the population.

Results: Of those respondents with arthritis, 28% reported being active: 19% participated in light activity and 9% participated in moderate-to-vigorous activity. The most common leisure physical activities reported by respondents were walking for exercise and home exercises. Back problems and high blood pressure were the most prevalent chronic conditions. Respondents who reported moderate to vigorous activity had less back problems (37%), high blood pressure (30%) and diabetes (8%) than respondents who reported light activity (back problems:39%; high blood pressure: 33%; diabetes 11%). Respondents with arthritis who had high blood pressure and smoked had the highest likelihood of participating in light activity, as opposed to moderate/vigorous activity (OR 2.34; 95% CI: 1.42, 3.87). Females (OR 1.29; 95% CI: 1.08, 1.53), respondents who were obese (obese class I) (OR 1.61; 95% CI: 1.28, 2.03) and current daily/occasional smokers (OR 1.75; 95% CI: 1.29, 2.37) had a higher likelihood of light activity than moderate/vigorous activity.

Conclusion: Demographic, behavioral and medical factors explained intensity of physical activity among respondents with arthritis. Because physical activity is a modifiable risk factor for osteoarthritis, arthritis management programs can be tailored to provide physical activity regimens that target suitable intensity of activity.

7

Case Report: Rheumatoid Arthritis Presenting with Acute Interstitial Pneumonitis Manifesting before Arthritis, a Rare and Atypical Presentation

Amina Lodhi (McMaster University, Burlington); Maggie Larche (McMaster University, Hamilton)

Abstract: A 50 year old male presented to ER with six month history of SOB. The chest X-ray was normal at that time and was diagnosed with the adult onset asthma and prescribed one week course of oral prednisone and bronchodilators. Ten days later his symptoms worsened with severe SOB and he developed severe pain and swelling of small joints of hands, wrists, elbows and knees bilaterally. He had no past history of arthralgia/arthritis. Review of systems was positive for 20 pound weight loss over the last six months and fatigue. He had 40 pack year history of smoking and worked as a construction worker, exposed to asbestos for 15 years and had pet parrots 30 years ago. BP was 114/64mmHg, RR 28/minute, T 36.3 C and saturating 87% on RA and bilateral diffuse crackles .All MCPs/PIPs were swollen/tender. Wrists, elbows and knees were swollen/tender. Chest X-ray showed bilateral diffuse alveolar densities suggestive of pulmonary edema. Chest CTPA showed diffuse ground glass opacification suggestive of ARDS/ acute interstitial pneumonia. Differential diagnosis at this point was infection vs inflammatory cause. He was supplemented with oxygen and was started on intravenous Tazocin. Blood /urine cultures were negative. Legionella urine antigen, HBV, HCV, HIV, and PCR for respiratory viruses were negative. Pasrovirus B-19 IgG was positive but IgM was negative. Aspergillus/Farmer's lung precipitants were negative. ESR 107, CRP 77.7mg/L. He was strongly positive for RF; 800IU/mL and Anti CCP was >124U/L. ANA, SS-A52, SS-A60 and Anti Jo-1 antibodies were positive. In the light of above evaluation, it was concluded that he had acute interstitial pneumonitis secondary to inflammatory arthritis. With positive RF and Anti CCP, rheumatoid arthritis with a rare and atypical presentation of acute interstitial pneumonitis presenting before arthritis was considered to be the most likely etiology. Other possibilities were Sjogren Syndrome with interstitial pneumonitis as primary manifestation and Anti synthetase syndrome. 1mg/kg body weight oral prednisone was given with significant improvement of SOB and arthritis but still high oxygen requirements. So he was given 125mg IV Solumedrol BID for two days with dramatic improvement. After two days he was switched to oral prednisone 1mg/kg body weight.
Conclusion: Extra-articular manifestations are not uncommon in RA. Arthritis precedes interstitial lung involvement in most cases. This case is atypical because the pulmonary symptoms manifested before the articular symptoms.

8
Spectrum of Musculoskeletal Inpatient Diagnoses at the Largest Pediatric Center in East Africa in 2011

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Objectives: Pediatric rheumatic diseases are among the most common chronic illnesses of childhood and can cause considerable disease burden and disability. The spectrum, frequency and outcomes of pediatric rheumatic conditions in East Africa are unknown. Defining the spectrum of in-patient diagnoses is critical to designing a context-specific educational program targeting African pediatricians and pediatric trainees to improve diagnosis and treatment of children with these conditions.

Methods: In order to assess the spectrum of diseases seen on the in-patient service from January to December 2011 at Gertrude's Children Hospital, the largest pediatric center in East-Africa, patients identified as having diseases of the musculoskeletal (MSK) system and connective tissues (CT) by ICD-10 diagnostic codes ("M-codes") at discharge were included. After IRB approval, the admission records of these patients were reviewed locally and the de-identified information sent to the McGill investigators. Diagnoses were validated by two independent rheumatologists using information gathered from the medical records as well as laboratory and microbiology investigations. True cases were defined as those with recorded clinical evidence corresponding to the standard definition of the M-code assigned by the local physician. Frequencies of each "M-code" identified were then calculated.

Results: The total number of admissions to Gertrude's Hospital during 2011 was 8,011. Among those, 35 patients were identified as having an "M-code" diagnosis at discharge. When the records were reviewed, non-MSK conditions accounted for 20% (7 cases) of all "M-code" admissions. Minor surgical procedures made up 14.3% (5 cases). When both of these were excluded, diseases of the MSK system and CT represented 0.28% of the total admissions in 2011. Validated diagnoses were classified as inflammatory arthropathies (39.1% or 9 cases), septic arthritis (30.4% or 7 cases); soft tissue and muscle infections (17.4% or 4 cases) and Kawasaki disease (KD) (13.1 % or 3 cases).

Conclusion: Diseases of the MSK and CT represented 0.28% of the total admissions to the largest pediatric referral center during 2011. The spectrum of rheumatic conditions requiring admissions included inflammatory and infectious arthropathies, soft tissue and muscle infections, and KD. Surprisingly, there were no admissions for lupus and other systemic vasculitides beyond KD. This may indicate under-diagnosis of these conditions, poor sensitivity of M-codes to identify these diseases or a true low frequency of these diagnoses. Although using "M-codes" to identify rheumatic conditions may have its limitations, this study was the first step at identifying the frequency of these conditions in this in-patient population.

9

Impact of Prokinetic Agents on Systemic Sclerosis-Associated Gastrointestinal Disease: A Systematic Review

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Objectives: More than 90% of patients with Systemic Sclerosis (SSc) have gastrointestinal (GI) involvement, particularly dysmotility causing complications such as gastroesophageal reflux and small bowel pseudo-obstruction. Treatment with prokinetic drugs is mostly modelled on their use in the general population, despite important pathophysiological differences between GI dysfunction in SSc and other etiology. Thus, our goal is to identify and appraise all studies evaluating the impact of prokinetics on GI outcomes in patients with SSc.

Methods: Three databases (Cochrane Central Register of Controlled Trials, Ovid MEDLINE, and Embase) were searched until November 2013 using the terms "scleroderma", "systemic sclerosis", "prokinetic", "anti-emetic", and generic and trade names of individual drugs. Studies were included if they evaluated any GI outcome with prokinetic treatment in at least 5 adults (age > 18y) with SSc, regardless of language or study type. Two reviewers independently evaluated all studies, and conflicts were resolved by a third.

Results: Of 492 search results, 21 studies from 12 countries met our criteria. All except one used an experimental design. Seven had a placebo arm, with cross-over design in 6. The sample sizes ranged from 5 to 64, with 362 participants in all. Using Cochrane guidelines, 5 studies had high risk of bias, 5, low risk, and the rest, moderate risk. The study subjects ranged in age from 30 to 80 years, and 83% of them were women. Six prokinetics were evaluated: cisapride in 9 studies, metoclopramide in 6, octreotide in 2, erythromycin in 2, and mosapride and clebopride in 1 study each. Only 2 studies evaluated >1 prokinetic. Outcomes included GI motility as evaluated by manometry (ex. esophageal sphincter pressure), scintigraphy (ex. gastric emptying time), and hydrogen breath tests; serum levels of motility-altering peptides (ex. motilin); and symptoms (ex. Index of Gastrointestinal Status). Each prokinetic was associated with a favourable outcome in at least half the studies that evaluated it, without serious adverse effects, except diarrhea with octreotide in one study. The heterogeneity in treatment duration and outcomes precluded any meta-analyses.

Conclusion: Available studies suggest a favourable side-effect profile and impact of prokinetics on SSc-associated GI disease, but are limited by small numbers, lack of uniform outcome measures, and risk of bias. Larger studies using validated outcome measures are required to confirm some of the findings in the smaller trials, and to help define the ideal type, dose, and duration of prokinetics for a given GI dysfunction in SSc.

10

Is Central Quantitative Computed Tomography (QCT) Superior to Dual Emission X-Ray Absorptiometry (DXA) for Fracture Risk Assessment in Post-Menopausal Women? – A Systematic Review and Meta-Analysis

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Objectives: Unlike DXA, QCT can assess volumetric bone mineral density (vBMD) and differentiate trabecular from cortical bone. Whether these QCT features translate to improved fracture risk assessment is unknown. This study was undertaken to ascertain if QCT-based bone parameters are superior to DXA measurements for determining fracture risk in post-menopausal women, as per area under the receiver operator characteristic (ROC) curve, or AUROC.

Methods: Medline, Embase, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews were searched for studies published until October 31, 2013, inclusive, comparing QCT-derived bone measurements at the spine or hip between fractured post-menopausal women and non-fractured female controls. Two authors independently selected and reviewed articles, and abstracted data. Discrepancies were resolved by consensus with a third author. For bone measures reported in >1 study, the standardized mean difference (SMD) between fractured and non-fractured groups was calculated. ROC curves were plotted for parameters reported in ≥ 3 studies.

Results: Of 6791 search results, 44 met our inclusion criteria, and were assessed using QUADAS-2, a tool for quantifying bias. All, except one study, were case-control. The AUROC for spinal trabecular vBMD (0.81 for spine and 0.80 for any assessed fracture) are higher than that for DXA measures (range 0.70-0.74), but with overlapping 95% confidence intervals (CI). There were inadequate numbers of studies to determine AUROC for trabecular vBMD of femoral neck or total femur. The AUROC for total vBMD at these sites were comparable to DXA BMD for any incident fracture.

Conclusion: QCT is comparable to DXA in fracture risk assessment in post-menopausal women. Spinal trabecular vBMD by QCT may be superior to DXA.

11
14-3-3η: A Mechanistic Biomarker That Supports the Concept of "Uncoupling" of Inflammation and Joint Damage

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Objectives: In RA, mitigating radiographic progression is a priority. It is well established that an "uncoupling" of inflammation and joint damage occurs along the disease course, highlighting the importance of radiographic assessment, to achieve target outcomes, alongside the measurement of acute phase reactant, C-reactive protein (CRP) and clinical evaluations. Approximately 40% of RA patients have sustained normal CRP levels where other early modifiable markers of joint damage progression risk, such as 14-3-3η, may assist in monitoring. This study examines 14-3-3η's relationship with CRP in an early RA cohort and whether its baseline expression in CRP-normal patients relates to radiographic outcomes.

Methods: Baseline serum 14-3-3η protein titres were measured using the 14-3-3η ELISA (cut-off ≥0.19 ng/ml) in a cohort of 409 early RA patients from the Reade Institute; all patients were treatment naive at baseline. Median patient age was 56 years and 73% were female. Differences in radiographic progression over 3 years based on 14-3-3η positivity across the whole group and in patients with normal CRP (≤10 mg/L) were assessed. Spearman correlations to compare relationships between variables and the Mann-Whitney u-test to assess median differences between groups were utilized.

Results: At baseline, 67% of patients were 14-3-3η positive and 60% of patients had elevated CRP. Spearman correlation revealed that there was no relationship between baseline CRP and 14-3-3η titres (r = 0.06). Baseline CRP titres correlated with Sharp/van der Heijde Score (SHS) at year 1 (r=0.17, p=0.0007) and the change in SHS (Δ SHS) from baseline to year 1 (r=0.17, p=0.0005) but not with baseline SHS. Patients who were 14-3-3η protein positive had more radiographic progression than 14-3-3η negative patients over years 1, 2 and 3; [0 (0-2) vs. 0 (0-1), p=0.006], [1 (0-6) vs. 0 (0-2.5), p=0.008] and [2 (0-7) vs. 0 (0-4), p=0.009], respectively. In patients with normal CRP, 14-3-3η positive patients (n=105) had higher year 1 mean (SD) radiographic progression of 1.4 (3.4) versus the negative group (n=55), 0.7 (2.3), p<0.05.

Conclusion: 14-3-3η is a mechanistic joint damage marker that does not correlate with the acute phase reactant CRP in early RA. These two markers provide unique information to assist in the clinical management of RA patients informing the uncoupling of inflammation and joint damage.

12
Working Status and Improvements in Work Productivity Over Time in an Early Rheumatoid Arthritis (ERA) Cohort

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Objectives: To describe working status in an ERA population in the first year of disease, and factors associated with improved work productivity.

Methods: Patients in the Canadian Early Arthritis Cohort who completed the Work Productivity and Activity Impairment (WPAI-RA) questionnaire at baseline and month 12 were included. Baseline differences among those working vs. not working were compared using chi-square or student's t-tests. Change in employment status and overall activity impairment was calculated for all patients at 12 months relative to baseline, whereas absenteeism (work hours missed) and presenteeism (impact of RA on work productivity) was calculated for those working at baseline. Multivariate logistic regression analyses tested whether age, sex, symptom duration, DAS28 score, HAQ-DI or type of treatment at month 6 were associated with improvements in WPAI domains.

Results: One hundred-ninety patients (age 56 years, symptom duration 5.6 months, baseline DAS28 4.85 were included); 110 were in paid employment at baseline. Individuals not in paid employment at baseline less frequently had high school or college education, had lower income, were older, had moderate-to-high DAS28 scores, and demonstrated greater disability HAQ-DI scores. Improvements in WPAI domains are shown (Table). Among working individuals, by 12 months, 78% had an improvement in working hours missed, 67% reported improved productivity and 72% had reduced activity impairments. The largest change of occurred for absenteeism (9.57 fewer hours missed). Younger age (OR 0.93, CI 0.89-0.98), DAS28 remission (OR 10.52, CI 1.4-79) and HAQ-DI at month 6 (OR 4.01, CI 1.2-13.1) were associated with gaining employment by month 12. Conversely, DAS28 remission was a negative predictor for improved work productivity (OR 0.04, CI 0-0.65) and higher HAQ-DI was associated with reduced activity impairment (OR 3.98, CI 1.89-8.37). DMARD or biologic use at month 6 was not associated with change in WPAI domains but corticosteroid use was negatively associated with presenteeism (OR 0.23, CI 0.06-0.89).

Conclusion: Differences in demographic and disease-related variables exist between ERA patients who are working versus those who are not. The majority of working individuals show improvements in WPAI domains over time but establishing the minimum clinically important difference for these domains is needed to help guide clinical interpretability. The impact of age, remission, disability and corticosteroid use on improved work productivity warrants further exploration in larger samples.

13

Time-to-Remission, Time-To-Relapse and Disease Severity at the Time of Relapse in RA-Results from the Ontario Best Practices Research Initiative (OBRI)

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Objectives: Clinical remission in RA is the desired goal, however the ability to sustain remission and the timing and severity of relapse is not well known. We aimed to describe time to remission, time-to-relapse and disease activity at the time of relapse.
Methods: We performed a longitudinal data analysis of patients enrolled in the Ontario Best Practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care. The prevalence of a first occurrence of clinical remission according to the DAS28-ESR <2.6 or CDAI £2.8 following cohort entry (baseline) was determined as was the average time-to-remission. Patients achieving remission with ³ 1 follow-up visit (typically spaced 3 to 6 months apart) were observed for the average time until relapse, defined as a DAS28 >2.6 or CDAI >2.8. The baseline disease activity level of those achieving remission and the disease activity level at the time of relapse was examined.
Results: The total cohort (N=2305) was 78% female with mean (SD) age 57 (13) years, disease duration 8.6 (9.6) years and mean DAS28 score 4.5 (1.5) at baseline. Remission was achieved in 1081 patients (47%); 140 of these patients had low baseline disease activity, 516 had moderate and 369 had high disease activity at baseline. The median time to remission was 279 days (interquartile range [IQR] 146 – 482) and remission was reached significantly faster among those starting with low disease activity (median 218 days, IQR 148-385) at baseline compared to more severe disease (median 357 days, IQR 173-563) (P<0.001). Nine hundred eighteen patients (85%) had continued follow up after remission and 582 (59%) went on to experience a relapse. The median time-to-relapse was 197 days (IQR 126-363). The majority switched from a state of remission to mild or moderate disease activity, in contrast to the moderate to severe levels of disease activity they experienced at baseline.
Conclusion: Clinical remission in routine care is achievable and occurs fastest in those with low to moderate levels of disease activity at baseline. Remission is not sustained in the majority of individuals and relapse occurs, on average, by 7 months. Further work examining the predictors and characteristics of patients who relapse to a low disease state (which may be an acceptable substitute to remission) vs. relapse to a high disease state is needed to determine the nature and timing of therapeutic intervention that may be required to prevent and manage disease flares.

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Disease Activity Scoring: Comparing Patient and Physician Global Assessment of Disease Activity in Rheumatoid Arthritis Patients Starting a First Biologic Agent

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Objectives: Visual analogue scales (VAS) are used in clinical practice and are part of composite scores such as the DAS, CDAI. Studies report weak to moderate positive correlations between physician (MDG) and patient (PtG) global assessment of disease activity. They may be driven by different considerations such as pain, fatigue and mental status for patients and more objective measures such as the joint count and acute phase reactants for physicians. We hypothesized that while absolute values of patient and physician global poorly correlate, changes in these measures may offer a better correlation. To evaluate these objectives, we looked at global evaluation changes before and after introduction of a first biologic agent in RA patients.

Methods: We included patients treated for at least 6 months with a first anti-TNF agent starting in January 2005.The patient and physician global assessments of disease activity of RA patients were extracted from RHUMADATA®. Pearson correlations coefficients between pre, post and pre-post changes in patient and physician assessments were computed (SAS v 9.3) and compared. We used t-tests to verify if pre-post differences in global assessments were related to disease duration (< 2 years vs > 2 years), age (< 50 years vs > 50 years), gender and DAS 28 (< 3.2 vs > 3.2). A general linear model (GLM) was used to further assess if disease duration, age, gender and baseline DAS28 score explain those discrepancies.

Results: The global disease activity scores from 83 patient-physician pairs were used for this analysis. The pre-treatment assessments were made within 0 and 176 days (mean 33 days) of biologic initiation while the post treatment assessments occurred between 182 and 799 days (mean 268 days). . The pre and post treatment Pearson correlations coefficients between patient and physician assessments are respectively r2=0.34 (p=0.001) and r2=0.19 (p=0.08). The correlation coefficient between patient and physician change in global assessment is 0.15 (p=0.19). Disease duration, gender, age and DAS28 scores did not influence the change in MDG. Similar results were observed in the PtG changes except for disease duration where patients with < 2 years had smaller changes The GLM revealed that no factors other than rater (physician or patient) explained the observed differences.

Conclusion: While the pretreatment global disease activity assessments showed moderate correlation, the change in these exhibited a weak relationship. Both physicians and patients agree on disease activity changes although their magnitudes differ. Only rater (physician or patient) seem to explain these differences.

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Real-World Use of Tocilizumab in Rheumatoid Arthritis Patients in Canada: Interim Results from the ACT_UP CARE Study

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Objectives: Tocilizumab (TCZ) is approved for the treatment of adults with rheumatoid arthritis (RA) either as monotherapy or in combination with disease-modifying antirheumatic drugs (DMARDs). However, data on its real-world utilization and durability are limited. This analysis aims to describe the pattern of TCZ use at baseline and after 6 months of treatment in Canadian moderate-to-severe RA patients enrolled in ACT-UP.

Methods: ACT-UP is an ongoing, multi-national, observational study with TCZ. As of June 2014, 1,375 patients were enrolled from 14 countries. Data from the 200 Canadian patients in ACT-UP were used. Descriptive statistics were produced; between-group comparisons were performed with the independent-samples t-test (continuous variables) and the chi-square test (categorical variables).

Results: Among the 200 patients, 67 (33.5%) started TCZ as monotherapy and 133 (66.5%) in combination with DMARD(s) (mean methotrexate dose: 19.9mg/week). Baseline age (55.2 vs. 55.6 years, respectively), gender (79.1% vs. 80.5% females) and disease duration (13.8 vs. 12.0 years) were similar between-groups. The initial TCZ dose was also comparable; 91.0% in each received 8mg/kg and the remaining <8mg/kg. Concomitant baseline corticosteroid use (38.8% vs. 36.1%; mean prednisone dose: 10.7 vs. 9.2mg/day) and prior biologic use (80.6% vs. 82.0%) were also similar in monotherapy vs. combination therapy, respectively. Lack of efficacy (70.4% vs. 68.2%) and intolerance (12.2% vs. 10.9%) were the predominant reasons for previous biologic discontinuation in both groups. However, a significantly higher proportion of monotherapy patients had been previously treated with >1 traditional DMARD (90.8% vs. 66.9%; P<0.001). Overall, baseline disease parameters were statistically comparable between treatment groups except for patient global which was significantly higher in the monotherapy group (68.1 vs. 60.6mm; P=0.017). At month 6, 86.6% and 85.0% of monotherapy and combination therapy patients, respectively, were still on TCZ. TCZ dose remained stable in 80.6% patients (76.9% vs. 82.5%, respectively) and was down-titrated in 14.7% (18.5% vs. 12.7%, respectively). Seven of 67 (10.4%) monotherapy patients added a concomitant DMARD within 6 months. Regardless of treatment group, significant improvements were observed over 6 months in all disease parameters examined (baseline vs. 6 months DAS28: 5.3 vs. 3.4; P<0.001).

Conclusion: In this real-world observational study, TCZ monotherapy was used in 33.5% of patients. Despite that 81.5% of patients had been previously treated with a biologic, more than 85% remained on TCZ after 6 months of treatment. TCZ therapy alone or in combination with DMARD(s) over 6 months was effective in inducing significant improvements in all disease parameters studied.

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Denosumab, Biologics and the Risk of Infection in Patients with Rheumatoid Arthritis

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Objectives: To evaluate the risk of infection in patients with rheumatoid arthritis (RA) treated with denosumab alone or concomitantly with a biologic agent (BA).

Methods: Patients with RA followed at the Institut de Rhumatologie de Montréal and who were prescribed denosumab were followed prospectively. Baseline demographics, co-morbidities, co-medication and infectious events were entered in the RHUMADATA® database. Patients were divided in 2 groups, the first received denosumab concomitantly with a biologic agent (BA) and the second group took only denosumab without ever taking a BA. The rate of infection was evaluated one year prior to the initiation of the denosumab and compared to the rate of infection during the exposure to denosumab in both groups. The data were analyzed using the SAS statistical software (Version 9.3).

Results: A total of 63 patients were ever prescribed denosumab, 20 concomitantly with a BA and 43 without a BA. Patients were on average 70.3 years of age, 92% were women, and had a mean (SD) RA disease duration of 18.6(13.5) years. Exposure to denosumab was on average 1.9 years for Group 1 and 1.6 years for Group 2. No differences were noted for co-morbidities or co-medication between the 2 groups. For Group 1, the rates of infections per 100 pt.-years were respectively 35.0 in the year preceding the start of denosumab and 15.7 during the concomitant use with a BA (p=0.16). For Group 2 the rates were respectively 18.6 prior to denosumab use and 25.0 during denosumab use (p=0.49).

Conclusion: In this cohort of RA patients whose baseline characteristics were similar, the risk of any infection was not increased by denosumab given alone or in combination with a biologic agent.

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Study of the Lymphatic System in Transient K/BxN Animal Model of Rheumatoid Arthritis

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Objectives: Autoimmune inflammatory arthritis reminiscent of rheumatoid arthritis (RA) spontaneously develops in the mouse strains called K/BxN. Arthritic development in the K/BxN mice is dependent of T CD4+ and B cells and production of immune complexes. Transient RA can be induced in recipient wild-type mice upon serum transfer. This model, known as the K/BxN serum transfer model of RA recapitulates several of the features seen in RA. Although most studies have focused their attention on the molecular events occurring in the joints during the development of arthritis, very little is known on the impact of arthritis on the lymphatic system. Here, our goal was to examine the changes occurring in the peripheral lymph nodes (LN) during transient arthritis induced by K/BxN serum transfer in wild type animals.

Methods: 18 C57BL/6 mice were either injected intraperitoneally with 150 ul K/BxN serum or diluent (PBS) on day 0 and 2. Mice were sacrificed at day 7 at the peak of the arthritis development and peripherals LNs were harvested and their weight measured. Left LNs were used for histology studies and right LNs were processed for cell population analysis using flow cytometry. Non parametric Mann Whitney T test was used and a p value < 0.05 was determined as significant difference.

Results: We observed a significant difference in weight and cell counts between the popliteal LN (PLN) of arthritic mice compared to control healthy mice. PLN of arthritic mice had a weight of 2.4 mg in average and contained 11.6×10^6 cells compared to healthy mice with PLNs, which had an average weight of 0.9 mg and a cell count of 5.6×10^6 cells. There was also a difference in the cell population comprised in the LN. Our results revealed an increase in the number of B cells (6.8×10^5 vs 1.8×10^5), dendritic cells (6.8×10^4 vs 3.1×10^4) and granulocytes (5.3×10^3 vs 1.5×10^3). Furthermore, we observed that a significant numbers of the PLN (37%) were filled with blood, suggesting that hemostasis is frequently perturbed at the levels of the lymphatic systems during arthritis. Intriguingly, no significant differences were observed in the axillary and inguinal LNs, pointing the occurrence of discrete cellular activation pathways taking place specifically in the PLN.

Conclusion: We observed significant changes in the draining LN in the transient model of RA. These findings underscore the need to decipher the molecular and cellular pathways that impact the lymphatic system during RA.

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Effectiveness of a Telemedicine Education Program for Adults with Inflammatory Arthritis Living in Rural and Remote Communities in Ontario

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Objectives: Telemedicine-based approaches to healthcare service delivery improve access to care. It was recognised that people with inflammatory arthritis living in rural areas had limited access to patient education and could benefit from the "Prescription for Education (RxEd)" program, an evidence-based inflammatory arthritis education program. The one-day program was adapted to be delivered via interactive videoconferencing through two workshops for local and rural facilitators: Telemedicine Best Practices/Adult Education Principles; Improved Public Speaking.   The objective of this study was to evaluate the effectiveness of telemedicine delivery of RxEd in improving arthritis self-efficacy and other secondary outcomes (arthritis knowledge, coping efficacy, illness intrusiveness, and effective consumer).

Methods: Two group, pre-post design comparing two methods of delivery, local (I, in-person) versus videoconferencing (R, remote using telemedicine), of the RxEd program. Data were collected at baseline (T1), immediately following RxEd (T2), and at 6 months (T3). Self-report questionnaires served as the data collection tool. Measures included demographics, disorder-related, and validated outcomes: Arthritis Self-Efficacy Scale (SE), previous knowledge [ACREU RA knowledge questionnaire (PK)], coping efficacy (CE), Illness Intrusiveness (II), and Effective Consumer Scale (ECS). Analyses included: Univariate comparison at baseline (I vs R); mean scores plotted over time (I vs R); and Generalized Estimating Equations (GEE) Analysis: Main effect of intervention over time, and Group by time interaction (comparison of I vs R).

Results: 123 persons completed baseline questionnaires (I n=36; R n=87), with follow-up of 81% (n=100) immediate post (T2) and 62% (n=76) at 6 months (T3). No significant baseline differences for: demographics, disorder-related, SE, PK, CE, II, and ECS measures.   Both groups (I and R) showed immediate effect (improved SE) after the intervention that diminished over 6 months. Both groups showed similar trends for improvement in all secondary outcomes over time.   GEE analysis: Main effect of RxEd statistically significant increase ($p<0.05$) in SE of 0.76 unit T1-T2, and not significant T1-T3; statistically significant increase in PK of 1.41 unit T1-T2 and increase in ECS of 4.31 unit T1-T3. CE and II not significant T1-T3. In all models (primary and all secondary outcomes), interaction between group and time was not significant, indicating that the in-person (I) and remote (R) changed similarly over time.

Conclusion: Improvements in arthritis self-efficacy and other secondary outcomes were similarly effective in local (in-person) and remote participant groups. Access to inflammatory arthritis education in rural and remote communities is greatly increased with using Telemedicine. Supported by a CIORA grant

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Discovery and Validation of Novel Urinary Biomarkers for Lupus Nephritis

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Objectives: Lupus nephritis (LN) is a major determinant of morbidity and mortality in Systemic Lupus Erythematosus. Variability in clinical course and response to treatment poses therapeutic challenges. Biomarkers that accurately reflect clinical change would aid in the management of LN. Renal biopsy establishes the extent and nature of renal injury, with serologic changes (anti-dsDNA antibodies) or measures of renal dysfunction (proteinuria) failing to anticipate impending flares and/or assess therapeutic response. We used a proteomics approach to identify urinary biomarkers associated with LN.

Methods: In a discovery cohort, urine was obtained from 60 LN patients within 2 weeks of biopsy, 25 active non-LN SLE patients, and 24 controls. 128 analytes were quantified by Luminex and normalized to urinary creatinine. Data was analyzed by hierarchical clustering using divisive analysis, linear modeling, and non-parametric statistics, correcting for multiple comparisons. Proteins preferentially elevated in active LN were validated in an independent cohort.

Results: LN and non-LN patients had comparable SLEDAI-2K scores (13.8±7.6 and 11.1±3.9, respectively), with the majority of the SLEDAI-2K in LN patients arising from the renal indices (8±4.3). The renal biopsy ISN-RPS classes were: I – 1; II-3; III or III/V-12; IV or IV/V-32; V-9; VI-2; TIN-1. The mean biopsy activity (6.68; range 0-19) and chronicity (3.13; range 0-10) scores were calculated. Following hierarchical clustering, significant clustering was seen for LN vs non-LN and controls. Linear modeling was used to determine the urinary proteins whose abundance differed significantly between disease states (SLE vs control) and between the presence or absence of LN (active LN vs active non-LN). Nine analytes differed significantly (q < 0.01) between SLE patients and controls and 42 between LN and non-LN, of which 37 differed only in LN patients compared to non-LN patients.   Several proteins, not previously proposed as LN biomarkers (e.g.,TIMP-1), and known candidate biomarkers (e.g.,adiponectin), were identified, with many of the novel biomarkers showing an enhanced ability to discriminate between LN and non-LN patients over biomarkers proposed in the literature. Ten proteins correlated with the biopsy activity score (q < 0.01), 5 of which (IP-10, vWF, adiponectin, IL-16, PAI-1) strongly discriminated between proliferative and non-proliferative/chronic renal lesions. Several of these proteins have been validated in an independent cohort.

Conclusion: Urinary biomarkers that correlate with the presence of active LN and/or renal biopsy changes were identified and validated. Experiments to assess the ability of these proteins to reflect clinically significant changes in LN are ongoing.

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Patient-Reported Outcomes in CAMEO, the Canadian Methotrexate and Etanercept Outcome Study
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Objectives: CAMEO was designed to evaluate effects of withdrawing methotrexate (MTX) following combination therapy with etanercept (ETN) plus MTX in patients with active rheumatoid arthritis (RA) who initiated ETN obtained by usual care. The purpose of this analysis was to evaluate health-related quality of life based on patient-reported outcomes (PROs).

Methods: This phase 4, randomized, open-label, noninferiority clinical trial enrolled RA patients who had inadequate response to MTX. All patients received combination therapy with ETN (50 mg weekly) and MTX for 6 months. At month 6, patients were randomized (1:1) to ETN monotherapy or to continue ETN+MTX for an additional 18 months. PROs included: Short Form-36 (SF-36) Health Survey questionnaire, Health Assessment Questionnaire Disability Index (HAQ-DI), and pain based on a visual analog scale, which were assessed at baseline and at months 6 (randomization), 12, 18, and 24. The SF-36 is a generic measure with higher scores representing better health; the minimum clinically important difference (MCID) for physical and mental component scores (PCS and MCS, respectively) is a change ≥2.5. The HAQ-DI is rated on a scale of 0-3 where higher scores represent greater disability; the MCID is a change ≥0.22. The pain VAS is rated on a scale of 0-100 mm where higher values represent greater pain; the MCID is a change of ≥10 mm. No statistical testing was performed because of the noninferiority study design.

Results: Of 258 enrolled patients, 53 were not randomized, 98 were randomized to ETN, and 107 were randomized to ETN+MTX. At month 6, mean change (standard deviation [SD]) from baseline in PCS was 7.9 (8.7); MCS was 5.5 (11.6); HAQ-DI was -0.4 (0.6); and pain VAS was -20.6 (28.7) for all patients. Mean change (SD) from month 6 (randomization) to month 24 in PCS was -3.1 (9.0) and -0.8 (9.4) for ETN and ETN+MTX, respectively; MCS was -1.3 (10.5) and 0.1 (10.7); HAQ-DI was 0.2 (0.4) and 0.0 (0.5); and pain VAS was 8.7 (26.1) and 5.1 (27.3). At month 24 the percentage of patients who achieved the MCID for PCS was 25.5% and 15.1% for ETN and ETN+MTX, respectively; MCS was 54.1% and 56.6%; HAQ-DI was 54.1% and 64.5%; and for pain VAS was 56.3% and 61.3%.

Conclusion: Clinically meaningful improvements in PROs were seen from baseline to month 6. In general, PRO improvements were maintained to month 24 in patients who discontinued MTX as well as those who continued on ETN+MTX.

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Risk of Hydrocephalus and/or Macrocephaly in Children Born to Mothers with Systemic Lupus Erythematosus

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Objectives: Evidence suggests that both hydrocephalus and macrocephaly could be potential manifestations of neonatal lupus. In a study of 87 children born to mothers with anti-Ro antibodies, prevalence of hydrocephalus was high at 8.0% and mean head circumference substantially larger than the age-matched normal values (Boros et al.,Arthritis Rheum,2007). Although up to 40% of women with SLE display anti-Ro antibodies, no one has assessed the occurrence of hydrocephalus and/or macrocephaly in SLE offspring. In a large population-based study, we aimed to determine if children born to women with SLE have an increased risk of hydrocephalus and/or macrocephaly.

Methods: The "Offspring of SLE mothers Registry (OSLER)" includes women who had ≥1 hospitalization for delivery after SLE diagnosis, using Quebec's universal healthcare databases (1989-2009). OSLER includes a randomly selected control group of women, matched ≥4:1 for age and year of delivery, who did not have a diagnosis of SLE prior to or at delivery. We identified children born live to SLE mothers and their matched controls, and ascertained hydrocephalus and/or macrocephaly based on ≥1 hospitalization or physician visit with a relevant diagnostic code. We performed multivariate logistic regression analyses, using generalized estimating equations, adjusting for maternal demographics and comorbidities, sex of child, and gestational diabetes.

Results: 719 children were born to 509 women with SLE, and 8493 children were born to the 5824 matched controls. Compared to controls, children born to women with SLE showed only a slight trend towards more records of hydrocephalus and/or macrocephaly diagnosis [8/1000 persons (95%CI 4-18) versus 6/1000 persons (95%CI 5-8), difference 2/1000 persons (95%CI -3-13)]. Similarly there was only a slight trend towards younger age at hydrocephalus and/or macrocephaly diagnosis in SLE offspring [respectively 0.6 year (95%CI 0.2-1.0) and 1.1 years (95%CI 0.5-1.7)]. Among the 6 cases of hydrocephalus and/or macrocephaly identified in SLE offspring, none had a diagnosis of cardiac conduction disturbance, suggesting no strong association with neonatal lupus. In multivariate analysis, the point estimate for the outcome was consistent with a trend for higher risk of hydrocephalus and/or macrocephaly in SLE offspring compared to controls, although the confidence interval was wide and precluded definitive conclusions (OR 1.37, 95%CI 0.58-3.22).

Conclusion: Compared to children from the general population, there was a slight trend for higher frequency (and earlier age at diagnosis) of hydrocephaly and/or macrocephaly among children born to mothers with SLE, but the results do not strongly suggest an important increase in the risk of hydrocephalus and/or macrocephaly.

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Assessing the Agreement of Patient Self-assessed Joint Count and Rheumatologist Joint Count Assessments in Patients with Inflammatory Arthritis: A Method Comparison Study

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Objectives: Identification of patients with inflammatory arthritis to permit expeditious assessment is a challenge for rheumatologists. Barriers include time constraints in busy family physicians' offices and family physicians' lack of expertise in evaluating inflamed joints. The purpose of this study was to assess whether untrained patients can perform joint self-assessment to provide information for rheumatologists.

Methods: Seventy-seven patients and 10 rheumatologists participated, with the number of patients seen by a single rheumatologist varying from 1 to 10. The joint count methodology used by the rheumatologists varied from 28 to 68. Patients were asked to record, on a homunculus, any tender peripheral joints. Bland-Altman (BA) plots were created to show the agreement between the patient count and their rheumatologist's count.

Results: Patient counts were higher than rheumatologist counts. BA-plots showed that the differences between the patients and rheumatologists increased with the magnitude of the mean of the patient and rheumatologist counts but were not discordant.

Conclusion: Patient-performed tender joint assessment can provide useful information to aid in selecting waiting list patients with possible inflammatory arthritis Weaknesses include the following: 1. This group of patients all had identified inflammatory arthritis and had previously had joint counts done by their rheumatologist; 2. The patient numbers are small; a larger study is planned.

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The Importance of Primary Care Providers for Managing Rheumatoid Arthritis for First Nations Patients: Discrepancies in RA Prevalence and Specialist Care Use

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Objectives: To estimate rheumatoid arthritis (RA) prevalence and health services use by First Nations (FN) and non-First Nations (non-FN) in Alberta, Canada.

Methods: Using population-based administrative databases in Alberta (1993/4 to 2010/2011), a prevalent RA cohort was defined by 1 hospitalization or 2 physician claims in 2 years for ICD-9-CA code 714.X and/or ICD-10-CM codes M05-M06.X. FN patients were identified using Alberta Health definitions based on premium payer status. Prevalence rates, stratified by FN status, were estimated. Annual rates for visits for RA to primary care physicians, rheumatologists and/or internists, as well as hospital admissions for hip and/or knee arthroplasty, and other hospitalizations (all-cause, RA-specific), per 100/person-years, were calculated for 4 fiscal years (2005/6 to 2008/9). Age and sex standardized-rate ratios (SRR) and 95% confidence intervals (95%CI) were calculated to compare estimates for FN relative to non-FN.

Results: In fiscal year 2008/2009, there were 2672 FN and 36259 non-FN who met the case definition for RA, with 61.3% (n=1637) of FN and 19.6% (n=7123) of non-FN residing in a rural location. The prevalence rate of RA in FN was 3.2 per 100 (95%CI 3.1-3.4) compared to 1.0 per 100 (95%CI 1.0-1.0) in non-FN, yielding an SRR of 3.15 (95%CI 2.92-3.40). FN patients with RA were more likely to see a primary care provider for their RA (SRR 1.68, 95%CI 1.67-1.68), and significantly less likely to see a rheumatologist or internist (SRR 0.64, 95%CI 0.63-0.64). There was no modification of these rates by location of residence (urban vs rural). Although the all-cause hospitalization rate for FN with RA was higher (31.3 compared to 15.1 per 100 person-years), RA-specific hospitalization rates were lower (SRR 0.81, 95%CI 0.80-0.81) relative to non-FN with RA. Hip and/or knee arthroplasty rates were lower in FN with RA compared to non-FN with RA (SRR 0.64, 95%CI 0.64-0.65).

Conclusion: First Nations in Alberta have a three-fold higher prevalence rate of RA. Despite the importance of specialty care for RA management, use of rheumatology and/or internal medicine services is significantly reduced compared to non-FN patients, regardless of location of residence. FN patients with RA are more frequently hospitalized for any cause, but are less likely to be admitted due to RA or for arthroplasty. Primary care physicians are delivering RA care to FN patients, thus increased alliance with these providers is critical to ensure treatment targets are being achieved. Supported by a CIORA grant

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Sociodemographic and Health Status Characteristics Explain Five Clinical Outcome and Radiographic Trajectories in Early Rheumatoid Arthritis: Data from the CATCH Cohort

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Objectives: Determine baseline characteristics that influence patient trajectories and radiographic progression in early rheumatoid arthritis (ERA).

Methods: Using growth-based trajectory modeling, subjects from CATCH (Canadian early ArThritis CoHort) were assigned to trajectory groups by their DAS28 scores over 24 months. Sociodemographic, disease and treatment variables distinguishing the groups were identified. Radiographic progression in the different trajectory groups was assessed.

Results: Five distinct trajectory groups within the cohort (n=1586) were characterized by their initial and final DAS28 scores: Group 1 (20.1%) high disease activity state (HDAS) improving to remission (REM); Group 2 (20.5%) moderate disease activity state (MDAS) improving to REM; Group 3 (30.1%) MDAS improving to low disease activity state (LDAS); Group 4 (19.3%) HDAS improving to LDAS; and Group 5 (10.0%) HDAS improving to MDAS only. Subjects in Groups 4 and 5 were older, had more comorbidities, lower education and employment. Subjects in Group 5 were more frequently of an ethnic minority population, and had lower income. Methotrexate and combination therapy use was lowest in Group 5, with higher steroid and biologic use. In the subset of patients with repeated radiographic examinations, those in Group 2 had lower odds of radiographic progression relative to Group 1 (OR 0.22, 95%CI 0.07-0.70, p=0.01) whereas more radiographic progression was observed in Groups 4 and 5.

Conclusion: Heterogeneous disease trajectories in ERA are influenced by sociodemographic and health status factors, resulting in differing degrees of radiographic damage. Personalized treatment strategies, early prediction of disease course and addressing social determinants of health could optimize outcomes.

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Treatment Outcomes with Biologic Therapies for Rheumatoid Arthritis in the Alberta Aboriginal Population

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Objectives: To compare the clinical outcomes of rheumatoid arthritis (RA) treatment with biologic therapies between Aboriginal and non-Aboriginal patients.

Methods: The Alberta Biologics Pharmacosurveillance Program (ABioPharm) is a longitudinal observational cohort of RA patients receiving biologic therapy. Outcomes captured include treatment efficacy and patient-reported outcomes including function (HAQ), quality of life (EQ-5D), and well-being (SF-36). We compared differences in disease phenotype, and baseline disease activity measures and patient-reported outcomes, between Aboriginal patients (self-reported First Nations, Metis or Inuit) and non-Aboriginal patients using Student's t-test or chi-squared tests as appropriate. Longitudinal mixed models were used to estimate the rate of change in disease activity measures and patient-reported outcomes over the first 12 months of treatment for Aboriginals and non-Aboriginals, with the ratio of the slopes of change adjusted for the baseline score of the variable of interest, as well as sex, age, baseline DAS28 and HAQ scores, and disease duration.

Results: Aboriginal patients (n=90) were younger at initiation of their first biologic (50 vs 55 years, p<0.001) despite similar disease duration to non-Aboriginals (n=1400), and had more comorbidities (mean Self-Administered Comorbidity Questionnaire score 5.4 vs 3.1, p<0.001). Prior use of DMARDs, disease duration at time of first biologic, and frequency of seropositivity was similar for both groups. Aboriginal patients had higher baseline DAS28ESR scores (mean 6.11 vs 5.19, p<0.001) with higher levels of pain (7.6 vs 6.7 by VAS, p<0.001), and worse SF-36 mental health (standardized score 40.1 vs 45.3, p<0.001) and physical scores (standardized score 25.3 vs 26.9, p=0.05). Over 12 months, Aboriginal patients had a slower rate of improvement for tender joint counts (adjusted ratio 1.15, 95%CI 1.02 to 1.29, p=0.017), swollen joint counts (adjusted ratio 1.14, 95% CI 1.00 to 1.28, p=0.043), and ESR (adjusted ratio 0.54, 95% CI 0.06 to 1.01, p=0.027). Despite this, Aboriginal patients were not more frequently switched to another biologic agent (mean switches 0.8 per patient). At 12 months, quality of life (EQ-5D adjusted difference -0.07, 95%CI -0.11 to -0.03, p<0.001), SF-36 mental health (adjusted difference -3.59 95%CI -5.05 to -2.13, p<0.001) and SF-36 physical scores (adjusted difference -2.34; 95%CI -3.90 to -0.78;p=0.003) remained lower in Aboriginal patients.

Conclusion: Aboriginal patients experience higher levels of disease activity through their first year of treatment with biologic therapies, even after adjusting for baseline characteristics, resulting in attenuated patient-reported outcomes. We have identified a need to intensify treatment regimes to achieve the desired treatment outcomes.

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Fine Particulate Air Pollution and Systemic Autoimmune Rheumatic Disease in Two Canadian Provinces

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Objectives: To estimate the degree to which fine particulate (PM2.5) air pollution is associated with systemic autoimmune rheumatic diseases (SARDs).
Methods: We used population-based administrative data from Alberta (1993-2007) and Quebec (1989-2010). The SARD case definition was based on at least 2 physician billing claim codes, or at least 1 rheumatology billing code, or at least 1 hospitalization diagnostic code (for systemic lupus, Sjogren's Syndrome, scleroderma, polymyositis, dermatomyositis, or undifferentiated connective tissue disease). Bayesian hierarchical latent class regression models estimated the probability that any given resident was a SARD case, given our three case definitions. Mean 2001-2006 residential exposures to ambient PM2.5 levels were assigned using satellite-derived data for Dissemination Area regions in Alberta, and Local Community Services Centre (CLSC) regions in Quebec (both assigned from postal code of residence). The sum of individual level probabilities provided the total cases per region in each province, according to age, sex, urban-versus-rural residence, income, and PM2.5 levels. In Alberta, we also stratified by First-Nations(FN) status. The hierarchical model generated odds ratio (OR) estimates for being a SARD case, based on age, sex, urban-versus-rural residence, income, and PM2.5 levels. The model accounted concurrently for these characteristics, as well as an interaction term between age and sex. The model generated Bayesian 95% credible intervals (CrI, which are similar to the non-Bayesian confidence interval) for the OR estimates
Results: The probability of being a SARD case was higher among females versus males and for residents aged > 45 versus younger, with the highest ORs for older females. Independently, the odds of being a SARDs case increased with PM2.5 levels. In Alberta, the effect was slightly greater for FN residents. Specifically, in Alberta, when we used a continuous variable for PM2.5, the adjusted OR (interpreted as increase in SARDs per unit increase in PM25) in FN residents was 1.38 (95% CrI 1.14, 1.68) whereas in non-FN Alberta residents the adjusted OR was 1.05 (95% CrI 1.01, 1.08). In Quebec, where information on FN status (1% of the Quebec population) was not available, the adjusted OR for PM2.5 as a continuous variable, was 1.05 (95% CI 1.05, 1.06).
Conclusion: Adjusting for demographics, exposure to PM2.5 is associated with an increased SARD prevalence. Our data suggest that FN populations may be particularly vulnerable to this effect. Improving air quality may be a key way to reduce chronic disease burden.

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A Novel Approach to Assess Wait-Times to Rheumatologists

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Objectives: Previous studies quantifying delays in assessment of patients by rheumatologists have studied patients from rheumatology clinics and thus include all patients who ultimately had access to rheumatologists. Our study estimates over-all wait times for initial rheumatology consultations for patients referred by their primary care physician.

Methods: We employed a novel approach to identify first-time rheumatology referrals from the primary care Electronic Medical Record Administrative data Linked Database (EMRALD), representing comprehensive EMR data from 168 primary care physicians across Ontario, Canada (32 rural, 39 suburban and 97 urban physicians). We randomly sampled patients with rheumatology referral letters and performed linkage with administrative data to retrospectively confirm that patients had no prior rheumatologist assessments. Using a standardized data abstraction tool, the entire patient medical record was reviewed to categorize each patient according to their diagnosis: systemic inflammatory conditions, mechanical/degenerative/arthritic conditions, chronic pain, regional musculoskeletal (MSK) syndromes, osteoporosis/osteopathies, and other (e.g., abnormal diagnostic tests). Administrative data were then used to identify the date of the first rheumatologist visit subsequent to the date recorded on the referral identified in the EMR. The time in days from the date the first referral letter was sent to the date of the first rheumatologist visit was determined overall and for each diagnostic category.

Results: Among 1086 patients with first-time referrals, 99% of referrals analyzed occurred between 2006 and 2013. The majority of referrals were for mechanical/degenerative conditions (34%) and systemic inflammatory conditions (30%). Overall, 36% of patients were seen by a rheumatologist within 6 weeks from referral and 67% within 3 months. 68 (6%) patients were waiting longer than 12 months to be seen. The average wait time to see a rheumatologist for any condition was 142 days (median 61) post-referral. For patients with systemic inflammatory conditions, the median time to be seen was 47 days (interquartile range 18-97). The median wait times for individuals with conditions deemed non-urgent (osteoarthritis, chronic pain) were roughly 2 weeks longer.

Conclusion: Using EMRs from a representative sample of Ontario primary care practices revealed longer wait times to see a rheumatologist than previous Canadian reports that sampled patients from urban rheumatology clinics. 33% of patients were still waiting >3 months to be seen, exceeding current Canadian recommendations. Individuals with systemic inflammatory conditions were seen earlier compared to other types of referrals. An analysis of wait times along each component of the care pathway is currently underway. Supported by a CIORA grant

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Methotrexate-Induced Lymphoproliferative Disorder Presenting in Lungs, Liver and Bone: A Case Report and a Literature Review

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A 73-year old male presented to emergency room with severe back pain. He was previously diagnosed with rheumatoid arthritis (RA) and treated with a maintenance dose of methotrexate (MTX) for 15 years. Bone scan revealed metastatic bone disease in T10 and L5-S1 regions. Further imaging demonstrated scattered numerous lung lesions up to a maximal diameter of 6.6 cm and hypoechoic well-circumsized liver lesions, all highly suggestive of metastatic disease with unknown primary origin. Lung biopsy showed large zones of necrosis without evidence of carcinoma or granulomatous inflammation. Staining for organisms was negative. Liver biopsy showed mild fibrosis and anisonucleosis, along with zones of prominent inflammation. Following these studies, patient was diagnosed with stage IV cancer and recommended 5 fractions of 20 Gy radiation. Patient declined therapy, deciding instead to withdraw all medications and was discharged under his family's care.

Follow-up imaging at 6 months showed clearing of most lung markings when compared to previous results. Imaging during an unrelated hospital admission 3 years later showed no liver or lung masses. Patient was subsequently diagnosed with methotrexate-induced lymphoproliferative disorder. There have been no symptoms of recurrence in the 4 years since MTX withdrawal. Patient's arthritis is currently not active.

MTX treatment is a known risk factor for lymphoproliferative disorders. To our best knowledge, this is the first reported case of non-EBV methotrexate-associated lymphoproliferative disorder localized to bone, liver and lungs. Literature sources on the topic of methotrexate-associated lymphoproliferative disorders are thoroughly examined following the case report.

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The Generalizability of the Ontario Best Practices Research Initiative to the Ontario Rheumatoid Arthritis Population and General Population

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Objectives: To compare the demographics of a clinical cohort of rheumatoid arthritis (RA) patients with all residents in Ontario (with and without RA).

Methods: We studied all patients in the Ontario Best Practices Research Initiative (OBRI), a clinical cohort of RA patients recruited from rheumatologists across Ontario (2008-present). All residents with RA as of 2010 were identified from the Ontario RA Database (ORAD) generated from provincial health administrative data. We used the 2011 Census from Statistics Canada and the National Household Survey to describe the general population. We evaluated the generalizability of the OBRI to the Ontario population with and without RA in terms of patient demographics.

Results: Of the 162 Ontario rheumatologists, 63 (39%) are participating in the OBRI representing both community-based (48%) and academic settings (52%). Among the 2354 RA patients in the OBRI, 78% are female and 36% are ages 65 years and older. Among the 97,499 RA patients in ORAD, 71% are female and 44% are ages 65 years and older. As expected, 92% of OBRI patients speak English as their primary language (followed by Punjabi (1%)), compared to 79% (followed by French (2%)) in the Ontario population. The three most frequent ethnicities include Caucasian (85% vs. 93%), Indian (4% vs. 8%) and Oriental (3% vs. 10%) in OBRI and Ontario population, respectively. Postsecondary (56% vs. 55%), high school (36% vs. 27%) and no education degree (8% vs. 19%) are relatively similar between OBRI and Ontario, respectively. The annual household income is also comparable. The regional distribution of RA patient residences in OBRI is similar to that of all Ontario residents (with and without RA), with the highest proportion of residents living in southern Ontario.

Conclusion: Overall, the OBRI has comparable demographics to the Ontario RA population and general population, increasing the confidence in the generalizability of OBRI for clinical research.

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Vasculitis in Patients with Inflammatory Bowel Diseases: A Study of 32 Patients and Systematic Review of the Literature

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Background/Purpose: Small case series suggested that vasculitis and inflammatory bowel disease (IBD; Crohn's disease [CD] or ulcerative colitis [UC]) can co-occur more commonly than the prevalence of the individual diseases suggest. This study aimed to describe this association through the analysis of a large cohort of carefully studied patients and a systematic literature review.

Methods: Clinical data was available from patients with both IBD and vasculitis with follow-up >6 months enrolled in the Vasculitis Clinical Research Consortium (VCRC) Longitudinal Studies, followed in Canadian Vasculitis research network (CanVasc) centers, and/or in the University of Toronto's IBD clinic. Individuals in which ANCA-associated vasculitis (AAV) and IBD were diagnosed within the same 12-month period were excluded. A systematic review of the literature (through 02/2014) for patients with IBD and vasculitis was conducted through a PubMed search. The main characteristics of patients with Takayasu arteritis (TAK) were compared to those patients in the VCRC with TAK but no IBD.

Results: 32 patients (17 VCRC, 15 CanVasc) with vasculitis and IBD that satisfied our study criteria were identified. The main group included 13 patients with large vessel vasculitis (LVV): 12 TAK and 1 giant cell arteritis; 8 patients had CD and 5 had UC. Eight patients had AAV (6 granulomatosis with polyangiitis, GPA), 2 eosinophilic granulomatosis with polyangiitis, EGPA, 5 isolated cutaneous vasculitis, and 6 other vasculitides (Kawasaki, IgA nephropathy, polyarteritis nodosa, or central nervous system vasculitis). Patients with LVV and AAV were mostly female (18/21) with a median age of 20 (8 to 52) and 27 (17 to 58) years at diagnosis of IBD and vasculitis, respectively. The diagnosis of IBD preceded that of vasculitis in 12/13 LVV and 8/8 AAV patients, 3/5 with cutaneous vasculitis and 3/6 with other vasculitides. 305 other patients with IBD and vasculitis were identified in the literature, distributed among 4 similar subsets: LVV (n=143, 116 female, 69 CD, 74 UC, 132 TAK, 87 with IBD preceding vasculitis), cutaneous vasculitis (n=66, 33 with IBD preceding vasculitis), AAV (n=19, 13 GPA, 3 MPA, 3 EGPA), and other vasculitides. Differences observed between patients with TAK with or without IBD included ethnicity and age at TAK diagnosis. Mortality was low in both groups.

Conclusion: These findings highlight the risk in patients with IBD (both CD and UC) to develop vasculitis, especially TAK. Further investigation of patients with both vasculitis and IBD may provide intriguing insights into common underlying mechanisms.

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What Investigations are needed to Optimally Monitor for Malignancies in SLE?

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Objectives: The overall cancer incidence risk in SLE is approximately 15-20% more than in the general population; the risk profile includes a higher and sometimes lower than expected risk of certain cancers. Concern also exists regarding higher rates than expected of cervical dysplasia (a precursor to cervical cancer) and cyclophosphamide-induced bladder cancer. Nevertheless, to date, the optimal malignancy screening measures in SLE remain undefined. Our objective is to determine what investigations are needed to optimally monitor for malignancies in systemic lupus erythematosus, SLE, in order to inform upcoming Canadian Rheumatology Association recommendations.

Methods: We conducted a systematic search looking at three scientific sources, Embase, Medline and Cochrane, in an attempt to identify cancer screening recommendations for patients with SLE. We used a filter for observational studies and included articles published in 2000 and onward.

Results: The initial search strategy led to 986 records. After removal of duplicates and articles unrelated to SLE we were left with 497 titles. From those, 79 research articles on cancer incidence in SLE were isolated and reviewed. Of the 79 original research papers, 25 offered screening recommendations, 14 suggested additional cancer screening whereas 11 studies simply promoted adherence to general population screening measures. The suggestions for more rigorous screening included recommending human papilloma virus testing in addition to routine cervical screening, and/or that cervical screening should be done annually and/or suggested urine cancer screening in SLE patients with history of cyclophosphamide exposure.

Conclusion: We found no original research studies directly comparing cancer screening strategies in SLE. Most studies argue for rigorous cervical screening strategies, and/or suggested urine cancer screening in SLE patients with a history of cyclophosphamide exposure, although some authors recommend adherence to general population screening measures.

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Disparities in the Treatment of Rheumatoid Arthritis in First Nations: A Population Based Study

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Objectives: Rheumatoid arthritis (RA) is more prevalent and severe in First Nations (FN) than nonFN populations yet FN with RA have fewer rheumatology visits. We used provincial administrative health data to determine potential resulting treatment disparities.

Methods: The provincial health research database (PHRD) contains health records for residents (population 1.2 million) including diagnosis based on ICD9/CM or CD10 codes, service provided, provider, prescribed medication and vital statistics. Records from April 1 1995 to March 31 2010 were accessed. FN people were identified by linking the Federal Indian Registry File which records all registered FN for the purposes of entitlement. Identification was expanded to include non-status Indians otherwise eligible or ineligible under the Indian Act. RA cases were identified using an administrative definition previously validated for use in this PHRD. Drug use (corticosteroids, Disease Modifying Anti-Rheumatic Drugs (DMARDs), biologics) was compared between FN and nonFN. Results are reported as median (range), mean (SD) or n(percentages).

Results: 8095 prevalent RA cases were identified. Compared to nonFN, FN with RA had more use (ever) of corticosteroids (835(76%) vs 4571(65%)) and less use of biologics (130(11.9%) vs 972(13.9 %)) with longer delays to first treatment with glucocorticoids (median 4 vs 2 months), DMARDs (median 2 vs 1.3 months) and biologics (median 47.2 vs 30.4 months). Although FN were more likely to have been prescribed combination DMARDs ever (46.6% vs 42.1%), FN received fewer combinations that included biologics (4.9% vs 12.1%). The duration of use (as estimated by the proportion of total RA disease duration on medication) was shorter in FN than nonFN for methotrexate (29.6% (0.05-0.96) vs 49.5% 0.03-1)), biologics (15.5% 0.01-0.65 vs 29.8% 0.04-0.94), and combinations including biologics (0.4 (0.28)vs 1.78(0.06) however was similar for standard DMARD combinations. FN were more likely to have interrupted treatment defined as no RA medication for at least 3 consecutive months (56.6 % vs 36.9%); gaps were more frequent (median 2 vs 1), of longer duration (587.9 vs 550 days) and FN were more likely to be prescribed steroids during treatment gaps (39% vs 33%). FN were younger at death than nonFN(53.0 years (CI mean 45.6-60.4) vs 75.9 (CI 74.4-77.3) p<0.0001). .

Conclusion: Despite higher prevalence rates of RA, clinically more severe disease and early mortality, FN with RA receive less aggressive treatment that is often interrupted. While comorbidity and other factors likely contribute to this disparity, these findings highlight the importance of improving rheumatic care delivery to this high risk population.

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Residual Lupus Disease Activity in a Large Canadian Cohort of Prevalent Patients

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Objectives: Treatment of systemic lupus erythematosus (SLE) aims at effectively controlling disease activity in order to prevent damage. We describe residual disease activity in a large multi-centre cohort of prevalent SLE patients.

Methods: We report disease activity, treatment and damage in a large cohort of prevalent SLE patients. Disease characteristics at cohort entry including demographics, the SLE disease activity index (SLEDAI2K), the SLICC/ACR damage index (SDI), serology, and treatment were collected. Four groups were created based on their SLEDAI2K score: low (<4), moderate (4 to <6), active (6 to <10) and highly active (>10). Cross-sectional comparisons of the characteristics in the four groups relied on bivariate analyses: chi-square tests for categorical 1-way ANOVA for continuous variables, and tests for trend.

Results: The cohort included 1454 participants. At cohort entry, the overall mean (sd) age was 44.0 years (15.9), age at diagnosis was 33.2 (15.3), disease duration 10.6 (9.7) years. There were 90.3% females, 81.7 % had completed high school, and 66.8% were Caucasians. At baseline, nearly half of the patients had low disease activity (n=655, 45.0%; 95%CI: 42.5-47.6%), one fifth had either moderate activity (n=288, 19.8%, 17.8-21.9%) or were active (n=318, 21.9%, 19.7-24.0%), while 193 (13.3%; 11.5-15.0%) were highly active. The low and moderate vs. active and highly active groups did not differ in age, sex, or education. In contrast, mean disease duration decreased significantly with increasing disease activity (p=0.01), from 11.3 (SD=9.8) for the lowest to 9.1 years (9.6) for the highest activity subgroup. Prednisone (p for trend= 0.002) and cyclophosphamide (p for trend= 0.001) use were associated with higher disease activity and antimalarial use with lower activity (p=0.019 for trend). Even in the low and moderate activity groups, more than half were taking prednisone >7.5mg/day, (56% and 53% respectively). Mean SDI scores were statistically significantly higher (p=0.012 for trend) but not clinically significantly different in the higher activity subgroups (4.2 in the active versus 3.9 in the low activity patients).

Conclusion: In our analyses higher SLEDAI2K score was associated with shorter disease duration, increased damage, higher use of prednisone and cyclophosphamide and lower use of antimalarials. Even after a mean of 11 years of disease, 35% of the subjects had active lupus, and even in those with low or moderate activity, more than half were taking prednisone >7.5mg/day suggesting ongoing need for more optimized treatment.

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Clinical Rheumatology Research in the Digital Age: Consent, and Governance Challenges

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Objectives: Canadian rheumatology clinicians are beginning to explore the issues of how data collected in electronic medical records can be used for quality improvement (QI), with the potential for data to be shared across several investigators, and ultimately used for clinical research. As clinicians incrementally move from clinical practice to research they experience difficulty distinguishing between QI and research activities. For example, a lack of guidance exists for patient consent in two areas: 1) electronic consent (e-consent) as patients provide self-reported clinical data electronically (tablets in physician office, online portals), 2) consent for the use of clinical data for research purpose. Presentation findings from the recent Canadian Association of Research Ethics Boards conference revealed clinicians experience difficulty determining what they are ethically permitted to do with clinical data and REB's are having difficulty distinguishing whether QI protocols submitted require review, since QI resides outside the domain of REB review. On this basis, a survey of literature was conducted to identify knowledge gaps and future directions

Methods: Established e-consent and electronic governance search terms were applied to English language articles from: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (1946-2012). CINAHL, Embase (1974-2012). Exclusion criteria: non-electronic articles, abstracts and meeting summaries. The initial search yielded 263390 citations. Combined search terms narrowed results to 379. After limiting articles to 2007-2012 and removing duplicates 83 remained, with 8 articles selected for review.

Results: Themes identified include: 1) Patient Privacy-Protection. 2) Consent-Integration, incorporating clinical care and research into the informed consent process, to satisfy ethical requirements for minimal risk studies. 2) Provision to opt out of study. 3) Governance-Authenticity, clinicians indicating consent conditions are met before accessing data. 4) Governance-Auditability, creating transparency within the research process for REB's.

Conclusion: Despite evidence in the literature that clinical data has been successfully implemented for research under certain conditions, our experience and feedback gained from the ethics community suggests that a large need still exists for clinicians and REB's to gain knowledge on how electronic clinical data can be used for research. Possible implementation challenges occur when attempting to use clinical data for research purposes; it becomes apparent that consent, governance, and compliance requirements will need to change as requirements suitable in a clinical setting are not appropriate for research. Further work is required to develop guidelines, targeting clinicians and REB's pertaining to consent, governance, and compliance requirements for clinical data transitioning to research use.

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Comparison of Patient Self-Reported and Physician Reported Rheumatoid Arthritis Medication Use - Results from the Ontario Best Practices Research Initiative
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Objectives: Patient self-reported medication histories may be prone to misclassification and recall bias. We aimed to assess the agreement between patient (Pt) and physician (MD) reported medication use in a cohort of RA patients.

Methods: Patients enrolled in the Ontario Best Practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care, were included. Following patient consent, data were extracted from physician charts using a structured questionnaire on patient demographics, comorbidities, disease activity and use of RA medications. Patients are assessed every 3 months through telephone interviews according to a standardized protocol to collect additional socio-economic characteristics, disease activities measures, and medication use. We examined the concordance of reporting medication names and the level of agreement between Pt and MD reported RA medications. RA medications (only DMARDs and BIOLOGICS) were categorized as (yes/no) for both self-reported and physician reported data and kappa statistics with 95% confidence intervals were computed at baseline and 12 month period to assess chance-corrected agreement between the two sources of data. Percent agreement was also calculated as a measure of agreement. In addition, dose reported for various drugs were compared at baseline and one year. Wilcoxon signed rank test was used to compare the mean difference of doses reported.

Results: Of the 2347 patients included in the study, 77% of patients were female with a mean (SD) age of 57.4 (12.9) years, and the majority (85%) were Caucasian. Patients had moderate disease activity according to both mean (SD) DAS28 scores 4.5 (1.5) and CDAI scores 21(14). At baseline, substantial agreement was found between Pt and MD reported medication use (kappa =0.78, 95% confidence interval (CI), 0.77-0.79); agreement=97.4%), and use of specific BIOLOGIC and DMARDS with agreement ranged from 88 to 100% (Figure, kappa range 0.50-0.85). The degree of agreement was lowest for methotrexate (kappa=88%). The MD reported mean dose was significantly higher than Pt except for MTX. At one year, the overall agreement of reported medication name increased with kappa=0.84 (95% CI 0.83-0.85) and there was no significant difference in reported dose between Pt and MD.

Conclusion: Similar level of agreement between patients and physicians suggest that differential misclassification is unlikely in the reporting of RA medication use. Furthermore, the accurate reporting of doses at one year suggests that patient's ability to report their medications improves over time.

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Characterization of Patient Reported Pain Medication in Rheumatoid Arthritis Patients – Results from the Ontario Best Practices Research Initiative (OBRI)

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Objectives: Optimal pain control is a cornerstone in the management of rheumatic diseases. Rheumatic pain is intricate and can involve inflammatory and non-inflammatory pathways. From the Ontario Best Practices Research Initiative, a clinical registry of rheumatoid arthritis (RA) patients, our goal was to characterize the use of pain medications according to the Anatomical Therapeutic Chemical (ATC) classification system (the World Health Organization classification of medicinal ingredients) and to characterize patient-reported pain disorders.

Methods: From the patient-reported OBRI cohort (N = 2,266), patients who received at least one pain medication during the study (N = 1,816) were selected. Patient-reported pain medications were categorized according to ATC classes and the numbers of events in each ATC category were identified. If a patient reported taking more than one pain medication within the same drug class it was counted as one event. Patients were also categorized based on self-reported pain disorders, and common medication classes used per category were reported.

Results: From our studied cohort (N=1,816), the mean age was 57.6 years, the mean disease duration was 8.98 years and 78.9% were female. A total of 3,445 events were reported, across all medication classes. The largest medication classes included NSAIDs (40.8%, N = 1405), opioid analgesics (15.9%, N = 548) and non-opioid analgesics (15.5%, N = 533). The use of antidepressants (14.3%, N = 494), benzodiazepines (8.04%, N = 277) and anti-epileptics (5.57%, N = 192) were also observed. Patients did not specify any indication for 48.5% (N=1670) of these pain medications. From the specified indications (N = 1,775), 6 most prevalent pain disorders reported were identified – generalized pain (28.0%, N = 497), joint pain (12.1%, N = 214), migraines (4.68%, N=83), fibromyalgia (3.83%, N=68), back pain (3.77%, N = 67) and neuropathic pain (3.10%, N = 55). Opioid and non-opioid analgesics were highly utilized amongst these groups (56.8%) followed by NSAIDs (33.8%).

Conclusion: Our study shows that in addition to inflammatory pain, many RA patients also suffer from neuropathic pain, fibromyalgia and migraines. Pain management in RA is complex and requires a multimodal approach. Concurrent use of antidepressants, benzodiazepines and anti-epileptics with traditional NSAIDs and analgesics is often required for optimal pain management. High utilization of these non-traditional therapies may indicate an association between pain and other comorbidities such as depression, anxiety and sleep disorders. Future work is required to identify these associations.

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Pilot Evaluation of an Electronic Research Platform Supporting e-Consent

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Objectives: As research participants begin utilizing electronic research platforms (e-platform) for their participation in research studies, technological advances have created a need to re-evaluate, and update current practices surrounding informed consent. Traditionally, consent to research has been expressed in writing, and was a one-time inflexible event. New e-platforms are making the historical consent process obsolete. The Consent and Data Management system (CDM) is an e-platform for electronic data collection of clinical data, participant self-reported data and electronic consent (e-consent). The e-consent process within CDM, gives participants the ability to dynamically and directly control: 1) consent to study participation, 2) access of data by researchers, and 3) electronic communication with researchers. A CDM pilot usability study was conducted which examined participant navigation preferences and analyzed the process of e-consent for rheumatology research.

Methods: A convenience sample of participants at the University Health Network were recruited using snowball methodology. Participants accessed the e-platform, participated in a mock study by completing study e-consent activities and questionnaires used for rheumatological research. The user experience was reported qualitatively and outcome measures were obtained utilizing the Computer System Usability Questionnaire (CSUQ) and the NASA Task Load Index (NASA-TLX).

Results: The pilot consisted of 21 participants, with 62% female. On a Likert scale of 1-7 (1=strongly agree), 58% of participants reported it was easy to learn to use CDM. 58% reported being overall satisfied with using an e-platform. 11 participants provided feedback on the e-consent process which used the same text as written consent in current use. Of these, 55% felt they did not understand what they were consenting to, 63% identified not being able to distinguish between the types of consent they were providing. Lastly, 71% raised ambiguity issues regarding implications of consent to communication with researchers.

Conclusion: While study participants are inclined to utilize e-platforms and researchers use electronic methods to collect data (tablets etc.); executing e-consent remains a challenge. Considerations for meaningful implementation of e-consent 1) Consent Clarity, ensuring terminology is clear and concise 2) Consent Distinction, distinguishing between types of consent a participant can provide (study participation consent is separate from consent to ongoing communication) 3) Contact Concatenation, ensuring participants ascertain the communications they may receive (invitations to join new studies, dissemination of study results, newsletters). Further work is required to determine participant comprehension of informed e-consent, their decision-making authority, and to separate the issues attributable to the consent text, and those due to the e-consent process.

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Bisphosphonates for Fracture Prevention in Steroid-Induced Osteoporosis: A Meta-Analysis

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Objectives: To assess the efficacy of bisphosphonates for fracture prevention in glucocorticosteroid-induced osteoporosis (GIOP) using a Cochrane Collaboration based systematic review and meta-analysis.

Methods: We searched MEDLINE and EMBASE databases and International Pharmaceutical Abstracts (IPA) via OVID (January 1997 to June 2013) for relevant articles and conference proceedings. We included randomized clinical trials satisfying the following criteria: 1) prevention or treatment of GIOP; 2) adults taking a mean steroid dose of 7.5 mg/day or more; 3) active treatment included bisphosphonates of any type alone or in combination with calcium and/or vitamin D; 3) Comparator treatment included calcium and/or vitamin D, alone or with a placebo; and 4) reporting relevant outcomes. We excluded trials dealing with transplant-associated osteoporosis. The primary outcome of interest was the number of participants with new vertebral fractures after 12-24 months. Our secondary outcome of interest was the number of participants with new non-vertebral fractures after 12-24 months. Data were analyzed with an existing Cochrane review by the same author. We assessed the overall quality and importance of the body of evidence using the GRADE Working Group approach.

Results: Pooled fracture analyses are reported using the Peto 0dds ratio. A total of 10 trials with 1247 patients were included in the meta-analysis for new vertebral fractures, and a total of 9 trials with 1245 patients were included in the meta-analysis for new non-vertebral fractures. The resulting odds ratio for the risk of new vertebral fracture in the experimental group was statistically significant at 0.57 [95%CI 0.35, 0.91]. The resulting odds ratio for the risk of new nonvertebral fractures in the experimental group was 0.75 [95%CI 0.44, 1.28]. There was no statistical heterogeneity in either fracture analysis. The quality of evidence was rated as 'moderate' for the vertebral fracture analysis and 'low' for the non-vertebral fracture analysis. Both outcomes were rated as being 'important' to the decisions regarding optimal management.
Conclusion: Between 12-24 months, bisphosphonate use resulted in a statistically significant 43% reduction in odds of vertebral fractures in the bisphosphonate group. Although there was a 25% reduction in odds of non-vertebral fractures in the bisphosphonate group, this result was not statistically significant. We conclude that bisphosphonates are effective at protecting against vertebral fractures up to 24 months in duration. Further research needs to be conducted into long-term fracture prevention in the GIOP population.

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Long-term Outcomes of Takayasu's Arteritis Patients with Renal Artery Involvement

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Objectives: Takayasu's Arteritis (TAK) is a chronic granulomatous inflammatory large vessel vasculitis involving the aorta and its branches. TAK incidence is 2.6/million annually in Minnesota. Prevalence is higher in Asian and Indian populations. TAK predominantly affects woman under 40 years of age. Renal artery involvement (RAI) in TAK is a poor prognostic factor; however, long-term outcomes have not been reported. Our objective was to report the long-term outcomes of TAK patients with RAI.

Methods: We performed a retrospective chart review of 50 patients. TAK diagnosis was based on the presence of constitutional symptoms, elevated inflammatory markers, and vascular abnormalities on angiography. RAI was identified based on conventional angiography, CTA or MRA. Patient demographics, presenting symptoms, signs, co-morbidities, blood pressure, medications and laboratory values were collated. Disease activity was assessed using the Indian Takayasu Activity Index 2010 (ITAS2010). Irreversible organ damage was assessed using the vasculitis damage index (VDI). Worsening renal function was defined as a drop in eGFR > 20%.

Results: Sixteen of 50 (32%) TAK patients were identified to have RAI. Fifteen (94%) were female, 13 (81%) were white. Mean age at presentation was 32 years (9-68). Fourteen (88%) met the ACR criteria for TAK. Ten (63%) had asymmetric blood pressures, nine (56%) had reduced pulses, seven (44%) had symptoms of vascular claudication, and five (31%) had bruits on exam. Median ITAS2010 was 13 (5-18). Eleven (69%) received prior therapy. Seven patients had unilateral and 9 bilateral disease. Eleven patients had hypertension. Six patients had renal asymmetry. Three patients had a moderate eGFR between 40 and 60 ml/min/1.73m2. Median follow-up duration was 8.8 years (10 months - 30 years). Fifteen (94%) received systemic treatment. Four patients underwent vascular intervention. ITAS2010 scores were available for 10 patients with a median of 7 (1-13) compared with 13 (9-18) at presentation. Median VDI was 5 (0-9). Fourteen (88%) had follow-up angiography: 12 (75%) had no change and 1 each had complete resolution and improvement of RAI. Thirteen patients were hypertensive. Six had renal asymmetry. The eGFR was unchanged in 7, improved in 4, and reduced in 3 patients. Among those with eGFR < 60 ml/min at presentation, 1 improved, 1 declined, and 1 remained stable.
Conclusion: The prevalence of RAI in this population (32%) is comparable to that in the literature. Hypertension was common. Most patients had normal eGFRs, despite severe disease. Disease progression was minimal. Our results suggest renal prognosis is better than previously thought.

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Persistence of Anti-TNF and nbDMARD use in a Population-Based Sample of Ankylosing Spondylitis (AS) in Quebec

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Objectives: To assess the rate of one-year persistence with anti-TNF or nbDMARDs therapy in Quebec, from 2006-2010.
Methods: We used physician billing data to identify potential AS cases, based on at least one ICD9 code 720 or ICD10 code M45. Analyses were restricted to individuals who initiated treatment with an anti-TNF or nbDMARDs between January 1, 2006, and December 31, 2010 (the initiation of the drug constituted the beginning of the patient's observation interval). Patients were excluded if they were not covered by the public drug plan 6 months before and one year after the first prescription of nbDMARDs and/or an anti-TNF agent. Persistence was calculated as the proportion of patients who remained on the initial therapy, allowing a 60-day gap between prescriptions. We also reported the number of days covered with the initial therapy over the first 365 days. The results are presented as mean and percentage, as well as the 95% confidence interval (95% CI) for the differences between groups.

Results: We identified 573 AS patients, 303 (52.9%) initiating treatment with anti-TNF (36.7 with etanercept, 34.8% with infliximab, and 28.5% with adalimumab) and 270 (47.1%) with nbDMARDs (45.3% with methotrexate, 21.5% with sulfasalazine, and 33.2% with other nbDMARDs). Patients first prescribed anti-TNF were more likely to be men (68.3% versus 58.9%) and younger (47.4 years versus 56.5 years) than those initiating nbDMARDs. Moreover, 88% of patients in the anti-TNF group had their first medication prescribed by a rheumatologist, versus 46% in the nbDMARDs group. The overall persistence was 56.7%, with a significant higher proportion in the anti-TNF group (67.0% versus 45.2% for nbDMARDs; 95%CI for the difference=13.9% to 29.8%). The mean therapy duration within the first year was 213 days; the mean duration was also higher in the anti-TNF group (234 days) than in the nbDMARDs group (191 days; 95%CI for the difference=24 days to 62 days).

Conclusion: Our data suggest that, among patients with a diagnostic code of AS in this administrative database, those initiating therapy with anti-TNF are more likely to continue their treatment over one year, versus those starting on nbDMARDs.

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LAMP-2 a Biomarker in Vasculitis: A Case Series of Polyarteritis Nodosa

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Objectives: Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculopathy typically affecting medium-sized arteries with occasional involvement of small muscular arteries. Unlike other vasculitides (e.g. Microscopic polyarteritis, granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA), PAN is not associated with anti-neutrophil cytoplasmic antibodies (ANCA) and outside an elevated ESR, does not have a biomarker identified for its diagnosis. We report serological profiles of 5 patients presenting with biopsy proven PAN.

Methods: Five cases of biopsy-proven PAN, meeting the American College of Rheumatology (ACR) criteria for PAN, were diagnosed between Jan 2010 and April 2012. Laboratory tests, therapeutic regimens and clinical correlations were studied retrospectively. Serum analysis included ANCA as detected by chemiluminescence (Bio Flash, INOVA Diagnostics, San Diego, CA) and atypical ANCAs including anti-LAMP-2 (lysosome associated membrane protein), were detected by addressable laser bead immunoassay. We used non-parametric analysis (Kruskal Wallis) to compare medians and IQR (Inter Quartile Range) between groups.

Results: 3/5 (60%) of the PAN had a high titer anti-LAMP2. By comparison, the frequency of anti-LAMP-2 in 14 giant cell arteritis sera was 0.0%, in 23 granulomatosis with polyangiitis was 0.0 %, and in 11 Takayasu arteritis, 18% of patients were positive for anti-LAMP2. Of the 3 PAN patients with high titer anti-LAMP2, the titres correlated with disease activity. Out of these 3 patients, 2 patients LAMP-2 titres decreased after initiation of immunosuppressive therapy. The two patients with low LAMP-2 titres had inactive disease or a milder form of the disease. The median anti-LAMP2 titer in the PAN group was 1217 (198-1729) which was higher than the other vasculitides (129-317), p = 0.0078.

Conclusion: Our studies, suggests that anti-LAMP-2 is a promising novel biomarker for PAN, a condition that otherwise had no previously documented biomarkers. Molecular biomarkers have changed our understanding of ANCA associated vasculitis and other disease entities that previously required confirmatory histological or clinical criteria. The role of anti-LAMP-2 in the pathogenesis and associated clinical phenotype of vasculitis needs further investigation, particularly given the evidence that autoantibodies to LAMP-2 represent a distinct marker of PAN with high disease activity. This report is leading the way for further testing of anti-LAMP-2 in a larger multi-center cohort of vasculopathies.

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Long-term (104-Week) Efficacy and Safety Profile of Apremilast, an Oral Phosphodiesterase 4 Inhibitor, in Patients with Psoriatic Arthritis: Results from a Phase III, Randomized, Controlled Trial and Open-Label Extension (PALACE 1)

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Objectives: Apremilast (APR), an oral phosphodiesterase 4 inhibitor, helps regulate immune responses in psoriatic arthritis (PsA). PALACE 1 compared the efficacy/safety of APR with placebo in patients with active PsA despite prior conventional DMARDs and/or biologics. We report the efficacy/safety of APR treatment over 104 weeks.

Methods: Patients were randomized (1:1:1) to placebo, APR 20 mg BID (APR20), or APR 30 mg BID (APR30) stratified by baseline DMARD use (yes/no). Patients whose swollen/tender joint counts (SJC/TJC) had not improved ≥20% at Week 16 were considered non-responders and were required to be re-randomized (1:1) to APR20 or APR30 if initially randomized to placebo, or continued on their initial APR dose. At Week 24, all remaining placebo patients were re-randomized (1:1) to APR20 or APR30. Double-blind APR treatment continued to Week 52; patients could continue APR up to 4 additional years.

Results: 504 randomized patients received ≥1 dose of study medication (placebo: n=168; APR20: n=168; APR30: n=168). At Week 52, modified ACR20 response was achieved by 63.0% and 54.6% of patients continually treated with APR20 or APR30 from baseline, respectively. Approximately 80% (285/344) of randomized patients completing Week 52 were still receiving apremilast at the data cutoff during their second year of apremilast exposure. Patients receiving APR from baseline demonstrated sustained improvements at Week 104 in: modified ACR20/ACR50/ACR70 response (61.3%/29.8%/16.0% [APR20] and 66.3%/35.6%/19.8% [APR30]), median percent change in SJC/TJC (-88.9%/-80.5% [APR20] and -87.5%/-76.7% [APR30]); mean change in HAQ-DI (-0.33 [APR20] and -0.43 [APR30]); mean change in DAS-28(CRP) (-1.61 [APR20] and -1.83 [APR30]); achievement of DAS-28(CRP) <2.6 (35.1% [APR20] and 38.6% [APR30]); and PASI-50/PASI-75 response (53.7%/36.6% [APR20] and 54.7%/30.2% [APR30]). No new safety concerns were observed with treatment through Week 104. During Weeks >52 to ≤104, AEs occurring in ≥5% of APR-exposed patients were nasopharyngitis and URTI; most AEs were mild/moderate in severity with no long-term increase in AE incidence/severity. Diarrhea and nausea occurred at lower rates in Weeks >52 to ≤104 (1.7% and 1.2%, respectively) than in Weeks 0 to ≤52 (15.3% and 12.4%, respectively). Serious AEs occurred in 6.4% (APR20) and 4.7% (APR30) over Weeks >52 to ≤104. Fewer discontinuations due to AEs occurred during Weeks >52 to ≤104 (1.5%) than Weeks 0 to ≤52 (8.2%).

Conclusion: Over 104 weeks, APR demonstrated sustained clinically meaningful improvements in signs and symptoms of PsA, physical function, and associated psoriasis. APR continued to demonstrate an acceptable safety profile and was generally well tolerated.

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Training Northern First Nation Nurses in Rheumatology: A Pilot Project

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Objectives: Remote First Nations (FN) communities in Canada have a high prevalence of rheumatic disease (RD) and worse outcomes than Caucasian communities. We examined the feasibility of training a local health care provider in RD with the goal of improving care of FN with RD in two remote communities.

Methods: We aimed to identify at least one nurse (BN or RN) from each of two remote communities in Manitoba in which outreach Rheumatology clinics are held. The nurses had to express an interest in RD and in assuming care for these patients. To minimize turnover we selected individuals who were permanent residents of their community. Both communities were supportive of the project. Nurses were brought to an academic rheumatology centre (AC) and given 3 days of lectures on RD and medications, joint exam sessions and shadowing time with nurse clinicians at the AC. Following training, nurses were to assume nursing-level responsibility for RD patients in the community, providing required injections, and facilitate appointments and bloodwork monitoring. They were supported remotely by the nurse clinicians at the AC and by the visiting rheumatologist. Primary outcome was the appointment attendance rates during outreach clinics.

Results: We identified one nurse from each community who was able to participate in the program. For community A, the nurse attended 2 of 3 days of training and was then unable to be contacted. For community B, the nurse attended all the training sessions. She has assumed responsibility for the RD patients in the community in addition to her other duties and works directly with the visiting rheumatologist during outreach clinics. Attendance appointment rates one year prior to training in community B were 36.7% and increased to 55.6% following the training.

Conclusion: Attempts to train local providers in remote communities in care of RD patients has met with mixed results but has the potential to improve performance markers for RD care. Appointment attendance rates remain poor even with this training suggesting further intervention may be required. Identification of the appropriate individual for training and community support are essential for success of this model. This model may be scalable to management of other chronic diseases in remote communities.

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Hydroxychloroquine-induced Cardiomyopathy Presenting as Heart Failure

David Shaw (University of Western Ontario, London); Gina Rohekar (University of Western Ontario, London)

We report a case of a 29 year-old man with a new diagnosis of seronegative rheumatoid arthritis, treated with hydroxychloroquine (HCQ), methotrexate, and sulfasalazine. He had no past medial history, and his only cardiac risk factor was smoking. After being treated with triple therapy for eight months with improvement of his arthritis, he developed progressive shortness of breath on exertion, requiring admission to the coronary care unit at a teaching hospital. He denied any chest pain or palpitations, and did not have presyncope or syncope.

In hospital, following effective diuresis, his investigations revealed cardiomegaly without pulmonary edema on plain film imaging, and mild elevation in troponin on blood tests, with a normal creatine kinase. Echocardiography revealed biventricular hypertrophy, as well as biventricular global hypokinesis with an ejection fraction of 25-35%, and bilateral atrial enlargement. Cardiac magnetic resonance imaging revealed concentric left ventricular hypertrophy and dilatation of the ventricle, with abnormal patchy delayed enhancement of both ventricles, consistent with infiltration. Edema was observed around the myocardium of both ventricles, consistent with an inflammatory process. He thereafter underwent right heart catheterization and endomyocardial biopsy, with hemodynamics consistent with restrictive defect. Histopathology showed nuclear hypertrophy and vacuolization, and electron micrography showed myelinosomes and curvilinear structures, consistent with HCQ toxicity. Serum alpha-galactosidase levels were normal, ruling out Fabry disease. He was treated for heart failure with acetylsalicylic acid, beta-blockers and angiotensin-converting enzyme inhibitors.

His HCQ was discontinued, with gradual improvement in his cardiac function and symptoms. Repeat echocardiography 6 months after initial admission revealed an ejection fraction greater than 60%, with some mild residual LV hypertrophy. Interestingly, he reported proximal muscle weakness and fatigue after discontinuation of the HCQ. He was seen by neurology and medical genetics for consideration of a myopathy or genetic cause for skeletal muscle dysfunction. He underwent electromyography and operative muscle biopsy, both of which were normal. Genetic testing did not reveal any abnormalities to explain his weakness, which gradually improved with time. His rheumatoid arthritis remains in remission on methotrexate and sulfasalazine therapy.

In summary, we report a young man presenting with cardiomyopathy likely related to HCQ treatment, which is a rare complication of antimalarial treatment. He has no known risk factors for toxicity, his imaging and biopsy results are consistent with antimalarial cardiotoxicity, and his symptoms have dramatically improved following discontinuation.

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Facilitation of Peer Assisted Learning in Rheumatology

Davina Morris (University of Toronto, Toronto)

Objectives: There is a lack of teaching administered by Rheumatology residents to core trainees. Peer-assisted learning (PAL) is the development of knowledge and skill through active help and support among peers. This study aimed to determine the barriers that rheumatology residents encounter which prevents PAL from occurring.

Methods: A survey was completed by nine rheumatology residents at University of Toronto. The survey was used to identify barriers to teaching as well as possible solutions to the current problem.

Results: Analysis of completed resident questionnaires revealed that the three most common barriers were lack or time (too busy with patient care) (3.5/5 on visual analogue scale), lack of time to prepare teaching materials (3.4/5), and trainee unavailability (3.2/5). 89% of rheumatology residents were interested in a teaching tool to facilitate teaching to junior trainees, 89% believed dedicated teaching time to teach junior trainees would be valuable, and 67% believed that a dedicated academic half day session on developing teaching skills would be beneficial.

Conclusion: Many barriers to PAL were identified including lack of time to prepare and administer teaching sessions. There was an overwhelming interest in the development of a teaching tool for rheumatology residents. The subsequent phase of this study is to develop a teaching tool that will be both efficient and effective to facilitate PAL.

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Training the Rheumatologists of Tomorrow: The Learners Experience

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Objectives: Canada faces a critical shortage of rheumatologists overall and more so in rural isolated communities. To address this problem we surveyed and interviewed learners and faculty/administrators affiliated with rheumatology programs across Canada to identify ways to attract more trainees. The views of learners are reported.

Methods: Participants were recruited locally and provided data in individual telephone interviews or from a web-based survey; analyzed by Thematic Framework Analysis.

Results: For most findings data differed by group -- junior learners (undergraduate medical students, PGY1-3s in internal medicine) and senior learners (PGY4-6s attending or recently graduated from a rheumatology program). There were 51 learners (45 surveyed, 6 interviewed), the main findings are presented with short excerpts labeled by group (Sr or Jr) and a unique ID number. The key to increasing interest in rheumatology is repeated exposure starting in medical school ("Tell them it exists; I didn't know about rheumatology until the start of Internal Medicine", Sr-8). Junior learners cited formal courses ("[Offer] more teaching by rheumatologists in the medical curriculum so students are aware of what the specialty is", Jr-6), observerships, mentoring opportunities, and information sessions that focus on professional and personal elements ("Emphasize [that you are] happy doctors", Jr-26). Messages could include the following: the intellectual challenges of being a rheumatologist ("It satisfies me on an intellectual level. Ultimately, at the end of the day this field fascinates me", Jr-19), the wide range of diseases encountered ("fantastically interesting diseases and presentations", Sr-4); the importance of basic science in developing new treatments ("I really enjoy the immunological/ autoimmune aspect", Jr-16), patients ("the opportunity to make a significant positive impact in a patient's life", Jr-7; "[forming] long-standing patient relationships", Sr-18), the existence of many job opportunities in academic and community settings, as well as a high quality of life due to the opportunity for a balanced work/personal life. The few learners who noted negative aspects to being a rheumatologist commented on earning less than other specialists.
Conclusion: This study, the first pan-Canadian qualitative investigation on how to increase the number of rheumatology trainees, noted the importance of early and continuing exposure to the multiple aspects of working in this field. The next step will be to form a national working group to collaboratively develop material and methods to further inform, recruit and educate potential trainees. Supported by a CIORA grant

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The Efficacy and Safety of Subcutaneous Tocilizumab Versus Intravenous Tocilizumab in Combination with Traditional DMARDs in Patients with RA at Week 97 (SUMMACTA)
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Objectives: To evaluate the efficacy and safety of tocilizumab subcutaneous (TCZ-SC) versus tocilizumab intravenous (TCZ-IV), including in pts who switched from TCZ-IV to TCZ-SC and vice versa, through wk 97.

Methods: SUMMACTA is a 2-year, randomized, active-controlled, parallel-group phase 3 study comprised of a 24-wk double-blind period, followed by re-randomization for a 72-wk open-label extension period. Pts (n = 1262) were randomized 1:1 to receive TCZ-SC 162 mg qw (n = 631) or TCZ-IV 8 mg/kg every 4 wks (q4w; n = 631) in combination with traditional DMARDs. After 24 wks, pts who initially received TCZ-SC were re-randomized 11:1 to TCZ-SC qw (n = 521) or TCZ-IV q4w (n = 48) and pts who initially received TCZ-IV were rerandomized 2:1 to TCZ-IV q4w (n = 372) or TCZ-SC qw (n = 186).

Results: A total of 76 (14.6%), 61 (16.4%), 8 (16.7%), and 26 (14.0%) patients from the TCZ-SC, TCZ-IV, TCZ-SC to TCZ-IV, and TCZ-IV to TCZ-SC groups, respectively, withdrew from the study through wk 97. The percentages of pts who achieved ACR20 responses [(TCZ-SC (83.6%), TCZ-IV (83.3%), TCZ-SC to TCZ-IV (82.5%), TCZ-IV to TCZ-SC (88.5%)]; ACR50 responses [(TCZ-SC (65.4%), TCZ-IV (62.5%), TCZ-SC to TCZ-IV (57.5%), TCZ-IV to TCZ-SC (67.3%)]; ACR70 responses [(TCZ-SC (44.8%), TCZ-IV (42.0%), TCZ-SC to TCZ-IV (37.5%), TCZ-IV to TCZ-SC (47.3%)]; DAS28 remission [(TCZ-SC (53.4%), TCZ-IV (46.4%), TCZ-SC to TCZ-IV (50.0%), TCZ-IV to TCZ-SC (55.6%)], and an improvement from baseline in HAQ-DI $\geq$ 0.3 [(TCZ-SC (72.4%), TCZ-IV (69.1%), TCZ-SC to TCZ-IV (56.4%), TCZ-IV to TCZ-SC (71.0%)] were sustained through wk 97 and comparable across all treatment groups. The safety profiles of switchers were similar to that of pts with continuous TCZ-SC or TCZ-IV treatment and consistent with the well-established safety profile of TCZ-IV. No anaphylaxis cases were identified. The proportions of pts who developed anti-TCZ antibodies remained low and were comparable across treatment groups through wk 97, and no association between anti-TCZ antibody development and clinical response or AEs was observed.

Conclusion: These data demonstrate that long-term efficacy and safety of TCZ-SC qw is maintained and remains comparable to TCZ-IV, with the exception of injection site reactions, which were more commonly seen with TCZ-SC but comparable to other SC RA treatments. The efficacy and safety profiles of pts who switched were comparable to those in pts who remained on TCZ-IV or TCZ-SC. Thus, TCZ-SC could provide a more convenient administration option and an opportunity of home injection in pts with RA.

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Do Patterns of Joint Swelling or Tenderness in Rheumatoid Arthritis Patients Impact Disease Activity Outcomes and Pain? Implications for Clinical Practice

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Objectives: This analysis aimed to describe the pattern of specific joint involvement (tender and/or swollen) pre- and post-TNFi treatment and the impact of specific joint pattern involvement on composite score outcomes and pain.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab (IFX) or golimumab (GLM). In this analysis, RA patients included those treated with IFX between 2002-2014 or with GLM between 2010-2014. Based on joint involvement 7 groups were created: shoulder(s), elbow(s), metacarpophalangeal (MCP(s)), wrist(s), proximal interphalangeal (PIP(s)), knee(s), and thumb(s). The impact of specific joints on disease activity indices and pain was assessed with the independent-samples t-test; linear regression produced adjusted estimates.

Results: A total of 1030 RA patients were included with 5177 assessments. At baseline, MCP(s) (84.8%) and wrist(s) (66.1%) were the most commonly swollen joints. Tenderness was most frequent at baseline in these two joint types (81.1% and 70.9% of patients, respectively). Swelling/tenderness rates in all joint groups were significantly lower (p<0.001) among patients enrolled in 2010-2013 vs. those enrolled in 2002-2005; no significant differences, however, were observed in joint involvement pattern. Swelling and tenderness in all joint groups were associated with significantly (P<0.001) higher pain. Upon adjusting for age, gender and the total number of swollen (SJC28) or tender (TJC28) joints, swollen shoulder(s) and knee(s), and tender shoulder(s) and elbow(s) had the biggest impact on pain. Swollen MCP(s), knee(s) and thumb(s) had the greatest impact on DAS28, while for CDAI and SDAI swollen thumb(s) and swollen thumb(s) and knee(s), respectively, showed the highest association. Tender wrist(s), shoulder(s), and knee(s) showed the highest association with DAS28, while tender MCP(s) had the greatest impact on CDAI and SDAI. However, all indices were significantly higher among cases with swollen thumb(s) (unstandardized coefficient (B): BDAS28=0.25, P=0.006; BCDAI=2.09, P=0.001; BSDAI=2.66, P=0.001).

Conclusion: Although joint swelling/tenderness documented at anti-TNF initiation has decreased over time, the profile of affected joints has remained stable. Swelling/tenderness in specific joint groups was differentially associated with pain, with larger joints having the greatest impact. Furthermore, differences were observed in levels of disease activity based on the type of affected joint which could be attributed to their impact on patient global assessment. These results suggest that location of joint involvement, in addition to the number of affected joints, has an independent impact on pain.

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Clinical and Imaging Efficacy of Etanercept in Early Non-radiographic Axial Spondyloarthritis; 48-Week Treatment Data

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Objectives: Our previous data show that etanercept (ETN) has superior clinical and anti-inflammatory efficacy to placebo (PBO) in patients with non-radiographic axial spondyloarthritis (nr-axSpA) and inadequate response to NSAIDs in a 12 week double-blind PBO controlled trial. The objective of the current analyses was to examine clinical and anti-inflammatory efficacy of ETN at wk 48 (12 wk double blind followed by 36 wk open-label treatment phase).

Methods: Patients with symptom duration >3 mths–<5 yrs, fulfilling ASAS axSpA criteria without meeting radiographic criteria for ankylosing spondylitis, having BASDAI ≥4, and failure with ≥2 NSAIDs were enrolled and randomized to ETN 50 mg QW or PBO. Both groups continued stable NSAID therapy. After 12 wks all patients received ETN 50 mg open-label. Clinical assessments (ASAS, ASDAS, BASDAI, BASFI) and MRI of sacroiliac (SI) joint and spine were performed (SPARCC and ASspiMRI scoring methods). Analyses used an ANCOVA model with baseline scores, treatment, MRI sacroiliitis +/-, as variables.
Results: Of 215 initially randomized patients (mITT population), 205 entered the open label phase (ETN=100; PBO=105). At week 12, 33.3% of patients treated with ETN and 14.7% PBO achieved ASAS40, improving to 52.7% by week 48 (combined groups). SPARCC MRI-SI joint and SPARCC 6 DVU scores were reduced from baseline–week12 in ETN (56.7%; 40.1%) and PBO (16.4%; 11.1%) groups and 65.2%, 60.8% (combined groups) by week 48, respectively. ASspiMRI improvements were 40.1% (ETN) and 7.7% (PBO) by week 12, and 40.9% by week 48 (combined groups). Infections (the most frequent AE) occurred in 43/208 (20.7%) patients and TEAE (pyrexia/bronchitis) caused 2 discontinuations between weeks 12–48.
Conclusion: In patients with early, active nr-axSpA and an inadequate response to ≥2 NSAIDs, clinical and imaging outcomes improved from baseline to a greater extent with etanercept therapy than with PBO, during the first 12 weeks. In the ensuing 36 week open label period, these outcomes continued to improve. There were no new safety signals.

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Substantial Structural Lesions on MRI in the Sacroiliac Joints of Patients with Non-Radiographic Axial Spondyloarthritis Even in the Absence of MRI Inflammation

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Objectives: To assess the relative importance of structural lesions on MRI in the sacroiliac joints (SIJ) of patients with non-radiographic axial SpA (nr-axSpA).
Methods: Patients had axial SpA per the Assessment of SpondyloArthritis (ASAS) classification criteria but did not meet modified NY radiographic criteria; symptoms for >3 months and <5 years; Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4; and failed ≥2 NSAIDs. Patients were randomly assigned to etanercept 50 mg/week or placebo, then after 12 weeks, all patients received open-label etanercept 50 mg/week. Clinical and health outcomes were assessed throughout the study, and MRI of the SIJ and spine was performed by two central readers at baseline, weeks 12 and 48 to assess bone marrow edema (BME) using the Spondyloarthritis Research Consortium of Canada (SPARCC) score. This analysis was conducted to score structural lesions using the SPARCC SIJ structural method, which assesses fat metaplasia, erosion, backfill, and ankylosis on T1-weighted spin echo (T1WSE) MRI. Two independent readers scored baseline and 48 week T1WSE MRI scans from 187 cases blinded to patients and short tau inversion recovery (STIR) MRI scans. Mean scores of the readers were used. SPARCC SIJ BME score ≥2 was used as the operational definition of positive MRI evidence of inflammation. For these analyses, all patients were combined, independent of randomization.

Results: Mean (SD) age was 32 (7.8) years, 60.5% were male, and duration of disease symptoms was 2.5 (1.8) years. A total of 73% of patients were human leukocyte antigen B27 (HLA-B27) positive and 81% met the ASAS MRI imaging criteria at baseline. Additionally, 61% had a structural lesion on MRI at baseline comprised of erosion (58%), backfill (23%), fat metaplasia (18%), and ankylosis (7%). Of the patients who were ASAS MRI positive, 65% had a structural lesion on MRI, compared to 43% who were ASAS MRI negative. Of the patients with SPARCC SIJ BME score ≥2 at baseline, 79% had a structural lesion on MRI compared to 35% with SPARCC SIJ BME score <2. Relative frequencies of MRI structural lesions in patients with SPARCC SIJ BME ≥2 vs <2 were: erosions (78% vs 30%), backfill (36% vs 5%), fat (22% vs 13%), and ankylosis (7% vs 7%).
Conclusion: Structural lesions on MRI occur frequently in nr-axSpA despite the absence of radiographic sacroiliitis and even in the absence of MRI inflammation. This finding strongly reinforces the concept of nr-axSpA as an early stage of axial SpA.

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The Ankylosing Spondylitis Disease Activity Score More Closely Reflects MRI Parameters of Sacroiliitis than the Bath Ankylosing Spondylitis Disease Activity Index in Patients with Non-radiographic Axial Spondyloarthritis

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Objectives: To assess which clinical measures best reflect the spectrum of MRI lesions in the sacroiliac joints (SIJ) of patients with non-radiographic axial SpA (nr-axSpA), and the effect of treating with an anti-TNF agent.
Methods: Patients had axial SpA per Assessment of SpondyloArthritis (ASAS) classification criteria but not modified NY radiographic criteria; symptoms for >3 months and <5 years; Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4; and failed ≥2 NSAIDs. Patients were randomized to etanercept (ETN) 50 mg/week or placebo for 12 weeks and then open-label ETN 50 mg/week. MRI of the SIJ and spine was performed by 2 central readers at baseline, weeks 12 and 48, to assess bone marrow edema using the Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ score). Structural lesions were scored using the SPARCC SIJ structural (SSS) method, assessing fat metaplasia, erosion, backfill, and ankylosis on T1-weighted spin echo (T1WSE) MRI. Two independent readers scored BL and 48-week T1WSE MRI scans from 187 cases blinded to outcomes and short tau inversion recovery (STIR) MRI. SPARCC score ≥2 for SIJ defined positive MRI evidence of inflammation. Week 48 change was analyzed using Spearman correlations, adjusted for treatment.

Results: Mean (SD) age was 32 (7.8) years, duration of symptoms was 2.5 (1.8) years, 60.5% of patients were male, 73% were human leukocyte antigen B27 (HLA-B27) positive, and 81% met ASAS MRI imaging criteria at baseline. A significant decrease in clinical (Ankylosing Spondylitis Disease Activity Score [ASDAS], BASDAI, CRP) and MRI (SPARCC SIJ inflammation, SSS erosion) measures of active disease was noted by week 48. There was significant baseline correlation between SPARCC SIJ inflammation score and ASDAS (r=0.19, p=0.005) and CRP (r=0.22, p=0.002), but not between BASDAI and MRI lesion scores. There was significant 48-week correlation between change in ASDAS and changes in SPARCC SIJ inflammation (r=0.40, p<0.0001), SSS erosion (r=0.25, p=0.0007), and SSS backfill (r=-0.23, p=0.002). Change in CRP correlated significantly with changes in SPARCC SIJ inflammation (r=0.35, p<0.0001) and SSS erosion (r=0.18, p=0.02). Change in BASDAI correlated significantly with changes in SPARCC SIJ inflammation (r=0.25, p=0.0008), SSS backfill (r=-0.18, p=0.02), and SSS erosion (r=0.16, p=0.03). Correlations between ASDAS and MRI measures of sacroiliitis were strongest in the ETN group through 48 weeks.
Conclusion: ASDAS is the preferred clinical measure of disease activity in nr-axSpA. Change in SPARCC SIJ inflammation seems most closely aligned with changes in ASDAS, CRP and BASDAI, though the correlations are modest.

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Reliability of Radiographic Assessment of Psoriatic Arthritis Mutilans
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Objectives: Psoriatic arthritis mutilans (PsAM) is the most severe form of Psoriatic arthritis (PsA). Research on PsAM has been hampered by the lack of an accepted disease definition. We recently performed a systematic review of the literature and conducted a survey of members of the Group for Research and Assessment of Psoriasis and PsA (GRAPPA) to identify radiographic features associated with PsAM. Based on the results of these studies, joint erosion involving entire articular surfaces on both sides of the joint, bone resorption leading to shortening of bone, pencil-in-cup deformity, ankylosis, and subluxation were deemed to be manifestations of PsAM. Thus, the aim of this study was to determine the reliability of assessing these five PsAM features on plain radiographs.
Methods: The radiographs of 35 PsA patients who have one of the five features in at least one joint of the hands or feet were retrieved and duplicated to generate 70 sets of images. Three rheumatologists, blinded to diagnosis, independently evaluated the radiographs for PsAM features in random order. A total of 42 joints, including wrists, all joints of the hand, all metatarsophalangeal joints and the interphalangeal joints of the first toes, were evaluated for each set of images. Inter- and Intra-observer reliability of the five features in each joint were determined using the Kappa statistic with standard errors calculated to accommodate an association between joints within patients.

Results: Moderate inter-rater agreement was observed for radiographic assessment of PsAM when the five PsAM features were considered as separate categories (kappa 0.63). The kappa improved to 0.83 when the PsAM features were grouped together as one category, indicating excellent inter-rater reliability in identifying severe joint damage. However, the specific agreement for each of the five PsAM features ranged from poor to moderate. Specifically, the assessment of joint erosion involving entire articular surfaces on both sides of the joint and bone resorption showed a kappa of 0.22 and 0.17, respectively whereas pencil-in-cup change, ankylosis and subluxation showed a kappa of 0.59, 0.76 and 0.52, respectively. Intra-rater reliability is excellent with an overall kappa ranging from 0.81 - 0.83.

Conclusion: These results indicate that there is moderate agreement in radiographic assessment of severe joint damage associated with PsAM. However, the agreement for specific features such as severe joint erosion and bone resorption was poor. Thus, new definitions of these features might be needed in order to improve the feature-specific and overall agreement in radiographic assessment of PsAM.

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Effective Knowledge Transfer: A Demonstration of Video Illustration in the Immunology Curriculum

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Objectives: A proper foundation in immunology is essential for the understanding and management of rheumatic conditions. An effective immunology curriculum is required for rheumatology trainees to meet the core competencies mandated by the Royal College of Physicians and Surgeons of Canada. However, we have demonstrated that Rheumatology Program Directors and trainees across the country believe that current immunology curricula, teaching and resources require significant improvement. We have developed a short video clip highlighting a well-defined immunology topic. Our objective is to assess its role in facilitating relevant knowledge acquisition in rheumatology trainees.

Methods: We enlisted an Education Information Technology (EIT) student to create a five-minute immunology video clip on T cell development. The topic was identified as "high yield" by rheumatology Program Directors and trainees across the country. Adobe Illustrator and After Effects were used to design the video. Immunology and rheumatology experts assisted in the creation of the video content. The video was piloted on adult and pediatric rheumatology trainees at the University of Toronto and qualitative feedback was obtained. Additionally, a quiz based on the video content was administered to the trainees before and after its viewing. The teaching effectiveness of this tool was evaluated by comparing pre and post video scores.

Results: A total of fourteen rheumatology trainees (eleven adult and three pediatric) participated in the video testing. All participants identified the immunology video as easy to follow and stimulating. Participants described the video as "engaging, excellent and effective." All trainees agreed that similar immunology video clips would be a valuable addition to their current immunology curriculum. There was a significant improvement observed between pre and post-testing ($p<0.0001$). The average pre-test score was 50.6% (+/- 26.9), compared to an average post test score of 85% (+/- 14.9). There was an average improvement in scores of 34.4% (+/- 22.2) with a 95% confidence interval of 22.7-46.0%. While only 5/14 participants received a passing score as set by our departmental guidelines (70% or higher) on the pre-test, 13/14 participants successfully passed the post-test.

Conclusion: Our pilot immunology video clip was an effective tool for improving short-term comprehension of a focused immunology topic amongst rheumatology trainees. The results are encouraging, and support the development of further immunology videos. This teaching aid has great potential as an educational deliverable, helping to improve and standardize immunology training across the country.

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"Eosinophilic Fasciitis as a Manifestation of GPA in the Setting of Allergen Immunotherapy and MDMA: A Case Report"

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Eosinophilic fasciitis, also known as Schulman's syndrome, has been previously described as one of several hypereosinophilic syndromes (HES). We report a case of a 22 year-old male presenting with ANCA-associated vasculitis (c-ANCA, PR3 positive) manifested as arthritis, biopsy-proven vasculitic rash, sinusitis, and pulmonary hemorrhage, in addition to peripheral eosinophilia and eosinophilic fasciitis involving his lower extremities. Interestingly, this patient had a long-standing history of sinus congestion and dust-mite allergy, for which he was undergoing allergen immunotherapy (AIT). He had received a dose 2 days prior to the onset of his symptoms. The patient also happened to consume 3,4-Methylenedioxymethamphetamine (MDMA), the primary constituent of Ecstasy and Molly, in an isolated incident 3 days prior to symptom onset.

His presentation of Granulomatosis with Polyangiitis (GPA) with the atypical features of eosinophilia and fasciitis raise the possibility of drug or AIT-induced eosinophilia. While delayed systemic reactions to AIT have been described, the role of AIT in the pathogenesis or induction of eosinophilic syndromes and autoimmune disease is not well-defined. Case reports have emerged describing AIT-induced eosinophilic esophagitis and peripheral eosinophilia. Eosinophilia has also been described following exposure to L-Tryptophan (Eosinophilia-myalgia Syndrome). L-Tryptophan can be included in the preparation of MDMA or co-ingested to enhance the overall drug use experience.

Our patient was diagnosed with Granulomatosis with Polyangiitis and his symptoms began to improve within 24 hours of high-dose Prednisone. He was ultimately treated with Rituximab induction therapy and remains asymptomatic on maintenance therapy.

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Clinical Audit of Infection and Vaccination Status Monitoring and Recording in Patients with Inflammatory Arthritis in a Rheumatology Clinic

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Objectives: To determine if infection and vaccination status were elicited during regular clinical encounters and clearly recorded in the electronic medical record (EMR) for patients with inflammatory arthritis.

Methods: A prospective audit in a single-centre Canadian rheumatology clinic. Audit standards were based on Canadian Rheumatology Association (CRA) infection surveillance guidelines. The standards included monitoring for infections (such as TB, hepatitis B and hepatitis C), counselling on vaccination status (such as influenza and pneumococcus), and having these results clearly recorded. We audited 23 appropriate consecutive patient encounters and reviewed the EMR to determine if the results were clearly recorded. After the initial audit, we implemented two interventions to improve recording on the EMR. 1) A "Measurement Group" on the OSCAR EMR system. 2) A web-based risk factor self-reporting form for patients to complete at home. Both interventions include yes/no questions related to risk factors for infections, GI bleeds, cardiovascular disease and osteoporosis.

Results: None of the 8 audit standards were being met, as the majority of participants were being appropriately screened but recording of infection and vaccination status in the EMR was deficient. For instance, 27% of patients on biologic therapy had a Mantoux skin test with recorded results, though 64% had a Mantoux test without clear recording. 30% of patients with inflammatory arthritis had hepatitis B serology with recorded results, though 48% had serology without clear recording. Results of our interventions are pending re-audit in November 2014.

Conclusion: Our defined standards of eliciting infection and vaccination status, and clear recording in EMR are not being met in typical non-structured patient encounters. The Risk Measurement Group in OSCAR, requires a healthcare provider to complete a Yes/No checklist during a clinic appointment, enabling the healthcare provider to conduct a systematic interview with results automatically recorded in the EMR. The online form elicits the same information as reported by the patient, and may serve as an additional patient education resource.

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Improvements in Bone Mineral Density and Health Related Quality of Life Maintained in Patients Treated with Teriparatide

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Objectives: The purpose of this study is to determine the effect of teriparatide (Forteo ®) and subsequent antiresorptive therapy on bone mineral density (BMD) and health-related quality of life (HRQL) during and up to two years after completion of teriparatide treatment.

Methods: A retrospective chart review of consecutive osteoporosis patients treated with teriparatide in a single Canadian rheumatology practice was conducted. Patients included in the study received teriparatide therapy for a period of either 18 or 24 months with baseline and follow-up BMD results up to two years after completion of therapy. Patient information was reviewed via electronic medical system records (EMR). Paper copies of patient files were reviewed if EMR data was unavailable. Baseline information collected included age, gender, height and weight. BMD, Mini-Osteoporosis Quality of Life Questionnaire (mini-OQLQ) data and medications taken were recorded at baseline, during and post-teriparatide therapy. A repeated measures mixed-model analysis was utilized to compare baseline and follow-up measurements for BMD at three sites (femoral neck, lumbar spine and total hip) as well as each of the ten questions (five domains) in the mini-OQLQ questionnaire. The analyses were adjusted for sex and baseline age, height and weight.

Results: 167 patients (143 women) were included in this study. The baseline characteristics were: mean (standard deviation) age 65.1 (11.4) years, height 159.8 (9.1) centimeters and weight 63.0 (13.1) kilograms. BMD information was shown to have quite significant improvement from baseline T-score to the first follow-up after therapy at all three sites: femoral neck (0.25, $p <$ .001), lumbar spine (0.77, $p <$ .001), and total hip (0.18, $p <$ .001). Statistically significant differences between baseline T-score and 3rd follow up, or up to two years after completion of teriparatide therapy, were also reported at the femoral neck (0.30, $p = 0.007$), lumbar spine (0.84, $p <$ .001) and total hip (0.26, $p = 0.003$). Significant improvements were also observed at the second follow-up post treatment in the OQLQ domains of pain symptoms, emotional functioning and physical functioning ($p < 0.05$ for the first six questions) as well as a trend towards significance in the domains of activities of daily living and leisure.

Conclusion: Teriparatide treatment and subsequent antiresorptive therapy was shown to improve both BMD, particularly at the lumbar spine, and HRQL. Furthermore, these findings are suggestive of maintained improvement in BMD for up to 2 years after completion of teriparatide treatment.

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Abatacept in Systemic Sclerosis: A Systematic Review of the Literature
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Objectives: Pre-clinical data support a role for T cells in the pathogenesis of systemic sclerosis (SSc). There have been anecdotal reports of the beneficial role of abatacept, a T cell co-stimulatory antagonist, in patients with SSc. The objective of this study was to systematically review the literature to determine the effects of abatacept in SSc.
Methods: A comprehensive search was conducted in November 2014 using Medline, EMBASE, the Cochrane Library and Web of Science, to identify original research studies reporting quantitative data on outcomes of interest, in particular joint, skin, lung and muscle, in SSc patients exposed to abatacept. Selected studies were reviewed for quality, and characteristics of the study samples and outcome data were extracted.

Results: Three studies were identified: one phase I/II double blind randomised controlled trial (high quality), one observational study (medium quality) and one case series (low quality). In the trial, subjects randomised to 24 weeks of abatacept (N=7) had improvement in the primary outcomes of absolute (-8.6 vs -2.3, p=0.059) and mean % change (-33% vs -6.2%, p=0.31) in modified Rodnan skin score (mRSS) compared to those in the placebo group (N=3). The results in secondary outcomes were mixed: those exposed to abatacept improved more in Health Assessment Questionnaire (-0.04 vs 0.25, p=0.56) and patient global assessments (-8 vs -2.7, p=0.023), but less in physician global assessments (-11.9 vs -17.3, p=0.048) compared to unexposed subjects. There were no differences in lung function between the two groups. No deaths or serious adverse events were reported. The observational study of SSc patients with polyarthritis (N=5) and refractory myopathy (N=7) revealed a decrease in Disease Activity Score (DAS28) after 11 months of abatacept (4.5 to 2.3, p=0.001) but no improvement in myopathy after 18 months of therapy. No significant change in skin or lung fibrosis was observed. Finally, a case series of four patients with diffuse cutaneous SSc with progression of skin thickening despite conventional therapy revealed reduction in mRSS, on average 1.3 units/month. Lung function improved in two patients, interstitial lung disease resolved in one patient and myositis improved in one patient.

Conclusion: Although there is strong rationale for the role of T cells in the pathogenesis and for T cell antagonism as a therapeutic target of SSc, there is a paucity of clinical data. Further studies are needed to determine the efficacy of abatacept in SSc. An additional phase II study is underway.

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Antimalarial Drugs Alone May still have a Role in Rheumatoid Arthritis

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Objectives: Antimalarials have been used for the treatment of Rheumatoid Arthritis for several decades. Current guidelines do not include the use of these drugs alone for rheumatoid arthritis patients. The purpose of the study is to review rheumatoid arthritis patients, to find those who have done well on antimalarials alone, and see if there are common features that predict good treatment outcome with these drugs

Methods: This is a retrospective chart review of patients who have been successfully treated with antimalarials alone. Patients who were attending routine follow up and were seemingly in remission defined by no swollen or tender joints were selected over a 6 month period. Those who had being doing well, but were now or had been on other agents are not included. The background data was reviewed to see if there were any common initial characteristics

Results: Thirty three patients were seen who had been started on antimalarials alone and where initial data was available. Patients remain in clinical remission. Based on clinical observation, inflammatory markers and X-ray reports, in the follow up visits, they remain with no signs of inflammation and no new erosions on X-ray. Initial bone erosions on 2 patients remain stable over the years

Conclusion: There are some patients with confirmed RA who definitely respond well to antimalarials alone. It is hard to objectively measure, whether mild disease activity, early treatment initiation, lack of smoking or other factors are contributing to a good treatment response

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A Retrospective Cohort of Aortitis Cases in a Canadian Centre over 10 Years

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Objectives: To determine: 1) the frequency of aortitis on aortic specimens at The Ottawa Hospital; 2) the clinical, radiological and histopathological characteristics of isolated aortitis; and 3) the approach to work-up, treatment and follow-up taken by the treating physicians, and subsequent outcomes, if available.

Methods: All cases of aortitis diagnosed on pathologic specimens of heart or aorta between January 1, 2003 and July 31, 2013 at The Ottawa Hospital were identified. Charts and pathologic specimens were then reviewed and data on patient demographics, clinical features, histopathology, laboratory markers, imaging findings, treatment and patient outcomes was analyzed.

Results: 49 cases of aortitis were identified (53% in women). Of those, 14% (n=7) were infectious. A definite systemic condition was diagnosed in 16% (n=8) – 4 cases with Giant Cell Arteritis (GCA), 2 with Rheumatoid Arthritis (RA), 2 with Polymyalgia Rheumatica (PMR), and 1 with each of Takayau's Arteritis (TA) and Systemic Lupus Erythematosus (SLE), respectively. One patient had both PMR and GCA and one had both PMR and RA. Of non-infectious aortitis, 79% (n=33) of cases were isolated. The majority of patients presented with symptoms of aortic aneurysm or had incidental findings of aortic aneurysm on echocardiography or imaging studies. Giant cells were seen on 25 pathologic specimens (60% of non-infectious cases). Corticosteroids were used in 40% (n=17) of patients with non-infectious aortitis. Doses and courses of treatment were highly variable. Death from all causes occurred in 6% (n=3) of patients. Recurrence rates of vascular lesions and other adverse outcomes are still being evaluated.

Conclusion: Isolated aortitis occurs without history or clinical evidence of systemic disease. It is commonly discovered only on examination of pathologic specimens following ascending aortic aneurysm repair. We did not find any gender predisposition for isolated aortitis. At this time there are no recommendations to guide the workup, treatment or follow-up of isolated aortitis, and it is not clear whether aggressive treatment or follow-up changes the outcomes. Better quality prospective studies are needed to address unanswered questions about this condition.

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Using Patient Reported Outcome Measures to Classify Disease Activity States in Rheumatoid Arthritis: A Comparison of Patient Activity Score (PAS) and Routine Assessment of Patient Index Data (RAPID)

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Objectives: Patient self-monitoring of disease activity may facilitate "treat-to-target" RA treatment strategy by alerting patients when they are off-target. The objective of this study was to compare the agreement between disease activity states from rheumatologists and those derived from patient reported outcome measures of disease activity.

Methods: Consecutive RA patients seen by seven rheumatologists were invited to participate. Patients completed a questionnaire before their visit. Rheumatologist joint count and lab values were obtained from charts. We evaluated 4 patient reported disease activity measures: i) PASII; ii) RAPID with 3 measures (RAPID3); iii) RAPID with 4 measures (RAPID4); iv) modified-RAPID4 (m-RAPID4) using HAQII instead of MDHAQ. The following rheumatologist-derived measures served as gold standards: i) Clinical Disease Activity Index (CDAI); ii) Simplified Disease Activity Index (SDAI); iii) Disease Activity Score 28 (DAS28). Disease states were categorized into remission, low, moderate or high, using published cut points. We also compared two categories: remission or low vs. moderate or high, to mimic when treatment change is recommended. Agreement between patient and MD derived disease states was evaluated using Agreement Coefficient 1 (AC1) for two category comparisons and Agreement Coefficient 2 (AC2), weighted with quadratic weights, for four category comparisons. AC values > 0.62 were considered good agreement. Z tests were used to evaluate the significance of the difference between pairs of ACs to compare agreement across instruments.

Results: We recruited 150 RA patients [mean (SD) RA duration: 11.9 (11.3) y; age: 57.8 (16.3) y; 81% female]. Most patient vs MD comparison showed good or moderate agreement. [DL1] Overall, PASII showed the best agreement with MD measures. When comparing ACs for four category disease activity states, all pairwise comparisons were significantly different (all but one p < 0.001), except when comparing agreement between RAPID4 and m-RAPID4 with CDAI (p = 0.054), and between RAPID3 and RAPID4 with SDAI (p = 0.075). When comparing ACs for two categories, significant differences were detected in the agreement between PASII and RAPID3 with CDAI, RAPID3 and 4 with CDAI, PASII and RAPID3 with DAS28, PASII and RAPID5 with DAS28 , RAPID3 and 4 with DAS28, and RAPID4 and m-RAPID4 with DAS28) (all p < 0.05).

Conclusion: Our results suggest that patients can self-monitor disease activity. PASII showed the best agreement with all MD measures. Given the similarities in the components of the measures compared, this difference may be due to cut points used to categorize disease states. Supported by a CIORA grant

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Incidence of Diabetes Mellitus in Rheumatoid Arthritis: A Population Based Cohort Study
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Objectives: Previous research suggests that people with rheumatoid arthritis (RA) have a higher risk of diabetes mellitus (DM) than non-RA individuals. Our objective was to evaluate the incidence of DM in a population-based incident RA cohort compared to the general population.

Methods: We conducted a retrospective cohort study using administrative health data among all incident RA cases in BC, identified in 1996-2006 and followed until 12/2010. RA cases were selected if they had ≥2 MD visits > 2 months apart with an RA diagnosis between 01/1996 and 03/2006 with no prior RA diagnosis since 1990. Cases were excluded if they had ≥2 subsequent MD visits for another inflammatory arthritis; if they saw a rheumatologist and RA diagnosis was never confirmed; or if there were no subsequent RA diagnoses over a follow-up >5 yrs. Controls were randomly selected from the general population, matched 1:1 to RA cases on birth year, gender and calendar year of cohort entry. Outcome: DM was defined as at least one physician visit or one hospitalization with a diagnostic code for diabetes (ICD-9 code 250.X, ICD-10 code E11.X) and at least one prescription for oral hypoglycemic agents or insulin. Cases and controls were excluded if they met criteria for diabetes prior to index date. Person-years of follow-up for cases and controls were calculated from index date to end of follow-up, last health care utilization, death or DM. Statistical analyses: Incidence rates of DM and 95% confidence intervals (CI) were calculated for the RA cohort and controls, along with incidence rate ratios. Hazard ratios (HR) were estimated using Cox proportional hazards model, adjusting for age, sex, and the Romano modification of the Charlson comorbidity index (excluding DM).
Results: The sample included 26,013 RA cases (67% female; mean [SD] age 58.6[17.2] years; follow-up 4.8 [4.1] years) and 25,823 controls (67% female; age 58.1 [17.1] years; follow-up 5.3 [4.5] years), contributing 175,231.5 and 192,506.8 person-years of follow-up, respectively. Diabetes occurred in 1,513 cases and 1065 controls. The incidence rate of DM was 8.63 per 1,000 person-years for RA cases, and 5.53 per 1,000 person-years for controls, yielding an incidence rate ratio for RA of 1.56 The aHR for DM in RA vs controls was 1.62 [95% CI: 1.49, 1.76].
Conclusion: In our population-based RA cohort, individuals with RA had an increased risk of incident diabetes compared to matched controls from the general population.

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Quality of Care for Diabetes Prevention in RA: Compliance with Plasma Glucose Screening Guidelines

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Objectives: Previous research suggests that RA populations receive sub-optimal care for their non-RA health related issues. Our aim was to evaluate the quality of care for cardiovascular disease prevention in RA by measuring compliance with general population diabetes screening guidelines in RA compared to the general population.

Methods: We conducted a retrospective cohort study among RA patients in British Columbia who received care between Jan 1996 and Mar 2006 and followed-up until Dec 2010, identified using previously described selection criteria (N=36,458). Controls were selected from the general population and matched 1:1 to RA cases on gender, age, and calendar year. Individuals with previous diabetes, in whom general population guidelines don't apply, were excluded. Administrative data was obtained on all physician visits, hospital admissions, tests ordered and medications. Compliance with screening guidelines for diabetes defined as testing for plasma glucose (PG) at least once every 3 years for individuals ≥ 45years was measured. Individuals' follow-up was divided into 3-year eligibility windows, when they were eligible for the screening guideline. Each individual could contribute up to four three-year eligibility windows. Compliance was measured as the proportion of eligibility windows with at least one PG test performed within the time period. Compliance rates between RA and controls, using eligibility windows as the unit of analysis, were compared via GEE model to account for the lack of independence of observations obtained from same patients, adjusting for age and gender. Compliance rate per patient was also calculated, as the proportion of eligible windows per patient during follow-up when screening was performed. Mean compliance rates in RA were compared to controls using Mann-Whitney U test.

Results: We identified 27,650 individuals with RA (68.8% female, mean [SD] age 62.5 [12.9] yrs), contributing 49,515 three-year eligibility windows; and 30,486 controls (68.6% female, age 62.3 [12.9] yrs), contributing 62,942 three-year eligibility windows. Overall, PG was measured in 71.2% of the eligible time windows in the RA sample and in 74.4% for controls (OR=0.89 [95% CI; 0.86, 0.92], p<.0001). RA individuals met the recommended screening guidelines in 72.1% (SD=37.1%) of their eligible time windows, compared to 74.1% (SD=35.3%) for controls (p<.001).

Conclusion: Compliance with screening guidelines for diabetes was slightly lower in our RA cohort than the general population. Although the difference was statistically significant, it may not be a clinically relevant difference. Regardless, given the increased prevalence and burden of cardiovascular diseases in RA, diabetes screening is sub-optimal for RA individuals.

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Quality of Care for Cardiovascular Disease Prevention in RA: Compliance Lipid Screening Guidelines

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Objectives: Previous research suggests that RA populations may receive sub-optimal care for their non-RA health related issues. Our aim was to evaluate the quality of care for cardiovascular disease prevention in RA by measuring compliance with general population hyperlipidemia screening guidelines in RA compared to the general population.

Methods: We conducted a retrospective cohort study among RA patients in British-Columbia who received care between Jan 1996 and Mar 2006 and followed-up until Dec 2010, identified using previously described selection criteria (N=36,458). Controls were selected from the general population and matched 1:1 to RA cases on gender, age, and calendar year. Individuals with previous diabetes, coronary artery disease, or hyperlipidemia, in whom general population guidelines don't apply, were excluded. Administrative data was obtained on all physician visits, hospital admissions, tests ordered and medications. Compliance with screening guidelines for hyperlipidemia defined as testing for lipids at least once every 5 years for women ≥ 50 and men ≥ 40 years was measured. Individuals' follow-up was divided into 5-year eligibility windows, when they were eligible for the screening guideline. Each individual could contribute up to two five-year eligibility windows. Compliance was measured as the proportion of eligibility windows with at least one lipid test performed within the time period. Compliance rate between RA and controls, using eligibility windows as the unit of analysis, were compared via GEE models to account for the lack of independence of observations obtained from same patients, adjusting for age and gender. Compliance rate per patient was also calculated, by measuring the proportion of eligible windows per patient during follow-up when screening was performed. Mean compliance rates in RA were compared to controls using Mann-Whitney U test.

Results: We identified 13,117 individuals with RA (64.5% female, mean [SD] age 59.0 [11.3] years), contributing 5,273 five-year eligibility windows; and 14,694 controls (65.0% female, age 59.0 [11.4] years), contributing 7,228 five-year windows. Overall, lipids were measured in 75.4% of the eligible time windows in the RA sample and in 76.7% for the control sample (OR[95% CI]=0.94 [0.86, 1.02], p=0.12). RA individuals met the recommended screening guidelines in 77.6% (SD= 37.5%) of their eligible time windows, compared to 78.5% (37.0%) for controls (p=0.22).

Conclusion: In our population-based RA cohort, compliance with general population guideline for hyperlipidemia screening was similar in people with RA and the general population. However, given the increased prevalence and burden of cardiovascular disease, lipid screening was sub-optimal for RA individuals.

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Using Patient Reported Outcome Measures to Classify Disease Activity States in Rheumatoid Arthritis: A Comparison of Patient-Derived Versions of Clinical Disease Activity Index, Simplified Disease Activity Index, and Disease Activity Score 28

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Objectives: Patient self-monitoring of disease activity may facilitate "treat-to-target" RA treatment strategy by alerting patients when they are off-target. The objective of this study was to compare agreement between patient and rheumatologist (MD) derived disease activity states using Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI) and Disease Activity Score 28 (DAS28).

Methods: Consecutive RA patients presenting for follow-up to seven rheumatologists were invited to participate. Patients completed a questionnaire and performed a self-report joint count before their visit. MD joint count and lab values were obtained from charts. Disease activity was evaluated using patient and MD versions of CDAI, SDAI and DAS28. Patient joint counts were used and global assessments from MD were replaced with patients' for patient-derived CDAI and SDAI. Disease states were categorized into remission, low, moderate or high, using published cut points. Instruments were also compared using two categories: remission or low vs. moderate or high, to mimic clinical decision making for treatment change. Agreement between patient and MD derived disease states were evaluated using Agreement Coefficient 1 (AC1) for two category comparisons and Agreement Coefficient 2 (AC2), weighted with quadratic weights, for four category comparisons. AC values > 0.62 were considered good agreement. Z tests were used to evaluate the statistical significance of difference between pairs of ACs to compare agreement across instruments.

Results: We recruited 150 RA patients [mean (SD) RA duration: 11.9 (11.3) year; age: 57.8 (16.3) year; 81% female]. There was good agreement between patient and MD derived disease activity states from the same measure (AC ranging 0.67-0.80), except when comparing patient and MD DAS28 across four categories, which had slightly lower agreement (AC 0.58 [95%CI:0.45;0.71]. There was no significant difference in the agreement between the patient and MD versions of the three measures when using four categories [CDAI vs. SDAI AC2: $p = 0.480$; CDAI vs. DAS28 AC2: $p = 0.633$; SDAI vs. DAS28 AC2: $p = 0.915$] or two categories [CDAI vs. SDAI AC1: $p = 0.580$; CDAI vs. DAS28 AC1: $p = 0.052$; SDAI vs. DAS28 AC1: $p = 0.062$].

Conclusion: Our results suggest that patients can self-monitor disease activity using patient derived CDAI, SDAI or DAS28 measures. Good agreement was found between the disease activity states derived from patient data and MD data from the corresponding measure, except for DAS28 when using four categories. There was no statistically significant difference in the agreement across measures. Supported by a CIORA grant

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Increases in Serum Cholesterol with Baricitinib Treatment are Associated with Favorable Changes in Apolipoprotein Content and with Improvement in DAS28-CRP in Patients with Rheumatoid Arthritis

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Objectives: Treatment with baricitinib (bari), an oral inhibitor of JAK1/JAK2, demonstrated improvements in signs and symptoms of RA through 52 wks in a Phase 2b study1, and also in dose- and time-dependent changes in serum lipids, LDL particle size and HDL and VLDL particle numbers2. Increases in HDL, but not LDL cholesterol, correlated with decreases in CRP at Wk-12. Changes in serum cholesterol, in apolipoprotein content of LDL, VLDL, and HDL particles were evaluated.

Methods: Patients (pts) with RA were randomized to QD doses of placebo (PBO) (n=98) or bari 1-mg (n=49), 2-mg (n=52), 4-mg (n=52), or 8-mg (n=50) for 12-wks. Pts assigned to 2-, 4-, or 8-mg bari continued blinded treatment for an additional 12-wks. Serum samples were collected through 52-wks for conventional lipid determinations (total cholesterol, LDL, HDL, and triglycerides). Apolipoprotein content was assessed at Wks 4 and 12 for PBO, 4-, and 8-mg bari groups.

Results: Pts treated with bari through 52-wks maintained a stable cholesterol and triglyceride profile with no further changes beyond Wks 12 and 24. Increases in apolipoprotein A-I, apolipoprotein B, and total apolipoprotein CIII were observed with 4- and 8-mg bari with no increase in LDL-associated apolipoprotein CIII. Bari treatment also demonstrated a significant reduction in HDL-associated SAA at the 4- and 8-mg doses compared to PBO while a significant reduction in Lp(a) was observed only in the 8-mg bari group (all $p < 0.05$). These changes in apolipoproteins coincided with the increases in serum lipids apparent by Wk-4. In pts treated across all doses of bari, a significant correlation was observed between change in HDL cholesterol and absolute DAS28-CRP score at Wk-12 ($r=-0.33, p<0.001$) as well as the change from baseline to Wk-12 in the DAS28-CRP ($r=-0.29, p<0.001$). Specifically, pts achieving DAS28-CRP <2.6 and larger decreases in DAS28-CRP demonstrated larger increases in HDL cholesterol. No significant correlations were observed in the PBO arm between HDL and disease activity measures and not between disease activity and total cholesterol or LDL levels in the bari arms.

Conclusion: In addition to increases in serum cholesterol and lipoprotein particle number (HDL and VLDL) and size (LDL), there were changes in apolipoprotein content of these particles in pts treated with bari. The increase in HDL cholesterol with bari treatment correlated with an improvement in DAS28-CRP.1Taylor P, et al. AnnRheumDis2013;72:A65-A662Kremer J, et al. AnnRheumDis2013;72(Suppl3):241

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What is the Level of Agreement between Disease Activity Indices and Response Criteria among Rheumatoid Arthritis Patients Treated with TNF Inhibitors?

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Objectives: Several standardized response criteria and disease activity indices are used to assess treatment efficacy in rheumatoid arthritis (RA). These measures comprise different types and number of variables resulting in different weighting of individual variables within each of them (1). The aim of this analysis was to compare the performance of ACR, SDAI major and minor, and HAQ response criteria and to determine their level of agreement with the DAS28, SDAI, and CDAI definitions of low disease activity (LDA) and remission in RA patients treated with infliximab (IFX) or golimumab (GLM) in a real-world, Canadian, clinical practice setting.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM. The analysis was based on RA patients treated with IFX between 2002-2014 or GLM between 2010-2014. Response was assessed with ACR20, ACR50, ACR70, HAQ improvement of 0.22 and 0.5, SDAI major (≥22) and minor improvement (≥10). Disease state was assessed with DAS28, SDAI, and CDAI definitions of LDA (<3.2, ≤11, ≤10, respectively) and remission (<2.6, ≤3.3, ≤2.8, respectively). The level of agreement was assessed with the proportion of concordant pairs over the total number of cases in each cross-tabulation and the Kappa statistic.

Results: A total of 830 RA patients with 4,100 available observations were included. The criteria for each definition of response/disease state were met for the following proportion of cases: ACR20 (66.4%), ACR50 (44.5%), ACR70 (26.4%), ΔHAQ≥0.22 (65.5%), ΔHAQ≥0.5 (53.4%), SDAI major improvement (55.8%), SDAI minor improvement (80.8%), DAS28 remission (29.4%), CDAI remission (20.4%), SDAI remission (21.8%), CDAI LDA (57.5%), SDAI LDA (58.1%), and DAS28-ESR LDA (46.0%). Statistically significant (Kappa P<0.001) associations were observed for all combinations of variables examined. Overall, the ACR response criteria performed better than the HAQ and SDAI response criteria in their agreement with LDA and remission. In general, higher levels of response in all three measures (ACR20 vs. ACR50 vs. ACR70; ΔHAQ≥0.22 vs. ΔHAQ≥0.5; SDAI minor vs. major) showed better agreement with LDA and remission. The highest level of agreement between response criteria and disease state was observed between the strictest definitions, namely between ACR70 and CDAI/SDAI remission; whereas, SDAI minor improvement showed the lowest level of agreement with remission, irrespective of definition.

Conclusion: This analysis showed that significant variation exists in the agreement between the various efficacy outcome measures. Thus, the choice of outcome measure used to make treatment decisions could have a significant impact on patient management.

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Safety and Efficacy of Baricitinib through 128 Weeks in an Open-Label, Long-Term Extension Study in Patients with Rheumatoid Arthritis

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Objectives: Baricitinib is an oral inhibitor of JAK1/JAK2 investigated for rheumatoid arthritis (RA) treatment. The safety and efficacy findings of baricitinib treatment in RA patients (pts) up to 128 weeks (wks) are reported here.

Methods: Pts were randomized to placebo (PBO) or 1, 2, 4, or 8 mg baricitinib QD for 12 wks (Part A). Pts assigned to 2, 4, or 8 mg continued assigned treatment and pts assigned to PBO or 1 mg were reassigned to 4 mg QD or 2 mg BID for an additional 12 wks of blinded treatment (Part B). Pts completing Part B were eligible to enter a 52 wk open-label extension (OLE; Wks24-76,Part C), where pts in the 8 mg group continued to receive 8 mg QD and all other pts received 4 mg QD. During Part C, doses could be escalated to 8 mg QD at 28 or 32 wks when ≥6 tender and ≥6 swollen joints were present. Pts completing Part C were eligible to enter 52 wk OLE (Wks 76-128,Part D) with 4 mg QD.

Results: Of 204 pts at sites participating in Part C, 201 (99%) were treated and 169 (84%) completed 52 wks. Among those remaining on 4 mg (N=108) in Part C, TEAEs occurred in 63%, SAEs in 16%, infections in 35%, and serious infections in 5%. Among those receiving 8 mg at any time (N=93) in Part C, TEAEs occurred in 68%, SAEs in 13%, infections in 40%, and serious infections in 3%. Of 150 pts at sites participating in Part D, 144 (96%) were treated and 133 (92%) completed an additional 52 wks. Among pts remaining on 4 mg (N=79) in Part D, TEAEs occurred in 53%, SAEs in 6%, infections in 32%, and serious infections in 3%. Among pts decreasing to 4 mg (N=65) in Part D, TEAEs occurred in 55%, SAEs in 6%, infections in 28%, and serious infections in 3%. No opportunistic infections, tuberculosis, or lymphomas were observed through 128 wks. One death due to myocardial infarction occurred in the 8 mg group in Part C. Among all pts combined, the proportions of pts achieving ACR20 or disease improvement at Wk 24 were similar or increased at Wks 76 and 128.

Conclusion: Among pts completing 128 wks of a phase 2b study, clinical improvements observed at Wk 24 were maintained or improved through Wk 128. Safety data collected during the OLE were consistent with previous baricitinib findings.

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Monitoring of Systemic Lupus Erythematosus Pregnancies: A Systematic Literature Review

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Objectives: Systemic lupus erythematosus (SLE) may result in significant obstetrical complications during pregnancy. Little data exist to guide the frequency and type of monitoring in SLE pregnancies. Our objective was to conduct a systematic review in this regard.

Methods: We conducted a systematic review of original articles using the following databases: Medline, EMBase, and Cochrane Library. No language restrictions were applied. We used Medical Subject Heading and free text terms adapted for each database. We included search terms for: 1) SLE, 2) pregnancy, and 3) monitoring parameters. All terms within each set were combined using the Boolean operator "OR" and then the 3 sets were combined using "AND". We hand-searched reference lists, review articles, and grey literature for relevant articles not captured by the electronic searches.

Results: The search yielded a total of 1032 articles. After removing 109 duplicates and 864 articles that were unrelated to our topic, 59 articles were included for in-depth review. Of these, 17 were excluded; 7 did not use a standardized scoring system for SLE activity, 5 did not specifically address SLE monitoring in pregnancy, the full-text article (in electronic or hard copy) was unavailable for 4, and one was a case series. Of 42 final articles evaluated, 20/42 (48%) addressed the value of serology, including antiphospholipid (aPL) and anti-Ro/SSA antibodies prior to pregnancy and/or during the first trimester, and 12/42 (28%) assessed monitoring of SLE flares with a validated scoring system, such as the SLE disease activity index (SLEDAI). 6/42 (14%) articles evaluated umbilical and uterine artery doppler monitoring. Consistently, across the studies included for full review, the presence of active disease, aPL and/or anti-Ro/SSA antibodies positivity, and abnormal uterine and umbilical artery doppler studies predicted poor pregnancy outcomes. No studies evaluated an evidence-based approach to the frequency of monitoring.

Conclusion: Few existing studies address monitoring for optimal care during SLE pregnancies. The available data imply roles notably for aPL and anti-Ro/SSA antibodies measurement (prior to pregnancy and/or during the first trimester), uterine and umbilical doppler studies, and following SLE disease activity with a validated scoring system such as the SLEDAI. However, optimal frequency of such monitoring is not addressed in the existing literature on SLE in pregnancy.

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Ethical Issues in Rheumatology - A Canadian Perspective

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Objectives: The frontlines in rheumatology have changed and the ethical issues that rheumatologists face today are expanding. The purpose of this study is to describe the frequency and nature of ethical issues as perceived by Canadian rheumatologists and to identify differences in ethical issues by type and location of practice.

Methods: A survey previously developed by the American College of Rheumatology Committee on Ethics and Conflict of Interest (Closed-ended [22 questions] and open-ended [2 questions]) was updated to include Canadian demographic information and used to collect information on participants views regarding their daily ethical challenges, industry relations, conflicts of interests and ethics training. Members of the Canadian Rheumatology Association were asked to participate. Participants responded in one of four categories: frequently ("always" or "often"); sometimes; infrequently ("rarely" or "never"); and no opinion; and frequencies were calculated. Open ended questions were analyzed for common themes by an independent investigator.

Results: Of the 476 emailed surveys, 140 responded completely for a 29% response rate. Participants were distributed equally between clinical practice and a combined clinical/researcher role; 60% indicated they were in an academic centre and the remaining in private practice/community. Respondents indicated that ethical issues arise more frequently in clinical research (56% responded always or often) than clinical practice (44% always or often) and 26% in basic research. The most frequently cited ethical issue was high cost of medications to society and patient (54% and 43% responded always/often, respectively) and doctor-pharmaceutical company relationships (35%). Unlike the other cohorts, Quebec respondents view profiting from enrolling patients in clinical research (30%) and practicing defensive medicine (20%) as issues that almost always or often arise. When respondents were asked the particular industry related activity that can pose an ethical issue, 87% believe serving on a company's board of directors is a problem. Analysis of the open-ended comments revealed a spectrum of industry related comments; from the monetary/profit related concerns, potential undue influence in prescribing habits, to their role in keeping rheumatologists abreast with new developments. Just over half of respondents (51%) felt they should disclose industry related activities to their patients.

Conclusion: This study rejuvenates a discussion on ethical challenges that rheumatologists face in their roles as clinicians and researchers. Costs of therapies is a common issue nationwide as was relations with pharmaceutical industries. Further work will compare and contrast ethical issues identified in the Canadian context with those noted in a US based survey of rheumatologists.

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The Treatment Dilemma in a Case of MDA5 Antibody Associated Dermatomyositis
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Dermatomyositis (DM) is classified as an idiopathic inflammatory myopathy along with polymyositis and inclusion body myositis. It is a systemic disease characterized by chronic inflammation in the skin and muscle. Circulating myositis specific antibodies can be found in 50-70% of patients with DM and the presence of certain antibodies predicts characteristic clinical phenotypes. One particular antibody, the MDA5 antibody, was only recently identified in Japan, and is present in 13-35% of patients with DM. Patients with this antibody tend to have mild or absent muscle disease compared to typical DM patients and are more likely to have palmar pustules, elbow lesions, cutaneous ulcerations and oral lesions. The presence of this antibody is an independent predictor of mortality in DM patients and death is often due to rapidly progressive interstitial lung disease, which does not respond to treatments typically recommended for DM. To date there have been few studies looking specifically at treatment of MDA5 associated dermatomyositis and there are currently no randomized controlled trials to help guide management. We present the case of a 67 year old female with rapidly progressive skin ulcerations involving her hands, feet, trunk and mouth as well as interstitial lung disease. She was diagnosed with dermatomyositis and found to be MDA5 antibody positive. Her skin manifestations did not respond to treatment with steroids or IVIG and she was started on mycophenolate mofetil therapy. Our aim is to review the clinical manifestations of MDA5 dermatomyositis and discuss the available literature regarding treatment of this condition.

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Increased Risk of Hematological Malignancies in Children Born to Women with Systemic Lupus Erythematosus

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Objectives: Patients with SLE have an increased risk of hematological malignancies compared to the general population. In utero exposures have been associated with the development of childhood hematological malignancies. However, until now, no one has assessed the risk of hematological cancers in children born to women with SLE. In a large population-based study, we aimed to determine if SLE offspring have an increased risk of hematological malignancies.

Methods: The "Offspring of SLE mothers Registry (OSLER)" includes women who had ≥1 hospitalization for delivery after SLE diagnosis, using Quebec's universal healthcare databases (1989-2009). OSLER also includes a randomly selected control group of women, matched at least 4:1 for age and year of delivery, who did not have a diagnosis of SLE prior to or at the time of delivery. We identified children born live to SLE mothers and their matched controls, and ascertained hematological malignancies based on ≥1 hospitalization or physician visit with a relevant diagnostic code. We performed multivariate logistic regression analyses, using generalized estimating equations to adjust for maternal demographics and comorbidities, sex of child, and gestational diabetes. In a subsample analysis of children with maternal drug coverage throughout pregnancy, we assessed relevant in utero medication exposures.

Results: 509 women with SLE had 719 children, while 5824 matched controls had 8493 children. Mean maternal age and follow-up were respectively 30.3 (SD 5.0) and 9.1 (SD 5.8) years. Children born to women with SLE experienced more hematological malignancies (9/719) compared to controls (38/8493) [1.3% (95% CI 0.6, 2.5) versus 0.5% (95% CI 0.3, 0.6), difference 0.8% (95% CI 0.1, 2.0)]. The most frequent type of hematological cancer in both groups was acute lymphoblastic leukemia. Primary non-Hodgkin lymphoma of bone was observed in 2 SLE offspring as opposed to 6 control children. In multivariate analyses (n=9212), children born to women with SLE appeared to have increased risk of hematological cancers versus controls (OR 2.80, 95%CI 1.33, 5.92). In the subsample of children with drug coverage (n=1925), in utero medication exposures were rare in the 10 hematological cancer cases: none were exposed to antimalarials, corticosteroids, or immunosuppressants.

Conclusion: Our data suggest that children born to women with SLE may have an increased risk of hematological malignancies. However, it must be emphasized that this outcome is extremely rare, and our findings remain to be confirmed by other study methods. The lack of association with in utero drug exposures may be viewed as re-assuring, though it is preliminary.

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Risk of Autism Spectrum Disorders in Children Born to Mothers with Rheumatoid Arthritis: A Systematic Literature Review

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Objectives: Recent evidence suggests in utero exposure to maternal antibodies and cytokines are important risk factors for autism spectrum disorders (ASD). Thus, we aimed to systematically review the risk of ASD in children born to mothers with rheumatoid arthritis (RA) compared to children born to mothers without RA.

Methods: We conducted a systematic review of original articles using the following electronic databases: PubMed, EMBase, and Web of Science. No language restrictions were applied. We hand-searched reference lists, review articles, and grey literature for relevant articles not captured by the electronic searches.

Results: Our literature search identified a total of 63 articles. Of the potentially relevant studies retrieved, 59 were excluded for lack of relevance and/or because they did not report original data. Four studies were included in the final analysis.   A case-control study, including 407 ASD offspring and 2095 control children, was unable to detect a difference in the prevalence of RA in ASD mothers versus control mothers [respectively 0.3% (95%CI 0.0-0.1) and 0.3% (95%CI 0.1-0.6)]. Another case-control study evaluated families of 61 ASD subjects and 46 healthy controls using parental report, and showed a statistically significant 8-fold increase in autoimmune disorders, including RA, in mothers of ASD offspring compared to controls. Forty-six percent of ASD offspring had a first-degree relative with RA (95%CI 34-58) compared to 26% of controls (95%CI 16-40). Moreover, in a population-based study including 3325 children with ASD and 689 196 control children, investigators observed an increased risk of ASD in children with a maternal history of RA compared to children born to unaffected mothers (OR 1.70, 95%CI 1.07-2.54). In a case-control study including 2431 ASD mothers and 653 control mothers, investigators observed that ASD mothers with fetal brain-reactive antibodies were approximately 3 times more likely to have RA compared to mothers of an ASD child without anti-fetal brain antibodies and control women of childbearing age.   Although these studies support the hypothesis of an increased risk of ASD in offspring of RA mothers, they had methodological limitations: none controlled for obstetrical complications nor medication exposures, nor considered the timing of RA diagnosis in relation to pregnancy, and all used a case-control study design. All estimates were relatively imprecise, and it is not clear to what extent the subjects represented the population base.

Conclusion: Observational studies suggest a potentially increased risk of ASD in children born to mothers with RA compared to children born to unaffected mothers, although data are limited.

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Ovarian Reserve and Fertility in Women with Systemic Lupus Erythematosus with Positive Anti-Ovarian Antibodies

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Objectives: Although anti-ovarian antibodies (AOA) have been associated with idiopathic premature ovarian failure in non-SLE populations and shown to be more prevalent in women with SLE than in unaffected women, no one has investigated the clinical significance of these antibodies in women with SLE. Therefore, we aimed to assess reproductive characteristics [i.e. time-to-pregnancy (TTP) and anti-Müllerian hormone (AMH) levels] and clinical features (e.g. disease activity and damage) in women with SLE with positive AOA compared to women with SLE with negative AOA.

Methods: Female subjects from the Montreal General Hospital Lupus Clinic were selected in accordance with the American College of Rheumatology classification criteria for SLE. Subjects were also required to be aged 18-45, and have ≥1 measurement of AOA. A detailed reproductive questionnaire was given, wherein TTP was assessed in those attempting to conceive. Disease damage index [i.e. SLICC damage index (SDI) score] and the mean disease activity (i.e. SLEDAI score) over a maximum of 5 years were recorded, as well as previous cyclophosphamide exposure (i.e. ever/never). As well, AMH levels were measured and subjects were defined as having low age-adjusted AMH levels if <5th percentile for age, indicating impaired ovarian reserve. A sensitivity analysis to avoid confounding by cyclophosphamide exposure was performed with the removal of all patients ever exposed. Descriptive statistics were calculated, including 95% confidence interval for difference in proportions.

Results: A total of 102 female SLE patients were studied, 11 of which had positive AOA (11%). Only one subject with positive AOA (1/7) and 26 subjects with negative AOA (26/79) had low age-adjusted AMH levels [respectively 14% and 33%, difference -19%, 95%CI -26, 35]. No difference was observed in the proportion of women with a TTP >12 months (in those attempting to conceive) between both groups [25% (1/4) of subjects with positive AOA versus 19% (7/37) of subjects with negative AOA, difference 6%, 95%CI -23, 60]. There was no difference in the mean SLEDAI score, as well as no difference in the proportion of subjects with a SDI score >1 (with or without the premature gonadal failure item) between both groups. In sensitivity analysis, removal of subjects exposed to cyclophosphamide did not substantially change the results previously described.

Conclusion: We did not observe an association between AOA and reduced fertility or impaired ovarian reserve, as measured respectively by TTP and AMH levels, in women with SLE. A larger study population would be necessary to confirm our results.

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Fibromyalgia: Twenty Year Follow-up and Possible Pathophysiology

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Objectives: Fibromyalgia is a condition characterized by chronic wide-spread pain, fatigue and sleep disturbance. There is little information on the long-term outcome. This is an observational study of a cohort of patients followed for 20 years until 2013.

Methods: The inception cohort consists of 384 patients seen in 2003 with the diagnosis of fibromyalgia. The records were reviewed and medical events noted.

Results: A total of 384 patients were diagnosed with fibromyalgia according to the ACR criterion of 1990. There were 81 males (21%) and 303 females (79%), yielding a sex ratio of 1:4. Average age of males was 44.4 years and of female was 46.6 years at time of diagnosis. Of these, 91 patients (24%) were followed for >20 years, 32 (8%) for 15-20 years, 32 (8%) for 10-15 years, 35 (9%) for 5-10 years and 70 (18%) for 1-5 years. The mean duration of follow-up was 107 months. Of the 91 patients followed for >20 years, 55 (60%) were found to have spinal stenosis of one or more levels, mainly due to hypertrophic facet arthritis with hypertrophy of the ligamentum flavum. Of these 65 (71%) developed psoriatic arthritis. Three have a seronegative arthritis that is psoriasiform but patients have eczema. Four patients have eczema.
Conclusion: Fibromyalgia could be a syndrome symptomatic of arthritis of facet joints, possibly as a part of a psoriatic arthropathy. There is a significant trend towards development of spinal stenosis.

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Medication Persistence among Rheumatoid Arthritis and Ankylosing Spondylitis Patients under DMARD and Anti-TNF Therapy in Brazil
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Objectives: We aimed to study one-year medication persistence among rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients initiated on disease-modifying anti-rheumatic drugs (DMARDs) and anti-tumor necrosis factor agents (anti-TNFs) therapy in Brazil.
Methods: We conducted a retrospective cohort study using data obtained from the administrative databases of the Brazilian public health system (SUS) in Minas Gerais. We included patients starting DMARD or anti-TNF therapy between July 2008 and June 2013 (no DMARD or anti-TNF in the previous 6 months). Patients starting both anti-TNF and DMARDs were considered in the anti-TNF group. Persistence was defined as the duration of time from initiation to discontinuation of therapy considering a permissible 30 day-gap between prescriptions. Medication possession ratio (MPR) was calculated by the division of the cumulative number of days of medication supply over the total number of days of follow-up. We calculated mean, percentage, and the 95% confidence interval (95%CI) for the difference between groups.

Results: Among 11,577 RA patients, 2,185 were in the anti-TNF group and 9,392 in the DMARD group. Of the anti-TNF group, 66.3% persisted on therapy at the end of the first year of follow-up compared to 54.1% of those in the DMARD group (95%CI for the difference 9.7% to 14.6%). Moreover, 5.1% DMARDs users started anti-TNF therapy while on DMARD use. The mean persistence was 309 days for anti-TNF users and 286 days for DMARD users (95%CI 17 to 28 days). The MPR was 0.68 and 0.59 for patients in the anti-TNF and DMARDs groups, respectively (95%CI 0.08 to 0.11). Among the 1,250 AS patients, 975 were in the anti-TNF group and 275 in the DMARD group, and 80.2% anti-TNF users and 41.1% DMARD users persisted on their therapy at one year (95%CI 36.8% to 49.9%). Also, 10.3% DMARDs users started anti-TNF therapy during the DMARD therapy. The mean persistence was 336 days for anti-TNF users and 249 days for DMARD users (95%CI 74 to 100 days). The MPR was 0.80 for anti-TNF users and 0.45 for DMARD users (95%CI 0.32 to 0.39). AS patients starting anti-TNF agents presented higher persistence compared to RA patients who started therapy with anti-TNF agents (95%CI 18 to 34 days).

Conclusion: RA and AS patients using anti-TNF therapy had higher persistence and medication possession ratios as compared to DMARD users. MPR among patients using DMARD was relatively low. Persistence for anti-TNF agents was longer among AS patients than RA patients.

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Pilot Test of a Pragmatic Randomized Controlled Trial of the OA GO AWAY, a Self-Management Intervention for Patients with OA of the Hip or Knee to Promote Exercise Adherence and Physical Activity: Preliminary Results

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Objectives: The current study seeks to assess the feasibility of conducting a full-scale pragmatic randomized controlled trial, testing the effectiveness of the OA GO AWAY on adherence to prescribed exercise, and effects on physical activity, goal attainment, pain, physical function, and quality of life. Another goal was to assess the feasibility and acceptability of the OA GO AWAY when used in routine clinical practice at The Arthritis Society (TAS).

Methods: The study will recruit a total of 40 patients with OA of the hip or knee at TAS in Ottawa, and 21 have been recruited to date. Participants were randomly assigned to one of two groups, the control group which received usual care at TAS and the experimental group which used the OA GO AWAY in addition to usual care at TAS. Participants completed a socio-demographic questionnaire, and measures of exercise participation, physical activity, goals, pain, function and quality of life at the beginning and the end of the study period. Participants in the experimental group were shown how to complete the OA GO AWAY, used it at home for 3 months, and assessed its acceptability and feasibility.

Results: Of the 21recruited participants, 14 completed the protocol, including 5 in the experimental group. Two experimental group participants dropped out citing changed personal circumstances. Participants in the experimental group reported the OA GO AWAY as acceptable for use at home. The majority of participants felt the Journal and Goals and Action Plan were acceptable regarding ease and time to complete. Participants unanimously agreed that the Exercise Log was quick and easy to complete. Two participants observed that the tracking of exercise in separate categories (aerobic, strengthening, range of motion, balance) helped them to link their OA goals with their exercise plan, and to see gaps in their actual versus planned activities. Some participants changed their goals from baseline to the end of the study or failed to complete the second and third Journal and Goals and Action Plan which made it difficult to assess goal attainment. Three participants said explicitly that the OA GO AWAY motivated them to be active.

Conclusion: Preliminary results suggest that the OA GO AWAY is feasible and acceptable for use in clinical practice at TAS, and may help to motivate patients to adhere to their exercise programs. Future work may be done to enhance the goal attainment self reflection capacity of the OA GO AWAY.

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14-3-3η Levels Predict Radiographic Progression in Recent-Onset Polyarthritis Patients
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Objectives: To determine if 14-3-3η serum levels predict joint damage progression in Early PolyArthritis (EPA).

Methods: Serum levels of 14-3-3η were measured at baseline and 18 months in EPA patients (median age 60 years; 62% female) from the EUPA cohort. Majority (97.4%) were treated with DMARDs between baseline and 18 months, aiming for clinical remission defined as 0 swollen joint out of 66; 24 also received biologics during that period. Radiographic progression was defined as a positive change in Sharp/van der Heijde score (ΔSHS). For 14-3-3η measurements, the manufacturer's (Augurex 14-3-3η ELISA) suggested diagnostic cut-off of ≥0.19 ng/ml was used. The difference in ΔSHS between positive or negative 14-3-3η status was analyzed with independent sample t-test. Generalized estimating equation with repeated measures was used to compare remission over time with positive or negative 14-3-3η at the same time points. Univariate linear regression (using ACPA, RF, anti-Sa, BMI, ESR, Age, Symptoms Duration, SJC66, gender and 14-3-3η) were performed to evaluate predictors of progression at 30 months.

Results: At baseline and 18 months, 154/332 (46%) and 150/325 (46%) of patients were 14-3-3η positive, respectively. Paired t-test revealed that 14-3-3η values significantly decreased between baseline and 18-month measurements (-0.72 ± 5.2, p=0.01). Patients with positive baseline 14-3-3η had higher mean ± SD progression at 30 months (7.6 ± 10.6 vs 4.7 ± 8.4, p=0.008). The difference was greater when progression was compared with 18-month positive 14-3-3η (8.5 ± 12.0 vs 4.0 ± 6.5, p<0.001). The likelihood of being in SDAI remission was reduced in the presence of positive 14-3-3η over time (RR (95% CI) 0.75 (0.62-0.91), p=0.004). In univariate analysis, all three antibodies, 14-3-3η, age and ESR were significant predictors of DSHS at 30 months. The variance (r2) of ΔSHS explained by baseline anti-Sa, RF and ACPA were 6.0%, 4.8% and 2.9%, respectively. For 18-month anti-Sa, RF and ACPA, r2 of ΔSHS was 5.8%, 9.0% and 4.1%, respectively. For 14-3-3η, r2 increased from 2.3% to 8% between baseline and 18 months.

Conclusion: Serum 14-3-3η is a mechanistic, joint-derived, serological marker that potently induces cytokines and joint damage factors. Positive baseline and 18-month 14-3-3η status in EPA are associated with an increased risk of joint damage progression at 30 months.

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What is the Effect of TNF Inhibitors on Employment Status in Rheumatoid Arthritis Patients and What are the Predictors of Progression to Unemployment?

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Objectives: The aim of this analysis was to evaluate the prevalence of unemployment due to work disability in RA patients initiating treatment with infliximab (IFX) or golimumab (GLM) and to identify determinants of disability.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM as first biologics or after having been treated with a biologic for <6 months. Data were obtained from RA patients treated with IFX (2002-2014) or GLM (2010-2014). Between employment group differences were assessed for statistical significance with the independent samples t-test or the chi-square. Time to employment and time to unemployment were assessed with the Kaplan-Meier (KM) estimator of the survival function. Cox regression was used to identify predictors of time to unemployment.

Results: A total of 581 RA patients were included; 374 (64.4%) employed and 207 (35.6%) unemployed due to disability. The following baseline parameters were associated with significantly increased likelihood of being unemployed due to disability: female vs. male gender (40.1% vs. 27.6%; P=0.006), earlier enrolment period (2002-05 vs. 2006-09 vs. 2010-14: 49.3% vs. 30.5% vs. 22.4%; P<0.001), insurance type (provincial vs. private vs. both: 54.9% vs. 23.8% vs. 20.0%; P<0.001), older age (P=0.033), and increased disease activity as evidenced by the higher DAS28 (P<0.001), SJC (P<0.001), TJC (P<0.001), HAQ (P<0.001), MDGA (P<0.001), PtGA (P<0.001), CDAI (P<0.001), SDAI (P<0.001), pain (P<0.001), and ESR (P<0.001). Among disabled patients, 10.1% were able to return to work upon treatment with TNF a mean KM-based duration of 119.5 months from baseline; whereas 6.4% of employed patients became disabled (2002-05 vs. 2006-09 vs. 2010-14: 7.0% vs. 10.1% vs. 1.7%; P=0.021) with a mean time to unemployment of 113.4 months. Multivariate survival analysis showed that, upon adjusting for enrolment period, higher baseline HAQ [HR (95%CI): 3.59 (1.64, 7.87), P=0.001], and higher baseline SJC [HR (95%CI): 1.09 (1.02, 1.16), P=0.011] were significant predictors of unemployment due to disability.

Conclusion: A significant proportion of RA patients are unemployed due to disability in Canada. At anti-TNF initiation, work disability was associated with higher disease activity, female gender, earlier enrolment period, and provincial insurance. Increased HAQ and higher SJC were significant predictors of progression to unemployment highlighting the importance of early anti-TNF initiation in order to prevent work disability. Anti-TNF treatment was effective in enabling a considerable portion of disabled patients to return to employment.

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Is the BASDAI Score Driven by Pain in Ankylosing Spondylitis Patients Treated with Anti-TNF?

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Objectives: The present standard for measuring disease activity in AS is the BASDAI which focuses on five major symptoms. Given that the BASDAI instrument contains two pain questions, the objective was to assess whether pain symptoms are the main drivers of BASDAI scores among AS patients treated with anti-TNFs in routine clinical practice.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab (IFX) or golimumab (GLM). Patients with AS treated with IFX or GLM and enrolled between 2005 and 2014 were included in this analysis. A modified weighted BASDAI score (m-BASDAI) was calculated excluding the axial (Q2) and peripheral (Q3) pain questions of the BASDAI. The correlation of BASDAI, each of its components, and the modified BASDAI (m-BASDAI) was assessed with the Pearson correlation coefficient. BASDAI low disease activity (LDA) and m-BASDAI LDA were defined as a score ≤3. The association between the number of administered analgesics (0, 1, >1) and BASDAI/m-BASDAI was assessed with one-way ANOVA.

Results: A total of 413 AS patients with 1,709 assessments were included in this analysis. Correlation analysis showed a strong correlation between the full BASDAI and m-BASDAI scores (r=0.98, P<0.001). With respect to the individual BASDAI questions, a strong positive linear correlation was observed between all questions and the BASDAI score as well as the m-BASDAI score. As expected, a lower correlation was observed between Q2 and Q3 with the m-BASDAI relative to BASDAI. Axial pain was most strongly correlated with the severity of morning stiffness, whereas the highest correlation of peripheral pain was observed with localized tenderness. The cross-tabulation of BASDAI LDA and m-BASDAI LDA showed a strong measure of agreement (kappa=0.871, P<0.001). Omission of the pain questions from BASDAI resulted in a comparable proportion of LDA cases (41.7% vs. 40.9%) when using the same LDA definition. Increased use of analgesics (0 vs. 1 vs. >1) over 2 years of follow-up was associated with significantly (P<0.05) higher mean scores in BASDAI, m-BASDAI, and each of the BASDAI components. No significant association was observed between increased use of analgesics and treatment retention.

Conclusion: Higher levels of AS pain are significantly associated with a higher BASDAI score and increased use of analgesic medications among patients treated with anti-TNFs. In addition to pain, fatigue, tenderness, and morning stiffness are likewise important contributing components in the BASDAI score and the disease burden of AS.

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Is Skin Disease More Important to Patients or Physicians in the Assessment of Disease Activity in Psoriatic Arthritis?

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Objectives: Patient (PtGA) and physician (MDGA) global assessment of disease activity are standard outcome measures used in clinical practice and research to ascertain patient and physician subjective perception of psoriatic arthritis (PsA) disease activity. The aim of this analysis was to assess the agreement between PtGA and MDGA, and to compare the correlation of PtGA or MDGA with the Psoriasis Area and Severity Index (PASI) in PsA patients treated with infliximab (IFX) in a Canadian real-world, routine clinical practice setting.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or golimumab as first biologics or after having been treated with a biologic <6 months. Eligible people for this analysis included PsA patients treated with IFX who were enrolled between 2005-2012. The correlation between disease parameters was assessed with the Spearman's rho coefficient (r), while the intraclass correlation coefficient (ICC) and Cronbach's alpha (CA) was used to assess internal consistency.

Results: 92 patients (52.2% male) were included with a mean (SD) age of 48.7 (9.9) years and disease duration of 6.8 (9.1) years. At baseline, mean (SD) disease parameters were: PASI = 3.3 (5.6); swollen joint count (SJC28)= 4.0 (3.8); tender joint count (TJC28)= 5.9 (5.3); PtGA= 5.0 (2.8); MDGA= 5.8 (2.2) cm. Prior to IFX initiation, 78 (84.8%) patients had been treated with a traditional DMARD (71.7% with methotrexate). Overall, a strong agreement was observed between PtGA and MDGA (r=0.632). The correlation of PASI with PtGA was low (r=0.213), whereas it was moderate with MDGA (r=0.343). Internal consistency was poor between PASI and both PtGA (CA = 0.373, ICC = 0.229) and MDGA (CA = 0.445, ICC = 0.286) although it was higher with the latter. Multivariate linear regression resulted in the exclusion of PtGA from the model, also supporting the stronger association of MDGA with PASI. When considering other disease parameters, PtGA showed a very strong correlation with pain (r=0.885) and strong with HAQ-DI (r=0.596), whereas a strong correlation was observed between MDGA and both pain and HAQ-DI (r=0.652 and r=0.520, respectively).

Conclusion: Our analyses show that the association of PASI is stronger with MDGA when compared to PtGA. However, patient-reported pain and HAQ-DI were better correlated with PtGA and MDGA when compared to PASI, suggesting that both patients and rheumatologists place more emphasis on pain and functional activity than on skin symptoms when evaluating the global status of PsA.

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What is the Real-World Effectiveness and Safety of Golimumab in the Treatment of Rheumatoid Arthritis over a 12 Month Period?

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Objectives: The efficacy and safety of anti-TNF in the management of rheumatoid arthritis (RA) has been demonstrated in numerous controlled clinical trials. However, real-world data demonstrating the true benefits of golimumab (GLM) in routine care are scarce. The objective of this analysis was to assess the long-term effectiveness and safety profile of GLM in routine clinical practice in the Canadian context.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM as first biologics or after having been treated with a biologic for <6 months. Analyses included RA patients treated with GLM who were enrolled between 2010-2014. Descriptive statistics were produced for clinical outcome measures and patient reported outcomes at baseline and 6 or 12 months of treatment. Within-group changes were assessed for statistical significance with the paired-samples Student's t-test. Safety was assessed with the incidence of adverse events (AEs)/100 patient-years.

Results: 170 RA patients were included in this analysis; 75.3% were female, mean (SD) age was 57.9 (13.5) years and disease duration was 8.1 (8.7) years. At baseline, 85.3% were taking concomitant DMARDs, 31.2% were on NSAIDS, and 23.5% received corticosteroids. Upon six months of treatment, statistically significant (P<0.001) and clinically meaningful improvements were observed in all parameters analyzed, which were sustained over 12 months of treatment. Mean (SD) disease parameters at baseline and 12 months of treatment were: HAQ: 1.32 (0.74) vs. 0.84 (0.72), P<0.001; CDAI: 27.1 (16.3) vs. 10.3 (9.3), P<0.001; SDAI: 30.3 (17.5) vs. 9.9 (9.4), P<0.001; and DAS28: 5.0 (1.6) vs. 3.1 (1.2), P<0.001. At 6 and 12 months of treatment, the proportion of patients who achieved CDAI remission was 14.9% and 21.6%, SDAI remission was 16.7% and 27.0%; DAS28 LDA was achieved by 46.6% and 53.8%, and DAS28 remission by 28.8% and 30.8%, respectively. A total of 147 AEs (107.0 events/100 patient-years) were reported by 66 (38.8%) patients and 8 serious AEs (SAEs) (5.8 events/100 patient-years) by 7 (4.1%) patients. Most frequently reported AEs were arthralgia (4.1%), sinusitis (4.1%), and upper respiratory tract infection (4.1%). There were three serious infections; one was a case of pneumonia and two were cases of herpes zoster. No deaths, tuberculosis cases or malignancies were observed.

Conclusion: The results of this Canadian longitudinal observational study have shown that treatment with GLM was safe and effective in reducing symptom severity and improving outcomes in RA patients over 12 months.

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What is the Correlation of Individual HAQ and BASDAI Questions with Disease Activity Measures in Ankylosing Spondylitis? Implications for Instrument Reduction

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Objectives: The aim of this analysis was to describe the correlation of individual HAQ and BASDAI questions with patient and physician reported measures used in AS and to examine whether the instruments could be reduced to better reflect routine clinical practice.

Methods: BioTRAC is an ongoing prospective registry of patients initiating infliximab or golimumab. Data from AS patients treated in 2005-2014 were used. The correlation of individual HAQ and BASDAI questions with patient (pain, BASDAI, HAQ and BASFI) and physician (MDGA) reported measures was described with the Pearson's correlation coefficient. The impact of each question on the need for help in each HAQ domain was assessed with logistic regression. Factor analysis was used to assess the variability due to each individual question in HAQ and BASDAI.

Results: A total of 413 AS patients with 1660 BASDAI and 1654 HAQ assessments were included. HAQ and BASDAI questions correlated at different extents with each AS measure. Questions related to "eating" and "gripping" showed the lowest correlation with patient and physician reported measures. All HAQ questions had higher correlations with patient reported measures than with MDGA. The BASDAI question on "fatigue and tiredness" showed the highest correlation with BASFI, while the question on "other joints pain/swelling" showed the lowest correlation with MDGA. None of the HAQ and BASDAI questions were associated with needing help for eating. All other HAQ individual questions were significantly associated with the need for help within their corresponding category, with the exception of Q5C and Q7A. BASDAI question on level of discomfort was significantly associated with the need for help in all HAQ categories, with the exception of "eating" and "walking". Q2A and Q7C accounted for 59.6% of the HAQ variance. The level of morning stiffness accounted for 73.8% of the BASDAI variance. When combining the HAQ and BASDAI, Q2A and Q3A from HAQ and Q1 from BASDAI accounted for 63.5% of the variance.

Conclusion: Variability exists in the correlation of HAQ and BASDAI questions with patient and physician reported AS measures. The results suggest that "standing up straight from an armless chair" and "turning faucets on/off" are the main drivers of HAQ, while the level of morning stiffness drives the BASDAI. Three questions were found to drive the combined HAQ and BASDAI which may have implications in the design of self-report instruments.

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Use of Rituximab Compared to Anti-TNF Agents as Second and Third Line Therapy in Patients with Rheumatoid Arthritis: A Report from the RHUMADATA® Clinical Database and Registry

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Objectives: To evaluate if patients with rheumatoid arthritis (RA) treated with rituximab (RIT) after failing a first or a second anti-TNF agents (TNF-IR) have a different drug retention rate than patients similarly prescribed anti-TNF agents (pooled adalimumab, etanercept or infliximab) and compare the treatment strategies of using RIT as second or third biologic treatment .

Methods: Data from TNF-IR RA patients prescribed adalimumab (ADA), etanercept (ETA), infliximab (INF) or rituximab (RIT) as second or third biologic agents on or after January 1st 2007 was extracted and subjects taking either ADA, ETA or INF were pooled to form the anti-TNF cohort. Baseline demographics included age, disease duration, HAQ-DI, fatigue and pain visual analog scale evaluations (VAS), TJC, SJC, DAS 28 ESR and SDAI. Five-year drug retention rates were estimated and compared using Kaplan-Meier survival estimates. Statistical analysis was performed using SAS version 9.3. RHUMADATA® is a clinical database and registry used in daily clinical practice at the IRM and CORQ.

Results: The data from 226 RA patients were extracted, 153 and 73 having respectively failed a first and a second anti-TNF agent. No clinically significant differences in baseline variables were observed between treatment groups in second and third intention. The 5 year retention rates of second line RIT and anti-TNF use were 74% and 36% respectively (Log-rank p=0.002). In patients having failed two anti-TNF, subsequent use of RIT and anti-TNF agents respectively demonstrated 5 year retention rates of 48% and 24% (Log-rank p=0.004). Although numerically superior (74% vs 48%) second line use of RIT did not reach statistical difference when compared to third line usage.

Conclusion: : As a second line agent, in TNF-IR patients, RIT demonstrates a better 5 year retention rate than anti-TNF agents. As third line therapy, RIT is also statistically superior to anti-TNF agents. Although no statistical difference was demonstrated between second and third line RIT use, it is evident that positioning RIT as second line offers a better long term outcome.

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Use of Monotherapy Anti-TNF Agents in Ankylosing Spondylitis Patients from the RHUMADATA® Registry: 8-year Comparative Effectiveness of Adalimumab, Etanercept and Infliximab

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Objectives: Anti-TNF agents namely adalimumab (ADA), etanercept (ETA) and infliximab (INF) are approved for the treatment of signs and symptoms of ankylosing spondylitis. Their efficacy for axial and extra-axial, such as enthesitis, uveitis, and inflammatory bowel diseases features have been demonstrated in randomized controlled trials against placebo. Antibodies and soluble receptors may have a different efficacy profile. The objective is to assess the retention rates of adalimumab (ADA), etanercept (ETA) and infliximab (INF) in patients diagnosed with ankylosing spondylitis (AS) and to compare patient reported response over a 8 year period.

Methods: Data of AS patients who had been prescribed adalimumab (ADA), etanercept (ETA) or infliximab (INF) in monotherapy on or after January 1st 2004 was extracted. Baseline demographics included age, gender, disease duration, HAQ-DI, fatigue and pain visual analog scale evaluations (VAS), morning stiffness, BASDAI, BASFI, ASDAS and HLA-B27. Eight-year drug retention rates were estimated and compared using Kaplan-Meier survival estimates. BASDAI improvement over time was assessed using proportional hazard model adjusted for age and disease duration at TNF initiation. Other differential measures of effectiveness were tested using general linear models (GLM). For these analyses, patients with baseline BASDAI of 4 or more were included. Statistical analysis was performed using SAS version 9.3.

RHUMADATA® is a clinical database and registry used in daily clinical practice at the IRM and CORQ.

Results: Data from 170 patients diagnoses with AS was extracted and no significant differences in baseline characteristics were observed between treatment groups except for age and disease duration. The 8-year retention rate of ADA, ETA and INF were 62%, 55% and 54% respectively and were not statistically different (Log-Rank p=0.90). Seventy-five patients were used to analyse time required to reach a BASDAI of 2 and compare rates of response. At baseline, ADA, ETA and INF BASDAI were 6.6, 6.2, 6.5 respectively. The adjusted hazard ratio for reaching a BASDAI of two was found to be 0.77 (95% CI = [0.32, 1.87]) and 0.92 (95% CI = [0.40, 2.14]) when comparing ETA and INF to ADA respectively. Overall 42%, 61% and 64% of ADA, ETA and INF patients reached a target BASDAI of 2 in average adjusted times of 9.6, 19.0 and 15.6 months (p-value=0.31).

Conclusion: Monotherapy adalimumab, etanercept and infliximab in AS patients show similar 8-years retention rates and similar improvement in BASDAI. They all represent good options for the treatment of AS in monotherapy.

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Tocilizumab use in Patients with Rheumatoid Arthritis having Failed One Previous Anti-TNF Agent: Comparison with Adalimumab, Etanercept and Infliximab from the Provincial Electronic Database and Registry Rhumadata®

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Objectives: Tocilizumab, as an intra-venous agent, has been approved for rheumatoid arthritis (RA) in Canada in April 30th, 2010. It was the seventh approved agent after adalimumab, etanercept, abatacept, infliximab, golimumab and rituximab. It has been demonstrated effective in the treatment of RA either in monotherapy or combo therapy after non-biologic or biologic DMARDS. The goal of this analysis is to describe its effectiveness in patients with RA failing a first anti-TNF DMARDs and to compare its retention rate versus adalimumab, etanercept and infliximab in the same clinical situation.

Methods: All patients with RA having failed a first anti-TNF agents and subsequently exposed to tocilizumab after the 1st of January 2005 were extracted from the Rhumadata® database. 4 cohorts were created according to the time tocilizumab or the subsequent anti-TNF agents was introduced: One cohort of patients starting tocilizumab and 3 other cohorts starting either adalimumab, Etanercept or infliximab. Demographics and baseline characteristics including age, gender, disease duration, Rheumatoid factor and anti-CCP antibodies, CRP and ESR, previous failed treatment number, DAS 28 ESR and CDAI, HAQ-DI were included for each cohorts.

Results: The data from 259 patients prescribed either tocilizumab (53=20%), adalimumab (97=37%), etanercept (82=33%) or infliximab (27=10%) as a second biologic agent were extracted from the Rhumadata® registry and clinical database. Mosts subjects were female (75%) and the average age of cohort subjects was 58.2 (StD=14.3). Mean CRP and ESR were respectively 17.0 (StD=29.5) mg per L and 26.6 (StD=24.1) mm per hour. No clinically significant differences at baseline were observed between groups. The four year retention rates of tocilizumab, adalimumab, etanercept and infliximab as second line biologic agents were 44.3%, 27.2%, 37.1% and 34.0% respectively. Kaplan-Meier survival analysis revealed significant differences in the drug retention rates (logrank p=0.0249).

Conclusion: In RA patient having failed their first anti-TNF agent, tocilizumab, an Il-6 inhibitor, could be a more valuable alternative than cycling to a second anti-TNF agent.

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Correlation of Individual HAQ Questions with Disease Activity Measures in Psoriatic Arthritis: Implications for Instrument Reduction

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Objectives: The aim of this analysis was to describe the correlation of individual HAQ questions with patient and physician reported measures used in PsA and to examine whether the instrument could be reduced to better reflect routine clinical practice.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab. Data from PsA patients treated with infliximab or golimumab in 2006-2013 were used. The correlation of each HAQ question with patient and physician (pain, patient global assessment (PtGA), SJC28, TJC28 and physician global assessment (MDGA)) reported measures were described with the Pearson's correlation coefficient. The impact of each HAQ question on the need for help in each HAQ domain was assessed with logistic regression. Factor analysis was used to assess the variability due to each question in HAQ.

Results: A total of 183 PsA patients with 596 HAQ assessments were included. Individual HAQ questions correlated at different extents with each PsA measures. All questions showed higher correlations with PtGA and pain compared to MDGA. Regarding patient reported outcomes, Question 5A ("Wash / dry your entire body") showed the highest correlation, specifically with pain. The majority of HAQ questions were significantly associated with the need for help within their corresponding ability category, with the exception of questions Q3B, Q3C, Q4B, Q5C and Q8B. The results of factor analysis showed that 2 (Q1A and Q3B) out of the 20 HAQ questions accounted for 61.5% of its matrix variance, suggesting that the question on the ability to "dress, tie shoelaces and do buttons", as well as the question on the ability to "lift a full cup or glass" may be the main drivers of HAQ in PsA.

Conclusion: Variability exists in the correlation of individual HAQ questions with patient and physician reported PsA measures. Pain and PtGA are significantly associated with the various domains of HAQ, while clinical outcomes (SJC28 and TJC28) and MDGA are less important. Among PsA patients, the HAQ is driven by components related to dressing and grooming and to eating abilities, suggesting that PsA patients may be facing different challenges than RA patients. This may have implications from an occupational health perspective and in the design of a shorter self-report instrument more suitable for PsA patients.

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Tocilizumab use in Daily Practice in Patients with Rheumatoid Arthritis: Description of the Profile using the Provincial Electronic Database and Registry Rhumadata®

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Objectives: Tocilizumab, as an intra-venous biologic agent targeting IL-6, has been approved for rheumatoid arthritis (RA) in Canada on April 30th, 2010. It was the seventh approved agent after adalimumab, etanercept, abatacept, infliximab. golimumab and rituximab. It has been demonstrated effective in the treatment of RA either in monotherapy or combo therapy after non-biologic or biologic DMARDS [1, 2]. The objective of this analysis is to describe the clinical and therapeutic profiles of patients starting tocilizumab in the three Rhumadata® centers using the software.

Methods: All patients with RA exposed to tocilizumab were extracted from the Rhumadata® database. 6 cohorts were created according to the time tocilizumab was introduced: Initial monotherapy, traditional DMARDS-ir or subsequent TNF-ir from one to more than four previous failure. Demographics and baseline characteristics including age, gender, disease duration, Rheumatoid factor and anti-CCP antibodies, CRP and ESR, previous failed treatment number, DAS 28 ESR and CDAI, HAQ-DI were included for each cohorts

Results: A total of 133 patients taking (n=82) or having taken tocilizumab in the past (n=51) were extracted for this analysis. Most subjects were women (84%) and the mean age at diagnosis was 58.8 (StD=12.9) years. Mean duration of disease from first symptoms was 15.3(StD=10.4) years. Most subjects were non-smokers (82%). Fifty-three (40%) were concomitantly treated with corticosteroids while on tocilizumab. As first biologic agent, DMARDS insufficient responders (DMARDs-ir) tocilizumab was used in 33(25%) subjects. As second, third, fourth or more agent in biologic agent insufficient responders (Biologic IR) in respectively 34(26%), 27(20%) and 39(29%). Tocilizumab was used as monotherapy in 25(19%) patients. The remainder were concomitantly treated with a variety of commonly used traditional DMARDs. The most commonly used DMARDS were methotrexate (86/108=80%) and hydrochloroquine sulfate (45/108=42%). Most frequent past DMARDs used include hydrochloroquine sulfate (63/133=47%), methotrexate (39/133=29%), leflunomide (37/133=28%) and sulfasalazine (30/133=23%). Success to therapy with tocilizumab will be evaluated using survival analysis.

Conclusion: In community practice, where new agents for the treatment of any medical condition are often used as last resort strategy, efficacy outcomes could certainly yield biased perception. Registry, such as the provincial electronic database and registry Rhumadata®, where larger number of patients are pooled, can help decision making as to the optimal order of therapeutic options.

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Life-Threatening Hypersensitivity Reaction to ACE Inhibitor Used in Scleroderma Renal Crisis

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A 68yo female presented to the emergency department after recently being discharged for renal crisis in diffuse systemic sclerosis. She had been discharged on an ACE-inhibitor, captopril, and returned three days later for fever, shortness of breath, rash and facial swelling. Her blood pressure was 215/90mmHg and her skin appeared diffusely swollen and tender with erythematous confluent patches covering 85% of her TBSA. Creatinine was 5.8 mg/dL with WBC casts on microscopy, and she was diagnosed with an acute hypersensitivity reaction to captopril with recurrent renal crisis. Skin biopsy revealed partial necrosis of the epithelium with vacuolar change and spongiosis consistent with major EM or Stevens-Johnson syndrome. Treatment with pulse dose steroids was initiated and captopril discontinued, noting the possibility that renal crisis may precipitously worsen. Over two days, her symptoms abated and the exfoliative rash was resolving, however, her renal function remained impaired with persistently elevated blood pressures. Preparations were made for hemodialysis. She was started on losartan, methyldopa and hydralazine for blood pressure control. Over several days, her renal function improved, and blood pressure returned to baseline. Hemodialysis was avoided, and the patient was discharged home in a hemodynamically stable condition with close rheumatology and nephrology follow-up. She was not started back on ACE inhibitor therapy and continues on ARB monotherapy without any significant adverse effects.

Discussion: Renal crisis in systemic sclerosis is a life-threatening condition, and ACE inhibitors have thus far been the standard pharmacological treatment. In a patient with a serious adverse drug reaction to ACE inhibitor therapy, other modalities such as hemodialysis and renal transplant are usually considered to treat this condition. Prior to subjecting a patient to these lifelong interventions, we may consider alternate management strategies to avoid this commitment. While employing the expertise of a rheumatologist and nephrologist, we may begin treatment with systemic steroids and strict blood pressure control. ARB monotherapy took the place of ACE inhibitors for the management of renal crisis in this case and thus, we ponder the hypothesis of whether ARB monotherapy may be of use in treating systemic sclerosis renal crisis, especially in those patients with adverse drug reactions to ACE inhibitors.

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Crowdsourcing Priority Setting: A Survey of Canadian's Priorities and Views about Using Digital Media in Arthritis Prevention and Treatment

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Objectives: Evidence in arthritis prevention and treatment continues to accumulate, but much of the knowledge has not been used by patients and health professionals. Digital technologies offer flexibility to implement research evidence in clinical practice and patient self-management. This study aims to assess the public's views and priorities in using digital media in arthritis management.

Methods: This study was co-led by researchers and patient/consumer leaders, including Arthritis Consumer Experts and Canadian Association of Retired Persons. A cross-sectional online public survey was conducted to address 3 areas: 1) challenges faced by people with arthritis, 2) individuals' views on how arthritis could be prevented and treated, and 3) opinions on how digital media (e.g., mobile apps, social networking tools and health tracking devices) should be used in arthritis management. The questionnaire was available in English and French. We used open-ended questions to elicit opinions from the public. Invitations were distributed through partner organizations' social media channels. A content analysis was initially performed on the first 200 responses to develop preliminary codes for the open-ended questions. These codes were subsequently refined and applied to all responses.

Results: In July-August 2014, 668 attempted the English survey and 500 individuals provided complete responses. 383 (76.6%) were women and 364 (72.8%) were over the age 55. 85.2% resided in a city with at least one hospital. 33.6% had OA and 12.4% had RA. 146 (29.2%) respondents had no chronic disease, but were providing care for someone with a chronic condition. Respondents identified pain (48.0%), loss of mobility (35.6%), and loss of functional independence (34.6%) as main challenges faced by people with arthritis. Exercise (33.8%), diet (21.0%) and healthy body weight (13.6%) were the most mentioned prevention strategies. Physical activity (44.0%), medication (37.8%), and physical therapy (15.2%) were the most mentioned treatments. 11.6% and 24.2% of respondents did not know how arthritis could be prevented or treated, respectively. Respondents indicated that digital media should be used to provide educational material (22.4%), monitor exercise (15.4%), and track symptoms (7.8%). However, 243 (48.6%) were unable to name a role, or felt that there was no role, for digital media in arthritis treatment.

Conclusion: Through crowdsourcing, we identified several areas where the public felt digital media should be used in arthritis management. This survey also uncovered gaps in the awareness of arthritis prevention and treatment, and the perceived role of digital media. These areas present opportunities for future knowledge translation endeavours.

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Real-life Drug Survival of Tumour Necrosis Factor-α Inhibitors in Inflammatory Arthritis
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Objectives: Inflammatory arthritis is a spectrum of diseases arising from immune dysregulation in the body causing pain, stiffness, swelling, and tenderness in the joints. Due to incomplete understanding of its pathogenesis, management has classically been directed at relieving symptoms in the short term, with no treatment capable of stemming the long-term progression of joint damage. Recently, tumour necrosis factor-α inhibitors (TNFi's) have revolutionized inflammatory arthritis treatment because of their ability to act on targets driving inflammation. As a result, most patients treated with TNFi's have significant reductions in disease activity and joint damage. Although randomized controlled trials (RCTs) have been instrumental in demonstrating this effect, observational studies examining the effectiveness and sustainability of TNFi's have been lacking. Such studies add value by ascertaining the long-term effects of an intervention in a highly generalizable population. Using an observational study design, our objective was twofold: to compare the efficacy of a first course of TNFi therapy in three forms of inflammatory arthritis (rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS)), and to compare the first-course efficacy of three widely used TNFi's (infliximab, etanercept, and adalimumab) within each of RA, PsA, and AS.

Methods: A retrospective cohort study design was used. All RA patients included met the 2010 ACR/European League against Rheumatism (EULAR) classification criteria for RA; all PsA patients included met the 2006 classification criteria for PsA (CASPAR); and all AS patients included met the 2009 Assessment of Spondyloarthritis Society (ASAS) classification criteria for AS. Efficacy was measured using the proven surrogate marker of drug survival. Crude TNFi survival was compared using Kaplan-Meier curves with log rank testing, and TNFi survival adjusted for several relevant covariates was compared using Cox regression with hazard ratios (HRs) for treatment termination.

Results: 332 patients were eligible for the analysis (114 RA, 58 PsA, and 160 AS patients). Crude TNFi survival was significantly greater in AS patients compared to RA (p = 0.028) or PsA (p = 0.045) patients. Both crude and adjusted TNFi survival was greater in RA patients taking adalimumab vs. etanercept (p = 0.010 and HR = 0.34 (95% confidence interval (CI) 0.14-0.80)). Male AS patients had superior TNFi survival than did female AS patients (HR = 0.51 (95% CI 0.27-0.95)).

Conclusion: This study helps to validate two key findings observed in previous studies: superior TNFi survival in AS vs. PsA and RA patients, and superior TNFi survival in male vs. female AS patients.

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"Factors Affecting Physicians' Confidence in Diagnosing Pediatric Rheumatic Diseases in East Africa"

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Objectives: With a limited rheumatology workforce in East Africa, the majority of pediatric rheumatic diseases are managed by primary care providers and non-rheumatology specialists. We evaluated physicians' confidence in diagnosing rheumatic conditions at Gertrude's Children's Hospital, the largest Pediatric Center in Nairobi, Kenya. We tested (1) the impact of physician demographics, country of education, level of specialization, and number of years in practice on their confidence in performing a MSK exam, and (2) whether physician's confidence in performing a MSK exam correlated with the physician's report of number of cases of Juvenile Idiopathic Arthritis (JIA) and/or connective tissue diseases (CTD) previously diagnosed.
Methods: Twenty two physicians affiliated with Gertrude's Children's Hospital completed a survey indicating physician demographics, country of education, level of specialization, and number of years in practice. In addition, they graded the level of self-perceived confidence in performing an MSK exam and the type and number of specific rheumatic conditions ever diagnosed. The survey was conducted in English, the working language of Gertrude's Children's Hospital.
Results: Data was obtained from generalists (general pediatricians and medical officers) (57%) and pediatric subspecialists (43%). Thirteen males (59%) and 9 females (41%) with an average of 22±13 years in practice completed the survey. Sixty two percent of the physicians were trained in Kenya exclusively, while 38% received training abroad. Twelve physicians (55%) reported low confidence in performing a MSK exam. The majority reported low confidence in diagnosing specific rheumatic conditions (68% physicians had low confidence in diagnosing JIA and 82% in diagnosing CTD). We did not find any definite correlations between higher physicians' confidence in performing a MSK evaluation and sex, country of education, specialization, number of years in practice or number of rheumatic cases they self-reported as having diagnosed, but the precision of our analyses may be limited by the small number of subjects. As predicted, in univariate statistics, higher confidence in performing a pediatric MSK exam correlated with higher self-perceived confidence in diagnosing inflammatory arthritis (Kappa=0.727, 95%CI 0.441-1), distinguishing mechanical vs inflammatory MSK conditions (Kappa=0.723, 95%CI 0.431-1), and diagnosing JIA (Kappa=0.530, 95%CI 0.168-0.892).
Conclusion: In a large pediatric referral center in East Africa, many primary care physicians and non-rheumatology specialists lack confidence in diagnosing rheumatic diseases. Further studies are required to evaluate the tools that might enhance the skills and confidence of physicians in performing the MSK examination to ultimately optimize the recognition and treatment of children with rheumatic diseases in East Africa.

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The Prevalence of Inflammatory Eye Diseases in Rheumatologic Conditions: Results from a Meta-Analysis

Jacqueline Hayworth (University of Toronto, Toronto); Janet Pope (St. Joseph's Health Care, London)

Objectives: This meta-analysis investigated the prevalence of ocular involvement in inflammatory rheumatic diseases to determine the frequency and type of eye involvement.

Methods: Medline, Web of Science and Cochrane databases were searched up to July 8, 2014, to identify full text publications related to inflammatory rheumatologic diseases and associated ocular conditions. Disease terms included; antiphospholipid syndrome, juvenile arthritis, rheumatoid arthritis, Sjogren's Syndrome, still's disease, giant cell arteritis, systemic lupus erythematosus, sarcoidosis, connective tissue disease, polychrondritis, scleroderma, myositis, polyarteritis nodosa, inflammatory bowel disease, ulcerative colitis, crohn's disease, spondyloarthropathy, ankylosing spondylitis, reiter's syndrome and vasculitis. For eye involvement terms were; ocular disease, conjunctivitis, keratoconjunctivitis sicca, xeropthalmia, uveitis, eye hemorrhage, eyelid disease, lacrimal apparatus disease, lens disease, cataract, glaucoma, opthalmoplegia, optic neuritis, papilledema, orbital disease, retinal artery occlusion, macular degeneration, macular edema, retinal detachment, retinitis, chorioretinitis, retinal vein occlusion, retinal neovascularization, scleritis, iridocyclitits, choroid hemorrhage, blindness and amaurosis fugax. Data regarding the rates of various ocular complications were extracted. Random effects models pooled rates to estimate the frequency of each complication in the included rheumatic diseases.

Results: Most of the 7124 studies were excluded, leaving 263 for full review. Preliminary pooled prevalence rates from these revealed the most commonly reported ocular manifestation in ankylosing spondylitis, Behcet's disease and juvenile idiopathic arthritis to be uveitis, at rates of 22.1%, 41% and 18.8%, respectively. Dry eye was the most prevalent ocular complication of rheumatoid arthritis and systemic lupus erythematosus, and was seen in 31.6% and 29% of patients respectively.

Conclusion: Extra-articular manifestations of inflammatory rheumatic diseases frequently complicate the ocular health of afflicted individuals. Although the rates vary, an awareness of potential complications can aid in early identification and treatment of these rheumatic complications.

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Parents' Perceptions of Health Care Professionals Support in the Transition of their Youth with Rheumatic Disease from Pediatric to Adult Care

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Objectives: Youth with a chronic disease must prepare for the transition from pediatric to adult healthcare. Parents play a vital role in supporting their youth through the transition process. The objectives of this study were to examine parents' perceptions of: 1) the process of transitioning from pediatric to adult health care for their youth with a rheumatic disease; 2) the strategies that health care professionals (HCPs) employ or could employ to assist parents in gaining the skills to enable promotion of self-care and independence in their youth throughout transition.

Methods: Using a qualitative approach and Appreciative Inquiry (AI), interviews were conducted with 9 parents of 6 youth with chronic rheumatic disease. A purposeful sample of parents of youth (15-21 years of age; 4 pre- and 2 post-transfer) was selected. Their experiences of caring for their youth, their role in promoting independence and self-management, and the support they have received from HCPs in the transition process were examined. Strategies to enhance parental support through the transition process were explored. A focus group with 4 of the parents verified the findings and suggestions for practical application. Findings were analyzed using thematic analysis.

Results: Four predominant themes emerged: 1) loss of control, 2) parents desire for knowledge and tools to enhance their involvement in transition, 3) the need for an inclusive, formal, defined transition process and 4) sustainability of transition practice changes through a restructuring of services (e.g. overlapping of services between pediatric and adult care as the time of transfer draws closer) and provision of education and skills for HCPs. Parents also voiced a desire to have an active role in the planning and implementation of transition. Current strategies viewed as working well included: youth attending appointments on their own; appointments with pediatric and adult care providers at the time of transfer; discussions about substance use and sexuality; and emotional support and provision of information. Parents suggested improvements including HCPs discussing the purpose of their youth attending appointments independently and more routine assessments around family coping. Parents would like to see parent and adolescent support groups, utilization of a systems navigator, and an environment exclusively geared towards adolescents.

Conclusion: Through the AI interview process parent participants were able to recognize helpful interventions within the pediatric system, however, they identified areas on which to build and had ideas for interventions that could enhance transition for their youth and themselves.

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JOINTS Study: Joint MD/pharmacist pilOt project to Increase adhereNce to RA TreatmentS

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Objectives: To determine the value and feasibility of a one-on-one pharmacist-led intervention on medication adherence in patients with active rheumatoid arthritis (RA) exhibiting treatment reluctance.

Methods: 24 subjects with active RA and verbalized treatment reluctance were recruited from rheumatology practice (JP) to attend one-on-one educational session with study pharmacist (LC, MC). One hour face-to-face session was followed by 1 or more supportive telephone conversations, frequency determined by patient need. Patients were surveyed initially as to educational needs and support required for adherence to recommended RA treatment. Medication reconciliation/consultation was completed, and study pharmacist contacted community pharmacist to inform them of medication changes and RA treatment plan. Calls were made to participants to assess treatment adherence. Patients were later assessed with exit questionnaire. The patient's clinical status was determined by study rheumatologist before and after pharmacist intervention. A drug history was obtained from patient at the end of study to determine actual medication list.

Results: Twenty-one of 24 patients (88%) referred to the program were seen by study pharmacist. 88% patients female, average disease duration 6.6 years, 75 % seropositive. Of the 21 who completed the study, 18 patients (86%) had positive outcome of treatment adherence (defined as remaining on therapy agreed to with treatment team, or else having contacted treatment team to indicate issues), including 12 who reached a low disease state. 100% of patients who attended pharmacist-led sessions felt they were valuable or very valuable. Average CDAI at entrance to study was 32 , declining to 16 at exit (for those completing study). The main reasons for lack of success were being lost to follow-up or choosing not to follow the advice of the MD or pharmacist. Total time spent by study pharmacists was 1.5 hours per patient including phone calls.

Conclusion: This project indicates that, in active RA patients who were treatment reluctant but willing to meet one-on-one with study pharmacist, treatment adherence can be achieved in 86% of cases over 6 months. Without this intervention, many of the patients stated they would not have been able to adhere to therapy. Those who did persist with treatment all had either good response to the selected therapy, or were willing to proceed to further treatment. The intervention was simple, easy to reproduce and required minimal space or time. Consideration for using similar approach in preselected treatment-averse patients may provide a useful tool to improve therapy adherence and outcomes in active RA patients.

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Effect of Age at Menopause on Disease Presentation in Early Rheumatoid Arthritis: Results from the Canadian Early Arthritis Cohort

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Objectives: Studies suggest that hormonal states affect disease characteristics in women with rheumatoid arthritis (RA). This study investigated how age at menopause affects disease presentation in women with early RA comparing premature menopause vs. normal age of onset.
Methods: This was a study of post-menopausal women with early RA under age 65 at time of enrollment in the Canadian Early Arthritis Cohort (CATCH) which is an incident cohort of suspected or proven early RA at multiple sites across Canada. RA-related disease characteristics in women who had early age at menopause (Early Menopause [EM], age at menopause < 45 years) were compared to those who had usual age at menopause (Usual Menopause [UM], age at menopause ≥ 45 years). T-tests were used for continuous variables and Chi-square tests for categorical variables. Multivariate logistic regression analysis was used to adjust for age, smoking, education, and use of exogenous hormones.
Results: A total of 534 women were included; 93 were in the EM group. The age at RA-onset was similar between groups. The EM group had higher mean patient global and pain scores and was more likely to be RF positive and meet 1987 ACR criteria for RA. Using multivariate logistic regression, the EM group was more likely to be RF positive (OR 2.2 [95% CI 1.3-3.8], P=0.005); using multiple imputation, they were more likely to be ACPA positive (OR 1.7 [95% CI 1.0-2.7], P=0.03) and seropositive (RF or ACPA positive, OR 1.9 [95% CI 1.1-3.4], P=0.02). Symptom duration, joint counts, DAS28, HAQ and inflammatory markers did not differ between groups.
Conclusion: Early age at menopause, compared to usual age at menopause, is associated with seropositivity in women with early RA.

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Educating Rheumatologists May Lead to Measuring More Disease Parameters and Treating to a Target in Psoriatic Arthritis and Spondyloarthropathy. Results from the Metrix II Study

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Objectives: To determine if education improved measurements and treating to a target in psoriatic arthritis (PsA) and spondyloarthritis (SpA).

Methods: Rheumatologists volunteered for this accredited, ethics approved program. A chart audit was performed on patients from each participant (10 with each PsA and SpA). A needs' assessment followed by an investigators meeting occurred and comparative chart audits were provided for each participant. Then 8 months later a repeat chart audit was done on serial patients with PsA and SpA who were recently seen in practice and a comparison group of rheumatologists who did not participate provided chart audits, all using standardized forms. This was followed by a final investigators meeting where new data were presented for performing outcome measurements and treating to a target. Comparative chart audit results were provided for individuals pre and post educational intervention and also compared to controls without the intervention. It was decided a priori that a 10% mean change in the frequency of performing measurements could be relevant.

Results: Nine participating rheumatologists performed a comparative chart audit feedback and educational intervention and 3 rheumatologists who performed chart audit as a comparison group. At the initial meeting the data on the performance of several physical examination measurements in SpA revealed that many were unhelpful in the management. Data were provided on earlier interventions and treating to a target in PsA improving outcomes and less data were present for SpA in the literature. After the intervention, for PsA, there was no change in performing SJC (96%) , TJC (91% vs. 95%), ESR (74% vs. 70%) and CRP (79% vs. 73%). However, MD (79% vs. 89%) and patient global (65% to 75%) increased allowing for more scores to be calculated, but HAQ decreased (76% to 56%). Less patients in the PsA group stopped methotrexate and less were using biologics and steroids. Both groups measured joint counts and inflammatory markers frequently (>70% of patients) in SpA whereas Schober's was done in approximately half and joint counts >90% in SpA. In SpA, measuring the Schober's increased (35% to 53%) but other physical examination measures decreased. MD global and BASDAI assessments were unchanged but were more frequent than the control group. There were no major treatment differences pre and post intervention or compared to the control group.

Conclusion: Measuring occurred more for global assessments in PsA and less for some physical examination variables in SpA. Treatment was slightly different pre and post intervention.   Supported by a CIORA grant

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Estimating Benefits from Immunesuppressive Treatment in Diffuse Cutaneous Systemic Sclerosis: Data from the Canadian Scleroderma Research Group

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Objectives: To determine the efficacy of immunesuppressive treatment over 1 year in early diffuse cutaneous systemic sclerosis (dcSSc) in an incident cohort study.

Methods: DcSSc patients with less than 3 years disease duration and at least one year of data enrolled in the Canadian Scleroderma Research Group (CSRG) database were included. Regression analyses for achieving at least minimal important differences (MID) for 5 outcomes (modified Rodnan skin score [MRSS], MD and patient global assessments, pain, and function as measured by the Health Assessment Questionnaire [HAQ]) over one year were done to determine baseline predictors of change and if immunesuppressive treatment yielded the attainment of the MID.

Results: One hundred twenty-five patients (mean age 52.3 years; 79.2% female) of 1434 in the CSRG database were eligible with a disease duration of 1.6 (SD 0.7) years. Twelve received prednisone alone and 23 in combination with immunesuppressives; 38 received immunesuppressives alone (27 on methotrexate, 5 on cyclophosphamide and 6 on mycophenolate mofetil). The percentage of patients who achieved MID were: 40.4% for pain, 54.1% for PTGA, 39.5% for MDGA, 32.7% for HAQ and 36.1% for MRSS. Variables associated with MID at one year were often the baseline variable and for some outcomes, age; sex, smoking, restrictive lung disease and treatment type. Despite univariate analyses illustrating that some outcomes were associated with treatment, treatment with immune suppressives was not found to be associated with achieving MIDs in multivariate analyses.

Conclusion: Treatment was associated with achieving a MID change at 1 year at the univariate level, but not when using multivariate models. These observational data do not support improvement with immune suppressives over one year but there could be confounding by indication. Using observational data, it is difficult to find a treatment effect in early dcSSc.

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A Review of Canadian Rheumatology Association Summer Studentships Demonstrates Positive Attitudes of Students for a Career in Rheumatology

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Objectives: There is a shortage of rheumatologists in Canada. The Canadian Rheumatology Association (CRA) has been attracting medical students to the discipline of rheumatology for more than a decade with clinical CRA summer studentships and for 6 years with research summer studentships. These have been sponsored by AbbVie (Abbott) and Roche and in past by Merck. The objectives were to determine medical student satisfaction with the program and the proportion who became rheumatologists due to the exposure.

Methods: Data from the CRA summer studentships including annual surveys to successful students asking about attitudes and satisfaction were analyzed. Additionally the number of students who studied in their first or second year of medical school and who would be at least PGY4s now were calculated to determine the proportion who were in or beyond rheumatology training.

Results: There were usually 20 clinical and 13 research students per year. There have been 283 medical students in the program since 2004. We have had many successes in both adult and pediatric rheumatology where this program was the tipping point for entering a rheumatology training program. Twelve of 159 (7.5%) eligible students have become rheumatologists and four more are applying to rheumatology. Overall, students were extremely satisfied with their summer experience (Example: The studentship made my summer research possible, and for that I am extremely grateful because I was surprised how much I liked it and am now seriously considering a career in Rheumatology.); 88% in the CRA-Roche research studentship said they would consider rheumatology as a career option and 84% of the clinical students strongly agreed that they would be interested in pursuing a career in rheumatology. All of the recent 19 CRA-AbbVie summer students strongly agreed the studentship was a valuable experience (19/19) and 18/19 would recommend this to other medical students. In general, the trainees said that their mentor would strongly influence their future career choices. Most of the CRA-Roche research students have had presentations/publications.

Conclusion: This program is invaluable for attracting trainees early into rheumatology. Trainees are more apt to consider a career pathway if they have early exposure. It is imperative that this program continues. The ability to have a clinical and a research experience attracts different students. Some students said they would like to have more contact after their experience with rheumatologists including learning about local grand rounds and guest speakers. We should systematically maintain further contact with interested trainees.

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Evaluating the Effect of Combination Therapy with Uricosuric Agents and Xanthine Oxidase Inhibitors versus Xanthine Oxidase Inhibitor Monotherapy on Serum Urate Levels: A Systematic Review

Jesse Heyland (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Division of Rheumatology, Edmonton)

Objectives: Gout is a crystalline arthropathy caused by an immune response to monosodium urate crystals within the synovium. Patients with refractory gout or intolerance to therapeutic doses of hypouricemic agents may benefit from a combination of a xanthine oxidase inhibitor and an uricosuric agent. Given the limited information on combination therapy, a systematic review was performed to evaluate the effect of uricosuric agents used in combination with xanthine oxidase inhibitors in comparison with xanthine oxidase monotherapy in treatment of patients with hyperuricemia and/or gout.

Methods: EMBASE, MEDLINE, Scopus, Proquest Theses and Dissertations, and the International Pharmaceutical Abstracts were searched for randomized controlled trials and observational trials. Trials focusing on patients with nephrolithiasis or urate nephropathy were excluded. Risk of bias was evaluated using the Newcastle Ottawa Scale for observational studies and the Cochrane Risk of Bias Tool for randomized controlled trials. The primary outcome was change in serum urate and secondary outcomes included impact on gouty flares, resolution of tophi, and adverse effects.

Results: After removing duplicates, 2367 papers were identified. After the abstract and title screen, fourteen papers were selected for full paper review, including three randomized controlled trials and eleven cohort studies. The mean age of the combination and monotherapy groups were 55.4 years and 58.2 years respectively. The study duration ranged from 4 days to 64 months. On average, combination therapy was able to decrease serum urate by an additional 16% in comparison with xanthine oxidase inhibitor monotherapy. Twelve studies including a total of 431 patients favored combination therapy over xanthine oxidase inhibitor monotherapy for reduction of serum urate. Two studies including 142 patients favored xanthine oxidase inhibitor monotherapy. Reports of important disease associations including tophi, acute gouty flares, chronic kidney disease and hypertension were not consistently reported across the studies. Both therapies were generally well tolerated.

Conclusion: Combination therapy of uricosuric agents and xanthine oxidase inhibitors appeared to be more favorable than monotherapy for lowering serum urate. Important limitations included small sample sizes, heterogeneity in the outcomes collected between studies, variability in study duration and medication dosing. In this climate of novel and expensive therapeutic agents with marginal clinical benefits, we would advocate for more robust studies to evaluate the effect of combining these relatively inexpensive efficacious classes of medication to optimize treatment of refractory gout.

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Premenopausal Females with Trisomy 21 and Gout: A Case Series and Review of the Literature

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Objectives: Gout classically presents in men and post-menopausal women and is not usually seen in pre-menopausal women or children. We present two cases of gout in pre-menopausal female Down syndrome patients with a review of the literature.

Methods: The charts of two patients with gout were reviewed after obtaining consent from the patients. A literature search was conducted using MEDLINE and the reference sections of relevant papers. Search terms included "Down syndrome + Gout", "Premenopause + Gout," and "Hypothyroidism + Gout."

Results: Two female patients were identified as having aspiration proven gout. Patient 1 is a 25 year female with symptoms extending back to 15 years of age. Her ongoing risk factors for gout included use of low dose aspirin and furosemide for management of her cardiac comorbidities, as well as hypothyroidism. Patient 2 is a 35 year old female who developed recurrent gouty flares beginning with podagra at age 30. Her risk factors for gout included use of low dose aspirin and furosemide, hypothyroidism, and secondary amenorrhea. Neither patient had chronic kidney disease, a significant family history of gout, significant alcohol intake, or a high-purine diet. Once diagnosed appropriately, both patients were well controlled with allopurinol.

In addition to being at increased risk of medication-induced hyperuricemia, hypothyroidism, and menstrual abnormalities, studies have shown that enzymes involved in early purine metabolism may upregulate uric acid production in Down syndrome. A combination of these factors likely led to the development of recurrent gout in these two cases.

Conclusions: Gout should be considered on the differential diagnosis of pre-menopausal patients with Down syndrome.

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Causes and Outcomes of Markedly Elevated Levels of C-Reactive Protein (CRP)

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Objectives: CRP has widely replace Erythrocyte sedimentaion rate as a marker of inflammation, infection, or tissue damage. The causes of markedly elevated CRPs have not been well established. This study will analyze the causes and outcomes of patients with markedly elevated CRPs.

Methods: We retrospectively reviewed adult cases with markedly elevated CRPs (more than 10 times normal or >100mg/L) in both inpatients and outpatients at a large referral centre over a 2 year period (2012-2013). Electronic and paper health records, in addition to telephone patient contact were used to determine characteristics, diagnoses, and outcomes of patients.

Results: Over the 2 year period, 40,843 CRPs were done, of which 9385 (5325 cases) were elevated and 839 (2%) were markedly elevated (range 100.1-576mg/L). For patients with CRP >100mg/L, the average age was 63 (18-101years) and 50.2% were male. The majority of cases of markedly elevated CRP were associated with infection (465 cases or 55.4%) including 38 cases of septic arthritis. Other disease states associated with markedly elevated CRP were rheumatologic disease (9.1%), other inflammatory conditions (5.2%), malignancy (5.1%), multiple causes (3.8%), drug reactions (1.7%) and other conditions (2.0%). A definitive diagnosis could not be established in 17.6% of cases. Of cases with CRP > 250mg/L (144 patients), only 8 were rheumatologic (6/8 crystal-induced arthritis); and of CRP > 300mg/L (72 cases) only 4 were rheumatologic (1 GCA, 3 crystal-induced arthritis). Above 350mg/L all 18 patients had infection, except 1 patient with polyarticular gout (CRP 361mg/L). 567 patients (67.6%) were hospitalized; of which 72 were treated in intensive care. Most rheumatologic patients (52.6%) remained outpatients, whereas the majority of patients with other diagnoses were hospitalized (78.1% with infection - 100% with multiple diagnoses). Hospitalization was longer and mortality was highest in patients with malignancy (37.2% mortality) and in those patients with multiple diagnoses (21.9% mortality) (vs. infection 9%, rheumatologic 3.9% mortality).

Conclusion: The majority of patients with markedly elevated CRPs have infection. Rheumatologic conditions account for only 5% of CRPs above 200mg/L (none above 361mg/L) and these are mostly due to crystal-induced arthritis. This data could help health professionals in the evaluation and management of patients with markedly elevated CRPs.

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IgA Cutaneous Purpura Post-Renal Transplantation in a Patient with Long Standing IgA Nephropathy: Case Report & Literature Review

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Background: IgA vasculitis (IgAV/ Henoch–Schönlein purpura (HSP)) is a small vessel vasculitis mainly affecting the pediatric population. IgA nephropathy is due to deposition of IgA antibodies in renal mesangium. IgA nephropathy and IgAV have long been considered related conditions; however the development of IgA vasculitis is uncommon in renal transplant patients with IgA nephropathy.

Objectives: (1) To describe the case of a patient with renal biopsy proven IgA nephropathy, who developed IgA cutaneous vasculitis for the first time two years post renal transplant after being treated with tacrolimus, mycophenolate mofetil and prednisone. (2) To perform a literature review of cases of IgA vasculitis after renal transplant due to isolated IgA nephropathy.

Methods: Chart review of one patient. Embase and Medline search was completed using the keywords: "IgA Vasculitis", "HSP vasculitis", "IgA nephropathy", "renal transplant", "prednisone"

Results: Case Description: 56 year old patient with renal transplant secondary to IgA nephropathy treated with prednisone, mycophenolate mofetil and tacrolimus. Two years post-transplant developed an acute onset of abdominal pain, palpable purpuric rash over the lower extremities and multiple swollen painful joints, following a gradual reduction in prednisone dose from 20mg to 5mg daily. Skin biopsy revealed IgA vasculitis and subsequent renal biopsy revealed recurrent IgA nephropathy. Literature review revealed the presence of only two similar cases. The first case was in a 69 year-old man who developed IgA vasculitis post renal transplant when his prednisone regimen was stopped. The second case occurred in a 49 year-old female who developed IgA vasculitis post renal transplant, 10 days after the annual seasonal influenza vaccine.

Conclusions: This is the third documented case of cutaneous IgAV after renal transplant due to isolated IgA nephropathy. While cutaneous vasculitis post renal-transplant is generally due to infections or drug reactions, it is important to recognize that it may herald the recurrence of underlying renal disease. The proper timeline for gradual tapering of prednisone or continuous use of the medication to prevent recurrence of IgA nephropathy or establishment of IgAV needs to be further evaluated.

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Does Methotrexate Lower Serum Uric Acid Levels? Data from the CATCH Cohort

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Objectives: Methotrexate is the cornerstone DMARD in the treatment of rheumatoid arthritis. The exact mechanism of action is elusive, but it is thought that the anti-inflammatory effect is related to increase in adenosine levels. Upon further analysis of this pathway, it is possible that methotrexate may be increasing the adenosine levels by blocking its' natural conversion to uric acid. The purpose of this project is to determine if methotrexate lowers serum uric acid levels in patients with rheumatoid arthritis.

Methods: A retrospective cohort analysis using data from the CATCH cohort was performed. All patients with a history of methotrexate use in the setting of early rheumatoid arthritis (ERA) diagonsis were included. Serum uric acid measurements from study visits were examined. Patients were identified according to methotrexate usage, baseline and follow-up serum uric acid levels. Patients with ERA who did not receive any methotrexate for treatment were used as comparator controls.

Results: Thirty-two ERA patients on methotrexate therapy with serial serum uric acid measurements were identified. In this group, the mean pre-methotrexate baseline serum uric acid level was 297 ± 94 µmol/L with a mean post-methotrexate serum uric acid level of 263 ± 66 µmol/L (single tail T-Test p 0.0487). The control group of ERA patients not taking methotrexate during this time had a mean baseline serum uric acid level of 278 ± 80 µmol/L and a follow-up level of 273 ± 74 µmol/L (one tail T-Test p 0.376).

Conclusion: Methotrexate is fundamental in the treatment of ERA and it is thought to work through increase in adenosine levels. By this postulated mechanism of action, uric acid levels were shown to be decreased in a clinical setting for patients taking methotrexate for ERA.

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High BMI Negatively Affects Patients' Ability to Achieve Sustained Remission in Early RA in a Multicenter Canadian Cohort

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Objectives: To determine if patients with early RA (ERA) with normal body mass index (BMI 20-25), low BMI (<18.5) or high BMI (≥ 25) are less likely to achieve sustained remission (susREM) in an early RA (ERA) cohort.

Methods: Initial BMI and disease activity (DAS28) prospectively measured over 3 years in patients with ERA from the Canadian Early Arthritis Cohort (CATCH). Multivariate regression using GEE was used to assess the odds that patients with extreme BMIs, based on World Health Organization (WHO) categories 1-6 (Cat1-6) would be less likely to achieve susREM defined as DAS28<2.6 x 2 at consecutive visits.

Results: 944/2524 eligible patients with available BMI and ≥2 consecutive DAS28 over 3 years formed the study cohort. Only 15(2%) of patients were underweight (Cat1). More ERA patients are overweight (34%) or obese (31%), (65% overall) compared to the national average of 47%. Characteristics of patients in the 6 BMI categories were studied. Patients with high BMI were older (p=0.0001), more often female (p=.001) with worse function at baseline by HAQ-DI (p=.001). Those with very low or high BMI had higher CRP (p=0.0004) and ESR (p=0.001), and those with low or normal BMI were more often smokers (p=0.0001). Patients in the highest BMI categories had higher Patient Global Assessments (PtGA) (p-0.03) and pain (p=0.04), though only PtGA remained an independent predictor of susREM. Physician's Global assessments (MDGA) did not differ between groups (p-value =0.9). There was no significant difference in ACPA (p=0. 16), RF positivity (p=0.26) symptom duration (p=0.66), or DAS-28 (p=0 06) at study entry and no difference in steroid (p=0.3) or methotrexate (MTX) use (p=0.9) over the first 3 months. In the multivariate analysis only low or normal BMI patients could achieve susREM. Obesity was an independent risk factor for poor outcome with an OR of .5 for Cat 5 (95% CI .3-.67) and an OR of .36 for Cat 6(95% CI .24-.53). Early MTX use, not smoking, and achieving a low disease activity state (LDAS) quickly increased the odds of susREM ((OR 1.72, 95% CI (1.43-2.05), OR 1.52, 95% CI 1.23-1.87), (OR 5.36, 95% CI 4.57-6.29).
Conclusion: Both obesity and overweight status decreases the probability of achieving sustained remission, with highest risk in the morbidly obese. Early use of MTX, an early response and non-smoking status improve the odds of sustained remission independent of BMI. BMI should be considered among the modifiable risk factors for poor RA outcomes.

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MRI Results from the Avert Study: A Randomized, Active-Controlled Trial to Evaluate Induction of Remission and Maintenance of Drug-Free Remission using Abatacept in Combination with Methotrexate or as Monotherapy in Patients with Early RA

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Objectives: To assess joint damage progression by magnetic resonance imaging (MRI) in pts with early RA from the AVERT study who were treated with ABA + MTX or ABA monotherapy, compared with MTX alone.

Methods: MTX-naïve, anti-CCP2+ pts with early RA (active synovitis in =2 joints for =8 weeks, DAS28 (CRP) >3.2 and onset of symptoms within =2 yrs) were included. Pts were randomized to 12 mths of weekly SC ABA 125 mg + MTX, ABA 125 mg monotherapy or MTX alone. Pts with DAS28 (CRP) <3.2 at Mth 12 entered a 12-mth withdrawal period with no treatment. All pts with protocol-defined flare after Mth 15 could receive open-label ABA + MTX. Gadolinium-enhanced MRI of the dominant hand-wrist was performed on all pts at baseline and at Mths 6, 12, 18 and 24. Changes from baseline in synovitis, osteitis and bone erosion MRI scores were assessed up to Month 18 in this analysis.

Results: During the 12-mth treatment period, benefits in synovitis, osteitis and erosion scores were numerically greater for ABA + MTX than for MTX alone; while numerically greater benefits were observed in synovitis and osteitis scores for ABA monotherapy than for MTX alone. A post hoc analysis of pts who maintained DAS28 (CRP) <2.6 to Mth 18 after treatment withdrawal did not show evidence of MRI progression compared to Mth 12 in those pts.
Conclusion: Consistent with the clinical outcomes of the AVERT study in pts with early RA with high disease activity, there were greater reductions in MRI outcomes with abatacept treatment in combination with MTX than with MTX alone. MRI changes with abatacept monotherapy treatment were intermediate between abatacept in combination with MTX and MTX treatment alone.

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What Role Do Patient Educators Play in Medical Students' Development as Medical Professionals?

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Objectives: Patient educators are one of many teaching modalities used to foster principles of patient-centred care in medical students. In addition to serving as effective teachers of clinical skills, patient educators have been shown to aid in development of patient-centredness by sharing their unique knowledge and personal stories around their illness experiences. In our published 2014 study of pre-clerkship students' perspectives of patient educators, five themes were identified.
Methods: In this longitudinal follow-up study using the phenomenology approach, five focus groups were conducted with fourth-year medical students and first-year residents who wrote reflections for the original study. We explored how perspectives on patient educators may have changed, and determined which themes identified during pre-clerkship remained relevant to clinical trainees. Learners were asked to give their impressions of patient educators and to react to the themes from the original study. The transcripts were then analyzed thematically.
Results: This study identified two new themes: "value of early clinical experience" and "development of professional identity". Themes from the pre-clerkship study that increased in relevance for clinical trainees included: "seeing condition within context of patients' lives", "recognizing patients' needs" and "recognizing complexity of practicing medicine". "Patients supporting students' learning" was equally relevant and "seeing the patient as a capable part of the team" received mixed responses.
Conclusion: While insights from pre-clerkship experiences with patient educators carry over into early clinical training, we identified shifts in emphasis and new perspectives. Further exploration of how patient educators help develop trainees' professional identity and patient-centredness is warranted.

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Induction of Clinical Remission followed by Drug-Free Withdrawal with Abatacept Combination and Monotherapy in Early RA: Results from the Avert Study over 18 Months

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Objectives: To assess ABA + MTX or ABA monotherapy in inducing clinical remission at 12 mths and then maintain it following rapid withdrawal of all RA treatment in pts with early RA.
Methods: MTX-naïve, anti-CCP2+ pts with early RA were included. Pts were randomized to 12 mths of weekly SC ABA 125 mg + MTX, ABA 125 mg monotherapy or MTX alone. Pts with DAS28 (CRP) <3.2 at Mth 12 entered a 12-mth withdrawalperiod with no treatment. All pts with protocol-defined flare after Mth 15 could receive open-label ABA + MTX. The co-primary endpoints compared ABA + MTX and MTX alone in pts achieving DAS28 (CRP) <2.6 at (1) 12 mths and (2) both 12 and 18 mths. ABA monotherapy was also assessed.
Results: 351 pts with early RA, highly active disease and poor prognosis (at baseline: mean RA duration of 0.56 yrs, mean DAS28 (CRP) of 5.4, mean HAQ of 1.4; 95.2% RF+ and anti-CCP2+) entered the study. At 12 mths, 60.9, 42.5 and 45.2% achieved DAS28 (CRP) <2.6 (ABA + MTX, ABA and MTX, respectively). Odds ratio (OR; 95% CI) for ABA + MTX vs MTX: 2.01 (1.18, 3.43) with p=0.01 and for ABA vs MTX: 0.92 (0.55, 1.57). At most time points, efficacy on signs and symptoms in the ABA monotherapy arm fell between the ABA + MTX and MTX arms based on DAS28 (CRP) as well as other measures. Following treatment withdrawal, most pts discontinued due to increase in disease activity (177/223; 79.4%). Rates of pts achieving DAS28 (CRP) <2.6 at both 12 and 18 mths were 14.8, 12.4 and 7.8% for ABA + MTX, ABA and MTX, respectively; OR (95% CI) for ABA + MTX vs MTX: 2.51 (1.02, 6.18), p=0.045 and for ABA vs MTX: 2.04 (0.81, 5.14). In a post hoc analysis, pts who maintained DAS28 (CRP) <2.6 at both Mth 12 and 18 tended to have numerically lower baseline mean symptom duration, DAS28 (CRP), HAQ score and DAS28 (CRP) <2.6 over time during the treatment period compared with pts who achieved only DAS28 (CRP) <2.6 at 12 mths.
Conclusion: In this study, in pts with highly active early RA with poor prognosis, abatacept + MTX resulted in significantly higher rates of remission and comparable safety vs MTX alone at 12 mths. At most time points, abatacept monotherapy was more effective than MTX alone.

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Patient Reported Stress Negatively Impacts Composite Patient Reported Outcomes in Early Rheumatoid Arthritis

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Objectives: We aimed to evaluate the effect of patient self-reported stress on composite patient reported outcomes (PROs) at disease presentation and over one year in patients with early rheumatoid arthritis (ERA).

Methods: Patients participating in CATCH (Canadian Early Arthritis Cohort), a prospective multicenter study reported on exposure to major stresses or life events within one year of study entry. We examined differences in PROs and changes of the RAPID 3 score over time using generalized estimating equations and survival curves of RAPID3 remission.

Results: Of 1596 patients 51% reported experiencing physical or psychological stresses 1 year prior to study entry. Compared to those not reporting stress, stress patients were younger (54.9 vs.52.6; P<0.001), more often female (77% vs. 69%; p<0.001), living alone (17% vs. 12%, P=0.005), and fewer had completed high school (41% vs. 48%, P=0.01). They reported significantly higher pain, fatigue, worse function, and worse global disease assessment. The RAPID 3 Scores (95% CI) were worse at study entry 4.2 (4.1-4.4) vs. 4.7 (4.5-4.8)(p=<0.001) and after 1 year were 2.3 (2.1-2.4) vs. 2.1 (1.9-2.2)(P=0.045). Multivariate analysis showed a significant negative effect of psychological stress on RAPID3 scores at baseline and over time. Fewer patients with a history of exposure to any stress achieved RAPID 3 remission (p<0.0017).

Conclusion: Exposure to stress within the preceding year of study negatively affects PROs at disease presentation and over time in ERA. A history of stress should be considered when interpreting patient reported composite disease activity measures such as the RAPID3.

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Management of Perioperative Tumor Necrosis α Inhibitors in Rheumatoid Arthritis Patients Undergoing Arthroplasty: A Systematic Review and Meta-analysis

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Objectives: Tumor Necrosis Factor α inhibitors (TNFi) are widely used in patients with RA (Rheumatoid Arthritis) undergoing orthopedic surgery, yet its optimal perioperative management is unknown. The objective of this study is to systematically review the available literature regarding perioperative TNFi management and post-operative infections and to formulate clinical practice recommendations for the optimum perioperative use of TNFi.

Methods: A librarian assisted search was conductedusing the following key terms: Rheumatoid Arthritis, TNF- α , antirheumatic agent, surgical site infections (SSI), surgery/infection, arthroplasty, anti-TNF- α , infliximab, etanercept, adalimumab, risk factor, perioperative, postoperative. Studies were included if most patients had RA, age ≥ 18, and were undergoing orthopedic surgery. The intervention was use of TNFi. The comparison group was patients not treated with TNFi. The outcome of interest was surgical site infection. Study quality was assessed using Oxford Center for Evidence Based Medicine Levels of Evidence. No randomized controlled trials were available; high quality cohort studies (2b) and case control studies (3b) were included.

Results: A total of 2,004 studies were found. After abstract review, 30 studies met inclusion criteria; 11 studies met criteria with low risk of bias, representing 3730 RA patients with recent exposure to TNFi's (TNF+) and 4,307 with no recent exposure . There was no consistent reporting of corticosteroid use. A forest plot is presented. Patients in the TNF+ group for all orthopedic surgeries had a 2.47-times greater likelihood of developing SSI compared to patients in the TNF- group (pooled random-effects OR=2.47 (95% CI = 1.66 to 3.68)]. A smaller group of cases with only total hip and total knee replacement were also meta-analyzed; here patients in the TNF+ group had a 3.08-times greater likelihood of developing SSI compared to patients in the TNF- group (pooled random-effects OR=3.08; 95% CI=0.87, 10.95; p=0.08). The Begg-Mazumdar test and Egger test did not reveal any evidence of publication bias (p = 0.88 and p=0.91, respectively).

Conclusion: Perioperative exposure to TNFi is associated with a higher risk of infection in all orthopedic surgery, although the risk in total hip and knee replacement is less clear. These data support withholding TNFi prior to orthopedic surgery.

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Gitelman's Syndrome: An Unusual Risk Factor for Hyperuricemia and Gout

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Gitelman's syndrome is a rare renal disease caused by a mutation in the thiazide-sensitive sodium chloride co-transporter, which has manifestations that mimic the effects of a thiazide diuretic. Gout is a common disorder characterized by hyperuricemia and arthritis most commonly seen in men and post-menopausal women with well described risk factors and metabolic comorbidities. We report an unusual case of gout in a young woman with Gitelman's syndrome contributing to the development of hyperuricemia.

A 27 year-old woman presented with chronic, intermittent right first toe pain and swelling. She was previously diagnosed with Gitelman's syndrome on the basis of hypokalemia, metabolic alkalosis, and acute renal failure. She also had a history of psoriasis and heavy alcohol intake. Synovial fluid aspirate revealed chalky-white tophaceous material with significant uric acid crystal burden under microscopy. Serum uric acid levels were elevated at 759 μmol/L. A diagnosis of chronic tophaceous gout was made, and managed by cessation of alcohol ingestion and urate lowering therapy using Febuxostat. At one-year follow up she was asymptomatic and uric acid levels had normalized to 141.0 μmol/L.

The diagnosis of gout in a young woman prompted investigations for secondary causes. Review of the literature did not reveal any association between Gitelman's syndrome and gout, or recognize it as a risk factor. However, studies have established that thiazide diuretics increase serum uric acid levels. In conclusion, several factors exacerbated hyperuricemia in this young woman including the thiazide-like effect of Gitelman's syndrome, renal failure, and excess alcohol ingestion. This case adds to the understanding of the pathophysiology of gout, and highlights Gitelman's syndrome as a rare but potential risk factor.

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Independent Validation of the 14-3-3η Assay: A Diagnostic RA Marker

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Objectives: 14-3-3η is a mechanistic biomarker that is complementary to rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) for the diagnosis of early and established rheumatoid arthritis (RA). The 14-3-3η ELISA has received Health Canada approval. The purpose of this study was to transfer the method to an automated platform, to support routine operation in a high volume clinical testing environment.

Methods: The Health Canada approved 14-3-3η ELISA relies on a manual testing method with a calibrator range of 0.16 to 20 ng/mL. Accuracy, intra and inter-assay variation were assessed using 5 serum samples with 14-3-3η titres ranging from negative to above the upper limits of the assay. To assess accuracy, recoveries were measured using 5 replicates and compared to pre-determined 14-3-3η values. Intra-day precision was determined with 20 replicates while inter-day precision was performed over 6 days with 5 replicates. Method linearity was conducted using 5 serially diluted samples within analytical measureable range (AMR). The cut-off for the normal population was performed in 147 presumed healthy individuals, setting the cut-off at the 89th percentile. For equivalency testing the automated and manual method (reference) were compared, each at different sites by testing 121 rheumatoid arthritis samples for 14-3-3η. Spearman correlations were performed to assess the relationship between 14-3-3η titres at both sites.

Results: Results of accuracy, intra and inter-assay testing were all within pre-specified parameters. Mean bias was 111% with a range of 104%-119%. Intra-and inter-day precision were all within the 20% target. Linearity recoveries was highly correlated delivering a R2 >0.99 and a mean accuracy of 86% from 0.20-16.3 ng/mL. Testing of the 147 presumed healthy individuals confirms the manufacturer's positivity cut-off of >0.19ng/ml. Mean 14-3-3η values generated at the two sites were compared and yielded a 90% qualitative concordance. Of the 58 samples within the AMR, the Spearman correlation revealed a statistically significant correlation of r=0.97, p<0.0001 between the two sets of results.

Conclusion: The 14-3-3η ELISA was successfully transitioned to an automated platform and demonstrates strong technical and clinical performance.

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The Incidence and Risk Factors for PsA in Patients with Psoriasis – A Prospective Cohort Study

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Objectives: We aimed to estimate the incidence of PsA in a prospective cohort of psoriasis patients and to identify risk factors for the development of PsA in these patients.

Methods: The setting is a prospective longitudinal cohort study of psoriasis patients without arthritis at baseline. Patient with a diagnosis of psoriasis confirmed by a dermatologist were enrolled. All patients were evaluated by a rheumatologist at baseline to exclude the presence of inflammatory arthritis or spondylitis. All study participants were then reassessed annually for signs of arthritis. Information was collected about their lifestyle habits, co-morbidities, skin activity and medications. Patients who developed inflammatory arthritis or spondylitis were classified as PsA if they fulfilled the CASPAR criteria. We summarize the results of 7 years of follow up and report the annual incidence of PsA from the onset of psoriasis that was estimated using an event per person-years analysis. Cox proportional hazard model, with fixed and time-dependent explanatory variables was used to compute the multivariate relative risk (RR) for incident PsA adjusting for sex and age at onset of psoriasis.

Results: The results of the 559 patients who were recruited from January 2006 and followed until December 2013 are summarized. The mean duration of follow up was 3.5 ± 1.9 years per person. A total of 51 patients developed PsA since enrollment. The annual incidence rate was 2.7 (95% confidence interval (CI) 2.1, 3.6) PsA cases per 100 psoriasis patients. The distribution of the time to development of PsA was fit with an exponential model, suggesting a constant hazard rate. The following variables predicted the development of PsA: Severe psoriasis (RR 5.4, p=0.006), low level of education (high school incomplete vs. college/university RR 5, p=0.005, high school complete vs. college/university RR 3.3 p=0.049), use of retinoid medications (RR 3.4, p=0.02), psoriatic nail pitting (RR=2.3, p=0.005), inflammatory eye disease (RR 4.3, p=0.03), pustular psoriasis (RR 4, p=0.04) and thyroid disease (RR 2.4, p=0.036).

Conclusion: The incidence of PsA in patients with psoriasis is higher than previously reported. More severe phenotype of psoriasis and several co-morbid conditions predict the development of PsA in patients with psoriasis.

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Cardiovascular Risk Assessment in Moderate to Severe Inflammatory Arthritis Patients

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Objectives: Increased cardiovascular (CV) risk is well-recognized in rheumatoid (RA) and psoriatic arthritis (PSA) patients and is felt to be secondary to inflammation and traditional CV risk factors. This study evaluates self-reported traditional CV risk factors in a population of moderate to severe inflammatory arthritis (IA) patients on biologic therapies.

Methods: A questionnaire evaluating features of IA disease, treatments and self-reported traditional CV risk factors was mailed to patients who had consented to be part of the RAPPORT database (Rheumatoid Arthritis Pharmacovigiliance Program and Outcomes Research in Therapeutics). Patients were asked complete fasting labs and were invited to participate in the Cardiovascular Risk Reduction Clinic for Inflammatory Rheumatic Diseases (CRRC – IRD). Questionnaire results were entered into a Microsoft excel database with descriptive statistics.

Results: Two-hundred and fifty (250) questionnaires (M:F 76:174) were returned, mean age 60 (SD 12), with 224 rheumatoid arthritis (RA) and 26 psoriatic arthritis (PsA) patients. Mean disease duration was 17.5 years (SD 13.5). Any life-time exposure (past/current) to IA-related medications included: prednisone 139(55%); non-steroidal anti-inflammatories (NSAIDs) 166(66%); TNF inhibitors 244(96%); rituximab 22(9%); abatacept 25(10%); and tocilizumab 11(4%). The mean number of traditional CV risk factors (age, gender, hypertension, diabetes, dyslipidemia, smoking, personal history of CV disease, family history of early CV disease and obesity) per patient was 2.53(SD 1.51). Four patients who had not reported diabetes had HBA1c in the diabetic range. History of CV disease was reported by 34(14%) patients (M:F 21:13). The mean age at first CV event was 54 years (SD 14) with14 (41%) patient reporting onset at an early age. The mean number of CV risk factors per patient was 4.03 (SD 1.42). The Fasting cholesterol profile (mmol/L) [mean (SD)] included: total cholesterol 4.5 (1), LDL 2.9 (0.8), HDL 1.5 (0.4), total cholesterol/HDL 3.5 (0.9).

Conclusion: Moderate to severe IA patients have a large burden of CV disease. CV risk reduction and aggressive IA management strategies should be emphasized. Untreated comorbidities remain an important problem that should not be overlooked.

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Characterisation of Mucosal-Associated Invariant T (MAIT) Cells in Ankylosing Spondylitis Patients

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Objectives: Ankylosing spondylitis (AS) is a rheumatic disease that is characterized by axial skeleton inflammation, often comorbid with peripheral arthritis. In addition, up to 70% of AS patients have subclinical gut inflammation. Previous research has demonstrated overlapping genetic risk loci between AS and inflammatory bowel disease (IBD), suggesting a pro-inflammatory role of the gut in AS. The gut associated cells, such as the innate lymphoid cells, that may mediate inflammation in AS are being uncovered. Mucosal-associated invariant T cells (MAITs) have an invariant T cell receptor and are restricted by the MHCI-like molecule MR1. These cells represent 10% of circulating CD8+ T cells, require gut microbes for maturation and have been implicated in IBD. In this study we aimed to characterize the frequency and function of these cells in AS patients.

Methods: Peripheral blood mononuclear cells (PBMCs) from 50 AS patients and 28 healthy controls were isolated using Ficoll-paque density centrifugation. Synovial fluid mononuclear cells were isolated from 8 patients. These cells were surface stained to identify MAITs (CD3+CD161hiVα7.2+CCR6+) and were further stimulated with PMA/ionomycin to assess granzyme B, IL-4, IL-17A, IFNγ and TNFα. Samples were analyzed by multicolor flow cytometry.

Results: We observed a marginal reduction in the frequency of circulating MAITs in AS patients, as compared to healthy controls (2.00% vs. 2.59%, $p<0.05$), with no alteration in the SF. Activation status as judged by CD69 was similar in AS and healthy control PBMCs, however was greatly elevated in the SF (11.0% vs 80.0%, $p<0.001$). In the periphery, MAIT cells displayed elevated IL-17A (8.40% vs 5.85%, $p<0.05$) and reduced IFNγ (74.3% vs 84.0%, $p<0.01$). MAITs in paired blood-SF showed equal IL-17A, increased granzyme B and reduced IL-4, IFNγ and TNFα.

Conclusion: MAIT cells are recruited to arthritic joints of AS patients where they are active. In the arthritic joint, MAIT cells display an aberrant activation profile with a lowering of selected cytokines and enhanced lytic potential. These results suggest a role for MAIT cells in AS and demonstrate a SF-mediated alteration of MAIT function.

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A Signal of Improvement in Lupus Disease Activity at 3 Months Predicts Further Valid Improvement at 6 Months

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Objectives: In patients with active disease, physicians look for an early signal in response to treatment to guide their therapeutic decisions. We aimed to determine if a signal of improvement in disease activity at 3 months predicts further improvement at 6 months.

Methods: Consecutive active lupus patients who attended the clinic between 2012 and 2014 were screened for inclusion. Patients were included if they: 1) had at least 1 of the following 5 Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) clinical organ systems active (vascular, renal, musculoskeletal, serosal or skin); central nervous system was excluded and 2) started or increased prednisone therapy and/or immunosuppressants. Outcome measures: Disease activity was measured by SLEDAI-2K at all visits and by SLEDAI-2K Responder Index 50 (S2K RI-50) at 3 months. Study definitions: Signal of improvement by SLEDAI-2K or S2K RI-50 is defined as any decrease in SLEDAI-2K or S2K RI-50 scores at 3 months respectively. Study endpoints: Based on the change in the total SLEDAI-2K score (baseline – last visit), each of the patients at last visit were grouped as: 1) improved (SLEDAI-2K decreased by ≥4) and not improved (SLEDAI-2K decreased <4). First, we identified the patients with SLEDAI-2K signal at 3 months and those who did not have a SLEDAI-2K signal were further evaluated for possible S2K RI-50 signal. Patients with signals were reevaluated at 6 months to determine if they had further improvement.

Results: 87 patients with mean SLEDAI-2K at baseline visit was 8.9±5.1 were studied. 90% were female, age at baseline visit was 40.0±12.4 and disease duration was 13.2±9.6years. Signals of improvement: Of the 87 patients, 54 (62%) had a SLEDAI-2K signal at 3 months. Of the 33 patients who did not have a SLEDAI-2K signal, a S2K RI-50 signal was identified in 11 (33%) patients. Study endpoints: Of the 54 patients with SLEDAI-2K signal at 3 months, 57% patients improved at 6 months. Of the 11 patients with S2K RI-50 signal at 3 months, 54 % improved at 6 months.

Conclusion: A signal of improvement at 3 months predicts further improvement in disease activity at 6 months. S2K RI-50 signal at 3 months, which is not discerned by SLEDAI-2K, predicts improvement in half of the patients at 6 months. S2KRI-50 can identify non responders at 3 months who will respond at 6 months.

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Impact of Patient's Priorities on the Management of Systemic Lupus Erythematosus

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Objectives: Systemic Lupus Erythematosus (SLE) greatly reduces the quality of life (QoL) and satisfaction with life of affected patients. SLE patients have numerous unmet needs and feel misunderstood by their health care providers. The aim of this study was to explore the priorities of SLE patients and the impact of these priorities on disease management.

Methods: Participants were ≥18 years of age, satisfied the ACR classification for SLE and were recruited from the Canadian Network for Improved Outcomes in Systemic Lupus Erythematosus (CaNIOS) Cohort at the CHU de Québec or by their respective rheumatologist. A qualitative approach based on audio-recorded focus groups was used to collect data. Interview guides were prepared prior to the meetings by an expert panel including: a resident in internal medicine, a psychologist, a rheumatologist, and nurse. The open-ended questions covered SLE patient priorities, the means of conveying these priorities to the medical team, and the impact of these priorities on their disease management. The transcriptions were coded by 2 analysts using different techniques: 1) a qualitative data analysis software (NVivo 10) and 2) manual analysis. The analytic approach was based on the grounded theory.

Results: Nineteen participants attended 3 focus groups in 2 different sites (university and community-based). Participants were female, ages ranged from 18 to >70 with a majority between 30 and 59 years of age. The average disease duration was 8.8 (7,7) years, ranging from 1 to 23 years, 68% were married/with spouse and 63% were employed. Five priorities were identified: 1) management of disability, in particular, loss of energy that prevents full engagement in daily activities, relationships, and social roles; 2) management of the unpredictable nature of SLE including, preventing flares and worsening of their condition, employment and financial issues associated with chronicity; 3) management of side effects; 4) access to information about lupus and support resources, in particular, support groups; 5) access to health care (improved communication between physicians, shorter wait times and longer time allotted with physicians.

Conclusion: It was difficult for SLE patients to articulate their priorities. Most probably this was due to the fact that there were so many to articulate. Health care providers need to develop strategies and communication tools to help SLE patients identify their priorities and help them in the self-management of their disease.

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A Case of Mucous Membrane Pemphigoid

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Objective: Mucous membrane pemphigoid (MMP) is a rare, immunobullous disease with predominant mucosal involvement and is caused by autoantibodies against components of the dermal–epidermal junction. Previously, this condition was known as 'cicatricial pemphigoid'; this term now exclusively refers to a clinical variant with scarring skin lesions and without significant mucous membrane involvement. Clinically, MMP most commonly affects the oral cavity (85%), followed by the ocular conjunctiva, skin, nasal cavity, anogenital area, respiratory tract, and esophagus. Laryngeal involvement is seen in 12% of patients, of which, the supraglottis is the most commonly affected site. MMP may have clinical, laboratory, or pathologic findings in common with other rheumatic conditions, including systemic vasculitis and bullous systemic lupus erythematosus. These commonalities may lead to diagnostic confusion, and thus, the importance of reviewing the diagnosis and treatment of this rare disease.

Method: The clinical features and response to treatment in a patient with MMP, is reported.

Results: A 43 year old female with a past medical history of chronic sinusitis and extensive nasal scarring presented with conjunctival injection, symblepharon, vesiculopapular rash, and respiratory distress with stridor secondary to supraglottic stenosis. A diagnosis of MMP was made on the basis of her clinical presentation (involvement of multiple mucosal sites with scarring) and histopathologically with direct immunofluorescence microscopy showing linear immunoglobulin G and complement component 3 (C3) deposits at the basal membrane zone. Initial treatment included ophthalmic and high-dose systemic corticosteroids and monthly intravenous immunoglobulin. This treatment appears to have halted further progression of her disease, but there has been minimal symptomatic improvement with regards to the supraglottic stenosis.

Conclusions: MMP is a chronic, inflammatory blistering disease. Complications related to scarring can be both vision- and life-threatening. Systemic immunosuppressive therapy is necessary for patients with progressive disease. Increased recognition of this rare disease is crucial, as its presentation can be clinically similar to other rheumatic conditions. Multidisciplinary collaboration is often necessary for the diagnosis and appropriate treatment of MMP.

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Prevalence of Cardiovascular Disease and its Associations with Disease Severity in Rheumatoid Arthritis Patients – Data from the Ontario Best Practices Research Initiative (OBRI)

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Objectives: Cardiovascular disease (CVD) is a major comorbidity and the leading cause of death among patients with rheumatoid arthritis (RA). Our aim was to compare the demographics, patterns of medication use, and disease activity in RA patients with and without CVD at cohort entry and 12 months of follow-up.

Methods: Physician and patient-reported data were collected from the Ontario Best Practices Research Initiative Rheumatoid Arthritis Registry (OBRI- RA), a clinical registry of RA patients followed in routine care. CVD was defined as the presence of coronary artery disease (CAD), congestive heart failure (CHF), hypertension (HTN), arrhythmia, stroke, transient ischemic attack (TIA), and/or other heart disorders upon entering the registry. Patient demographics, clinical characteristics, socioeconomic status and treatment regimens were compared between CVD and non-CVD patients at cohort entry using Chi- square and t-tests. Mean disease activity and functional status scores at cohort entry and 12 months of follow-up were estimated by generalized linear regression, adjusting for confounders, including age, sex, smoking, socioeconomic factors, disease activity at cohort entry (for 12-month follow-up analyses only), and RA duration.

Results: Among 2226 RA patients, 360 (16.2%) had CVD at cohort entry. Among which, 101 (28.1%) had CAD, 51 (14.2%) had arrhythmia, 12 (3.3%) had CHF, 28 (7.8%) had CVA, 8 (2.2%) had PE, and 160 (44.4%) had other/unspecified CVD. Patients with CVD were older (66.7 ± 10.1 vs. 53.6 ± 12.9yrs, $p<0.0001$), had longer RA duration (10.6 ± 11.8 vs. 8.1 ± 9.0yrs, $p<0.0001$) and more extra-articular features (35.0% vs. 26.3%, $p<0.05$). Male sex, lower education and income, lack of private insurance, and smokers were more frequent among CVD patients ($p<0.001$ for all). CVD patients were more frequently treated with glucocorticoids (34.9% vs. 28.3%, $p<0.05$) but less frequently with NSAIDs (29.9% vs. 49.3%, $p<0.05$). After adjusting for confounders, patients with CVD had higher RADAI and HAQ-DI, but similar DAS28, CDAI, or SDAI scores at cohort entry, and at 12 months, CVD patients were more likely to have significantly higher DAS28 and ESR than patients without CVD.
Conclusion: At cohort entry, RA patients with CVD have worse disease activity (RADAI) and functional status (HAQ-DI). At 12 months of follow-up, disease activity (DAS28) remained worse among CVD patients. The higher ESR found in CVD patients may suggest heightened systemic inflammation. The lower use of NSAIDS may be due to their known CVD risks, but the higher utilization of glucocorticoids may require further investigation.

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Feasibility of a Pilot-test to Measure Construct Validity and Test-retest Reliability of the "Which Health Approaches and Treatments are you using?" (WHAT) Questionnaires

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Objectives: Complementary and alternative medicine (CAM) is commonly used by children with juvenile idiopathic arthritis (JIA). Since no validated questionnaires exist to assess its use in JIA, we have developed and assessed the content validity of the child self-report and parent proxy-report "Which Health Approaches and Treatments are you using?" (WHAT) questionnaires. The objective of this study was to describe the feasibility of a pilot-test to measure construct validity and test-retest reliability of the WHAT questionnaires.
Methods: A purposive sample of 4 youth with JIA (8 to 18 years) and their parents was recruited at the Children's Hospital of Eastern Ontario to complete a questionnaire package including the self-report and proxy-report WHAT questionnaires, separately, once at the rheumatology clinic and then again in their home 4 to 7 days later to determine test-retest reliability. They also participated in an interview to determine the understandability and feasibility of the WHAT questionnaires at the clinic. Parents and youth then completed a daily diary monitoring CAM use for two weeks, followed by the WHAT questionnaires for a third time, to determine construct validity. Participants were asked about the feasibility and helpfulness of the WHAT questionnaires at the end of the study.

Results: Youth took a mean of 9.9 minutes (SD=4.1 minutes) and parents took a mean of 8.3 minutes (SD=3.1 minutes) to complete the WHAT questionnaires in clinic. All participants found the questions of the WHAT questionnaires to be essential and clear. However, three youth and three parents mentioned that the format of a table asking about CAM use should be simplified. Families completed questionnaires on time, with one reminder sent for each package, except for two families who needed up to two additional reminders. All participants felt that the questionnaires were useful to complete (e.g., facilitating communication within the family and with health providers), but did not change their perception of CAM.

Conclusion: Modifications to the format of the WHAT questionnaires may help to ensure their understandability and feasibility. Rigorous validity and reliability testing with adequate reminders may facilitate communication about CAM within the family and with health providers. SD: Standard deviation

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Are Patients' Views Considered when Developing Instruments for Assessing Shared Decision Making Outcomes? A Systematic Review to Inform Rheumatology Practice and Research

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Objectives: Shared decision making (SDM) is an essential component of high quality care in rheumatology. However, it is currently unclear which instruments should be used to evaluate SDM outcomes in rheumatology. To ensure the clinical relevance of these instruments, patients' views should inform their development. Therefore, we sought to describe the extent of patient involvement in developing and validating instruments that assess SDM outcomes, as well as their applicability to rheumatology practice.

Methods: A systematic review was conducted using the search strategy and methods of a systematic review of SDM instruments published by Scholl and colleagues in 2011. We updated Scholl's electronic search on January 20, 2014, using PubMed and the Web of Science databases. Experts in the field of SDM were also consulted to identify relevant instruments. Two members of the research team independently screened the citations to identify instruments assessing SDM outcomes, and extracted information about patient involvement in studies reporting their development and validation, as well as their measurement properties. Methodological quality of the studies reporting measurement property testing of instruments was assessed using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist. Measurement properties of the instruments were rated using the Terwee criteria.

Results: A total of 684 citations were screened for relevance by title and abstract, yielding 10 citations that met the eligibility criteria. We identified five instruments, supplementing the nine already derived from Scholl's review. Of the 14 instruments, two considered patients' views of decision making in their development (i.e. Hip/Knee Osteoarthritis Decision Quality Instrument (HK-DQI) and COMRADE), and five included patients in their validation process (i.e. HK-DQI, Decisional Conflict Scale (DCS), SURE screening test, Decision Evaluation Scales, and perceived behavioral control subscale of the Theory of Planned Behaviour). Two instruments included rheumatology patients in their development or validation (the SURE screening test and the HK-DQI), but studies assessing their measurement properties did not meet all the COSMIN criteria for validity, reliability and responsiveness, and their measurement properties were indeterminate according to the Terwee criteria.

Conclusion: To date, six instruments considered patients' views of decision making in their development or validation process, and two of those included rheumatology patients. However, these were not thoroughly validated. Future studies should find effective ways to consider patients' views in the development and validation of SDM instruments, and should use a rigorous evaluation of measurement properties.

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Training the Rheumatologists of Tomorrow: The WOMAC Experience

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Objectives: Globally there is an increasing shortage of rheumatologists. Currently there are 371 rheumatologists in Canada, 147 of them in Ontario. This is approximately half the number needed. Recognizing this problem, nine post-graduate rheumatology programs across the country participated in a CRA/CIORA-funded qualitative study to determine how best to address this issue. Data from the two Ontario programs are presented.

Methods: Learners (undergraduates, junior and senior residents), faculty, and administrators associated with the rheumatology programs were interviewed or surveyed. The objective was to gather respondents' opinions of how rheumatology programs might increase the number of trainees, and what messages might be important to disseminate to achieve this goal. Data were examined for themes and patterns using Thematic Framework Analysis.

Results: Results were combined across sites. Faculty and administrators' views were similar and data were combined. There were 28 respondents from the two Ontario sites: 16 learners and 12 faculty/administrators. Twenty-one of these respondents completed the online survey and 7 were interviewed. Of the learners, most (50%) were rheumatology residents (PGY4-5) (all currently in training), 44% were junior residents (PGY1-3, nearly 75% of whom had completed a rheumatology rotation prior to the study) and one was an undergraduate. Both learners and faculty/administrators identified exposure as key to recruiting future trainees. Examples include undergraduate musculoskeletal (MSK) clinical skills courses, and information and networking sessions (eg.. "Joy of Rheumatology, "Rheumatology Weekend," "MSK Bootcamp"). Learners suggested increasing interest through general information sessions, undergraduate courses ("promote the specialty at the curriculum level – I didn't know about it until I did a rotation as a resident"), and rotations and observerships for undergraduates and junior residents. Faculty/administrators concurred, also noting the importance of introducing students early to the field. When asked about messages to attract future rheumatologists the learners suggested focusing on the variety of patients and diseases seen and the likelihood of a good quality of life as a practitioner. Faculty/administrators again agreed and also suggested mentioning the availability of jobs.

Conclusion: As part of a Canada-wide effort to increase the number of rheumatologists, learners, faculty and administrators of rheumatology programs have provided the insiders' view on how to meet this goal. The next step will be to form a country-wide working group to review suggestions and collaboratively develop material and methods to inform, recruit and educate potential trainees. Supported by a CIORA grant

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Statins and the Risk of Rheumatoid Arthritis - A Population Based Study from the General Practice Research Database

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Objectives: The immunomodulatory properties of statins, including in rheumatoid arthritis (RA), have been described. Although some observational studies suggest a lower risk of RA with statin exposure, robust estimates are lacking. Our aim was to assess the risk of new onset RA in people exposed to statins.

Methods: We conducted a cohort study with a nested case-control analysis in adults of at least 40-years of age in the General Practice Research Database. Subjects entered the cohort with a first-time statin prescription between 1997 and 2010 after at least 1 year of up-to-standard follow-up. Subjects with prevalent RA or previous immunomodulatory drug exposure were excluded. The cohort was followed until death, diagnosis of RA, or end of the study period. Cases were defined with one RA diagnostic code and a DMARD prescription or 2 diagnostic codes without an alternative diagnosis of arthritis, earliest of which was the index date. We selected 10 random controls for each case matching on gender, age at index date and year of cohort entry using risk-set-sampling. Each statin preparation was assigned a relative intensity based on the respective percent reduction of low density lipoprotein established in a meta-analysis of randomized controlled trials. Time-dependent exposure categories were defined as quintiles of duration-weighed average treatment intensity up to index date in controls. We used conditional logistic regression to compute the odds ratio of RA, an estimate of the hazard ratio (HR) when using a nested case-control approach, comparing high versus low intensity statin groups, adjusted for smoking status, body mass index, baseline cholesterol level, history of cardiovascular disease, non-iatrogenic hypothyroidism and previous history of other autoimmune diseases.

Results: Among 522,608 new statin users, there were 1357 incident RA cases that were matched with 13,570 controls. Mean age was 67+/-9.6, 60.8% were females and follow-up duration was 39+/-30 months. The adjusted HR of RA for the highest versus lowest intensity quintile was 0.75(95% confidence interval (CI) 0.61-0.93). The HR was 0.76(95%CI 0.58-1.02) when the analysis was restricted to include subjects with more than 80% compliance. After excluding RA cases diagnosed within the first year of statin treatment, HR was 0.80(95%CI 0.64-1.00).

Conclusion: This population-based cohort study of statin users suggests that the risk of RA is lower in subjects exposed to high as compared to low doses of statins. This finding may be of particular relevance in individuals at high risk of RA who require statin therapy.

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Improving Access to Rheumatologists: The Utilization and Benefits of an eConsultation Service

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Objectives: It is recognized that the burden of rheumatologic disease in Canada has surpassed the capacity of current rheumatologists. Locally, this has resulted in wait times of two to three years for non-urgent referrals. An innovative eConsult service (Champlain BASE) has been introduced in our region that enables the primary care provider to access specialist advice through a secure web-based eConsult system in lieu of a formal referral. As the impact of eConsults within rheumatology is not known, we have analyzed all rheumatology eConsults submitted to the Champlain BASE service since its inception to quantify the characteristics of referred cases and the impact on improving timely access to rheumatology advice.

Methods: 154 eConsults completed through the Champlain BASE service from May 9, 2011 to August 31, 2014 were reviewed. Demographic information was obtained from the eConsult database. Each eConsult was characterized based on the type of question asked, as well as the rheumatologic diagnosis or primary symptom. Rates of referral avoidance, as well as physician satisfaction and impact on patient care, were obtained from the mandatory end of case survey.

Results: Of the 154 eConsults reviewed, the average time to response from the rheumatologist was 2.8 days (median 1.9 days). In the majority of cases, time required for eConsult review and response by the rheumatologist was less than 10 minutes (ranging from less than 10 minutes to 20 minutes). The most common type of clinical question asked was treatment related (40%) or request for further direction (36%). The eConsults pertained to a diverse set of diagnoses, with osteoporosis being the most common (23%) followed by inflammatory polyarthritis (14%). In 38% of the cases, a referral to a rheumatologist was originally contemplated but was avoided due to the availability of the eConsult service. Feedback from primary care providers regarding the service was positive, with high or very high value ratings in 88% and 92% of cases with regards to clinical value and patient value, respectively.

Conclusion: While certain clinical questions necessitate a traditional face-to-face consultation, we have shown that there are clinical questions that can be answered within days through an innovative eConsult service while receiving excellent satisfaction ratings from referring primary care providers. The appropriate use of eConsults can improve timely access to rheumatologists, on average decreasing wait times to specialist response to 3 days, when compared with traditional referral-consultation process.

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Patient Priorities in RA Research – An Exploration of Patient Perspectives from those Enrolled in the Ontario Best Practices Research Initiative (OBRI) Clinical Registry
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Objectives: Patient experiences with rheumatoid arthritis (RA) symptoms, treatments, and rheumatology care are critically important in the assessment of treatment-effectiveness and quality of care for RA. Despite recommendations for more patient-centered research, measures to evaluate the effectiveness of RA therapies often fail to reflect patient priorities.[1] The Ontario Best Practices Research Initiative (OBRI) is a clinical registry focused on improving the quality of care and health outcomes of patients with RA through long-term data collection on therapies, clinical practices, and health-care utilization. Patient self-reported data is collected using structured interviews and validated questionnaires. These provide valuable data but may fail to reflect patient priorities and experiences. The objectives of this study were to explore patient priorities in RA research, identify gaps in OBRI data collection, and explore options for communication with patients.

Methods: RA patients enrolled in the OBRI clinical registry were invited to participate in one of three patient sessions in 2014 to provide feedback on how OBRI data collection could be improved to better capture patient needs/priorities. In small groups facilitated by a moderator, patients were asked to identify gaps in OBRI data collection and share experiences with RA and rheumatology care. Approximately 48 RA patients participated. After each discussion, patients completed a questionnaire on their use of social media.

Results: Four overarching themes were identified: 1) A need for research focused on patient experiences with RA including journeys to diagnosis, symptoms, treatments, side effects, and challenges/concerns; 2) A need for research into patient satisfaction with rheumatology care including rheumatologist accessibility, communication, and disease management; 3) A need for OBRI research addressing patient social support networks, strategies for coping with flares, diet and exercise, and the use of alternative therapies; and 4) A need for more information from rheumatologists on medication risks. Additionally, of those who completed the social media questionnaire, all (n=26) reported using email and some (n=15) reported using Facebook, however only (n=14) indicated a preference to communicate through email.

Conclusion: Patients expressed that some of their most important experiences are not captured through structured questionnaires, suggesting a need for mixed-methods RA research to capture qualitative and quantitative patient-reported outcomes. This study identifies patient research priorities and opportunities for improved care and communication.

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Relevant Determinants Influencing Walking Adherence among Older Individuals with Knee Osteoarthritis: Participant Exercise Preference (PEP) Pilot Randomised Clinical Trial

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Objectives: Osteoarthritis (OA) is the most common disabling disorder affecting joints, such as the knees and hips (Klippel et al. 2008) with over 4.4 million Canadians suffering from this joint disease (Statistics Canada, 2011). The main objective of this pilot RCT was to evaluate the effect of participants' exercise preference. We did examine the hypothesis that participants who follow their preferred aerobic walking program: 1) supervised (S) or 2) unsupervised (U), combined with a BI component, will be more encouraged and satisfied, thus enhancing their walking adherence through the 3-month study period, compared to individuals who do not obtain their preferred choice of aerobic walking program. We wanted to evaluate the potential influencing factors that would determine the adherence rates to an effective aerobic walking program after 3 months, among people diagnosed with knee OA.

Methods: This is a single blind RCT, based on a patient treatment preferences model (Cahill et al. 1996). Sixty nine adult individuals with OA were recruited in Ottawa. The selected participants were randomized to one of two groups: (1.1) a 9-month supervised community-based walking program with BI (WBS), or (1.2) a 9-month self-directed unsupervised walking program supplemented with a multifaceted BI (WBU). It was performed by analyzing the data collected from a survey related to the implementation of Ottawa panel evidence-based clinical practice guidelines for aerobic walking programs in the management of OA (Ottawa Panel 2012), using multifaceted interventions.

Results: Data analysis was oriented towards the interaction between 5 different factors, selected as more important to predict the adherence of elderly diagnosed with knee OA following a proven walking program, at 3 months. Participants who attended and completed at least 66% of the prescribed walking sessions were considered and included in the calculation of adherence (King et al, 1997). It is necessary to act on modifiable factors in enabling individuals with mild to moderate osteoarthritis of the knee, in order for them to benefit optimally from the positive effects of walking.

Conclusion: Older individuals with OA who received a supervised structured community-based aerobic walking program combined with a multifaceted BI (WBS) demonstrated greater adherence rate compared to a self-directed unsupervised/unstructured walking program supplemented with a multifaceted BI (WBU). It addresses questions of clinical and scientific importance to identify the main strategies to promote the long-term adherence of community-based walking program. Therefore, preference for improving adherence rates is an innovative approach that addresses a new knowledge gap.

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Good Agreement between the Framingham Laboratory and Non-Laboratory Calculators in Assessing Cardiovascular Disease Risk in Rheumatoid Arthritis Patients

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Objectives: The overall standardized mortality ratio for RA is approximately two and the excess mortality is mostly due to cardiovascular (CV) disease (CVD). Although CV risk (CVR) assessment using national guidelines is recommended for all RA patients the adherence to this recommendation is suboptimal. The lack of lipid data available at the time of the rheumatology consultation may limit the use of the Framingham Laboratory Risk Calculator (FLRC). We tested the agreement between the FLRC and a simpler-non-laboratory based CVD risk prediction model (i.e. Framingham office-based calculator FOBC) in estimating a patient's 10-year risk of developing cardiovascular disease.

Methods: Each of the FLRC and FOBC was calculated in a total of 75 consecutive RA patients assessed at the MUHC RA Program between July 2013 and July 2014.

Results: Participants were mostly female (76%), with a mean ±SD age of 59.6 ±16.1 years, and with established (disease duration: 7 ± 8.1 years) and seropositive (RF+ 65.3%; CCP+ 62.7%) RA. 12% of the patients were current smokers, 29% were treated for diabetes mellitus and 38.7% were on anti-hypertensive medications. According to the WHO classification criteria, 29.3% of the patients were classified as obese. Using the FLRC, 18.7% of the RA patients were classified as being at high risk of developing CVD, while 36% of the patients were at risk according to the FOBC. The agreement between the two calculators in identifying high-risk patients was moderate (kappa value of 0.580; p-value <0.001) however all the at risk patients according to the FLRC were classified as at-risk by the FOBC.

Conclusion: Despite the limitations of using the Framingham risk calculators in high CVD risk populations such as RA patients, FOBC could facilitate the calculation of risk in settings where lipid data is not readily available. This could thus allow physicians to expedite the implementation of treatment measures to improve CVD outcomes in RA patients. However, since FOBC is more conservative than FLRC more people would be classified as at risk by this calculator.

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Lipid-Lowering Therapy is underused in Patients with Rheumatoid Arthritis

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Objectives: Cardiovascular disease (CVD) is the leading cause of mortality in rheumatoid arthritis (RA). CV risk assessment, risk factor modification, and treatment according to national guidelines established for the general population are recommended for RA patients. We assessed a key component of risk factor management in RA, which is the treatment of dyslipidemia.

Methods: We used the "2012 Canadian Cardiovascular Society Guidelines for the Diagnosis and Treatment of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult" to risk-stratify RA patients and define indications for lipid-lowering therapy, within the McGill University Health Centre (MUHC) RA Program. A total of 75 consecutive RA patients assessed at the MUHC RA Program between July 2013 and July 2014 were included in the study.

Results: Subjects were mostly female (76%) and seropositive (RF+ 65.3%; CCP+ 62.7%) with a mean ±SD age of 59.6 ±16.1 years, and mean disease duration 7 ± 8.1 years. 12% of the patients were current smokers, 29% were treated for diabetes mellitus, 38.7% were on anti-hypertensives, and 29.3% were obese according to WHO criteria. According to the 2012 Canadian Cardiovascular Society Guidelines, 18.7% of the patients were classified as high risk, 26.6 % as intermediate risk, and 54.7% as low risk. Based on the Canadian recommendations, 38 (36%) of the 75 RA subjects studied would benefit from lipid-lowering therapy. Only 21 of these 38 (55%) were on any such agent.

Conclusion: A third of our RA patients fulfill treatment thresholds according to current national recommendations for lipid-lowering therapy. Only half of the patients that would benefit from lipid-lowering therapy are on statins. Future studies should address the reasons for the under treatment of dyslipidemia in RA.

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Development of an Arthritis Patient Charter

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Objectives: In 2014, the Canadian Arthritis Patient Alliance (CAPA) led the creation of an Arthritis Patient Charter (Charter), an update of the Arthritis Society's 2001 Canadian Arthritis Patient Bill of Rights. In the nearly 15 years since the Bill's original development, the landscape of arthritis and its care has changed significantly, and we wished to provide patients and their healthcare providers a new tool with which to stimulate conversation, and hopefully an overall better partnership and outcomes for patients. Along with rights associated with care, responsibilities for patients were also included. We will present the course of the Charter's development throughout 2014 and its subsequent launch in time for September's Arthritis Month.

Methods: CAPA drove this project with financial and in-kind support from arthritis stakeholders (including the Ontario Rheumatology Association, the Arthritis Society, the Arthritis Alliance of Canada, the Canadian Rheumatology Association, Arthritis Consumer Experts, Patient Partners, the Canadian Spondylitis Association, and some individual patients). One Board member acted as project manager and sought to include input and feedback for the Charter's development from all members of the arthritis community. Methods to achieve this included phone calls, in person meetings, email updates, and an online survey. Subsequent distribution and promotion of the Charter were achieved through CAPA's efforts and with substantial stakeholders help.

Results: An Arthritis Patient Charter (http://arthritispatient.ca/projects/arthritis-patient-charter/) was created with input from patients, family and friends, health care professionals, and not for profit and industry stakeholders. Through meetings (phone, in person) throughout the course of a year, the stakeholders outlined a draft Charter. Public feedback was sought through an online survey that was publicized by stakeholder networks (e.g. newsletters, social media, websites). The survey responses (>730) shaped the Charter wording and the Charter (postcard and poster versions in English and French) resides on the CAPA website and was delivered to Canadian Rheumatology Association members. In the same spirited capacity in which the Charter was developed, partners disseminated news about the Charter for September's Arthritis Month.

Conclusion: The Arthritis Patient Charter was created via collaboration by arthritis stakeholders in Canada. CAPA aims to help patients engage in more dialogue with their healthcare providers through this Charter, and ultimately for them to achieve better outcomes by understanding their arthritis care and their own responsibilities associated with that care.

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Identifying and Addressing Real and Perceived Barriers to Therapeutic Education Programs to Inform a New Model of Care

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Objectives: To identify real and perceived barriers to attending a classroom-based Therapeutic Education Program (TEP) for patients with Inflammatory Arthritis (IA); ii) To understand patient preferences regarding alternative technology-based methods of TEP delivery.

Methods: Individuals with IA referred to The Arthritis Program at Southlake Regional Health Centre are invited to attend a classroom-based TEP. This program runs for half a day, every day for 2 consecutive weeks and is offered monthly. To understand barriers to attending this program and preferences for alternative methods of TEP delivery, patients with IA were mailed questionnaires created. Respondents included individuals who elected not to participate in the program, those who attended less than half of the sessions, and those who completed the program. Questionnaires were piloted with a small group of participants to ensure face validity prior to mailouts. Questionnaire responses were entered into an SPSS database and frequency statistics were calculated.

Results: Questionnaires were returned by 103 individuals who attended all 10 in-class sessions (Group A), 24 individuals who attended between 0 and 4 sessions (Group B), and 33 individuals who never attended any session (Group C). The vast majority of respondents were female and over 45 years of age. The most common barrier to attendance for respondents in Groups B (67%) and C (76%) was time. Distance to the in-class sessions was the second most popular barrier for Group B (42%) and Group C (55%) respondents. The third most popular barrier was personal health status (Group B 46%, Group C 55%). Health status (28%), distance to the sessions (26%), and cost (24%) were listed as barriers that had to be overcome to attend the program by Group A participants. Pre-recorded, online e-learning interactive education modules were considered the most favourable alternative learning option with ≥64% of respondents in all groups expressing interest in this option. Pre-recorded in-class sessions available online and on-demand were also favoured by ≥59% of respondents in each group. Less than one third of respondents in each group said that they would participate in live online chatting with other RA patients as an electronic learning option.

Conclusion: Given the barriers identified by all respondents, time and distance being most popular, an alternative method of education delivery may increase access to information. For those who did not attend or attended few sessions, online interactive e-learning modules that can be viewed from home is the most popular alternative. Supported by a CIORA grant

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Does a Clinical Definition of Fragility Fracture Based on its Cause and Circumstances Adequately Classify Women with Characteristics Predisposing to Osteoporosis?
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Objectives: To identify the characteristics associated with a clinical definition of fracture type (traumatic or fragility) determined from the cause and circumstances of fracture, in a cohort of fractured women aged ≥50 years.

Methods: In the Recognizing Osteoporosis and its Consequences in Quebec programme, a cohort of recently-fractured women was recruited. At baseline, each fracture was defined as a fragility fracture (FF) or traumatic fracture (TF) based on the associated trauma. FF was defined as occurring spontaneously, from a fall from standing height, sitting, lying (<1m high), from missing three or fewer steps, from coughing or sneezing or from a movement outside of the normal range of motion. All other fractures were classified as a TF. Six to eight months following fracture, women were contacted to complete a follow-up questionnaire detailing personal and clinical characteristics related to osteoporosis (diagnosis, treatment, comorbidities, risk factors, etc.). To identify the characteristics related to the two distinct fracture types, a logistic regression model was constructed using a stepwise algorithm.

Results: A total of 2712 women (2079 FF and 633 TF) completed the follow-up questionnaires. Risk factors significantly associated with FF included (odds ratio; 95% CI) increasing age from 50 years of age (per year: 1.04; 1.02-1.05), smoking tobacco (vs never smoked: 1.47; 1.09-2.01), history of fracture after age 40 years (1.31; 1.05, 1.63), family history of fracture (1.25; 1.04-1.52), and having a low level of physical activity (<1200 kcal/week vs ≥3600 kcal/week: 1.65; 1.24-2.18). Interestingly, obese women (BMI>30 kg/m2) were more likely to experience a FF compared to those with a normal BMI (vs 18.5-25.0 kg/m2: 1.56; 1.21-2.01). Being socially deprived and less educated were also associated with FF.

Conclusion: A simple clinical definition of FF based on the cause and circumstances of fracture is useful for identifying fractures associated with well-known risk factors for osteoporosis. Moreover, although obesity is known to be associated with a higher bone mineral density, we observed that it was associated with an increased risk of FF.

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The Relationship between Body Mass Index and Level of Trauma in a Cohort of Women who have sustained a Fracture

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Objectives: To investigate the relationship between body mass index (BMI) and the level of trauma in a cohort of fractured women aged 50 and older.

Methods: In the Recognizing Osteoporosis and its Consequences in Quebec programme, a cohort of recently-fractured women was recruited. Information on circumstances of the fracture and skeletal sites were collected at baseline, and fractures were classified as low or high-energy trauma fractures. A low-energy trauma fracture was defined as occurring spontaneously, from a fall from standing height, sitting, lying (<1m high), missing three or fewer steps, coughing or sneezing or from a movement outside of the normal range of motion. All other fractures were classified as high-energy trauma fractures. Six to eight months following fracture, women were contacted to complete a follow-up questionnaire detailing personal and clinical characteristics related to osteoporosis. Bone mineral density (BMD) of participants who reported having had a BMD measurement within 2 years of the fracture event were obtained from patients' clinics. BMD data was imputed for women who did not have a BMD result available. To evaluate the association between BMI and the level of trauma, a multivariate logistic regression model including adjustment variables and an interaction between BMI and fracture site was constructed. Results were presented by fracture site category.

Results: The analysis included 2633 women who suffered a low- (n=2037) or high- (n=596) energy trauma fracture. Women who suffered a foot, ankle, tibia or fibula fracture were more likely to have experienced a low-energy trauma fracture if they were overweight (O.R. [95% C.I.] = 1.80 [1.20; 2.70]) or obese (O.R. [95% C.I.] = 2.91 [1.85; 4.58]) than if they had a normal BMI (Table 1). For the humerus and elbow fracture, women with an obese BMI tend more to have experienced a fracture following a low- than a high-energy trauma (O.R. [95% C.I.] = 2.08 [1.22; 3.55]). No significant association was detected between BMI and the level of trauma in women who suffered a hip/pelvis/femur or wrist/forearm fracture.

Conclusion: This study suggests that the association between BMI and level of trauma differs depending on the fracture site. For the foot/ankle/tibia/fibula or humerus/elbow fracture sites, a higher BMI is associated with a higher risk to experience a fracture following a minor than a major trauma in women aged 50 and older.

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Comparing Abatacept to Adalimumab, Etanercept and Infliximab as First or Second Line Agents in Patients with Rheumatoid Arthritis. Experience from the RHUMADATA® Clinical Database and Registry

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Objectives: The order of use of biologic agents is still a question for debate. Phase III trial data in MTX-IR patients show comparable efficacy results across biologic agents and limited head-to-head studies have been published. Registries offer a unique opportunity to prospectively monitor the effectiveness of these agents in a clinical setting. Objectives: To evaluate if patients with rheumatoid arthritis (RA) treated with abatacept after failure to either a first line agent (MTX-IR) or a second line anti-TNF agents (TNF-IR) have a different drug survival rate than patients similarly treated with adalimumab, etanercept or infliximab.

Methods: RA patients prescribed a first biologic agent after January 1st 2007 were included in the present analysis. Two cohorts were extracted. The first included all patients prescribed their first biologic agent, abatacept (ABA), adalimumab (ADA), etanercept (ETA) or infliximab (INF); the second included all patients failing their first biologic agent and switching to a second one. Baseline demographics for both cohorts included age, disease duration, HAQ-DI, fatigue and pain visual analog scale evaluation (VAS),tender joint count (TJC), swollen joint count (SJC), DAS 28 ESR and SDAI. Person-years of treatment were also compared across biologic agents. Statistical analysis was performed using SAS version 9.3. RHUMADATA® is a clinical database and registry used daily in clinical practice at the IRM and the CORQ.

Results: A total of 526 patients were analysed, 340 were included in the first cohort and 186 composed the second cohort. No clinically significant differences in baseline characteristics were noted between treatment groups. The 5 year retention rate of ABA, ADA, ETA and INF post MTX failure were 64%, 40%, 49% and 42% without significant statistical differences (Log-Rank p=0.29). Similarly, the 5 year retention rates for patients having failed a first anti-TNF agent are not statistically different (44% (ABA), 36% (ADA), 41% (ETA) and 16% (INF) (Log-Rank p=0.07)) except when comparing ABA to INF (Bonferroni adjusted log-rank p-value=0.04).

Conclusion: Abatacept, adalimumab, etanercept and infliximab after MTX failure have similar 5-years retention rates. Prescribing abatacept after failing a first anti-TNF agent offers a similar effectiveness as ETA and ADA, but a significantly better retention rate than INF.

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Therapeutic Exercises are Effective Strategies for Pain Management of Juvenile Idiopathic Arthritis

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Objectives: There is a need for high quality up to date evidence-based clinical practice guidelines for juvenile idiopathic arthritis (JIA) that are rigorously developed using structured and quantitative methods. To create guidelines for the use of physical activity in the management of JIA through the identification and assessment of existing randomised controlled trials and evidence-based research

Methods: The Ottawa Methods Group identified and assessed existing comparative controlled trials evaluating the efficacy of physical activity interventions on JIA. Evidence-based recommendations were endorsed by members of the Expert Panel with experience in juvenile rheumatology. Guideline recommended grades were determined according to experimental design, statistical significance, and clinical importance using a hierarchical alphabetical grading system. Included studies were assessed according to the PEDro scale to determine methodological quality.

Results: Five RCTs met the selection criteria and four were considered high-quality. Positive recommendations from the high quality studies included: 1) Pilates for improving health-related quality of life, pain, functional ability and range of motion (grade A), 2) individualised home exercise programs for improving quality of life and functional ability (grade A), 3) aquatic aerobic fitness for decreasing the number of swollen and tender joints (grade A), 4) and Cardio-Karate aerobic exercise for improving range of motion and number of active joints (grade C+).

Conclusion: The Ottawa Panel recommends physical activity such as Pilates, strength training, cardio-karate, individualised home exercise, and aquatic aerobic exercises for the management of JIA.

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What is the Therapeutic Validity of the Trials Involving Physical Activity in the Pain Management of Fibromyalgia?

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Objectives: Exercise therapy is recognized to be effective, relatively economical, easily accessible and widely used in clinical practice. The application and prescription of exercise vary and likely affect therapeutic validity. To evaluate the therapeutic validity of various exercise programs in high-quality RCTs in the management of fibromyalgia (FM) and explore whether therapeutic validity affected pain relief in FM patients.

Methods: The therapeutic validity on included RCTs was evaluated based on 1) the Consensus on Therapeutic Exercise Training (CONTENT) scale and 2) the 2013 American College of Sports Medicine (ACSM) recommendations for FM. The strength of evidence of the pain relief effect of the various exercise programs was also considered. Cohen's kappa coefficients with 95% confidence intervals were used to determine the relationship between therapeutic validity and effectiveness on pain relief.

Results: The CONTENT mean total score was 4.42 out of 9, demonstrating generally low therapeutic validity of the 28 included RCTs. Kappa statistic results showed poor concordance (k= 0.01) between statistical significant (p<0.05) pain relief values and achievement of ACSM criteria. There was poor concordance (Kappa values ranging between -0.6 to 0.57) for therapeutic validity and pain relief.

Conclusion: Therapeutic validity is low even amongst high-quality RCTs consisting of exercise therapy for the management of FM. This is mainly due to the incomplete descriptions of therapeutic application of the various exercise programs. Improved standardised reporting is recommended to identify optimal exercise therapeutic application for FM.

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Foot Imaging Study - Ultrasound is better than Clinical Exam at Detecting Synovitis
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Objectives: To compare clinical examination (CE) of tender and swollen joints with ultrasonographic findings of synovial thickening (ST) and power Doppler (PD) in metatarsophalangeal (MTP) joints in patients with early rheumatoid arthritis at baseline (i.e. is ultrasonography (US) better than clinical examination (CE) in detecting active or damaged joints?).

Methods: A total of 40 patients with newly diagnosed treatment naiive RA will be recruited from the clinics of Dr Maggie Larche and Dr Ed Keystone. Xrays, US and MRI, along with clinical joint counts and demographics will be conducted at baseline. In this interim analysis, 25 patients have completed baseline measurements. Comparative statistical analyses are used to compare CE to US scores at baseline.

Results: 84% of the patients were female with a mean age of 52 years. The mean baseline ESR was 23.5mm/hr (range 2-89) and CRP 17.4mg/dl (range 1.5-71.5).46% were RF positive, with 25% strongly positive; 58% were anti-CCP Ab positive, with 33% strongly positive. 11 joints had erosions detected by ultrasound (5.5%) 43% of joints (bilat MTP2-5) had synovial thickening on US, 16% had power Doppler signal; 16% had joint swelling detected by CE and 45.5% were tender. There was no correlation when comparing synovial thickening detected by US to swollen joint count by CE, either in individual MTPJs or as a group of 8 joints (MTP2-5 bilaterally).For right MTP2 r=0.302, p= 0.183, for right MTP2-5 r =0.221,p=0.045 and for bilateral MTP2-5 r=0.317, p= 0.00003). There was also no correlation between power Doppler and tender joint counts (r = 0.211, p = 0.006)

Conclusion: With no correlation between US findings and CE, US adds an extra dimension when examining the MTPJs in RA. The next step is to assess whether positive US findings predict erosions at 12 months.

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T Cell Epitopes Stimulating TGFβ in Patients with Systemic Sclerosis: Towards a Vaccine

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Objectives: The target of autoimmune insult in Systemic Sclerosis (SSc) may be HLA genes. HLA-sensitized individuals (through previous transplants, blood transfusions or pregnancies) awaiting renal transplantation have increased T cells responding to HLAclass 1 peptides (α3 and transmembrane regions) These responses are associated with chronic graft rejection and with chronic Graft vs Host Disease (GvHD). cGvHD has similar clinical findings to SSc. Hypothesis HLA peptides will stimulate cells from patients with SSc compared to healthy controls.

Methods: Peripheral blood mononuclear cells (PBMCs) from 23 patients with SSc were compared to 28 healthy controls PBMCs were stimulated with HLA α3 peptides. Cytokine and chemokine production was measured by ELISPOT analysis for TGFbeta, IL-6 and IL-17; and MCP-1 and MIP-1alpha),.

Results: There were increased levels of TGFbeta responses with no changes in the other cytokines or chemokines measured) in patients with SSc compared to healthy controls following stimulation with peptides from the α3 chain of HLA class I. 60% positive responses in SSc vs 35% positive responses in controls for TGFbeta ($P<0.05$).

Conclusion: PBMCs from patients with SSc respond to HLA peptides with increased levels of TGFbeta. This suggests a (probable) T cell response. Mouse models are underway with HLADR4 and HLA-A2 to develop this as model for immunotherapy. The next step will be treatment of these transgenic mice with a mixture of HLA peptides to prevent or reverse GvHD (as a model of SSc).

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First Reported Case of Charcot Arthropathy of the Shoulder in Sjögren's Syndrome

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Background: Sjogren's syndrome (SS) is an autoimmune disorder predominantly affecting the exocrine glands but with a wide spectrum of extraglandular manifestations including neuropathy. The most common neuropathy in SS is sensory ganglionopathy, but small fibre neuropathy, sensorimotor neuropathy, mononeuropathy multiplex, autonomic neuropathy, and rarely central nervous system involvement can also be seen. Charcot's arthropathy is the progressive destruction of a joint in the setting of an underlying neuropathy. It is most commonly seen in diabetes mellitus however no literature to date has described the development of Charcot's arthropathy in SS.

Case Report: We present a case of a 68-year-old female who had been diagnosed years earlier with SS on the basis of serology, keratoconjunctivitis sicca, arthralgias, and mild altered sensation in the right arm, but was subsequently lost to follow up. She presented 11 years after diagnosis with acute pain and functional loss of the right arm. X-ray of the right shoulder showed destruction of the right humeral head and glenoid which had progressed rapidly compared to imaging two months prior. Magnetic resonance imaging of the spine revealed no syrinx and joint aspiration showed no bacterial growth. Assessment revealed a longstanding history of right arm numbness, a recent decrease in right leg sensation, and longstanding sicca, dry mouth, and arthralgias. Other than an intermittent erythematous facial rash, no other connective tissue disease symptoms were present. Physical examination was remarkable for bilateral clouded corneas, edentulousness, and mild synovitis of the right wrist and proximal interphalangeal joints bilaterally. The right shoulder was swollen with limited range of motion and no sensation on the entire right arm. There was decreased sensation on the entire right leg. Electromyography (EMG) revealed diffuse sensory neuropathy with intact motor function. Serology was significant for 1:1280 positive speckled ANA, negative extractable nuclear antigens, double stranded deoxyribonucleic acid antibody, and rheumatoid factor. Inflammatory markers were elevated. Syphilis and Borrelia burgdorferi serology were negative. She was initiated on hydroxychloroquine, low dose prednisone, natural tears and monthly intravenous immunoglobulin (IVIG). The arthralgias improved with hydroxychloroquine and the neuropathic symptoms in her right leg resolved. However, there was no change in the right arm neuropathy despite IVIG treatment and repeat EMG revealed ongoing sensory neuropathy.

Conclusion: No literature to date has described the development of a neuropathic arthropathy in the shoulder in SS. This case illustrates an unusual and severe presentation of longstanding SS-associated sensory neuropathy with minimal improvement with IVIG therapy.

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Temporal Trends in Incidence and Mortality for Rheumatoid Arthritis and Systemic Autoimmune Rheumatic Diseases in Quebec, Canada: A Population-based Study

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Objectives: Administrative healthcare databases are increasingly used in Canada to develop chronic disease surveillance indicators. Examining trends in incidence and mortality over time can assist in monitoring disease burden and evaluating the effectiveness of treatment. The purpose of this population-based study was to assess prevalence and to explore time trends in incidence and mortality for rheumatoid arthritis (RA) and selected systemic autoimmune rheumatic diseases (SARD) (SLE, sclerosis, myositis, sjögren's, vasculitis and polymyalgia) using administrative data.

Methods: Using previously developed case definitions; two population-based cohorts for RA and SARD (1996-2009) were defined. To identify incident cases, a «run-in» period of five fiscal years (1996-2000) was used to exclude cases that were prevalent at the beginning of the study period. Age and sex-specific incidence rates were calculated using the number of incident cases as the numerator and the counts of population eligible for the Quebec health insurance registry as the denominator. For each fiscal year, age-standardized rates were calculated and rates were directly adjusted using the 2001 age-structure of the Quebec population (census data). The Quebec health insurance registry file was also used to identify deaths among RA and SARD cohorts and, for each fiscal year, mortality rates in each cohort were compared with mortality rates in the general population using standardized mortality ratios (SMRs). Joinpoint regression and negative binomial regression analyses were used to test for linear change in incidence trends and SMR over time.

Results: Prevalence using all years from 1996 to 2009 was estimated at 1.1% for RA and 0.53% for SARD. For RA, 69.2% of cases were females, while for SARD, this percentage was 73.5%. In 2009, we calculated an incidence rate of 0.9 per 1,000 for RA and 0.6 cases per 1,000 for SARD. Our analyses did not confirm statistically significant linear changes in incidence over the study period. The mortality rate in both RA and SARD patients was significantly higher than the expected rate in the general population (2009: RA SMR=1.32 [95% CI 1.27-1.38], SARD SMR=1.95 [95% CI 1.85-2.05]), and no significant improvement in these parameters was observed over time.

Conclusion: In this study, we could not establish time trends in RA or SARD incidence between 2001 and 2010. Mortality is substantially higher in RA and SARD compared to the general population, and elevated SMRs persisted over the study period. This suggests that further efforts are needed to optimize long-term outcomes in these diseases.

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Industrial Pollution Emissions are associated with Anti-CCP Antibodies

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Objectives: To estimate the prevalence of anti-CCP antibodies in a sample of a large population-based Quebec cohort, and determine the associations between anti-CCP antibodies and exposure to industrial emissions of fine particulate matter (PM2.5) and sulfur dioxide (SO2).

Methods: The CARTaGENE cohort includes 20,000 general population subjects randomly drawn from four census metropolitan areas (Montreal, Quebec City, Sherbrooke, Saguenay–Lac-Saint-Jean). Available are demographics, health data, and stored serum. On a random sample of 3,579 CARTaGENE cohort members, we determined serum anti-CCP3 antibodies (INOVA Diagnostics). We performed multivariable logistic regression models, for the outcome of positive anti-CCP, assessing for independent effects of our pollution variables, adjusting for age and sex. Using the residential postal code for each subject, two models assessed distance to main industrial emitters of PM2.5 and SO2 (those averaging >100 tons/year), and two models assessed tons of PM2.5 and SO2 annual emissions. All models had two exposure variables. For models with tons of emissions (of SO2 or PM2.5), the first variable was a binary variable capturing whether in proximity to the postal code of residence for a given subject, there was emissions; the second variable was a continuous variable for those exposed to emissions (providing the effect per 1000 tonnes). For models with distance, a binary variable captured whether the postal code of residence for a given subject was farther than 7.5 kilometres of a major industrial emitter; the second variable provided the effect per 1000 metres for those living close to a major emitter.
Results: Of the 3,579 individual CARTaGENE samples, 236 (6.6%) were low positive for anti-CCP antibodies, 98 (2.7%) were medium positive, and 53 (1.5%) were high positive. Our further analyses included the 1,721 subjects with a valid postal code. For those exposed to emissions of both SO2 and PM2.5, there were strong trends towards a positive association between the presence of anti-CCP antibodies, and annual industrial emissions in residential area. As well, there were strong trends towards a negative association between the presence of anti-CCP antibodies, and distance for those living in proximity to a major industrial emitter of both SO2 and PM2.5. The results of adjusted analyses were more robust for PM2.5 than for SO2, however.
Conclusion: We provide compelling evidence that pollution emissions, and proximity to major industrial emitters, are associated with anti-CCP antibodies. Our results are more robust for PM2.5 than SO2, and require validation in other datasets and with more precise exposure estimates.

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Risk of Breast, Ovarian and Endometrial Cancers in Women with Rheumatoid Arthritis
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Objectives: Previous studies found that breast, ovarian and endometrial cancer risk in women with rheumatoid arthritis (RA) is lower versus the general population, although authors do not always agree. Perhaps the dichotomy in findings is due to the differing age compositions of the populations examined. The objective of this study was to examine the risk of breast, ovarian, and endometrial cancers in RA patients, stratified by age groups, versus the general Quebec population.

Methods: Incident RA cases were identified from Quebec physician billing data between January 1, 2002, and December 31, 2008. Patients were included if they had 2 or more physician billing code diagnoses for RA (i.e. ICD 9 code 714) at any time. Cancer cases occurring after the RA diagnosis and up to the end date were identified from hospitalization billing diagnoses. Cancers were classified according to International Classification of Diseases, ICD codes, as follows: breast (ICD-9 174, ICD10 C50); ovary (ICD9 183, ICD10 C56); and body of uterus (endometrial), (ICD9 182, ICD10 C54-55). RA subjects were stratified by age into 5 year groups. We then compared the observed cancer incidence to the cancers expected according to Quebec's age-specific general female population cancer incidence rates between 2002 and 2008. We derived a standardized incidence ratios (SIR) for the malignancies of interest, with the corresponding 95% confidence intervals, CIs.

Results: We assessed 46,859 female incident RA patients followed an average of 3.26 (total 152,523) patient-years. Versus the age-matched Quebec population, we found a lower incidence of breast (incidence 1.46/1000 patients, SIR= 0.62, 95% CI 0.54-0.71), ovarian (incidence 0.19/1000, SIR= 0.64, 95% CI 0.43-0.92) and endometrial cancers (incidence 0.27/1000, SIR= 0.60, 95% CI 0.43-0.82). When stratified by age, for breast cancer, all RA age groups seem to have a decreased risk versus the general population. However, for endometrial and ovarian cancers, in younger age groups the confidence intervals were wide, so we cannot provide definitive conclusions for those demographics.

Conclusion: Overall, RA patients demonstrate lower breast, ovarian, and endometrial cancer rates versus the general population. However, a limitation of our study is the use of administrative records, as the RA and cancer diagnoses were not otherwise clinically confirmed. When stratified by age, for breast cancer, all RA patient age groups had a decreased risk. However, in ovarian and endometrial cancers, we cannot provide definitive conclusions in younger age groups. The lower risk of these cancers in RA should be further studied.

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Societal Preferences for Rheumatoid Arthritis Treatments: Evidence from a Discrete Choice Experiment

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Objectives: The cost-effectiveness of new interventions is increasingly assessed using the cost per quality-adjusted life year (QALY). QALYs are calculated by multiplying the length of time spent in a health state by the value of that health state, usually representative of the general public and estimated using a generic preference-based measure such as the EQ-5D. A limitation of generic preference based instruments is that they may fail to describe benefits of a treatment that patients experience and that society might value such as the method or convenience of treatment. The aim of this study was to determine the value society places on aspects of rheumatoid arthritis treatment, including mode of administration.

Methods: A discrete choice experiment (DCE) was administered using a web survey in a representative sample of the Canadian general population using an online panel. Focus groups led to the development of a DCE with 7 attributes (route and frequency of administration, chance of benefit, chance of serious and minor side-effects, confidence in benefit and side-effect estimates (based on GRADE definitions), and life expectancy. A conditional logit regression model was used to estimate the significance and relative importance of attributes in influencing preferences.

Results: 733 respondent provided rational responses and were included in the analysis. They were recruited from all provinces and territories in Canada, and their mean age (44), gender (55% female) and education were representative of the general population. Six attribute levels within four attributes significantly influenced preferences for treatments. Respondents were willing to give up to a year of life expectancy over a 10 year period to increase the probability of benefitting from treatment, or two thirds of a year to reduce minor or serious side-effects to the lowest level or improve the confidence in benefit/side-effect estimates. There was some evidence of a preference for oral drug delivery and sub-group analysis suggested this preference was restricted to injection naive respondents.

Conclusion: As expected, our study found society values the benefits and side-effects of treatments. However, our study also found that people also value the degree of confidence in the estimates of risks and benefits of treatments, and to a lesser extent, the route of administration. Since economic evaluations typically focus only on the health outcomes of treatments, they may miss process aspects of treatment that are valued by society. This study provides important evidence to policy makers determining the cost-effectiveness of treatments in arthritis.

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Harnessing the Power of Administrative Data Linkage: Results from the Ontario Best Practices Research Initiative Clinical Linked Cohort

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Objectives: The Ontario Best Practices Research Initiative (OBRI) is a longitudinal observational cohort of rheumatoid arthritis (RA) patients recruited from 63/162 Ontario rheumatologists. This abstract describes the "OBRI RA Clinical Linked Cohort"; it includes 95% of OBRI cohort patients (all who consented to administrative data linkage).

Methods: In January 2014, clinical data from patient baseline visits were linked with the Institute for Clinical Evaluative Sciences (ICES) administrative data, providing a complete profile of all medical services used. We included all patients with a rheumatologist enrollment form who also completed a telephone questionnaire administered by a trained interviewer within 60 days (n=1841) as of July 15, 2013. Exclusion criteria were patients who had not consented to ICES linkage, and patients without provincial health care coverage. Selection of data for linkage was conducted using expert opinion from the OBRI Planning and Review board including clinicians, academics and ICES data experts and encompassed 6 main categories: Physician information (de-identified investigators, joint counts), patient information (demographics, SES, smoking, insurance, comorbid conditions), medications (current and past), and RA history. In addition, standard questionnaires related to pregnancy, tuberculosis, employment/work productivity, HAQDI, RADAI, Quality of Life (EQ5D), DAS 28 score, ESR and CRP were linked.   Regular data logic checks were performed on the clinical cohort to ensure high quality data. All patient reported medications were coded using ATC WHO codes reviewed by a pharmacist and 2 senior pharmacy students.

Results: Baseline data from the OBRI were linked with ICES administrative data, with n=1841 patients linked. Our administrative data linked clinical sample was predominantly female (88%), caucasian (85%) and English speaking (93%) with an average age of 57.3 and disease duration of 8.5 years. 26% of patients received a new biologic at baseline and 51% received a new DMARD at baseline. Patients had a mean DAS28 of 4.5 SD(1.5), CDAI 21.8 SD(13.6) and HAQ DI 1.2 SD(0.8).Researchers have the ability to look forward and backward through administrative databases including medication and health care resource utilization with adjustment for baseline clinical confounding.

Conclusion: Our unique dataset is the largest existing linked dataset and the first to include patients irrespective of medication course. The depth and breadth of our clinical covariates linked with administrative data will be an indispensible tool for researchers and health care stakeholders answering questions about of drug safety and efficacy, clinical practice patterns, and health care resource use.

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Derivation and Comparison of Utility Scores for Economic Evaluation in Large Datasets: Modelling Patient Level EQ-5D Using the Ontario Best Practices Research Initiative
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Objectives: Quality of life scores such as the EQ-5D are essential for the economic evaluation of clinical interventions. In large databases (e.g. administrative datasets), primary data collection for EQ-5D assessments is impractical and expensive. This can be avoided by statistically modeling EQ-5D scores from demographic and clinical characteristics in existing databases that include both measures. We used a large Canadian dataset to create an EQ-5D reference index for Canadian RA patients indicating the average EQ-5D quality of life score for patients based on their demographic and clinical characteristics. We compared our Canadian index to that of an American sample (Sullivan, 2006).

Methods: Our data were obtained from the Ontario Best Practices Research Initiative (OBRI), an observational cohort of RA patients, recruited from 62/162 Ontario rheumatologists from both academic and community sites. Baseline assessments were analyzed (n=2086) with the main outcome of EQ-5D score (0-1). Covariates were categorical variables for age, sex, education, income, number of comorbid conditions (NCC) and race. A Censored Least Absolute Deviations (CLAD) regression was chosen, as it is robust to traditional regression assumptions and accounts for the right censoring of data. To obtain confidence intervals and standard error values for the CLAD regression we performed bootstrap replication of our sample with β=2000 replicates. Unadjusted EQ-5D scores and number of comorbidities were compared to American values for the 25th, median and 75th quantile.

Results: The average age of our sample was similar to US data; μOBRI=58 vs. μUS=59 with disparate NCC quintiles OBRI: 25th =1, 50th=2, 75th=3 vs. US data: 25th=3, 50th=5, 75th=7. The unadjusted results for the EQ-5D percentile scores were 25th=0.70, 50th=0.80, 75th=0.82 compared with US sample reporting 25th=0.446, 50th=0.778, 75th=0.816 with 0 being the worst possible health and 1 being perfect health. The unadjusted EQ-5d mean μOBRI=0.770 for the OBRI cohort showed better quality of life compared to the American group μUS=0.661. The CLAD model for the median quintile showed a bias corrected EQ-5D median of 0.799, SE=0.0174, CI:(0.763, 0.832), with significant covariates for income.

Conclusion: Our results suggest a higher quality of life score for rheumatoid arthritis patients in Ontario, Canada compared with the United States especially in the most severe patients. Our index set will allow researchers to conduct patient level economic analysis using the entire population of RA patients by providing EQ-5D scores. This index value set will be the largest and most robust ever created for rheumatoid arthritis patients.

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Microscopic Polyangiitis with Spontaneous Spinal Intradural Hemorrhage: A Case Report and Review of the Literature

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Background: Microscopic polyangiitis (MPA) is a systemic, necrotizing, pauci-immune vasculitis primarily affecting small vessels. The renal and pulmonary systems are commonly affected while CNS involvement is rare. We review a case of MPA presenting with spinal intradural hemorrhage and intracerebral hemorrhage.

Objectives: (1) To describe a patient presenting with MPA affecting the CNS; (2) perform a literature review of MPA with CNS involvement and approach to management.

Methods: We performed a chart review followed by a literature search of the following databases: Medline, Embase, Scopus, and Proquest. The following keywords were used: "microscopic polyangiitis", "ANCA associated vasculitis", "central nervous system", "brain", "spinal cord", "intracerebral-, subarachnoid-, subdural-, intradural hemorrhage."

Results: BD, a previously healthy 53-year-old male, presented to the University of Alberta Hospital with acute onset mid-thoracic back pain, bilateral leg weakness, and urinary retention. MRI of the spine revealed intradural hemorrhage extending from the level of T2 to T12 with a mass lesion seen at the level of T3. An emergent decompressive laminectomy was performed. Pathology of the mass revealed diffuse infiltration of inflammatory cells with a focus of tightly packed and hyalinized vessels. There was no evidence of neoplasm and the differential included vascular malformation, infection, or inflammatory process.

Post-operatively, BD developed acute testicular pain with an ultrasound showing multiple testicular hemorrhages. The patient became increasingly confused and CT revealed acute intraparenchymal hemorrhage requiring emergent craniectomy and hematoma evacuation. Pathology showed necrotizing vasculitis with an absence of granulomatous inflammation. There was a positive p-ANCA with elevated anti-MPO. BD was diagnosed with MPA and treated with intravenous solumedrol followed by oral prednisone. Unfortunately, the patient developed sepsis with multi-organ failure post-operatively and passed away.

Our review of the literature confirms CNS involvement in MPA is rare. Reported cases include involvement of cranial nerves, brain, and meninges, with only 2 previously reported cases of spinal disease. Previous cases of MPA with CNS disease have seen clinical improvement with steroids and cyclophosphamide. Use of plasma exchange in emergent situations has also been proposed. Maintenance therapy includes azathioprine, methotrexate or mycophenolate mofetil.

Conclusion: MPA can rarely present with brain and spinal cord involvement, even in the absence of pulmonary and renal findings. CNS disease carries a high mortality rate; however, there have been case reports of patient response to immunosuppressive therapy with steroids and cyclophosphamide.

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Inflammatory Arthritis Patients' Perspectives, Priorities, and Opinions on Interventions for Medication Adherence

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Objectives: In light of inconsistent and disappointing research on the impacts of adherence interventions in arthritis, incorporating patients' views in study development is a crucial step that ensures research aligns with patients' needs and experiences with medication taking. Our objectives are: 1) to describe the conception, development, and implementation of qualitative research demonstrating collaboration with arthritis patients; and 2) to report preliminary findings from the pilot focus group conducted with arthritis patient collaborators.

Methods: On February 11th, 2014, we presented our research program on medication adherence in arthritis, including proposed focus groups to better understand patients' experiences with taking medications, at a meeting of the Arthritis Research Centre of Canada's (ARC) Patient Advisory Board (APAB). Composed of men and women living with arthritis, the APAB participates in arthritis research decision-making with ARC researchers. We established a dedicated team of APAB collaborators for the resulting focus group-based research study "INflammatory arthritis patients' perspectives, priorities, and opinions on interventions FOR MEDication adherence (INFORMED)." We applied an iterative, thematic approach using a constant comparative approach informed by aspects of grounded theory and analyzed the transcript using the constant comparison method. Four study team members independently read and annotated the transcript and after discussion agreed on an initial coding framework.

Results: APAB members were involved in all stages of the INFORMED study including grant proposal and research instrument development (e.g. focus group topic guide). Six APAB members agreed to participate in the pilot focus group session, which was digitally recorded and transcribed verbatim. Qualitative analyses of the pilot focus group resulted in identification of 8 emerging categories including: relationships, stage of illness, strategies of adherence, patient beliefs/attitudes, effects of medications, peer relationships, activities of daily living, and information/education.

Conclusion: Gaining an in-depth understanding of arthritis patients' experiences, priorities, and motivators around medication use is crucial for guiding successful medication adherence interventions. The INFORMED study collaboration demonstrates the value of establishing patient research partnerships to better inform research questions, design, and interpretation. Findings from the pilot focus group will be used to guide subsequent focus groups to better understand arthritis patients' perspectives and experiences of medication use and in particular, their views on various strategies and interventions to improve adherence. Supported by a CIORA grant

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Prevalence of Medicinal Marijuana use among 1000 Rheumatology Patients attending a Community-based Rheumatology Clinic: A Prospective Cross-sectional Study

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Objectives: With a worldwide groundswell of medicinal cannabinoid use, and with few pharmacologic cannabinoid options available, rheumatology patients may be using marijuana to self-medicate. "Severe arthritis" was cited as the diagnosis for 65% of persons legally authorized to possess medicinal marijuana in Canada in 2014. With knowledge that most medicinal marijuana is obtained illegally, and by extrapolating from Canadian census data of 2011, conservative estimates are that 4% of persons with rheumatic complaints may be using cannabis, with an even higher rate expected for rheumatology patients. We have prospectively examined herbal cannabis use for 1000 rheumatology attenders.

Methods: Over two months (April-May 2014), consecutive patients attending an academic, community based rheumatology clinic staffed by 3 rheumatologists were invited to participate. Patients were either newly referred or attending for a follow up visit. The study comprised 2 questionnaires completed at the time of the visit: 1) demographic and disease related information completed by the rheumatologist, 2) patient anonymous report of current health status, pain severity and past or current marijuana use for either recreational or medicinal purposes, or both. Ethics approval and signed consent was obtained.

Results: Of the 1067 patients attending, 1000 (96%; 74% females; mean age 63 ± 15 yrs) agreed to participate. Thirty seven patients refused to participate, 30 were not eligible. Diagnoses were: inflammatory arthritis 516 (52%), osteoarthritis/ back pain, 489(49%) soft tissue rheumatism/ fibromyalgia, 218 (22%), others, 99(10%) with some overlapping diagnoses. Medicinal marijuana was used by 28 (2.8%; 95% CI: 1.9-4.2). Users vs. non users were more likely to be younger, 53.vs.63 yrs (p=0.0003), unemployed or disabled 46% vs. 8% (p<0.0001), and tended to be male. Diagnoses did not differ between the users and nonusers, but users reported poorer global health 5.5 vs. 3.9 (p=0.0029), more pain 6.3 vs 4.8 (p= 0.0088), and previous recreational cannabis use 82% vs 19% (p< 0.0001). The physician global assessment did not differ significantly between the groups 3.2 vs 2.8 (p=0.2991).

Conclusion: Contrary to the expected rate, only 2.8% of patients, receiving rheumatology care for multiple rheumatic disease categories, reported current use of medicinal marijuana. With use observed across all disease categories, familiarity with marijuana as a recreational product may explain use for some. Perceived health status was poorer for users, with almost half not working. The low rate of marijuana use reported by rheumatology attendees questions the often self-reported diagnostic label of "severe arthritis".

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Impact of Age on Symptom Severity and Disease Management at Fibromyalgia Diagnosis
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Objectives: Population studies indicate that older persons experience more pain generally. Fibromyalgia (FM) affects persons of all ages, with previous studies on the impact of age on symptom severity reporting conflicting findings. The aim of this analysis was to describe the association between age at FM diagnosis and patient and clinical characteristics among Canadian patients in routine clinical care.

Methods: A cohort of FM patients prospectively followed at a tertiary care multidisciplinary clinic was included in the analysis. Demographic and disease severity measures included: pain visual analog scale (VAS), patient global assessment (PGA), Health Assessment Questionnaire (HAQ), Pain Disability Index (PDI), Pain Catastrophizing Scale (PCS), FIQ, MPQ, anxiety and depression by Arthritis Impact Measurement Scale (AIMS). General linear models and logistic regression were used to assess the association between age and, continuous or categorical, respectively, patient or disease parameters at baseline.

Results: The cohort comprised 248 patients with a mean ± SD age 47.89 ± 10.34 years, disease duration 10.84 ± 9.80 years, and 91.13% female. Baseline values were: pain VAS 6.52 ± 2.29, PGA 6.58 ± 2.23, FIQ 66.97 ± 16.82, HAQ 1.19 ± 0.61, MPQ 40.82 ± 15.22, PDI 37.69 ± 14.44, PCS 29.39 ± 12.17, AIMS anxiety 6.34 ± 1.84, AIMS depression 4.91 ± 1.84, with a mean medication count of 2.38 ± 1.67 per patient. Increased age was associated with significantly (P<0.001) longer pain duration (B=0.34; i.e. increased duration of pain by 0.34 years for each additional year of age) and lower odds of having allodynia (OR=0.97; P=0.037). Furthermore, increased functional disability was observed in older patients as evidenced by the higher HAQ scores (B=0.01; P=0.007). However, no significant association was observed with pain severity, PDI, PCS, PGA, FIQ, MPQ, anxiety and depression. Older patients were more likely to be treated with tranquilizers (OR=1.03; P=0.039), with a statistical trend towards more analgesics (OR=1.03; P=0.096) but less antidepressant use (OR=0.98; P=0.091). No significant differences were observed for other treatments, cigarette smoking, or substance abuse.
Conclusion: Although older age at baseline was associated with significantly longer duration of pain, no significant differences in disease parameters were observed based on age; the only exception being HAQ which was worse among older patients. Patient management differed based on age without, however, reaching statistical significance. Further study is necessary to establish whether response to treatment is associated with age.

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Profile of Rheumatology Patients using Medical Marijuana

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Objectives: Self-reported diagnosis of musculoskeletal pain is a common reason for medicinal marijuana use. Specific patient or disease characteristics for rheumatology patients using medicinal marijuana, or its effectiveness are unknown. With marijuana recognized as a medicinal product in many jurisdictions, evidence is lacking for effect for rheumatology patients. To better understand medicinal marijuana use by rheumatology patients, we have examined the profile of users with a rheumatologist confirmed diagnosis.
Methods: One thousand consecutively attending patients with a rheumatologist-confirmed diagnosis reported on the use of medicinal marijuana. Rheumatic disease treatments, co-morbidities and information about use were obtained through a physician and patient-completed questionnaire. Physician (MD global) and patient global (Pt global) assessment of disease severity was scored by VAS (0=very good, 10=very poor), and patient assessment of effectiveness of marijuana, VAS (0=very poor, 10=excellent). The study was ethics approved and participating patients provided written informed consent.

Results: Among the 1000 patients screened marijuana use was reported by 28 (2.8%). Diagnoses were: inflammatory arthritis 9 (RA 2, PSA 2, SpA 4, PMR 1), OA 15 (small joints 4, large joints 7, spine 9), and soft tissue 7 (FM 5, tendonitis 2), more than 1 diagnosis 3. Eight (29%) had no other comorbid condition, with psychological disease identified for 8 (29%). MD global score was <4 for 18 (64%), ≥4 for 10 (36%), with 3 (11%) ≥6. Rheumatic drug treatments were a mean of 1.75 drug categories/patient: NSAIDs 12, DMARDS 6, biologics 6, antidepressants 6, anticonvulsants 4, opioids 11, steroids 2, tranquilizers 2, and 4 using no concurrent medications (tendonitis 1, large joint OA and FM 1, Spa 1, OA small joints 1). Marijuana users reported past and present use respectively for cigarettes (89% vs 35%), recreational marijuana (82% vs 39%). Methods of use were smoking (24 patients), vaporized (6), ingested (5) and topical application (1). Reported symptom relief included decreased pain (24 patients), improved sleep (5), decreased anxiety (6) and relief of gastrointestinal symptoms (4). Eleven patients reported relief for more than one symptom. Effect for marijuana was rated as 7.2±2.10.

Conclusion: Two thirds of users were categorized by the rheumatologist as having mild global disease activity. Psychological contributors, cigarette smoking and current recreational marijuana use characterized current marijuana users. Although patients report good effect, these findings raise concerns about indication for use and the accumulated health risks related to medicinal marijuana.

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Efficacy and Safety of Cannabinoid Treatments in the Rheumatic Diseases: A Systematic Review of Randomized Controlled Trials

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Objectives: The endocannabinoid system functions to maintain homeostasis in the human body and thereby has effects on modulation of pain and inflammation. Cannabinoid preparations are available as synthetic or plant derived products and may be effective for the management of musculoskeletal pain. We have conducted a systematic review to examine the evidence for efficacy and side effects of cannabinoids (phyto- and syntheto-) in rheumatology care.

Methods: A literature search was conducted of MEDLINE; Embase Classic + Embase ; BIOSIS Previews; Scopus; CENTRAL; DARE; CINAHL; PsycINFO; AMED, with additional searches in ClinicalTrials.gov, International Clinical Trials Registry Platform, Current Controlled Trials, Natural Standard, various Drug and Device Regulatory Approval Sites, Web of Science and Scopus. Included were RCT's in rheumatology patients with pain and sleep disturbance outcomes. Study quality was assessed using the JADAD scale (out of 5).

Results: Of the 1407 articles screened, 12 underwent full text examination. Excluded were survey reports, observational studies, case series, case reports and commentaries, with 7 remaining articles. Of these 3 were excluded: two included patients with non-rheumatic diseases, 1 was an open-label study of effect of THC on experimentally induced pain. The remaining 4 studies comprised 201 patients (58 RA, 72 FM, and 74 OA). One study examined the effect of nabiximols in RA, two studies examined nabilone in FM (one a non-inferiority study with amitriptyline as comparator), and one examined effect of a fatty acid amide hydrolase-1 (FAAH1) inhibitor in OA. The quality of the trials was good, with a mean 3.75 JADAD score. The study of FAAH1 inhibitor was stopped at interim analysis for futility. For the remaining 3 trials, duration was from 5-8 weeks, with significant analgesic effect in two, significant sleep effect in two, and one in FM reporting improved quality of life. No serious adverse events were reported, with dizziness and drowsiness the most common adverse effects for about a quarter of patients. There were no studies of inhaled herbal cannabis identified.

Conclusion: Small sample sizes, heterogeneity of rheumatic conditions and products, only a single comparative trial and absence of any study of herbal cannabis allow for only limited conclusions. The results suggest that pain relief and positive effect on sleep may have some potential for therapeutic benefit for rheumatic patients, but in view of this small body of current evidence cannabinoid treatments cannot be recommended for management of rheumatic complaints.

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Early Erosions in Rheumatoid Arthritis (EERA) Software Reliably Measures Erosive Damage on MRI in the Metacarpophalangeal Joints of Rheumatoid Arthritis Patients

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Objectives: Advancements in automated segmentation algorithms aim to improve the efficiency and reliability of monitoring erosive damage to joints in RA patients. One emerging software, Early Erosions in Rheumatoid Arthritis (EERA), is designed for use by a novice reader to semi-automatically quantify bone erosion volume of the metacarpophalangeal (MCP) joints captured by MRI. Here, we assess the reliability of EERA to quantify individual images (status-measurements) and monitor erosive progression (change-measurements).

Methods: MR images were acquired for the dominant hand of 68 RA patients from a single rheumatology clinic. Twenty-four patients were subsequently imaged at follow-up times of either 6, 12, 18 or 24 months. Two novice readers trained in EERA, but otherwise inexperienced with conventional quantification techniques, used EERA to evaluate and sum the erosion volume of the 2nd through 5th MCP joints of each MR image. One reader repeated all measurements after 72h. Image evaluations occurred in a random order and readers were blinded to each other's measurements. To assess intra- and inter-rater reliability, intra-class correlation coefficients [ICC (2,1)] were calculated with 95% confidence intervals (CI) for status-measurements and change-measurements. Using the 95% limits of agreement method, the smallest detectable difference (SDD) was computed for status-measurements and change-measurements. To examine EERA reliability in early disease, SDDs were also assessed for only those images with mean total bone loss <100mm3.

Results: From 68 participants, 48 (70.6%) were female, 56 (82.4%) were Caucasian, mean (SD) age was 57.4 (10.3) years, and mean (SD) baseline DAS28-ESR3V was 4.0 (1.5). For n=92 status-measurements, intra-rater reliability ICC=0.987 (95% CI 0.981 to 0.991), and inter-rater reliability ICC=0.956 (95% CI 0.934 to 0.970). Intra-rater SDD=31.1mm3, and inter-rater SDD=59.6mm3. Including only the n=70 images with mean total erosion volume <100mm3, intra- and inter-rater SDD dropped to 5.5mm3 and 11.8mm3, respectively. For n=24 change-measurements, intra-rater ICC=0.934 (95% CI 0.855 to 0.971) and inter-rater ICC=0.613 (95% CI 0.281 to 0.813). For change-measurements, intra-rater SDD=34.4mm3 and inter-rater SDD=74.0mm3. Including only the n=18 image pairs with mean baseline total erosion volume <100mm3, intra- and inter-rater SDD for change-measurements dropped to 9.3mm3 and 17.1mm3, respectively.

Conclusion: Evidenced by good to excellent ICCs, EERA is reliable for quantifying erosive damage to the MCP joints on individual MR images and in measuring erosive progression over time. SDDs were especially low when less erosive damage was initially present. This evidence suggests that EERA is highly reliable for quantifying and monitoring erosive damage to the MCP joints in early RA.

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The Effect of Cigarette Smoking and Alcohol Intake on Patient Reported Outcome Measures in Psoriatic Arthritis

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Objectives: To assess the effect of alcohol and smoking on patient reported outcome measures (PROs) in psoriatic arthritis (PsA).

Methods: Data from the International Psoriasis And Arthritis Research Team (IPART) cohort was used to assess alcohol intake prior to diagnosis (PreDx), at diagnosis (Dx), and at current study (CS). PROs included EuroQoL (EQ5D), Health Assessment Questionnaire (HAQ), Functional Severity Score (FSS), Functional Assessment of Chronic Illness Treatment (FACIT), Dermatology Quality of Life Index (DLQI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index, Ankylosing Spondylitis Quality of Life Index (ASQoL) and Short Form Health Survey (SF-36). Analysis included simple statistics and Pearson correlation, deemed statistically significant at p<0.05.

Results: We assessed 3571 patients (73.7% male, mean (SD) age 50.2 years (13.2), disease duration 14.3 years (10.5). Mean units/week (SD) alcohol intake Pre-Dx, Dx and CS were 0.4 (SD 3.3), 0.3 (SD 2.7), and 1.2 (SD 3.3) respectively. Mean (SD) number cigarettes smoked/day 5.8 (11.4) at Dx and 4.1 (8.5) at CS; at CS mean (SD) years smoked 5.8 (SD 11.4). Mean (SD) PROs: EQ5D of 0.763 (0.19), HAQ 0.61 (0.67), FSS 4.52 (2.96), FACIT 36.0 (12.8), DLQI 3.41 (4.60), BASDAI 3.53 (2.43), BASFI 2.84 (2.64), ASQoL 6.82 (5.86), physical component SF-36 39.2 (11.5) and mental component SF-36 47.1 (11.8). Smoking at Dx, number of years of smoking at Dx, smoking at CS and number of years smoking at CS each weakly but significantly negatively impacted HAQ, HAQ pain, HAQ stiffness, FSS, FACIT, BASDAI, BASFI, ASQoL and both physical and mental components of SF-36 ($r2 < 0.2$ for all correlations). Smoking status or number of years smoked did not correlate with DLQI at any time. Alcohol use at CS was very weakly, but significantly correlated with poorer outcomes on EQ5D, HAQ pain, HAQ stiffness, FSS, FACIT, DLQI, BASDAI, BASFI, ASQoL, and physical and mental components of SF-36 ($r2 < 0.2$ for all correlations). Very weak but significant correlations were found between alcohol use at Dx and worse outcomes on physical component of SF-36 ($r2 < 0.1$ correlations). Alcohol use Pre-Dx was significantly weakly correlated with poorer outcomes on HAQ pain, HAQ stiffness, FSS, FACIT, BASDAI, BASFI, ASQoL and both components of SF-36 ($r2 < 0.1$ for all correlations).

Conclusion: Smoking weakly correlated with several PROs, with the notable exception of the DLQI. Alcohol intake during the course of PsA also negatively impacted several PROs. However, while these correlations were statistically significant, they were quite weak.

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The Effect of Alcohol Consumption on Patient Reported Outcomes in Ankylosing Spondylitis

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Objectives: To examine the effect of alcohol intake on patient reported outcomes (PROs) in ankylosing spondylitis (AS).

Methods: Using data from the Spondyloarthritis Research Consortium of Canada (SPARCC) cohort, data sets from patient visits were analyzed to determine correlations between alcohol intake prior to diagnosis (PreDx), at diagnosis (Dx) and at current visit (CS). PROs included Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), AS Quality of Life (ASQoL) Short Form Health Survey (SF-36), Patient Global Assessment of Disease Activity (PGA), EuroQoL (EQ5D) Scores, Health Assessment Questionnaire (HAQ) scores, and Functional Severity Score (FSS). Analysis included simple statistics and Pearson correlation. Correlations were deemed statistically significant at a level of $p < 0.05$.

Results: There were 1330 patients (57.3% males) with a mean age of 49.92 years (SD 13.3 and average disease duration of 18.02 years. Mean (SD) PROs BASDAI of 4.06 (2.49), BASFI 3.46 (2.78) EQ5D 0.72 (0.21), HAQ 0.605 (0.611) HAQ Pain 1.13 (0.865) and FSS 4.88 (2.89). Mean weekly alcohol intake was 1.6 units PreDx, 1.4 units at Dx and 2.2 at CS. EtOH use at CS was statistically significantly, but very weakly correlated with poorer outcomes as assessed by BASFI, BASDI, ASQoL, HAQ, FSS, and SF-36 (Physical Component Score [PCS] and Mental Component Scores [MCS]) (r2 all <-0.2 or 0.2; many r2 <0.1). Alcohol use at Dx had only one very weak, but statistically significant negative correlation (r2 = -0.05). Alcohol use prior to diagnosis also had one statistically significant, yet very weak, negative correlation with EQ5D (r2=0.06).

Conclusion: Current alcohol intake and HAQ pain and stiffness scores correlate negatively whereas there was a positive correlation between current alcohol intake and SF scores. Further studies into the physical and psychological mechanisms underlying these relationships are ongoing.

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Limited Scleroderma (CREST Syndrome) is Associated with Worse Xerostomia and Xerophthalmia than Primary Sjogren's Syndrome Patients.

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Objectives: Objectives: The severity of mouth and ocular dryness in patients with CREST syndrome, was compared with Primary Sjogren's Syndrome (PSjS) alone.

Methods: Methods: Patients were pre-screened for objective evidence of dry eyes or dry mouth, abnormal serology or history of salivary gland enlargement as an adult. Six hundred and nine patients were subsequently examined on protocol. The evaluation included a visual analogue score (VAS) for severity of xerophthalmia and xerostomia, Schirmer's-1 test, Rose Bengal staining, unstimulated salivary flow (USSF), minor salivary gland biopsy and serological profile. Sjogren's Syndrome was classified according the American European Consensus Group (AECG) Criteria. Sicca referred to patients with objective dry eyes or mouth who did not meet AECG criteria. Patients with anticentromere antibody (ACA) were designated as Limited Scleroderma (CREST Syndrome) whether or not they met criteria for Sjogren's. A 2-tailed student t-test with heterogenous variance was used to compare measures of severity.

Results: Results: Among 609 patients, 446 met the AECG criteria for PSjS. One hundred and sixty-three patients were designated as sicca. Thirty-four patients were ACA positive, and although they all had dry eyes or dry mouth, 26 of them met the AECG criteria for PSjS as well. Among the 34 CREST patients, Raynaud's phenomenon was seen in 88% (compared to 28% of the PSjS (p < 0.001)). Furthermore, elevated IgG was seen in 24% of the CREST patients and 57% of the pSjS (p < 0.001). Of the CREST patients who met the AECG criteria, only 35% were anti-Ro or anti-La positive compared with 77% of the PSjS patients (p < 0.001). Among all 34 CREST patients, esophageal dysmotility was seen in 18 (53%), sclerodactyly in 16 (50%), and telangiectasia in 14 (44%). Fourteen had 3 or more CREST features. Whether or not the CREST patients met AECG criteria made no difference. They had more severe symptoms of xerostomia (higher mean VAS) than patients with PSjS alone 8.3 vs 6.9 (p < 0.001), whereas mean VAS for xerophthalmia (6.6 vs 6.4) was similar. The USSF in CREST compared with PSjS was 0.1 vs 0.4 ml/15 minutes (p < 0.001). The mean Schirmer's test was 3.5 vs 4.1mm/5 minutes (p = 0.038).

Conclusion: Conclusions: Patients with CREST Syndrome had Xerostomia that was subjectively and objectively worse on average than patients with PSjS. Furthermore, CREST patients had more severe objective xerophthalmia than PSjS patients.

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Systematic Review of the Effect of TNFα-inhibitors on Cardiovascular Events in Patients with Rheumatoid Arthritis

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Objectives: Rheumatoid arthritis (RA) is strongly associated with cardiovascular morbidity and mortality. Previous studies have demonstrated that a group of biologically active drugs, TNFα inhibitors, may reduce cardiovascular events (CVE) in patients with rheumatoid arthritis. There is an inherent treatment bias in these cohort studies and it is possible the selection of RA patients for TNFα inhibitors favours those with an inherently lower risk of CVE. Randomized controlled trials would reduce this bias, however, they are not powered to detect CVE. Thus, to obtain appropriate power for statistical analysis the most appropriate study design is a systematic review. The purpose of this systematic review was to evaluate the ability of TNFα inhibitors to reduce the risk of CVE in patients with RA. This study will update the systematic reviews by Barnabe et al. (2011) and Westlake et al. (2011) by including an additional five years of data.

Methods: A search of Medline, Embase, Medline IPAIC, ACP Journal Club, DARE, and the CCRCT was conducted for observational cohorts reporting on CVE in RA patients since 2009. Conference proceedings for the CRA, ACR, and EULAR were also searched between 2009 and 2014. Abstracts were assessed for inclusion by two reviewers and studies identified by either reviewer were brought forward to full-text review. Studies undergoing full-text review were further assessed based on predefined inclusion and exclusion criteria and the quality of selected papers was evaluated using the Newcastle-Ottawa Scale.

Results: The search identified 6089 abstracts and 14 articles were included in the final systematic review. Of the studies included, 8 reported on the effect of TNFα inhibitors on overall CVE, 10 reported on coronary artery disease (CAD), and 6 reported cerebrovascular disease (CVD). 5 studies demonstrate a significant reduction of CVE with the other 3 studies trending towards positive results. 4 studies demonstrate significant reduction of CAD, and only 1 study reported reduction of CVD.

Conclusion: TNFα inhibitors appear to reduce the likelihood of CVE in individuals with RA. The reduction is not as significant in the individual outcomes of CAD and CVE. These results are consistent with the findings of Barnabe et al. (2011) and Westlake et al. (2011) that TNFα inhibitors are likely useful in the prevention of cardiovascular complications of RA.

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Clinical Correlates of Monospecific Anti-Ro52/TRIM21 Antibodies in a Tri-nation Cohort of 1574 Systemic Sclerosis Subjects

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Objectives: Autoantibodies directed against Ro52/TRIM21 are common in systemic sclerosis (SSc) but the clinical significance of these antibodies remains uncertain. Although they have been reported to be associated with interstitial lung disease (ILD), this relationship may have been confounded by the presence of other concomitant SSc-specific antibodies known to be associated with ILD, in particular anti-topoisomerase I. The aim of this study was to assess the clinical correlates of monospecific anti-Ro52/TRIM21 antibodies, i.e. in subjects with isolated anti-Ro52/TRIM21 antibodies in the absence of other SSc-specific antibodies.

Methods: A Tri-nation (Canada, Australia, United States) cohort of 1574 SSc subjects was formed, demographic and clinical variables were harmonized and sera were tested for anti-Ro52/TRIM21 antibodies using a common diagnostic platform (Euroimmun line immunoassay). Descriptive statistics were used to compare 20 selected variables between monospecific anti-Ro52/TRIM21 antibody positive versus negative subjects. After adjusting for multiple comparisons, $p < 0.0025$ was considered statistically significant.

Results: 103 (6.5%) SSc subjects had monospecific anti-Ro52/TRIM21 antibodies. They generally had similar demographic profiles compared to the rest of the cohort (N=1471), including mean age at disease onset (45.2 vs 45.5) and mean disease duration (7.9 vs 9.6). Of note, subjects with monospecific anti-Ro52/TRIM21 antibodies were less likely to be white than the rest of the cohort (66 (68%) vs 1178 (83%), p<0.0003). In univariate analysis, ILD was the only clinical variable significantly associated with anti-Ro52/TRIM21 antibodies (odds ratio=2.55, 95% confidence interval 1.69-3.85, p<0.0001).

Conclusion: The prevalence of monospecific anti-Ro52/TRIM21 antibodies in this large SSc cohort was low. Nonetheless, the results obtained from this unique dataset represent the strongest evidence to date that anti-Ro52/TRIM21 antibodies are independently associated with the presence of ILD and provide strong support for the prognostic value of this serological biomarker in SSc.This study underscores the critical importance of international collaborations to the understanding of the clinical correlates of less common SSc serological profiles.

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Rate of Infections in Anti-Neutrophilic Cytoplasmic Antibody Vasculitis Patients treated with Cyclophosphamide: A Meta-Analysis

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Objectives: To determine the rate of severe infection in cyclophosphamide (CYC) induction therapy for anti-neutrophilic cytoplasmic antibody (ANCA)-associated vasculitis (AAV).

Methods: We performed a literature search of the following bibliographic databases: Medline, Embase, and Cochrane database from 1947 to July 2014 and abstracts from the American College of Rheumatology, and European League Against Rheumatism annual meetings. Systemic reviews and meta-analysis, clinical trials, cohort studies, and case series were excluded. Our search strategy combined the terms: anti-neutrophil cytoplasmic antibody or ANCA-associated vasculitis (granulomatosis with polyangiitis, microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis) treated with cyclophosphamide (CYC). We performed a random effects meta-analysis. Both oral and intravenous CYC were included. The cumulative dose of CYC was calculated based on the study description of the CYC dosing regimen and the duration of treatment.

Results: Fifty-nine studies met the criteria. There were 4 abstracts, 14 randomized-controlled trials (RCTs), and 41 observational studies. Only the RCTs were meta-analyzed; the sample size ranged from 25-197, mean age 42.9 to 67.8 and total cumulative CYC dose 114.5 g to 5333 g. Prophylaxis for pneumocystis jiroveci pneumonia was recommended in 10/14 studies. Rates of vaccinations for influenza or pneumonia were not reported. Everyone in the trial received corticosteroid as part of the induction regimen for AAV. 2 trials compared CYC vs. rituximab, and 5 trials compared oral CYC vs. intravenous CYC (both arms were included in the analysis). Duration of follow-up period ranged from 6 to 60.8 months.   Random effects analysis showed the rate of severe infection per 100 g of CYC was 9.49 per 1000 person years (95% CI: 9.48-9.49; p-value ≤ 0.0001).

Conclusion: The rate of severe infection among patients with AAV treated with CYC and corticosteroid induction therapy was 9.5 per 1000 person years. The rate was highly variable between studies even accounting for cumulative CYC dose. Other factors, such as patient age, disease severity, and co-morbidities should be considered.

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A Case of Mixed Connective Tissue Disease with Features of SLE and SSc, Livedoid Vasculitis, Severe Vasculopathy

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These are pictures and arteriogram (to be presented on the poster) of a 51-year-old woman with mixed connective tissue disease with features of SLE and SSc (ANA positive at 1:640 with a speckled nucleolar pattern, double stranded DNA, RNP and SSA positive, low C3 and C4), livedoid vasculitis, severe vasculopathy with multiple amputations of fingers.

She initially presented with a longstanding history of Raynaud's phenomenon. During the last few years, it substantially worsened to the point of being spontaneously triggered, affecting her toes in addition to her fingers, and occurring frequently up to 12 times a day. She also began to notice puffiness involving the entire length of her fingers.

Otherwise, she had no pertinent medical history or family history at the time of initial assessment. Initial examination revealed multiple telangiectasias on her face, upper chest and hands as well as dilated capillaries in several proximal nail folds. Initial investigations including bloodwork, pulmonary function test, and echocardiogram were non-contributory.

She rapidly deteriorated with marked cyanotic changes with Raynaud's phenomenon, which progressed to digital infarction of both hands. Arteriogram showed small vessel long segment variable narrowing almost exclusively within the hands, with multiple small vessel occlusions in the digits, compatible with severe vasculopathy. This caused significant pain and impaired mobility. During this period, she also developed interstitial lung disease and lost significant weight due to dysphagia, lack of appetite, and recurrent vomiting, likely due to the gastrointestinal tract involvement.

She was aggressively treated with nifedipine, sildenafil, iloprost, prednisone, cyclophosphamide, rituximab and various analgesics. However, we were unable to salvage her digits, and she required multiple amputations of fingers and debridement of toes.

Her current immunosuppressive regimen includes cyclophophamide 50 mg p.o. daily and prednisone 5 mg p.o. daily. She remains on sildenafil 50 mg p.o. b.i.d. Her condition has stabilized in the last several months; she is regaining weight and undergoing physiotherapy. The pictures were taken at various time points to demonstrate progression of digital infarction in this patient. Although not included in this case study, her toes were also involved, became infarcted, and were subsequently debrided.

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Juvenile Localized Scleroderma Presenting with Finger Contractures: A Case Report and Review of the Literature
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Juvenile localized scleroderma (LS) (or "morphea") is a subtype of scleroderma that lacks internal organ involvement. It is an uncommon inflammatory condition that involves excess collagen deposition in the skin and can progress to underlying connective tissue, including fascia, muscle, and bone. Depending on the extent of disease, LS can result in significant morbidity. Although larger joint contracture involvement is often reported in LS, small joint contractures are seldom reported. We present a case of finger contractures in a 6-year-old boy with LS and updates on treatment modalities.
Observation: A 6-year-old boy presented with a 6-month history of finger contractures of the right third and fourth metacarpal-phalangeal and proximal inter-phalangeal joints. A brown-colored indurated lesion with an erythematous border was seen on the right palm. Routine lab investigations were all normal, including complement levels, ANA, and RF. With a suspected diagnosis of Dupuytren's contracture, the patient underwent a fasciectomy, which revealed inflammation of the tenosynovium and granular deposits infiltrating the flexor tendons. The patient later developed an indurated lesion on the palmar aspect of his right wrist. A skin biopsy from the wrist displayed a sclerotic dermis with lymphocytic infiltrates, findings consistent with a diagnosis of LS.
LS generally presents as a subtle localized area of erythema with waxy induration that may evolve to ivory-colored thickened skin. LS is commonly classified into 5 subtypes: circumscribed, linear, generalized, pansclerotic, and mixed. The most common subtype in children is linear LS. Some patients present with musculoskeletal symptoms, including arthralgias, synovitis, and contractures. The extension of fibrosis into deeper connective tissue can lead to impaired growth, limb-length discrepancy, joint contractures, myositis, arthritis, and significant disability, particularly in a growing child.

Current treatment regimens include methotrexate combined with oral prednisone or intravenous methylprednisolone. This treatment can be supplemented with topical corticosteroids or calcineurin inhibitors and regular physiotherapy. Other adjuvant therapies have also been documented with varying results, including phototherapy treatment, systemic treatments (acitretin, imatinib, infliximab, antimalarials, mycophenolate mofetil, ciclosporin), and topical treatments (tacrolimus, imiquimod, calcipotriol-betamethasone dipropionate).

Conclusions: Small joint contractures can be the initial presentation in children with LS, as the disease can progress beyond the superficial layers of the skin into underlying connective tissue, muscle, and bone. This is the second case of linear LS finger contracture presentation reported in the paediatric population. Advanced LS can lead to significant morbidity and disability making early recognition and treatment critically important.

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Isolated Aortitis with Acute Aortic Dissection: Atypical GCA or Typical Fulminant Variety of Isolated Aortitis?

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Introduction: Aortitis is a chronic, progressive inflammatory condition of the aorta, most commonly associated with giant cell arteritis (GCA) or Takayasu arteritis (TA). Isolated aortitis refers to the clinical presentation of aortitis not meeting criteria for GCA or TA, and with no evidence of infectious or other autoimmune etiologies. The histopathological findings are often indistinguishable between GCA, TA, and isolated aortitis. A new entity of the latter, termed fulminant variant of isolated aortitis which often presents with acute, severe aortic dissection, has been inadequately described in the literature.

Case Description: 56-year-old female smoker, previously healthy, presented with a one-day history of bilateral leg numbness and weakness, and sudden-onset chest pain confirmed to be type A aortic dissection on imaging. The dissection was extensive, extending from the ascending aorta to bilateral iliac arteries resulting in paraplegia, bilateral leg ischemia and compartment syndrome, and bilateral renal ischemia requiring dialysis. She underwent repair for her type A aortic dissection, axillary to right femoral artery bypass, and bilateral lower limb fasciotomies. Histopathological analysis of the resected aorta revealed inflammation and intimal thickening with many histiocytic giant cells in the intima-medial junction, with infiltration of young-type fibroblasts and no evidence of chronic fibrosis. She was started on prednisone 50mg daily, along with acetylsalicylic acid and denosumab for stroke and osteoporosis risk reduction, respectively.

Discussion: We elected to empirically manage this patient as an atypical case of GCA. However, the patient does not meet criteria for either GCA or TA, and neither typically present acutely with aortic dissection. There are case reports in the literature of first-presentation aortic dissection in the setting of large vessel vasculitis (LVV). Our patient represents a fulminant and rare subset of those cases, which has been termed fulminant variant of isolated aortitis. We will review cases of aortitis presenting with aortic dissection, in both patients who meet and do not meet criteria for GCA or TA. We hope to better delineate distinguishing characteristics of isolated aortitis from aortitis occurring in established LVV.

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Comparison of Medication Use in Rheumatoid Arthritis Patients Between University and Private Settings – Results from Ontario Best Practice Research Initiative

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Objectives: The objective of this study was to compare the characteristics and patterns of medication use among rheumatoid arthritis (RA) patients in university and community settings.

Methods: Descriptive analyses were performed using data collected from the Ontario Best Practice Research Initiative (OBRI), a clinical registry of RA patients followed in routine care. Patients were categorized as university if their rheumatologist worked in a teaching hospital, mentored medical students and/or had their Research Ethics Board (REB) located at a hospital. The patients of a community rheumatologist worked at a community center and/or had their REB at a location other than a hospital. A group of mixed Physicians (n=12), who were affiliated with an academic site, but practiced at a community site were excluded from the analysis. Patient baseline demographics, clinical characteristics, socioeconomic features and treatment regimenswere compared between university and community patients using chi-square and t-tests.

Results: Among 1583 RA patients, 512 (32%) were from university and 1071 (67%) from community sites. Compared to community patients, university patients were younger (55.5 ± 12.9 vs. 57.9 ± 13.3 yrs, p=0.004), had longer RA disease duration (11.3 ± 10.9 vs. 6.9 ± 8.5yrs, p<0.0001), and were highly educated with higher household incomes. Prevalence of depression was higher among community patients (26%) compared to university (21%), p=0.04. The disease activity measures and functional status at baseline were similar between the two groups. The use of Biologics was more in university patients (31% vs. 17%, P<.0001) with fewer use of DMARDS (61% vs. 73%, P<.0001).

Conclusion: RA patients in community settings appeared to be older with longer disease duration, had lower socio-economic status and a lower utilization of biologics. The results do not represent the clinician practice patterns as the referral criteria might have biased the patients enrolled in the study. Further analysis is required to evaluate whether the care gap due to differential utilization of biologics have an impact on disease severity in subsequent years.

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Disease Activity in Moderate Rheumatoid Arthritis Patients - Results from Ontario Best Practice Research Initiative

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Objectives: Randomized trials in Rheumatoid Arthritis (RA) usually include patients with severe disease activity; however, patients with moderate disease activity represent a large proportion of RA patients in the real world. The aim of this study is to describe characteristics of RA patients with moderate disease activity at time of entry into the Ontario Best Practice Research Initiative (OBRI) cohort, and to compare patient characteristics and disease activity in those on Biologics versus DMARDs. We also aim to determine the proportion of patients in low, moderate and severe disease activities at 6 months.

Methods: Data was collected from OBRI, which includes a clinical registry of RA patients followed in routine care in Ontario, Canada. Patients with moderate disease activity were identified based on the Clinical Disease Activity Index (CDAI) at entry into OBRI. These patients were further classified into two subgroups based on their medications at time of entry into the cohort: Disease Modifying Antirheumatic Drugs(DMARDs) or Biologics. Patient characteristics at baseline and the proportions of patients with low, moderate, and severe disease activity at 6 months were compared.

Results: In the OBRI cohort (n=2305), 512 (22%) patients with mean (SD) age 57.3 (13.3) years were found to have moderate CDAI at baseline with follow-up data at 6 months. Among these, 271(53%) reached low activity, 177(35%) stayed in moderate activity, and 64(13%) progressed to high activity at 6 months. At the time of entry into OBRI, patients on Biologics had longer RA duration (11.3 vs 7.2 years, p<0.0001), with a higher proportion of females (85% vs 74%, p<0.05) compared to those on DMARDs. Patients on biologics also had significantly more previous biologics use (p<0.0001), and higher Health Assessment Questionnaire (HAQ) score (p<0.001) compared to patients on DMARDs. Age, education, private insurance, income, race, smoking history, comorbidities, tender joint count, swollen joint count, and other disease activities at entry into the cohort were not significantly different between the two groups.

Conclusion: Among patients with moderate disease activity at time of entry into OBRI, half achieved low disease activity at 6 months, while 1/3 remained in moderate disease activity. At entry into the cohort, socioeconomic factors and comorbidities between patients on Biologics and DMARDs were the same. The next steps are to evaluate clinical and functional responses at 6 months in patients taking Biologics in comparison with DMARDs in moderate RA patients.

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Takayasu's Arteritis: Natural History of the Disease

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Background: Takayasu's Arteritis (TAK) is a rare systemic inflammatory disease of unknown origin that most commonly affects woman before age 40. It is defined as granulomatous inflammation of the aorta and its major branches. Approximately 80% of patients are managed by Rheumatologists. There is little epidemiologic data on the disease. The first phase of disease involves a systemic inflammatory stage manifesting as constitutional symptoms and fever. This is followed by the vascular inflammatory phase that may manifest as claudication, neurologic, cardiac or gastrointestinal symptoms secondary to arterial insufficiency, arthralgias, myalgias or rash secondary to skin vasculitis. Most patients are treated with corticosteroids, and other immunosuppressant medications. With therapy, the final inactive phase is usually achieved, but only maintained in approximately 20% of patients. The majority of patients have progressive relapsing disease, associated with significant morbidity.

Objective: To describe a case of untreated monophasic Takayasu's arteritis.

Methods: We present a unique case of a 62 year old woman with untreated Takayasu's Arteritis for 34 years. This case presents the disease's natural history

Results: CC, a 62 year old woman, was recently referred to Rheumatology for initial management of TAK, diagnosed at the age of 29. She developed her symptoms post-partum. She presented with an acute headache, right sided hemiplegia and had a stroke confirmed by angiogram due to narrowed blood vessels. She did not describe constitutional symptoms prior to her stroke. Standard treatment for Takayasu's with steroid was never initiated. Bypass was not feasible. She was advised to stay on lifelong anticoagulation and cardiovascular risk reduction. She completed rehabilitation and returned to work six months later. She remained asymptomatic. In 2013, she developed a cold right upper extremity and was referred for this reason. Subsequent CT angiography was grossly abnormal showing complete occlusion of the left common carotid artery, left subclavian artery and subtotal occlusion of the right brachiocephalic with significant collateral vessel formation. We evaluated her further for disease activity; her ESR and CRP were normal and a PET-CT showed no activity. She remains on warfarin, ASA and statin. She has been referred to vascular surgery for possible revascularization.

Conclusion: Takayasu's arteritis is treated with corticosteroids, and if unresponsive then other treatment agents are often added. It is unusual to describe a patient presenting decades after the initial diagnosis with no prior corticosteroid usage. This case report provides a description of the natural history of the disease, without corticosteroid usage.

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Longitudinal, Incremental Healthcare Costs of Sjogren's Syndrome in British Columbia, Canada: A General Population-Based Cohort Study

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Objectives: Estimates of healthcare resource use and costs in Sjögren's Syndrome (SjS) are scarce, and the incremental burden of SjS (extra costs due to treating SjS) has not been determined. We estimated the incremental healthcare costs of a general population-based cohort of incident SjS for five years after diagnosis.

Methods: Data sources: Our administrative data captured all provincially-funded outpatient visits, investigations, and hospitalizations (from 1990-2010) and all dispensed prescriptions, regardless of funding source (1996-2010). Cases: A population-based cohort of incident SjS (no prior SjS encounter from Jan 1990 to cohort entry) for the years 1996-2008 was identified using the following algorithm: ICD-9/10 code for SjS on: a) at least two visits within a two-year period by a non-rheumatologist physician; or b) at least one visit by a rheumatologist or from hospitalization. Controls: Individuals from the general population matched to cases 10:1 on sex, age at diagnosis, and index year. Cost Calculation: Costs for outpatient services and prescriptions were summed directly from billing data. Case-mix methodology was used for hospitalization costs. Statistical Analysis: Mean per-patient-year (PY) costs were estimated for cases and controls. Generalized linear models were then used to determine the incremental healthcare utilization, and cost ratios between cases and controls, after further adjustment for urban/rural residence, neighbourhood income quintile, and Charlson's co-morbidity index at baseline. Costs are reported in 2010 Canadian dollars.

Results: We matched 691 incident SjS cases (91% female, mean age 57±15.0 years) to 6,910 controls. Unadjusted mean per-PY costs for controls in the first year after diagnosis (Year 1) were $4,213 (95% CI=$3,762-$4,665). Costs for SjS cases were 2.8-times greater, averaging $11,748/PY ($9,640-$13,856), with 49% from hospitalizations, 25% from outpatient, and 26% from medications. Following adjustment, costs for cases were 2.7-times higher than matched controls (95% CI=2.4-2.9). Cases averaged 16.5 additional outpatient visits/PY than controls in Year 1 (95% CI=15.1-17.9, $p < 0.01$), and were dispensed 10.7 more prescriptions/PY (7.2-14.2, $p < 0.01$). 29% of cases were hospitalized in Year 1 (versus 11% of controls, $p < 0.01$); adjusted hospitalization costs amongst hospitalized cases were 28% higher than those of hospitalized controls ($19,487 vs. $15,225, $p < 0.01$). Mean per-PY costs decreased in the second year after diagnosis (Year 2), but remained two-times higher for cases versus controls, and this trend continued through Year 5 (adjusted cost ratio=2.6 (2.3-3.1)).
Conclusion: The incremental healthcare burden of SjS is high (averaging $7,535/PY in the year after diagnosis), and is sustained over time.

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Triage of Rheumatology Referrals by an Advanced Practice Physiotherapist Facilitates Wait Time Benchmarks

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Objectives: In June 2014 the CRA (Canadian Rheumatology Association) published wait time benchmarks for inflammatory arthritis and connective tissue disease to improve patient outcomes. Furthermore, many hospitals have established quality indicators with respect to triage of referrals, including both time to confirmation of receipt of referral and time to notification of appointment. The study aim was to determine if both centralized triage by an Advanced Practice Physiotherapist (APP), and the introduction of quality improvement initiatives would facilitate achievement of wait time benchmarks. Quality initiatives included priority assignment of referrals, booking templates, and monthly audits of indicators against benchmarks.
Methods: All referrals triaged by a rheumatologist from September to November 2012 were evaluated and compared to referrals triaged by an APP from January to March 2014. Each referral was assigned a priority ranking based on a previously described triage system. All referrals were categorized into one of two groups: 1) suspected inflammatory arthritis (IA) / connective tissue disease (CTD) or 2) non-IA/ CTD. Time to initial consult and time to notification of appointment from receipt of referral was assessed.

Results: A total of 558 referrals were evaluated, with 11 (2%) identified as urgent at time of referral receipt and 24 (4%) had insufficient information or were duplicate/cancelled referrals. 227 referrals and 331 were received in a three month period in 2012 and 2014, respectively. In 2012, 72 (33%) patients were diagnosed with IA at time of initial consult, with 149 (67%) patients identified as non-IA. Mean wait times for IA patients to be seen was 33 days, 95% CI [25.5, 40.5], while mean wait times for non-IA patients was 37 days, 95% CI [33, 41]. In 2014, the triage system used by the APP identified 131(43%) patients with suspected IA based on information in referral outlining distribution of arthralgias/joint swelling, family/personal history, duration of disease, morning stiffness, and serology. Mean wait times for patients with suspected IA based on the triage tool criteria was 15.5 days, 95% CI [5.5, 25.5], while non-IA patients had a mean wait time of 51.5 days, 95% CI [45.5, 57.5]. Time to notification of appointment was improved from 17 days to 4.37 days.

Conclusion: Triage of rheumatology referrals by an APP is effective in improving wait times for priority patients thereby improving patient outcomes. Centralized triage, booking templates, monthly auditing and implementation of benchmarks facilitated decreased wait times for inflammatory arthritis and connective tissue disease.

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Case Report: Tapazole Associated Cutaneous Vasculitis
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Introduction: Agranulocytosis and p-ANCA-associated vasculitis are rare complications of anti-thyroid therapy, and generally do not occur simultaneously. The pathophysiology of these reactions is poorly understood, however autoimmunity is thought to play a role in conjunction with direct toxicity. Among those with anti-thyroid medication induced vasculitis, reactions may resemble lupus-like disease or idiopathic systemic vasculitis. Reported cases describe leukocytoclastic infiltrates on skin biopsy, however there has been at least one case that also described the presence of thrombi.

Objective: We report a case of an eighteen year old woman with Grave's hyperthyroidism treated for one year with methimazole who presented with necrotic skin lesions of the lower extremities. These lesions, taken during a period of coinciding agranulocytiosis, were inconsistent with typical histopathological biopsy findings of leukocytoclastic vasculitis.

Results: The rash began as two erythematous lesions on the left leg which became centrally ulcerated with eschar. Lesions appeared on the right leg five days later. There was no preceding palpable purpura, arthritis, or pruritis. Past medical history included mild asthma and acne treated with a combination oral contraceptive. Family history is significant for maternal hyperthyroidism and gestational diabetes of as well as a sister with hypothyroidism. The patient denied drug use, is sexually active with no history of STI, and has piercings and a tattoo.

Investigations revealed aseptic lesions with mixed dermal inflammation on biopsy including extravasated RBCs and possible fibrin or thombi in the dermal vessels suggestive of a thrombotic vasculopathy. There was an absence of neutrophilic infiltrate. The patient had an isolated, severe neutropenia of zero with an otherwise unremarkable peripheral smear. ENA, RF, ANA, anti-dsDNA, anti-tTG, cryoglobulins, and anti-centromere B were negative; however anti-MPO and anti-intrinsic antibodies were positive. Complement levels and renal function were normal. Hepatitis B and C, HIV, EBV, and CMV serology were negative. Drug testing was negative. Two days after discontinuation of methimazole there were no observable neutrophils; G-CSF treatment was given, with neutrophil normalization after four days. The patient's rash improved after ceasing methimazole but was still present at discharge 12 days later.

Conclusion: We report a case of methimazole-associated agranulocytosis and necrotic skin lesions, in the absence of typical leukocytoclastic vasculitis on biopsy. To our knowledge, this is the first case to report a mixed inflammatory appearance as opposed to a leukocytoclastic vasculitis. This may suggest a novel reaction to methimazole or the result of coinciding agranulocytosis at the time of skin biopsy.

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Characterization of the Immune Basis for Reduced IFN-α Production in Serologically Active Clinically Quiescent SLE

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Objectives: Serologically active clinically quiescent (SACQ) SLE patients maintain high levels of anti-DNA antibodies and/or low levels of complement for sustained periods of time in the absence of clinical activity. Previous studies have shown that the IFN signature and levels of other pro-inflammatory cyto/chemokines are significantly decreased in SACQ, as compared to serologically active clinically active (SACA) patients. Our objective was to determine the mechanisms underlying the lack of IFN-α and pro-inflammatory cyto/chemokines in SACQ patients.

Methods: Control peripheral blood mononuclear cells (PBMCs) were incubated with SACQ, SACA, serologically quiescent clinically quiescent (SQCQ) or healthy control (HC) serum (1/20 dilution) in the presence or absence of HeLa nuclear extract as a source of nuclear antigen for 24 hours. The levels of pro-inflammatory cyto/chemokines in the supernatants were measured by ELISA. Mixing experiments, where SACQ, SQCQ or HC serum was added to SACA serum or supernatants of CpG-stimulated PBMCs, were performed to assess the presence of inhibitors.

Results: Incubation of PBMCs with SACQ serum induced significantly decreased levels of detectable IFN-α as compared to SACA serum (p=0.0008), with the levels for SACQ serum being comparable to those induced by SQCQ and HC serum (p=0.14; p=0.88). Even in the presence of nuclear antigens, the levels of IFN-α that could be detected following incubation of PBMCs with SACQ serum were significantly reduced as compared to SACA serum (p=0.0001), suggesting that this reduction was not due to a lack of nuclear antigens. In mixing experiments, the addition of SACQ serum to SACA serum dramatically reduced the levels of detectable IFN-α. The mechanism of this inhibition appeared to vary with the autoantibody profile of SACA serum, suggesting the presence of multiple inhibitors in SACQ serum. In some cases, similar inhibition was seen for SACQ, SQCQ and HC serum (compatible with possible nuclease activity), whereas in others only SACQ serum inhibited, and this inhibition was abrogated by IgG depletion. Notably, the presence of IgG inhibitors appeared to correlate with the ability of SACQ serum to block detection of IFN-α by ELISA, raising the possibility that these are anti-IFN-α antibodies. In contrast, there was no difference between SACQ, SQCQ and SACA serum in their capacity to induce IP-10 production by PBMCs, although the addition of exogenous nuclear antigens led to increased IP-10 production only for SACA serum.

Conclusion: The results suggest that there are multiple inhibitors of cyto/chemokine production/detection in SACQ serum. These could include anti-cytokine antibodies and nucleases.

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Prevalence, Severity and Impact of Fecal Incontinence in Systemic Sclerosis: Preliminary Results of a Cross-Sectional Study

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Objectives: Fecal incontinence (FI) is a complication of systemic sclerosis (SSc), but its exact epidemiology and optimal management remain unknown. The primary aim of this study was to establish the prevalence and severity of FI in SSc. Secondary aims were to determine the association between FI and constipation, diarrhea, small intestinal bacterial overgrowth (SIBO) and other predictors of FI, and to determine the impact of FI on health-related quality of life (HRQoL) in SSc.

Methods: A cross-sectional study was initiated in March 2014 in three sites participating in the Canadian Scleroderma Research Group (CSRG; Sherbrooke, Montreal and Hamilton). In addition to the standardized data collection protocol, participants were asked to complete three validated questionnaires: Bristol stool scale (BSS; measures consistency of stool from 1, being hardest, to 7, being completely liquid stool), Jorge-Wexner score (JWS; FI severity score ranging from 0-20, with 20 being most severe), and Fecal Incontinence Quality of Life scale (FIQOL; measuring 4 domains: lifestyle, coping/behaviour, depression/self perception, embarrassment). The Rome III criteria were used to define constipation. Descriptive statistics and associations between the JWS and clinical variables were computed. P-values ≤0.05 were considered statistically significant.

Results: As of August 2014, 70 subjects had been recruited. Mean age was 61.2±11.4 and 82.9% of subjects were women. The mean BSS was 3.0 (2.0-4.0), 30(43.5%) subjects met the Rome III criteria for constipation and 14 (20.0%) had been treated with antibiotics for SIBO since disease onset. According to the JWS, 17 (25.0%) subjects had FI; among them 10 (14.7%) were mild (score 5-9) and 7 (10.3%) moderate to severe (score ≥10). The JWS was significantly higher in patients with associated constipation (p=0.004), urinary incontinence (p=0.00002) and past history of forceps use (p=0.015). No significant relation was found between the JWS and the BSS (p=0.101), use of antibiotics for SIBO (p=0.757), and other predictors of FI including disease duration (p=0.138) and disease type (p=0.215). There were strong correlations between the JWS and 3 domains of the FIQOL: lifestyle (p=0.001), coping/behaviour (p=0.0003) and embarrassment (p=0.003). The correlation was not significant with the depression/self-perception domain (p=0.207).

Conclusion: In this multi-site study, FI was common and often severe in SSc. Constipation, but neither diarrhea nor malabsorption, was significantly associated with FI. FI had a strong negative impact on HRQoL. A larger study is underway to obtain more robust estimates. These data will inform the design of future interventions aimed at improving this serious complication of SSc.

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Improving Decision-Making about Medications in Individuals with Suspected Knee Osteoarthritis using a Web Application

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Objectives: Concerns persist that many individuals with suspected knee osteoarthritis (OA) self-treat with over-the-counter (OTC) medications, particularly NSAIDs, without understanding the risks of side-effects or understanding the alternative medication options that exist. To test whether an online web application can help improve individuals: a) knowledge of medication options, b) medication preference, c) utilization of physicians and pharmacists, and d) adherence to medication.

Methods: Participants over 50 were recruited from adverts at pharmacies and on google to access a website. Individuals who passed validated screening questions for suspected knee OA were then consented and asked questions about their medication use, interactions with health care professionals, their decisional conflict and their perceived level of risk of side-effects. They were then randomized to receive information about medications for knee OA from either 1) Control: package inserts, or 2) Intervention: a web application (called DeCIDA) that displayed personalized risks of the medications which best matched each individual's profile. Each group were then asked to indicate their preferred medication, their decisional conflict, their knowledge based on pre-set questions, and were then advised to discuss the results with their physician or pharmacist. Comparisons between groups. Participants will then be followed up after 6 months.
Results: Of the 232 individuals that consented to begin the study, 53(23%) were using high doses of OTC NSAIDs without advice from a health professional. All but 3 of these respondents underestimated their risks of either acute gastrointestinal hemorrhage or cardiovascular disease. Only 98 individuals completed the web application vs 111 who completed the control arm with problems in usability cited as a concern in a follow up of drop-outs. Overall for completers, decisional conflict was reduced in both groups, but significantly more in the DeCIDA group (Δ18 vs Δ9, p=.04). More individuals in the DeCIDA arm indicated their preferred medication was different to their current medication (22% vs 10%, p=.06), and improved their knowledge score (4.2 vs 3.1, p=0.01). The proportion of individuals that indicated they planned to discuss the information with a health professional was marginally improved (42% vs 35%, p=.09).
Conclusion: We found that providing an online web application improved knowledge and medication preference and reduced decisional conflict. Ongoing follow-up will measure whether individuals engage with the health care system and adhere to their medication preferences. Concerns with navigation of the tool were identified.

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Estimating Cost Savings Attributable to Increased use of Triple Therapy

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Objectives: Recent randomized controlled trials in rheumatoid arthritis (RA) patients have determined that a strategy of first adding sulfasalazine and hydroxychloroquine to methotrexate (Triple Therapy or TT) is neither inferior nor less safe than first adding anti-TNF drugs in patients with active disease despite methotrexate. The implication is that inexpensive TT should be initiated prior to expensive biologic therapy. In this study we examine historical biologic and TT use in British Columbia (BC), Canada over the past 10 years. We sought to estimate the potential savings in expenditures if TT use had been more prevalent, and project potential future cost-savings.

Methods: We examined a population-based cohort of all BC patients with a rheumatologist diagnosis of RA identified from administrative data. We selected prevalent RA cases who used a biologic for the first time between 2001 and 2010 and examined their prior DMARD history from prescription billing data. For each year, we calculated the proportion of patients that had used TT, the average drug prices, and the average duration patients remain on TT. Since not all patients can use TT, we conducted a series of scenarios which estimated costs that would have been saved if a higher proportion of patients had used TT.

Results: In total, we examined 2726 RA patients who started their first biologic over the time period. TT use prior to biologic therapy has increased over time, from 15.2% in 2001 to 24.4% in 2010. The average duration patients remained on triple therapy was 1.13 years. Of the $62million spent on patients first year of biologics, a scenario where 80% would have received TT instead would have resulted in cost savings of $47.3 million over the 10 year period. Assuming similar patterns of TT use across Canada, projections suggest future cost-savings of over $12 million per year if triple therapy is used in 80% of patients prior to biologic use. Various sensitivity analyses are performed.

Conclusion: Higher utilization of TT will require a willingness for rheumatologists to prescribe it, and a willingness for patients to use it. With the benefit of hindsight, higher use of TT would have released a substantial amount of pharmaceutical spending to alternative treatments. Importantly, with less than 25% of patients currently receiving TT prior to a biologic, there is still a considerable potential for future savings. Strategies such as academic detailing and patient decision aids may be good investments if they can change treatment choices. Supported by a CIORA grant

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Osteonecrosis in Systemic Lupus Erythematosus: Prevalence, Patterns and Outcomes

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Objectives: Osteonecrosis is a serious comorbidity of systemic lupus erythematosus (SLE). The reported frequency of symptomatic ON in SLE is variable, ranging from 4% to 15%. The aim of this study is to provide an update of the prevalence, patterns and outcomes of symptomatic osteonecrosis in SLE.

Methods: SLE patients with osteonecrosis were identified from the Lupus Clinic Database containing patients with 4 ACR criteria of SLE or 3 criteria and a biopsy diagnostic of lupus. Osteonecrosis was defined as those patients with clinical symptoms and confirmed osteonecrosis by imaging (x-ray, bone scan, CT, MRI). Demographic and clinical data of affected patients were collected prospectively, stored in an Oracle database and analyzed using descriptive statistics.

Results: Of the 1729 patients with SLE registered in the database as of 1970, 235 patients (13.6%) developed symptomatic osteonecrosis. 86.0 % were female, with a mean age of 34.8 +/- 12.8 years at first osteonecrosis diagnosis. This involved a total of 542 joints, 383 joints of which were identified at the time of first osteonecrosis occurrence. The mean time from diagnosis of SLE to diagnosis of first osteonecrosis was 8.2 +/- 8.1 years, and the time from first osteonecrosis diagnosis to second osteonecrosis diagnosis was 3.4 +/- 4.8 years. 111 out of 235 (47%) patients had multiple site involvement at first osteonecrosis occurrence, affecting from 2 to 6 sites. At the time of first diagnosis affected sites included the hip (245), knee (86), shoulder (28), ankle (15), wrist (3), other joints (3) and elbow (2). Those that progressed to surgical intervention included: hip 131/245 (53.5%), knee 18/86 (19.8%), wrist 1/3 (33.3%), shoulder 1/28 (3.6%), ankle 0/15 (0%), elbow 0/2 (0%), and other joints 1/3 (33%). The mean time from osteonecrosis diagnosis to surgery of the hip was 3.8 +/- 5.5 years, while the mean time from osteonecrosis diagnosis to surgery of the knee was 5.5 +/- 6.2 years.

Conclusion: Osteonecrosis continues to be a significant comorbidity of SLE as 13.6% of patients developed symptomatic osteonecrosis. In patients developing osteonecrosis, the presentation occurred after 8.2 +/- 8.1 years of SLE disease duration. 47.2% of patients had multiple site involvement at first ON diagnosis. Large weight-bearing joints, including the hip and knee, were most frequently involved. The majority of hips required surgical intervention. To our knowledge, this is the largest cohort of SLE patients with symptomatic osteonecrosis. Better strategies to prevent this serious complication are needed.

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A Survey of Safety Needle Use in Joint Injection Amongst Canadian Rheumatologists
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Objectives: Needle safety devices are mechanical modifications to needles and/or syringes in order to reduce the risk of inadvertent needle stick injury (NSI). Following research showing reduction in NSI, these devices have been introduced to many hospital systems. To date, no research has been performed on the effects of these devices on reducing needle stick injuries amongst Canadian Rheumatologists performing joint injection and aspiration procedures. However, due to hospital policies, these devices are often the only available needles available for procedures. No data currently exists regarding the preference of Rheumatologists for safety needles versus standard needles or the effect of these devices on NSI during joint injection and aspiration.

Methods: An online survey was distributed via SurveyMonkey to actively practicing Canadian Rheumatologists who are currently performing joint aspiration or injection procedures. The survey assessed the use of safety devices by Rheumatologists and their perceptions regarding the usefulness and safety of such devices.

Results: A total of 138 Rheumatologists responded to the online survey. The survey showed the majority of Rheumatologists polled (65.9%) use standard needles over needles with safety devices. Of the devices, the Becton Dickinson devices were the most commonly used (65.8%). Rheumatologists were agreeable to the use of safety devices (57.7%). Of those not interested in use of safety needles, the most common complaints were the perceived cumbersome nature of the device (38.1%) and interference with joint injection/aspiration technique (31.0%). 17.2% of responding Rheumatologists have suffered at least one NSI during joint injection or aspiration post fellowship. Of those with NSI, 57.1% of Rheumatologists did not change their practice to reduce risk of further NSI and 45% have had multiple (between 2 and 5) NSI. At present, only one responding Rheumatologist is actively using ultrasound guidance for joint aspiration or injection.

Conclusion: Despite safety data on the use of needle safety devices in other healthcare settings, there is minimal data on the safety and effectiveness of safety needles in the setting of joint injection and aspiration by Rheumatologists. Rheumatologists in Canada have a preference for standard needles over needles with safety devices. Design changes to safety needles to improve ease of use during joint injection and aspiration could improve safety while also increasing compliance.

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Improving the Diagnostic Value of Ultrasound in Giant Cell Arteritis

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Objectives: To study whether determination of intima-media thickness in carotid and axillary arteries can improve the diagnostic value of Temporal Arteries (TA) ultrasonographic (US) exam in patients with proved or suspected Giant Cell Arteritis (GCA).

Methods: From May 2011 to August 2014, 45 patients had a US examination of TA because of a clinical suspicion of GCA. US of the common, frontal and parietal branches of the TA were done with a MyLab70 device and Color Doppler technique. Findings were considered compatible with the diagnosis of GCA if a there was a halo sign, stenosis or occlusion. Carotid and Axillary arteries were also examined and the intima-media thickness recorded in 40 of our patients, at least 2 cm from any atherosclerotic plaque. The clinical diagnosis was considered positive if made by an expert or if treatment with at least 40 mg of prednisone/day was started.

Results: 68,9% of our patients were women, with an average age of 72 years; 40% had at least 3 ACR criteria for GCA. The specificity of the US findings in TA was 85% when compared to ACR criteria. Of the 7 patients who had a TA biopsy, the one that was positive demonstrated US findings in the TA compatible with GCA. Sensitivity of our diagnosis was increased if there was an intima-media thickness of more than 0,8 mm or TA findings on US, compared to TA findings on US only (70,6% vs 64,7%), while keeping a very good specificity of 95,7%. Increased thickness smaller than 0,8 mm had no impact on the diagnostic value of US.

Conclusion: Previous work has shown that a significant percentage of patients with GCA also presented inflammation of larger vessels. A limit of intima-media thickness of more than 1.5 mm was previously recommended in the literature for the diagnosis of GCA without any experimental support. Our objective was to determine if lower values could add to the diagnostic value of TA US. Several limits were used (0.5, 0.6 and 0.8 mm) but only 0.8 mm had a positive impact on the sensitivity and specificity of the US evaluation. Normal values for these parameters have not yet been defined in the literature. Our perspective is to study a group of persons without vasculitis aged 65-75 to determine the normal range of intima-media thickness. These future results may improve the impact of US in the diagnosis of GCA.

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What Proportion of Patients Fail to Achieve DAS, CDAI, SDAI Remission based on Patient Global Assessment? An Analysis from the Prospective, Observational Registry, BioTRAC

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Objectives: PtGA is included in the formula of all disease activity indices despite the fact that it may not accurately reflect RA disease activity, but rather reflect disease activity related to fibromyalgia, low back pain, depression or other conditions. We previously assessed the impact of the PtGA on the ability to achieve Boolean ACR/EULAR remission state. The aim of this analysis was to assess the proportion of patients failing to achieve DAS, CDAI and SDAI remission based on a real-world, routine clinical care setting in Canada.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM. In this analysis, RA patients treated with infliximab between 2002-2014 or with golimumab between 2010-2014 were included. Modified versions of DAS28 (mDAS28), CDAI (mCDAI), and SDAI (mSDAI) were calculated by omitting PtGA from the formulas. Correlation of the standard and modified versions of each index was assessed with the Pearson's correlation coefficient. In the absence of validated thresholds for remission and LDA for the modified versions, the standard definitions were considered as the gold standard and ROC curve analysis was used to identify new thresholds for the modified versions. Cross-tabulations with the Chi-square test were used to assess the agreement between the standard and modified definitions of remission and LDA.

Results: One thousand nineteen RA patients with a mean (SD) age of 56.1 (13.5) and disease duration of 8.5 (9.1) were included in the analysis. A strong correlation was observed between the standard and modified versions of DAS28 (r=0.98; P<0.001), CDAI (r=0.99; P<0.001), and SDAI (r=0.99; P<0.001). Based on ROC analysis the new thresholds for remission and LDA were: DAS28 (remission=2.6, LDA=3.1), CDAI (remission=2.5, LDA=10.5), SDAI (remission=3.3, LDA=10.9). Cross-tabulation of the standard and modified thresholds showed that an additional 10.1%, 10.6%, and 17.8% of non-remission cases for DAS28, CDAI and SDAI, respectively, would be classified as remission with the modified definitions. Similarly, an additional 11.5%, 21.2%, and 20.6% of non-LDA cases for DAS28, CDAI and SDAI, respectively, would be classified as LDA.

Conclusion: The results of this analysis have shown that PtGA could account for up to 10% of non-remission cases and up to 20% of non-LDA cases as measured by DAS, CDAI and SDAI. Further analyses are required to identify the determinants of patient global assessment.

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Effect of Smoking on Antimalarial Efficacy in the Treatment of Cutaneous Lupus Erythematosus and Systemic Lupus Erythematosus: A Systematic Review

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Objectives: Antimalarials are frequently used as first-line agents in the treatment of cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE). Studies have suggested smoking not only increases disease activity but may also decrease antimalarial efficacy in lupus patients. The direct effect of smoking on antimalarial efficacy remains unclear and existing observational studies have shown mixed results. Our objective was to evaluate the effect of smoking on antimalarial treatment response in CLE and SLE patients.

Methods: MEDLINE, Embase, Cochrane Library, CINAHL, and Google Scholar were searched for full-length articles and abstracts published up to May 2014 describing the effect of smoking on antimalarial efficacy in lupus patients. Papers were included if they described any outcomes for SLE or cutaneous lupus patients (discoid, subacute cutaneous, chronic cutaneous) on antimalarials with reported smoking status (eg. smoker vs non-smoker).

Results: Out of 232 references, 101 studies were included for full-paper review, out of which 8 observational cohort studies (5 retrospective: 3 prospective) met the inclusion criteria. Seven out of eight studies (575 patients in total) were English, one was French. Antimalarial usage between studies included hydroxychloroquine (HCQ) (200-600 mg daily), chloroquine (CQ) (250-300 mg daily), and quinacrine (Q) (100 mg daily). Concomitant immunosuppressant therapy was not consistently reported between studies. Heterogeneity existed between studies regarding which outcomes were reported for disease response (e.g. CLASI vs author-defined skin response). Four out of eight studies reported no difference in SLE- and skin-related outcomes whereas 3 out of 8 studies reported a lower response rate to antimalarials in smoking patients. One study had mixed results, reporting an initially greater response of the CLASI to antimalarials in the smoking group in the first 7 months whereas non-smokers showed greater improvements in the CLASI after eight months on antimalarial treatment combined with at least one other immunosuppressant. Smokers on HCQ were found to use more quinacrine in this study.

Conclusion: The effect of smoking on the efficacy of antimalarials in SLE is complex, as evidenced by the conflicting results of this systematic review. Larger SLE cohort studies or randomized controlled trials would be helpful to better define this possible attenuation of disease response to antimalarial treatment while adjusting for the contribution of smoking to SLE disease activity in general. Clear definitions of SLE outcomes (e.g. skin scores) would allow for better comparability between cohorts.

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Inflammatory Pseudotumour of the Skull Base: A Case Report and Review of the Literature

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Inflammatory pseudotumours (IPTs) are non-malignant collections of mixed inflammatory and fibroblastic cells due to an unknown etiology. IPTs have been most commonly described in the gastrointestinal and respiratory tract, but can occur anywhere in the body. The diagnosis of IPT is one of exclusion and rheumatologists are often asked to assess for entities such as granulomatosis with polyangiitis (GPA) or IgG4- related disease.

Here we describe a case of a 27 year old female who presented with several months of right sided temporal headache and new-onset dysarthria, dysphagia and rightward tongue deviation. MRI revealed a mass at the skull base extending into multiple cranial nerve foraminae. Blood work revealed negative ANCA studies, elevated inflammatory markers, and normal IgG4 and ACE levels. She also had an incidentally discovered pulmonary nodule that was biopsied and showed focal necrosis with no granulomas or vasculitis. The skull base mass was biopsied and found to be consistent with IPT, without any features of vasculitis, lymphoma, sarcoidosis, infection or IgG4-related disease. She initially improved with high dose glucocorticoids followed by two doses of IV cyclophosphamide but unfortunately worsened after several weeks. A second biopsy was done to ensure that her diagnosis was correct and was again consistent with IPT. Currently, she remains symptomatic on glucocorticoids and is awaiting Rituximab therapy.

We reviewed the literature for similar cases of adult patients with IPT involving the skull base with cranial nerve involvement and found seven articles detailing 10 patients. The average age of reported patients was 44±12 years. In most cases patients had symptoms that had been present for months to years. All patients had an acute deterioration that led to diagnosis of IPT, usually with vision symptoms, hearing loss or worsening pain. All patients underwent imaging to localize the IPT and all had biopsies performed for definitive diagnosis. Treatment of IPT varied, two patients were managed with surgery alone, eight had variable doses and durations of glucocorticoids, and four patients also received cyclophosphamide therapy. Four patients had recurrence of symptoms after initial treatment. Overall outcomes were favourable, with resolution of symptoms and improvement of neurological deficits in eight patients. Two patients died; one from sepsis and the other from internal bleeding after the IPT infiltrated a carotid artery.

Inflammatory pseudotumours have diverse presentations that may mimic rheumatologic conditions. Rheumatologists are often asked to rule out other diseases as well as aid in management with immunosuppressive medications.

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Safety of Rapid Rituximab Infusion in Rheumatoid Arthritis in a Single Community Practice

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Objectives: To evaluate the safety, tolerability, and practicality of a rapid infusion protocol for rituximab in RA patients (n=28) in a single community setting.

Methods: Patients, who were prescribed rituximab for the treatment of moderate to severe RA, were recruited from October 2006 to November 2013 and given the opportunity to participate in the rapid infusion protocol. All patients provided written informed consent. Each treatment course consisted of 2 rituximab 1000 mg infusions given 2 weeks apart. The first infusion followed the conventional infusion schedule. Rapid infusion protocol was administered on the second and/or all subsequent infusions over 2 hours. All patients received premedication. Vital signs were recorded at baseline and at 15, 30, 60, 90, and 120 minutes.

Results: A total of 57 patients received rituximab infusions (280 infusions) from October 2006 to November 2013. Out of these, 50 patients with a diagnosis of rheumatoid arthritis met the criteria to be followed on the short infusion protocol. A total of 28 patients agreed to be followed on rapid rituximab protocol. 132 infusions were included in this analysis with the mean treatment interval of 9.4 months. 93% of the patient population had failed or were intolerant to prior TNF-alpha inhibitors and 7% were biologic naïve. A total of 7 infusion reactions were reported over 132 rapid rituximab infusions (28 patients), as compared to 8 infusion reactions over 148 conventional infusions (22 patients). There was no significant difference in the incidence of infusion reactions between rapid and conventional infusions (p=0.97). In both rapid and conventional infusions, no patients discontinued rituximab due to infusion related symptoms or reactions. Overall, all symptoms reported were mild and resolved within 24 hours after the infusion. No serious infections or serious adverse events were reported in either rapid or conventional infusion groups.

Conclusion: The current analysis provides reassurance that rapid rituximab infusion is safe and well tolerated. Our experience of administering this protocol over 7 years proves that rapid infusion is as safe as the conventional infusion. In addition to safety, patients reported greater satisfaction with the short infusion duration. This data and previously reported data on rapid infusion in rheumatoid arthritis patients assures physicians that this strategy can be safely implemented in a single community practice setting.

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What Is the Treatment Durability and Safety Profile of Rheumatoid Arthritis Patients Treated with Infliximab Plus Methotrexate and/or Leflunomide? An Analysis from the Real-world Registry, BioTRAC

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Objectives: Clinical trials of anti-TNF therapies have shown that concurrent methotrexate (MTX) therapy enhances the efficacy of TNF inhibitors. A scarcity of data exists on the benefits of combination therapy with IFX and MTX vs. leflunomide (LEF) in a real-world setting; therefore the BioTRAC Registry database was used to explore this question.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or golimumab as first biologics or after having been treated with a biologic for <6 months. RA patients treated with IFX who were enrolled between 2002-2014 were included in this analysis. Treatment durability was assessed with the Kaplan Meier (KM) estimator of the survival function and Cox regression.

Results: 723 RA patients were included; at baseline 516 (71.4%) were on IFX+MTX, 115 (15.9%) on IFX+LEF, and 92 (12.7%) on IFX+MTX+LEF. The mean (SD) age was 55.5 (13.6) years, 76.2% were female and mean (SD) disease duration was 8.7 (9.2) years. The majority of patients were from Ontario (50.6%), followed by Western Canada (25.8%), and Quebec (20.9%). There were 217 (30.0%) patients who discontinued due to lack/loss of response, disease progression, adverse event (AE) or change in therapy with a KM-based mean (SE) time to discontinuation of 83.9 (3.0) months. Upon adjusting for potential confounders, higher durability was observed for the IFX+MTX group vs. IFX+LEF [hazard ratio -HR- (95% CI): 0.50 (0.25-1.01), P=0.055]. Moreover, factors independently associated with premature treatment termination were earlier enrolment period [HR2006-09 vs. 2002-05 (95% CI): 0.15 (0.02-1.15, P=0.068; HR2010-2014 vs. 2002-05 (95% CI): 0.09 (0.01-0.70), P=0.021], shorter baseline disease duration [HR (95% CI): 0.97 (0.93-1.00), P=0.054], and increased baseline pain levels [HR (95% CI): 1.14 (1.03-1.26), P=0.013]. 2,016 AEs were reported by 343 patients (106.8 events/100 patient-years) and 156 SAEs by 96 patients (8.3 events/100 patient-years). The incidence density ratio (IDR) (95% CI) was higher in the groups IFX+MTX vs. IFX+LEF for both AEs and SAEs with 1.44 (1.25-1.67) and 1.60 (0.94-2.73), respectively, however the latter was not statistically significant. When examining the triple combination therapy (IFX+MTX+LEF), higher durability was observed compared to both IFX+MTX [HR (95% CI): 3.68 (1.14-11.92); P=0.030] and IFX+LEF [HR (95% CI): 6.34 (1.72-23.34); P=0.006].

Conclusion: The results of this real-world observational study have shown that combination therapy with IFX+MTX is associated with significantly higher treatment durability compared to IFX+LEF in RA patients with increased risk for AEs but not for SAEs.

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Prevalence of Smoking and Impact on Disease Parameters Among Ankylosing Spondylitis, Rheumatoid Arthritis and Psoriatic Arthritis Patients Treated with Infliximab or Golimumab in Canada

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Objectives: Smoking can compromise the response to biologic treatment in rheumatoid arthritis (RA) patients. The aim of this analysis was to compare patient characteristics and baseline disease parameters based on smoking status at initiation of anti-TNF treatment and to assess the impact of smoking on anti-TNF effectiveness in RA, ankylosing spondylitis (AS), and psoriatic arthritis (PsA) patients treated with infliximab (IFX) or golimumab (GLM).

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM. The analysis was based on patients with available smoking status treated with IFX or GLM between 2010-2014. Between-group differences were assessed for statistical significance with the independent-samples t-test or Chi-square test.

Results: Among the 478 patients included in the analysis, there were 143 (29.9%) AS, 237 (49.6%) RA, and 98 (20.5%) PsA patients. At baseline, the proportion of current smokers was 27.3% in AS, 19.8% in RA, and 19.4% in PsA (P=0.186). Overall, no significant differences in baseline characteristics were observed based on smoking status except for gender among AS patients and TJC28 which was higher among smoking PsA patients. Upon 6 months of treatment, statistically significant and clinically meaningful improvements in almost all parameters were observed, regardless of smoking status and diagnosis. Although statistical significance was not achieved, a greater proportion of non-smokers achieved CDAI LDA (RA: 49.0% vs. 34.8%, P=0.252; PsA: 68.3% vs. 50.0%, P=0.296), SDAI LDA (RA: 56.7% vs. 33.3%, P=0.152; PsA: 69.0% vs. 57.1%, P=0.664) and DAS28 LDA (RA: 50.0% vs. 38.1%, P=0.458; PsA: 59.4% vs. 37.5%, P=0.430) at 6 months. After 6 months of treatment, no significant between-group differences were observed in the improvement of disease parameters in all diagnoses with the exception of PtGA in RA patients which was greater among non-smokers (-21.8 vs. -6.2, P=0.047), and ESR (-21.2 vs. -6.4, P=0.006) and CRP (-19.8 vs. -7.9, P=0.052) levels in AS patients which were greater among smokers.

Conclusion: The results showed that the rate of smoking among Canadian RA and PsA patients treated with anti-TNF is comparable to the general population. Smoking rates among AS patients, however, were greater. Numerical, although not statistically significant, differences were observed in the response to 6 months treatment based on smoking status. Regardless of smoking status, treatment with IFX or GLM was effective in improving disease severity outcomes and reducing symptom severity among AS, RA or PsA patients.

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Drug Survival of Tumour Necrosis Factor-α Inhibitors in Patients with Ankylosing Spondylitis and Axial Spondyloarthritis

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Objectives: To compare the drug survival of tumour necrosis factor-α inhibitors (TNFis) etanercept, adalimumab, infliximab and golimumab used in the treatment of ankylosing spondylitis (AS) and axial spondyloarthritis (SpA).

Methods: All AS and SpA patients treated with TNFis under the care of two community rheumatologists in Mississauga were included in this chart review. Charts dating back to 2001 were assessed in May – July 2014. Patient demographics, non-steroidal anti-inflammatory and disease modifying anti-rheumatic drug use, and TNFi therapies undertaken with reasons stopped, erythrocyte sedimentation rate, C-reactive protein and Bath Ankylosing Spondylitis Disease Activity Index values were extracted. Drug survival was compared for first and second line TNFi therapies using a Kaplan-Meier survival analysis and log rank test. The analysis was conducted using STATA 13.

Results: A total of 107 first TNFi patients were included in this study. The raw survival rates were 46.67%(7/15) for etanercept, 70% (14/20) for adalimumab, 68.12%(47/69) for infliximab and 66.67%(2/3) for golimumab. Through the Kaplan-Meier analysis, only etanercept demonstrated a less than 50% survival, with a median survival time of 63.78 months (CI: 34.68 - ∞). Adalimumab, infliximab and golimumab have greater than 50% survival; therefore no median survival is available. The log-rank test yielded an insignificant p-value of 0.6413. A total of 37 patients required changing to a second TNFi. Reasons for switching included 12 (2 etanercept, 1 adalimumab and 9 infliximab) due to adverse reactions, 23 due to lack of efficacy (6 etanercept, 5 adalimumab, 11 infliximab and 1 golimumab) and 1 (infliximab) for lack of convenience and 1 (infliximab) for loss of coverage. A total of 37 second TNFi patients were included, in which the raw survival rates were 50% (4/8) for etanercept, 73.33% (11/15) for adalimumab, 66.67% (2/3) for infliximab and 54.54% (6/11) for golimumab. The Kaplan-Meier analysis reports median survival for was 7.13 months (CI: 3.48 - ∞) for etanercept, 61.55 months (CI: 61.55 - ∞) for infliximab and 26.56 months (CI: 6.05 - ∞) for golimumab. Adalimumab has a greater than 50% survival (no median survival is available). The log-rank test yielded an insignificant p-value of 0.2766.

Conclusion: Our analysis concludes that there are no differences in survival of the TNFis etanercept, adalimumab, infliximab and golimumab, used as a first or second line TNFis. The disparity in the patients per treatment group warrants further investigation.

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Serum CXCL10 is Elevated in Psoriasis Patients Prior to Psoriatic Arthritis Onset

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Objectives: To determine whether inflammatory cytokines and chemokines CXCL10, IFNA2, IL15, IL17A, IL23, and TRAIL are elevated in the serum of psoriasis patients who develop psoriatic arthritis (PsA), compared to psoriasis patients who do not develop PsA.

Methods: Psoriasis patients were followed prospectively beginning in 2006, and were assessed yearly by a rheumatologist for the presence of PsA. Psoriasis patients who developed PsA were termed 'converters'. Patients who did not develop PsA over the same duration of psoriasis were termed 'non-converters'. Serum CXCL10, IFNA2, IL15, IL17A, IL23, and TRAIL were measured using a multiplexed microsphere-based assay on the Luminex 200 platform. Protein levels were compared between samples taken before and after PsA diagnosis by paired t-test, and between converters and non-converters by logistic regression.

Results: At baseline, converters (n=46) were 54.3% males, with a mean age of 46.1 ± 13.0 years, mean psoriasis duration of 25.5 ± 14.9 years, mean age at psoriasis onset of 20.9 ± 16.5 years, and mean PASI of 7.0 ± 7.2. Non-converters (n=46) were 50% males, with a mean age of 45.5 ± 12.3 years, mean psoriasis duration of 27.5 ± 16.0 years, mean age at psoriasis onset of 18.9 ± 16.3 years, and mean PASI of 6.3 ± 6.1. Proteins were first tested in half of the converter and non-converter samples (discovery cohort), then were validated in the remaining samples. In the discovery cohort, CXCL10 was significantly elevated in baseline samples from converters compared to non-converters (OR=1.6, 95% CI 1.2-2.2, p=0.005). TRAIL was also elevated in converters at baseline (OR=1.0, 95% CI 1.0-1.1, p=0.05) however it was not independent of CXCL10 in multivariate analyses. IFNA2, IL15, IL17A, and IL23 were below the detectable range in several samples and were not significant. CXCL10 remained significantly elevated (OR=1.3, 95% CI 1.1-1.5, p=0.003) in a combined analysis of the discovery and validation cohorts. Twenty-three converters had samples taken at both baseline and at PsA diagnosis. Although mean CXCL10 level was high in baseline samples, it declined significantly following PsA onset from 932 ± 458 pg/ml to 543 ± 310 pg/ml (p<0.001), which is not significantly different from the mean CXCL10 levels observed in non-converters (421 ± 218 pg/ml, p=0.06). **Conclusion:** Serum CXCL10 is elevated in psoriasis patients who develop PsA, but decline following PsA onset. Further studies are needed to elucidate of the dynamics of serum CXCL10 levels in the progression from psoriasis to PsA.

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Impact of Arthritis on Engagement in Farming Related Physical Activities

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Objectives: Agricultural workers have physically demanding occupations. In this study of Saskatchewan farmers, we examine: 1) self-reported prevalence of physician-diagnosed rheumatoid arthritis and osteoarthritis; and 2) the impact of these chronic arthridities on engagement in physical tasks related to farming.

Methods: This study was conducted through a cross-sectional analysis of baseline data from the Saskatchewan Farm Injury Cohort Study in which 2,473 adult residents upon 1,216 farms participated. Collected survey data included: demographic and health information; regional musculoskeletal symptoms for each participant assessed via the Standard Nordic Questionnaire; and engagement in various specific physical tasks or activities associated with mixed farming practices.

Results: Of the 2,473 respondents, 13% reported chronic arthritic diagnoses (10% osteoarthritis, 4% rheumatoid arthritis, with 1% from each category overlapping with both forms of arthritis). Participants reporting arthritis were more likely to also report disabling musculoskeletal symptoms involving their shoulders, elbows, hands, lower back, hips, knees and ankles. Disabling musculoskeletal symptoms were reported by 54% of farmers with arthritis compared to 25% of those without arthritic diagnoses. Farmers with arthritis reported less participation in all physical farming activities studied including various machinery operations, herd maintenance and veterinary activities, overhead work, shovelling/pitchfork work and lifting/carrying. When adjusted for age, gender and co-morbidities, operation of combines and shovelling/pitchfork work continued to be significantly less engaged in by farmers with arthritis.

Conclusion: The overall prevalence of arthritis was consistent with general population prevalence, although the category of rheumatoid arthritis was over-represented. Farmers with arthritis were significantly less likely to participate in combine operation and shovelling/pitchfork chores compared to their counterparts without arthritis.

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Utilization of Health Care Services for Rural and Remote Rheumatoid Arthritis Patients in Saskatchewan

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Objectives: The objective of this study was to inventory geographic availability of medical and allied health services to rheumatoid arthritis (RA) patient care in rural and Northern Saskatchewan and to identify potential barriers to the utilization of these services and perceived impact of such barriers.

Methods: The study population consisted of patients (sample size = 100) who lived in rural or Northern Saskatchewan (100 km or more from Saskatoon), were above 18 years of age and had rheumatologist-diagnosed rheumatoid arthritis. Patients were recruited from the clinical practices of the two rheumatologists based at the Royal University Hospital, University of Saskatchewan, Saskatoon, Canada. Using a standardized interview script and questionnaire, an interview was conducted with the patient to collect information on their understanding of the closest geographic locations for health care services, distance travelled, difficulties including travel costs, lost work time, demands on family members, frequency and wait time of their accessing the service and level of satisfaction in patient access to various health services.

Results: Patient access to general practitioners (GP) was high (98/100), but lower for Physiotherapy (PT, 53/100), Occupational Therapy (OT, 26/100), and Nurse Practitioners (NP, 18/100). Patients visited their GPs more often than their rheumatologists (6.1 vs 3.4 times per year, p=0.0001), however, there was no relation between the visits, resulting in significant variance in number of physician visits per year (9.4 visits per year, 95% CI: 7.8, 11). Patients had similar driving distances for their GP, PT, Pharmacy and Laboratory services, but typically commuted significantly farther for OT services. Patients were significantly more satisfied with their rheumatologist appointments than their GP, OT or PT appointments (8.96 vs 8.04, 7.46 and 6.82 on a 10-point scale respectively), and there was a very small but significant pattern of patients with long travel times being more satisfied with their appointments compared to in community visits. Patients that travelled 1, 2 and more than 2 hours had satisfaction scores 0.93, 0.88 and 1.32 points higher on a 10 point scale. (p<0.03).

Conclusion: Clinician access is a significant issue in this rheumatoid arthritis population, with significant commute times for all services. The inverse relationship between distance and satisfaction suggests that patients do not resent commuting. However, the effect of geographic residential location and therefore possibly commute time on service access and utilization is evident particularly in low frequencies of PT and OT care.

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Self-resolving Limited Respiratory Tract GPA or Something Else?

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Prior to the introduction of effective therapy, Granulomatosis with Polyangiitis (Wegener's) was universally fatal within a few months of diagnosis. The following case report describes a 67 year old man's apparently spontaneous near-remission of this disease. Initially he reported worsening constitutional symptoms, recurrent sinusitis, and airway congestion. His history was also significant for intermittent episodes of hemoptysis, epistaxis, and a possible remote history of sarcoidosis. He denied any musculoskeletal, cutaneous, or other extra-pulmonary manifestations. A physical examination revealed crusted lesions surrounding the nares and inflamed nasopharyngeal passages. A CT-head identified chronic inflammatory changes of the sinuses. A CT-Chest detected a large 12-cm paravertebral pulmonary mass with central cavitation surrounded by multiple small satellite lesions in the lung parenchyma. The patient was noted to have stenotic airways on bronchoscopy, and bronchial washings performed at that time were negative for malignancy. A vasculitic work-up yielded an elevated ESR, a strongly positive PR-3 ANCA, and normal renal parameters. An initial radiologic guided biopsy of the lung lesion and of the nasal lesions were inconclusive. Subsequent larger biopsy specimen and examination of a mediastinal lymph node revealed chronic inflammatory cell infiltrate, consistent with but not diagnostic of GPA. Prior to this point no specific therapy had been initiated during the diagnostic evaluation. At this juncture, the patient was offered standard immunosuppressive treatment, but declined as he felt his symptoms had been progressively improving during the course of the investigations. The risks of further delay in therapy were discussed, and an agreement reached to re-evaluate his laboratory and chest radiographic parameters. Subsequent ANCA titres were approaching normal and acute phase markers had normalized. Chest imaging revealed near resolution of the previously identified masses. The patient will be periodically re-evaluated for recurrence of active disease involvement or sequelae. It is not yet clear whether this case history represents an atypical self-resolving case of limited GPA, a mere lull in disease activity, or a GPA "mimic" disease process.

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Addressing Rural and Remote Access Disparities for Patients with Inflammatory Arthritis through Telehealth/Videoconferencing and Innovative Inter-professional Care Models

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Objectives: The purpose of this 2-year research project, funded by the Canadian Initiative for Outcomes in Rheumatology Care (CIORA), is to evaluate the efficacy of providing long-term follow-up care to patients with Rheumatoid Arthritis (RA) living in rural and remote areas using videoconferencing technologies. RA patients require regular follow-up to ensure their disease is well-controlled, resulting in substantial travelling for people who live in rural/remote regions. Using telehealth/videoconferencing technology to perform their follow-up appointments would allow people to stay in or nearer their home communities and continue to receive care. We have designed an innovative inter-professional care approach using videoconferencing technology to combine rural-based physiotherapist evaluators with urban-based rheumatologist support. In this study we will evaluate: 1) whether a physiotherapist performing a patient assessment with the support of a rheumatologist via videoconferencing can provide follow up care with equivalent outcomes to traditional clinics and 2) whether people monitored utilizing this videoconferencing approach will have comparable satisfaction compared to traditional rheumatology clinics.

Methods: This project will be conducted in two phases. In Phase 1, RA patients will be recruited to participate in a series of examinations. The patients will be evaluated five times during a single day: twice by rheumatologists, twice by physiotherapists, and once by a physiotherapist supported by a rheumatologist via video-conferencing. Resulting evaluations will be compared between and within specialties to ensure that reasonable equivalency of examination findings exist. In the second phase of the study, remote RA patients (those that live 100 kilometers or more from Saskatoon) will be randomized to the videoconferencing group or traditional rheumatology clinic. Both groups will have three follow-up appointments at 3, 6, and 9 months after recruitment: the intervention group will be followed up by a physiotherapist supported by a rheumatologist via videoconference, while the control group will continue to travel to Saskatoon for follow-up care. The patients will be monitored for disease severity including DAS-28 CRP values, quality of life metrics and overall satisfaction. Economic impact of each intervention will be measured through patient diaries.

Results:

Conclusion: Follow-up care for people with chronic diseases such as RA, who reside in rural and remote areas places a significant burden on both patients and health care delivery systems. Through this project we hope to demonstrate that ongoing care provided through an innovative inter-disciplinary model and utilizing distance technologies such as videoconferencing can provide equivalent outcome measures compared with traditional clinic structured care. Supported by a CIORA grant

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Road Blocks Perceived by Canadian Dermatologists for Referring Patients with Suspected Psoriatic Arthritis

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Objectives: The current system of referral by Canadian dermatologists of patients who may have psoriatic arthritis (PsA) to rheumatologists is suboptimal. Hypothesizing that knowledge level, attitude and confidence in being able to refer appropriately impacts the ability of dermatologists to refer patients who may have PsA to a rheumatologist, we aimed to define their current awareness of, and practices relating to, the diagnosis and referral of PsA.

Methods: Based on recommendations from our advisory group comprising rheumatologists, dermatologists, methodologists and patient-partners, questions for structured interviews and focus groups with practicing dermatologists were developed. Dermatologists from across Canada at different stages of their career were recruited via electronic mail. Telephone or face-to-face interviews and focus groups were conducted by trained research associates. The interviews and focus groups were recorded, transcribed, and analyzed by 2 experts and key themes identified.

Results: 8 interviews and 2 focus groups involving a total of 20 dermatologists in community practice (10 males, mean years in practice 18.4) were conducted and data saturation reached. The following themes were identified- (1) Self-perceived knowledge of psoriasis and associated co-morbidities was fairly high [mean of 8.5 (out of 10) across the interviews and 7.1 across focus groups]. (2) The number of patients with psoriasis seen was quite variable, 30-50 weekly on average. Of these, the percentage with PsA or suspected PsA ranged from 5%-50%. (3) Co-morbidities, including PsA, diabetes, obesity, heart disease, depression, metabolic syndrome, and hypertension were consistently mentioned. (4) Red flags noted for PsA included morning stiffness and joint pain. Fewer mentioned nail lesions and joint swelling. (5) All dermatologists recognized the importance of identifying PsA early, both for the patient and for the broader healthcare system. (6) There was a notable divide between their perceived role in screening for PsA and in making the diagnosis. A minority of respondents felt comfortable managing PsA if it was mild without confirmation by a rheumatologist. (7) If arthritis is perceived to be mild, dermatologists perceive an ongoing role in patient management. Other aspects of the healthcare system that affected dermatologists' perception included the nature of the local healthcare context, access to rheumatologists, and the role of primary care.

Conclusion: This qualitative study shows that dermatologists have high self-perceived knowledge of psoriasis, PsA and its associated comorbidities, and recognize the importance of identifying PsA early. However, the nature of the local healthcare context and access to rheumatologists are significant road blocks to appropriate referral. Supported by a CIORA grant

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The Safety and Efficacy of Certolizumab Pegol in Rheumatoid Arthritis used in Routine Canadian Clinical Practice: Interim Analysis of the FasT CAN Study

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Objectives: Certolizumab pegol (CZP), a PEGylated Fc-free anti-TNF, has previously demonstrated a fast and sustained clinical response in rheumatoid arthritis (RA). This 2 year prospective, observational study was designed to assess the safety and efficacy of long term CZP use in routine clinical practice for RA in Canada. The primary objective of the study is the rate of Disease Activity Score (DAS28) remission (<2.6) at 2 years. Secondary objectives include change in the Health Assessment Questionnaire Disability Index (HAQ-DI), clinical disease activity index (CDAI) and work and home productivity.

Methods: This pre-determined interim analysis includes data from all visits up to study termination at week 104. The cut-off for this analysis was July 25, 2014. A total of 494 patients were enrolled to date and received at least one dose of CZP and therefore included in the safety analysis. Of these patients, 387 were included in the full analysis set having received at least one dose of CZP and had at least one post-baseline DAS28 measure. Non-responder imputation was conducted on the DAS28 measures for subjects who discontinue from the study for any reason.
Results: At baseline the mean age of patients was 56 years, 79% were female, the average disease duration was 7.7 years and the mean DAS28 was 5.2 and HAQ was 1.45. Of the 387 full analysis set patients, DAS remission (<2.6) was achieved by 62/387 patients (16%) at week 12, 73/359 (20%) at week 24, 54/297 (18%) at week 52 and 32/166 (19%) at week 104. DAS low disease activity (<3.2) was achieved by 115/387 patients (30%) at week 12, 116/359 (32%) at week 24, 85/297 (29%) at week 52 and 47/166 (28%) at week 104. Similar improvements were seen in HAQ, CDAI, work and home productivity and other secondary endpoints. Of the patients in the safety analysis 185/494 (37%) reported an adverse event and 26/494 (5%) experienced a serious adverse event with most frequent being pneumonia (3/494) within the SOC of infections and infestations (9/494 1.8%). There were four deaths in the study which were determined to be not related to study medication.
Conclusion: In the real-world FasT CAN study, RA patients treated with CZP achieved a rapid reduction in disease activity during the first 12 weeks of treatment and this improvement was maintained for up to 2 years. The safety results were consistent with previous CZP reports.

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Frequency of Psychiatric Disorders in the Classic and Hypermobility Types of Ehlers-Danlos Syndrome and Association with Systemic Findings

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Objectives: Ehlers-Danlos Syndromes (EDS) are a heterogeneous group of hereditary connective tissue disorders characterized by joint hypermobility, widespread musculoskeletal pain and tissue fragility. Psychiatric disorders and psychosocial impairment are common yet poorly characterized findings in EDS patients. Some systemic features of EDS, such as chronic pain, are speculated to be related to the increased prevalence of psychiatric comorbidities, although these associations are poorly defined in the literature. The purpose of this study was to investigate the frequency and types of psychiatric disorders in a cohort of EDS patients and to investigate the relationship between systemic manifestations of EDS and psychiatric disorders.
Methods: A retrospective analysis was undertaken by systematic database search for patients diagnosed with EDS classic and hypermobility types seen at the genetics clinics at Lakeridge Health Oshawa (Oshawa, Canada) and the Fred A. Litwin Centre for Genetic Medicine (Toronto, Canada) from 2008 to 2013. Medical and psychiatric findings were recorded and coded according to the International Classification of Diseases (ICD-10).

Results: In total, 106 patients (90 females; 84.9%) were identified to have confirmed EDS classic, hypermobility or overlapping classic/hypermobility diagnoses. The frequency of psychiatric disorders was found to be 42.5%, with 22.69% of patients affected with 2 or more psychiatric diagnoses. Anxiety and mood disorders were most commonly reported, with frequencies of 23.6% and 27.4% respectively. A variety of other psychiatric diagnoses was also identified. Abdominal pain (odds ratio (OR)=7.38), neuropathic pain (OR=4.07), migraines (OR=5.21), joint pain (OR=2.85) and fatigue (OR=5.55) were significantly associated with the presence of a psychiatric disorder. The presence of any pain symptom was significantly associated with having a psychiatric disorder (OR=9.68). Muscle pain (OR=2.79), abdominal pain (OR=5.78), neuropathic pain (3.91), migraines (OR=2.63), fatigue (3.78) and the presence of any neurological symptom (OR=2.3) were significantly associated with having an anxiety or mood disorder. Joint hypermobility, recurrent joint dislocations and skin hyperextensibility were not associated with psychiatric disorders.

Conclusion: The findings of this study suggest that increased awareness and surveillance for mental health issues in EDS patients is warranted, particularly in those with pain symptoms.

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"Appropriate Investigations and Costs in Rheumatology: Residents' Attitudes and Knowledge"
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Objectives: This study aims to: 1) assess internal medicine and rheumatology residents' attitudes towards appropriate ordering of rheumatology investigations and cost-conscious decision-making; 2) assess residents' knowledge of costs of care in rheumatology; and 3) identify areas of need in the post-graduate rheumatology curriculum with respect to this topic.

Methods: In July and August 2014, a 16-question survey created using Google Forms was emailed and distributed at the rheumatology academic half-day to rheumatology trainees and internal medicine residents in their rheumatology rotation at Sunnybrook Health Sciences Centre. Demographic details were obtained. Participants were asked to rate statements on a 5-point Likert-scale to assess attitudes. They were then asked to estimate costs of common rheumatology investigations. Descriptive statistics were conducted using Microsoft Excel.

Results: The survey was completed by 10 out of 15 eligible participants (response rate 66.7%). Seven participants (70%) were female. Responders included nine rheumatology residents and one internal medicine resident. All participants agreed or strongly agreed that all physicians should be familiar with appropriate use of investigations and costs of care. All agreed that internal medicine/rheumatology residents should receive training on this topic. Eight participants (80%) believed that inappropriate ordering of investigations is a problem among medical residents in general. Six participants (60%) felt that formal teaching on this topic should be mandatory. Six participants (60%) consider pre-test and post-test probabilities and test sensitivity/specificity in clinical decision-making, while only three (30%) consider costs. None of the responders felt confident in appropriately ordering a whole-body bone scan, and fewer than half felt confident in appropriately ordering HLA-B27 and DEXA scans. The mean estimated cost by residents was greater than the true cost for all investigations included in the survey. The average discrepancy between estimated and true cost was greatest for MRI spine, DEXA scan and whole-body bone scan.

Conclusion: The results reveal areas of need in the post-graduate curriculum with regards to appropriate ordering of rheumatology investigations and costs of care. Future steps include surveying more trainees and developing a teaching tool outlining this topic for internal medicine and rheumatology residents.

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A Case of Scrotal Tophaceous Gout and Review of the Literature

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Tophaceous gout is a complication resulting from hyperuricemia, uric acid crystals and chronic inflammation. It most commonly affects the digits, pre-patellar and olecranon bursae and helix of the ear; although it has been reported to deposit in other places such as over the Achilles tendon. Here, we present a 43 year old male with a long standing history of seronegative inflammatory arthritis and chronic kidney disease with chronic tophaceous gout affecting his foot digits, helices of his ears and scrotum and penis.

Our patient is a 43 year old male that presented with multiple firm painless nodules in his scrotum which progressively doubled and extended into the shaft of his penis. Eventually, the nodules were associated with intermittent acute erythematous periods ultimately erupting into exudative discharge associated with white chalky discharge. A scrotal ultrasound suggested calcified subcutaneous nodules. Despite numerous topical and laser treatments, the lesions continued to progress. As a result, his scrotum was surgically resected with pathology in keeping with uric acid crystals. Retrospectively, his urate levels were markedly elevated near 785 microM and his baseline estimated glomerular filtration rate was approximately 35 (mL/min/1.73 m2). Because of his underlying renal dysfunction, he was started on Febuxostat 80 mg and Colchicine 0.6 mg daily with successful reduction of urate level to 452 microM one month later. Tophaceous gout affecting the scrotum is very uncommon, as only two other cases have been reported in the literature. Our patient is the only reported case with inflammatory arthritis and scrotal tophaceous gout. Our case highlights the importance of obtaining a tissue diagnosis in directing appropriate definitive therapy.

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Combined Hereditary Heterozygous C2 and C4 Deficiencies: Variable Clinical and Serological Manifestations among Three Sisters

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Introduction: The causal link between inherited complement deficiencies and systemic lupus erythematosus (SLE) has been well established, although it remains a rare cause of the disease. SLE is found in approximately 90% of patients with C1q deficiency, 75% with C4 deficiency, and 10% with C2 deficiency. We present the case of three biological sisters with combined hereditary heterozygous C2 and C4 deficiencies, but who differ widely in their clinical and serological manifestations.

Clinical case: Patient 1 is 25 years old. She was diagnosed with SLE at the age of 12, with initial clinical manifestations of malar rash, photosensitivity and arthritis. Further testing revealed World Health Organization (WHO) type III glomerulonephritis, hemolytic anemia, lymphopenia, positive ANA, anti-dsDNA, anti-CENP-B and antiphospholipid antibodies (APL), as well as decreased C2, C3 and C4 levels. She also had two thrombotic events in the context of an antiphospholipid syndrome (APS). Patients 2 and 3 are both 21 years old and are dizygotic twins. Patient 2 also has SLE, diagnosed at the age of 12. Her initial clinical presentation was choreiform movements of the right arm, with the laboratory findings of lymphopenia, positive ANA, anti-dsDNA and APL (but no APS), and low C2 and C4, but normal C3 levels. She is currently asymptomatic. Patient 3 has always been completely asymptomatic. Serologically, she has positive ANA and APL, and low C2 and C4, but normal C3 levels.

Conclusion: A small proportion of SLE is caused by inherited deficiencies of the early complement components. We presented a case of combined familial heterozygous C2 and C4 deficiencies with different disease phenotypes among three biological sisters. All three sisters have documented partial C2 deficiencies. Their low C4 is most probably inherited as well, because C4 consumption is unlikely in the absence of C3 reduction and in the context of inactive disease (for Patients 2 and 3). In addition, our patients' disease phenotypes differed substantially from what has been described in SLE associated with C2 hypocomplementia alone. Therefore, additional congenital C4 deficiency likely contributed to their disease presentations. Combined C2 and C4 deficiencies is extremely rare. To our knowledge, only four reports of such combined hypocomplementemia have been described in the literature. The presence of positive APL in all 3 patients is noteworthy, as this association has also been rarely reported. The variable clinical and serological manifestations among our patients further reflect the complex and multifactorial nature of SLE.

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Immunization Status and Barriers in Childhood Rheumatic Diseases

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Objectives: To determine the vaccination status of children with rheumatic diseases, and identify immunization knowledge of families and potential barriers to vaccination.

Methods: A cross-sectional study of children with rheumatic diseases followed at a tertiary care center outpatient clinic was performed between October 2013 and September 2014. Demographics, diagnosis and current treatments were obtained from health records. Children were considered immunosuppressed, if they were currently received corticosteroids, non-biologic or biologic disease-modifying agent. A unique provincial electronic database that records accurate vaccine history was used to obtain actual patient vaccination history. Perceived immunization barriers, concerns and knowledge regarding contraindications to vaccination, and sources of immunization information were captured from a patient/parent questionnaire. Descriptive statistical methods were used to analyze the data.

Results: A total of 120 children were recruited into the study. Of these, 86 (72%) children were considered immunosuppressed.Vaccination database: Patients received most recommended vaccines, with the exception of the Influenza (2013/2014) and Hepatitis B vaccines (recommended for age of 10 [grade 5] in Canada). Influenza was missed 25% of the time in the 1 – 3 years old group, 28.2% of the time in the 4 – 9 years old group, and 27.6% of the time in the 10 – 17 years old group. Hepatitis B was missed at a rate of 8% in the 10 – 17 years old group. Patient/parent questionnaire: Fourteen patients reported previous adverse reactions to vaccination (Influenza [5], Measles, Mumps, and Rubella (MMR) [2], Hepatitis B [2] and Varicella [2]). In 33% at least one vaccination was withheld, most commonly for active disease (30%), recommendation against receiving vaccinations by health care provider (25%), uncertainty about whether or not a vaccine should be given (13%) and concerns about disease flare (15%) and/or side effects post vaccination (20%).Several sources of information were utilized by patients and families for vaccination information, and satisfaction with this information was fairly high. Patients and parents identified the following information gaps: 1) risks and contraindications of vaccinations in childhood rheumatic diseases, 2) age-appropriate vaccination schedules and modalities, 3) best practice of vaccination documentation. Vaccination reminders were identified as useful, with several comments indicating that e-mail alerts, reminders, and a method to track this information would be useful.

Conclusion: The majority of children with rheumatic illnesses received the recommended vaccines. Immunisation gaps were identified for Influenza and Hepatitis B. Knowledge regarding contraindications to vaccination is good. Concerns about perceived safety limit vaccination completeness.

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What is the Best Screening Instrument to Identify Lupus Patients with Cognitive Impairment in an Ambulatory Setting?

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Objectives: There is an unmet need for a clinical assessment of cognitive function that can be administered in an ambulatory setting to patients with systemic lupus erythematosus (SLE). We aimed to determine (1) the validity of the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE) as screening tests of Cognitive Impairment (CI) in SLE, and (2) the validity of patient self-reporting in screening for CI.

Methods: Consecutive patients with SLE, visiting the Toronto Lupus Clinic between February and August 2014 that agreed to participate, were included in this study. Patients underwent a battery of cognitive screening tests by one trained assessor: Hopkins Verbal Learning Test-Revised (HVLT-R) and Controlled Oral Word Association Test (COWAT) via telephone interview and MoCA and MMSE via face-to-face assessment. Patients completed the Perceived Deficits Questionnaire – 5-item (PDQ-5). HVLT-R and COWAT scores were considered the external constructs. HVLTR and COWAT)are both validated assessments of CI and were considered the "Gold Standard". The agreement and correlation of MoCA and MMSE, HVLT-R and COWAT, were studied. Sensitivity/specificity of MoCA and MMSE in detecting CI was studied. PDQ-5 scores were compared in patients with and without CI (T-test).

Results: 61 patients participated, 92% were female, mean age, disease duration and SLE Disease Activity Index 2000 (SLEDAI-2K) were 48±13 and 18±12 years, and 3.7±4.3 respectively. 34% had CI using the HVLT-R and 15% using COWAT. MoCA and MMSE identified CI in 44% and 16% of patients, respectively. Kappa coefficients (κ) showed moderate agreement between HVLT-R and MoCA (κ 0.46), fair agreement between HVLT-R and MMSE (κ 0.30), and slight agreement between COWAT and MoCA and MMSE (κ 0.14 and 0.17, respectively). Sensitivity was markedly higher in MoCA (76%) compared to MMSE (33%), though MMSE was more specific (93%) than MoCA (73%). HVLT-R correlated significantly with MoCA (Spearman 0.45, $p < 0.001$). PDQ-5 showed higher scores in CI patients compared to patients without CI (10.58±5.01 vs. 8.17±3.76, $p = 0.05$).

Conclusion: CI among SLE patients was highly prevalent (34%) in this study. HVLT-R and MoCA are valid and are the best screening tests for detecting CI in SLE in an ambulatory setting. Considerations of cost and administrative burden, particularly ease of use and time needed for an assessment, make the MoCA the preferential screening test for CI in patients with SLE. A valid test, like MoCA, should be used when screening for CI in SLE in an ambulatory setting.

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Quantified Differences in Erosion Number and Size in the First Year of Inflammatory Arthritis Using High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT)

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Objectives: To quantify changes in erosion number and size in early inflammatory arthritis (EIA) using HR-pQCT.

Methods: EIA subjects were recruited for HR-pQCT scanning (Xtreme-CT I, Scanco Medical AG, Switzerland) of the 2nd and 3rd MCPs of their dominant hand at diagnosis and following one year of DMARD therapy. Disease activity measures and plain radiographs were collected at both time points. HR-pQCT images were assessed for erosions using Osirix software, applying the erosion definition and margin landmarks proposed by the SPECTRA Collaboration. The smallest detectable change (SDC) was calculated to assess for significant progression in erosion size. HR-pQCT standard evaluation scripts provided measures of bone densitometry and microarchitecture, and a custom script estimated joint space width parameters.

Results: At baseline with a mean symptom duration of 195 days, 41 (87%) subjects had RA by 2010 ACR/EULAR criteria and 6 had an indeterminate diagnosis, with a mean DAS28-ESR of 4.76 (SD 1.43), HAQ of 1.17 (SD 0.74), and 71% (n=32) were seropositive. Radiologists determined 11% (n=5) to have erosions, however an additional 6 subjects met HR-pQCT criteria for erosive lesions. The mean dimensions of the erosions were: axial depth 1.11 mm (SD 0.81); axial width 2.22 mm (SD 1.91), perpendicular depth 1.23 mm (SD 0.77), and perpendicular width 1.85 mm (SD 1.39). A total of 27 subjects have completed their follow-up period, achieving a mean DAS28-ESR of 2.03 (SD 1.19) and 48% (n=13) meeting the ACR RA Boolean remission definition. Fifteen subjects remained free of erosions, and in 2 subjects existing erosions were undetectable at 1 year. Six subjects with erosions at baseline did not develop new lesions, whereas 4 developed additional erosions. Increases in erosion size were observed (axial depth 0.24 mm, axial width 0.09 mm, perpendicular depth 0.07 mm), but with a decrease in perpendicular width (0.18 mm). By the SDC, progression in axial depth (n=4), perpendicular width (n=2), perpendicular depth (n=1) or axial width (n=1) was determined. No significant changes were observed in bone densitometry or microarchitecture over 1 year (p>0.05). Euclidian joint space width improvements were seen at the 2nd MCP (mean 0.27 mm, median 0.13 mm, minimum 0.46 mm), although the joint space width volume decreased non-significantly (12.1 mm3).

Conclusion: We have applied a highly sensitive imaging technology to characterize erosion development and regression, and quantify size differences, in EIA. The majority of erosive lesions do not significantly progress when effective DMARD therapy is used.

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Engagement by Rheumatology Patients with the EdmontonRheumatology.com website
Steven Katz (University of Alberta, Edmonton); Tharindri Dissanayake (University of Alberta, Edmonton); Jill Hall (University of Alberta, Edmonton)

Objectives: A website (www.EdmontonRheumatology.com) was developed and launched in 2010 as an online (Internet) resource for rheumatologists and patients in Edmonton. The website includes resources for students and staff, as well as a patient portal for submitting information for appointments, verifying clinic locations, asking questions, and learning about rheumatological conditions and the medications used to treat them. While there has been substantial growth in the use of the website, it is unclear how well the website has been utilized by rheumatology patients, the primary target audience. The purpose of this study is to determine rheumatology patient engagement with the website.

Methods: As part of an observational cross-sectional survey conducted at the two largest Edmonton rheumatology clinics over 2 months in 2013, patients anonymously were asked questions regarding the EdmontonRheumatology.com website. Response items included whether patients had visited the website, and if so, for what purpose. Data were analyzed using descriptive statistics and then correlated to patient characteristics, including age, gender, employment, and visit type.

Results: Of 1063 patients (response rate 36%) who participated in the study, one third indicated that they had visited the website. Reasons for accessing the website included clinic location verification, online appointment confirmation, first appointment information submission, disease education, medication education, patient portal access, accessing other resource links, and the Ask the Rheumatologist webpage. Patient access to the website did not differ significantly based on age, employment status or visit type (first versus follow-up). There was a statistically significant difference based on educational background, with those less educated accessing the website more often. Women also accessed the website more often than men.

Conclusion: The EdmontonRheumatology.com website was regularly accessed by patients surveyed for a variety of reasons, despite socioeconomic background. Future work to identify gaps in information being sought may be helpful to lead to further develop for this local online forum.

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Survey of Patient Perspectives on the Introduction of Subsequent Entry Biologics in Canada

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Objectives: Subsequent entry biologics (SEBs) are medications that are similar but not identical to innovator biologics. Despite a paucity of comparative trials, SEBs are poised to enter the Canadian market. We conducted a survey of Canadian arthritis patients currently taking innovator biologics to understand their perspectives on SEBs.

Methods: A survey consisting 14 multiple choice format questions was administered sequentially to 208 patients at a biologic infusion clinic. Patients were asked about their understanding of SEBs, and after providing a definition, were asked about factors that might influence them to switch to an SEB. The survey results were analyzed using SAS version 9.3.

Results: Of the patients surveyed (n=208), mean age was 56 years, 67% were female, 56% of patients had an annual household income of less than $75, 000, and 63% had private drug insurance. The majority of patients had a diagnosis of rheumatoid arthritis (76%) and had been on their current biologic for 1-5 years (55%). When asked about the definition of a SEB, 58% indicated they did not know, 26% chose correctly, and 16% chose incorrectly. When asked about their interest in using a SEB, 30% were neutral, 40% were somewhat or very interested, and 30% were somewhat or completely opposed to it. Potential lower cost of a SEB did not greatly influence this decision, though if an insurance company mandated use due to lower cost most opposed this (54%). The lack of testing in North American patients led to 79% of patients being somewhat or completely opposed to SEBs. Most patients were interested in continuing to use the innovator biologic if there was no further expense (70%) and felt their doctor's opinion would influence their decision (85%). Demographics, household income, diagnosis and type of current biologic therapy did not affect patient opinions.

Conclusion: Given the comparative lack of efficacy and safety data for SEBs, there is understandable concern as these medications enter the biologic landscape. This survey identifies a lack of patient understanding of SEBs and highlights a need for further education. Patients are hesitant to use SEBs that are not tested in a North American population and would prefer to stay on innovator biologics if cost was not an issue. Patients value their doctors' opinions to help them make informed decisions about SEBs. Open dialogue is needed between patients, physicians, industry and regulatory bodies in order to safely introduce SEBs into practice.

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Geocoding the Rheumatoid Arthritis Population of Northern Alberta
Jason Soo (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)
Objectives: The geographical home of a patient may have significant impact on their health and the provision of their health care. Therefore, this information may be important to examine determinants of disease, but also in the implementation of models of care and working toward quality improvement in health care delivery. The geographical home of established rheumatoid arthritis patients followed by rheumatologists in Northern Alberta is currently unknown. This preliminary report aims to identify and map this patient population and describe early findings.
Methods: Using rheumatologists' electronic health records, we identified patients with a rheumatology clinic visit between May 1, 2012 and April 30, 2014 who had a diagnosis of rheumatoid arthritis (ICD codes 714.0, 714.1, 714.2) and a documented postal code. Using geocoding software (batchgeo.com, copyright 2014) postal codes were converted to their corresponding geographical location for further analysis.
Results: The records of 8/18 rheumatologists were accessible. Three rheumatologists do not keep electronic records and were excluded. 8 rheumatologists' records were not searchable for these parameters using our search protocol. Nonetheless, 1886 patients with rheumatoid arthritis were identified. 1848 were from Alberta with the majority of the remainder from Saskatchewan and British Columbia. 70 Patients travel to see an Edmonton rheumatologist from Southern Alberta - south of Red Deer - for disease management, while 164 patients live in Northern Alberta (>54 ° latitude North). Approximately half the patients identified live in the Greater Metropolitan Edmonton Area (N=788).

Conclusion: This preliminary report demonstrates a wide geographic distribution of rheumatoid arthritis patients under the care of Edmonton based rheumatologists. This work will continue to ensure all Northern Alberta rheumatology data is included for completeness. This will allow for a powerful tool in the work towards health care delivery optimization in rheumatic disease, as well as analysis of distribution of disease and potential determinants.

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Getting a Grip on Arthritis Online: Web-based Continuing Education Supports the Dissemination of Arthritis Clinical Practice Guidelines among Rural/Remote Primary Care Providers

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Objectives: Primary care providers (physiotherapists, occupational therapists, nurses, family physicians) are often challenged with accessing relevant up-to-date arthritis information to enable delivery of optimal care. An online arthritis continuing health education program based on arthritis clinical practice guidelines (CPGs) was developed to address this issue.

Methods: Online learning modules were developed for Osteoarthritis (OA) and Rheumatoid Arthritis (RA) based on a needs assessment, published CPGs adapted for primary care (best practices), and input from subject matter experts. The program was piloted in two rural/remote areas with high arthritis prevalence and health human resource shortages. Best practices included: exercise; education; weight management; occupational therapy/joint protection; use of assistive devices; social support; analgesics; NSAIDs; and intra-articular injections for both OA and RA, with the addition of surgical consultation for OA and rheumatology consultation, adjuvant oral corticosteroids and DMARDs for RA. Knowledge of best practice guidelines was measured by assigning one point for each best practice applied to a hypothetical case scenario. Points were then summed into a total possible best practice score (OA=10; RA=12). The program was evaluated using paired samples analyses comparing total best practice scores at baseline and immediately post program.

Results: Participants (OA module, n=34; RA module, n=32) represented various disciplines, including physiotherapists (OA, n=19; RA, n=18), occupational therapists (OA, n=2; RA, n=2), registered nurses (OA, n=5; RA, n=4), nurse practitioners (OA, n=3; RA, n=5), social workers (OA, n=1; RA, n=1), dieticians (OA, n=1; RA, n=0), and family physicians (OA, n=3; RA, n=2). Participants demonstrated significant improvements in total best practice scores immediately following the program (OA pre=2.76, post=3.82, $p<0.01$; RA pre=3.91, post=4.63, $p<0.01$). Most improvements were seen for non-medical interventions. There was a significant increase in recommendations for occupational therapy/joint protection for the OA case scenario (pre=32.4%, post=58.8%, $p=0.01$) and patient education for the RA case scenario (pre=46.9%, post=68.8%, $p=0.04$).

Conclusion: With knowledge gained from the online modules, participants were able to apply a greater number of arthritis best practices. The modules had the most impact on the application of non-medical best practices, such as patient education and recommendations for occupational therapy/joint protection. The Grip Online modules have demonstrated that they can provide the information rural/remote primary care providers need to deliver optimal care and support patient self-management.

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Is the Heart in the Right Place? Cardiac Risk Profiles of Early Rheumatoid Arthritis Patients

Tanja Harrison (University of Calgary, Calgary); Cheryl Barnabe (University of Calgary, Calgary); Liam Martin (University of Calgary, Calgary)

Objectives: To describe the prevalence of cardiovascular disease (CVD) risk factors in early rheumatoid arthritis (ERA) patients. A secondary objective was to determine how CVD risk was addressed by rheumatologists.

Methods: We conducted a retrospective chart review of randomly selected patients seen at a tertiary care Early Inflammatory Arthritis (EIA) Clinic between 01/2009 to 12/2012. Variables extracted at baseline, 6 month and 12 month visits included demographic information, disease activity scores (DAS28-ESR), medications, traditional CVD risk factors, diagnoses of CVD and treatment for these. Framingham Risk Scores (FRS) based on lipids and BMI, and QRISK®2 scores were calculated from these data. We also extracted the rheumatologists' recommendations for CVD risk reduction.

Results: 150 patients (70% female, 89% Caucasian, mean age 52 years), who met ACR/EULAR 2010 criteria for RA were included. The mean baseline DAS28 score was 5.17(SD 1.31). At 12 months, 63% of patients achieved low disease activity or remission. Of these 150 patients, 89(60%) had at least one CVD risk factor (exclusive of RA). Of the 89 patients with risk, 18% (n=16) had two, 17% (n=15) had three, and 10% (n=9) had more than three risk factors. Obesity(30%), smoking(28%) and hypertension(23%) were the most common risk factors. Documentation of the discussion around CVD risk was only found for 1 patient. The FRS risk score could only be calculated in 123 patients with 13% at high risk using the FRS Lipid calculation and 17% at high risk using the FRS BMI calculation. QRISK®2 could be calculated for 52 patients of which 23% had high-risk scores of ≧20%. Once the EULAR recommended 1.5 times multiplication factor for RA was applied, the number of patients nearly doubled in the high-risk category for both FRS calculators. For 38 patients who had existing CVD risk, 35 had this risk managed to some degree by another physician. If there was new or poorly managed CVD risks, rheumatologists initiated or requested to have the risk addressed in 13 patients. There were 3 cardiac events observed during the first year of disease.

Conclusion: Although ERA patients are receiving anti-rheumatic therapy to achieve disease targets, nearly half of this cohort had intermediate to high FRS and QRISK®2 risk scores before applying the recommended RA multiplication factor. This highlights a missed opportunity to educate patients about their cardiac risk and intervene on modifiable risk factors earlier in their disease, which could be facilitated through a multidisciplinary and multi-target care model.

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Risk of Pneumocystis Jirovecii Pneumonia in Patients with Vasculitis

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Objectives: The objective is to determine the incidence rate of PJP in patients with vasculitis, namely polyarteritis nodosa (PAN) and granulomatosis with polyangiitis (GPA).

Methods: Adult patients with ≥ 1 hospital discharge diagnosis of vasculitis defined by ICD-9-CM code 446.x (ICD-10 code M31.x), or ≥ 2 billing codes at least 8 weeks apart of those same codes made by a specialist physician. Subgroups for specific diagnosis of PAN (ICD-9 code 446.0) and GPA (ICD-9 code 446.4) were defined by the same method. Cohort subjects were followed from the index date of diagnosis until the first of either: 1) PJP infection defined as ICD-9-CM code 136.3 (ICD-10 code B59), 2) death, or 3) end of study period. Data was collected from the Quebec provincial health administrative database (RAMQ) from Jan 1, 1994 - Dec 31, 2003. Age and sex-matched controls identified from the general population data within the same database were used to generate rates of PJP in the general population.

Results: The cohort included 836 patients with a diagnosis of vasculitis, including 124 with PAN and 152 with GPA. Overall, 20 cases of PJP were identified in the vasculitis group, including 11 in those with PAN and 7 in those with GPA. Overall, the incidence rate of hospitalization for PJP in all patients with vasculitis was 4.7 per 1000 person-years. The incidence rate of PJP was more than 3 times higher in males compared to females (9.7 per 1000 person-years [95% CI 5.5-17.1] in males versus 2.5 per 1000 person-years [95% CI 1.2-5.2] in females). The overall incidence rate of PJP in PAN was 19.0 per 1000 person-year (95% CI 10.5 – 34.4) with sex-specific rates of 24.9 per 1000 person-year (95% CI 11.9-52.2) in males versus 13.5 per 1000 person-year in females (95% CI 5.1-35.9). In GPA the overall incidence rate of PJP was 8.7 per 1000 person-year (95% CI 3.9 – 19.4) with 10.2 per 1000 person-year (95% CI 3.3-31.6) in males versus 7.6 per 1000 person-year (95% CI 2.5-23.5) in females. The incidence rate of PJP in the general population was 0.08 per 1000 person-year (95% CI 0.05 – 0.11) in females and 0.16 (95% CI 0.12-0.21) in males.

Conclusion: The incidence of PJP was increased in patients with vasculitis when compared to the general population. There was an evident difference in incidence rates of PJP according to sex, with males with vasculitis being affected more than 3 times more frequently.

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The Economic Impact of Psoriasis at a Single Centre in Toronto, Ontario
Taryn Gitter (University of British Columbia, Toronto); Michal Bohdanowicz (University of Toronto, Toronto); Vinod Chandran (University of Toronto and University Health Network, Toronto); Cheryl Rosen (University Health Network, Toronto Western Hospital, Toronto); Dafna Gladman (Toronto Western Hospital, Toronto)

Objectives: Psoriasis is an immune mediated inflammatory skin disease affecting 2-3% of the population. Approximately 30% of patients with psoriasis develop psoriatic arthritis (PsA). While psoriasis causes some disability, PsA can lead to significant joint damage and reduced quality of life. With the advent of biologic therapies the course of psoriasis and PsA may change and there may be a reduction in the incidence of PsA. High cost and strict prerequisites for drug approval however have prevented many patients from accessing biological therapies or have resulted in them receiving the drugs too late. The economic impact of PsA has been previously studied and this study aims to determine the economic impact among patients with psoriasis without arthritis in order to compare between the two aspects of the disease and determine if the use of biologic agents earlier in the course of disease is cost effective.

Methods: This study includes a cohort of 200 patients with psoriasis who are consented participants to the International Psoriasis & Arthritis Research Team (IPART) program and have been confirmed by a rheumatologist not to have PsA. Questionnaires have been administered to these participants to assess direct and indirect health costs in the preceding 12 months. Direct costs include the cost of medications, therapies, health care services and physician visits and indirect costs include cost of missed work and early retirement.

Results: Of the 200 patients in this study, 73.4% were using topical therapies, 6.8% were taking NSAIDS, 14.1% were taking DMARDS, and 9.5% were taking biologic agents over the past year. The average PASI score for these patients was 4.1±5.3. The average SF36-PCS, SF36-MCS and HAQ were 51.3±8.4, 50.7±9.5 and 0.11±0.28, respectively. The average annual costs for topical therapies, NSAIDS, DMARDS, biologic agents, phototherapy and OTC medications were $89.43, $1.92, $90.76, $1,849.88, $55.70, $157.10 respectively. The average annual cost per patient for clinic visits, lab tests and hospital admissions was $1,663.19 and the cost for alternative medicines was $1,341.57. Patients with psoriasis lost on average 1.83 days of work per fiscal quarter due to their health. Six patients (3%) were unemployed due to psoriasis, losing on average 6.8 years of employment and $24,501 per year.

Conclusion: Comparison of these results with the economic impact of PsA will determine if the use of biologic agents earlier in the course of disease is cost effective.

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Natural Health Product use in Patients with Rheumatological Conditions Based on Gender, Age, Education Level and Work Status

Tharindri Dissanayake (University of Alberta, Edmonton); Karen Hagen (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton); Jill Hall (University of Alberta, Edmonton)

Objectives: Natural health products (NHPs) are naturally occurring substances available without a prescription, such as vitamins, minerals and herbal supplements, frequently used to restore or maintain good health. Previous literature has shown that NHP use is higher in patients with rheumatological conditions compared to the general population and that NHP users are more likely to be female, middle aged, college educated, and relatively wealthy. We aimed to describe the prevalence of NHP use in patients with rheumatological conditions and determine whether there is an association with various patient specific factors.

Methods: We conducted an observational cross-sectional survey of patients attending the 2 largest rheumatology clinics in Edmonton, Alberta over a two-month period in 2013. The survey collected self-reported NHP use, rheumatological and other medical conditions and the medications used to manage them, as well as demographic data. In this study we analyzed NHP use based on age, gender, education level, work status, and visit type. Data were analyzed using descriptive statistics and included an inflammatory arthritis subgroup.

Results: Of the 1063 patients who participated in this study (36% response rate), 557 self-identified as having inflammatory arthritis. Female patients were more likely to utilize NHPs compared to male patients ($p<0.01$). Female patients and those on a return (follow-up) visit also used more NHP products ($p=0.05$ and $p=0.04$, respectively). Patients aged 45 -74 most frequently used NHPs, however, there was no relationship between age and number of NHP products used overall. Work status also demonstrated variability in NHP use, with those working part time using more NHP products and NHPs more often, however these findings were not statistically significant. Patients with a post secondary education also consumed more NHP products than those without ($p<0.05$). There were no significant differences between the entire cohort and the inflammatory arthritis subgroup for any of the patient specific factors.

Conclusion: This study confirmed that NHP use is more prevalent in female and middle-aged, patients and demonstrated that patients who are female, have a post-secondary education, or are on a follow-up visit used more NHP products. Conversely, in our study we did not find a significant relationship between work status (a surrogate for income) and NHP use. Obtaining an improved understanding of NHP use patterns may prompt health care practitioners to regularly seek and provide information during patient visits.

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Natural Health Product use in Patients with Rheumatological Conditions

Tharindri Dissanayake (University of Alberta, Edmonton); Karen Hagen (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton); Jill Hall (University of Alberta, Edmonton)

Objectives: Natural health products (NHPs) are naturally occurring substances available without a prescription, such as vitamins, minerals, and herbal supplements, frequently used to restore or maintain good health, often in addition to or in place of conventional therapy. Previous literature has shown that the prevalence of NHP use is higher in patients with rheumatological conditions compared to the general population. However, NHP use is frequently under-reported and thus represents a common but often overlooked aspect of the patient medication history. Obtaining information on NHP use is essential to the provision of pharmaceutical care to this population, as significant drug-drug and drug-disease interactions may exist, potentially impacting the efficacy and safety of disease modifying anti-rheumatic drugs. The aim of this study was to describe the population-based rates and patterns of NHP use in patients with rheumatologic conditions.

Methods: We conducted an observational cross-sectional survey of patients with rheumatological conditions in Edmonton, Alberta. Patients attending the 2 largest rheumatology clinics over an 8-week period were invited to participate. Response items included self-reported NHP use, rheumatological and other medical conditions and the medications used to manage them, as well as demographic data. Data were analyzed using descriptive statistics and included an inflammatory arthritis subgroup.

Results: Of the 1063 patients who completed the survey (response rate, 36%), 60% reported using of one or more NHPs, with a mean of 2.9 products. When excluding vitamins and minerals, the prevalence decreased to 40% and the mean number of NHPs to 1.8. There were no differences between the entire cohort and the IA subgroup. The most common indication for NHP use was for the management of joint health or 'rheumatologic condition'. A variety of NHP products were used, however the most common non-vitamin/mineral NHPs were omega-3 fatty acid products, glucosamine/chondroitin, and coenzyme Q10. The majority of patients stated that they would not discontinue conventional prescribed medication in favour of NHPs. Almost 65% of NHP users stated they informed their physicians of NHP use, however, only 20% informed their pharmacist and even fewer informed other health care professionals. A minority of patients noted any benefit or adverse effect from therapy.

Conclusion: Our study, the largest Canadian study to date, confirmed the frequent use, but underreporting, of NHPs by patients with rheumatologic conditions. Obtaining an improved understanding of NHP use patterns may prompt health care practitioners to regularly seek and provide information during patient visits.

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Disease Modifying Anti-Rheumatic Drug Efficacy and Safety in Chronic Kidney Disease and Dialysis: A Literature Review

Thirza Carpenter (University of Alberta, Edmonton); Jill Hall (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

Objectives: Recommendations regarding the use of DMARDs in both chronic kidney disease and renal replacement therapy are limited in guiding clinicians in the choice of a DMARD. In order to find the best current evidence to assist clinicians in prescribing safe and effective therapy for their patients with inflammatory arthritis and co-existing chronic kidney disease, we performed a literature review regarding the safety and efficacy of disease modifying agents (DMARDs) in this patient population.

Methods: The Medline and EMBASE databases were searched. Studies eligible for inclusion evaluated the safety and efficacy of DMARDs in patients with chronic kidney disease or requiring renal replacement therapy and were published in English. Studies examining the serum concentrations and other pharmacokinetic properties of DMARDs in hemodialysis or peritoneal dialysis were also included. Additionally, relevant studies cited within the search criteria were also included.

Results: There were 93 relevant studies examining DMARDs in chronic kidney disease or renal replacement therapy. The vast majority of studies were case reports or case series. While limited, the current literature suggests that antimalarials, azathioprine and TNF-a inhibitors can be used safely in patients with chronic kidney disease with appropriate dosing adjustments. In renal replacement therapy, antimalarials, leflunomide, TNF-a inhibitors, and non-TNF biologics appear to be safe. Azathioprine may be safe but require post-dialysis administration, while sulfasalazine requires more clinical and pharmacokinetic studies before a recommendation can be made. Data suggest methotrexate and gold are unsafe.

Conclusion: This literature review suggests that many DMARDs are likely safe to use in patients with inflammatory arthritis and co-existing chronic kidney disease. However, more prospective studies are needed to support these results and to guide the creation of clinical practice guidelines for this population.

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Tocilizumab for Treating Takayasu's Arteritis and Associated Stroke: A Case Series and Updated Review of the Literature

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Objectives: Takayasu's arteritis (TA) is a rare disease that can result in stroke, for which long-term use of corticosteroids (CS) are the mainstay for its therapy.   Objective: To retrospectively assess the effectiveness of tocilizumab® (TCZ) in inducing remission and reducing CS doses in patients with refractory TA and/or those with TA and stroke.

Methods: We retrospectively reviewed all patients with TA treated with TCZ from 2009 to 2013 and determined their response to therapy and adverse effects. We also summarized all reported TA patients treated with TCZ in the literature by conducting a search in Pubmed and Medline with no date or language restrictions and determined the utility of TCZ in inducing remission, acting as a CS sparing agent and its adverse effects.

Results: TCZ induced remission and reduction of CS doses in all three cases of TA we identified in our cohort. Of note, remission was induced in two of these patients where stroke was the only initial manifestation of their disease. In total, 3 out of 4 patients with TA and stroke (2 from our study and 2 from other studies) treated with TCZ achieved remission and stability of their disease. We also identified 30 patients (from 12 studies) with TA treated with TCZ from our literature search, of which 76.7 % (23 patients) achieved remission despite not achieving sustained remission with other biological agents in a large proportion (34.8 %). In addition, TCZ resulted in a statistically significant reduction of CS in patients on CS prior to using TCZ (median -8.8 mg/day (IQR -19.4, -3.4 mg/day), Wilcoxon p-value 0.0002).

Conclusion: TCZ is a promising therapeutic option for TA patients refractory to other medications and for those with stroke as one of its complications that is effective in inducing remission and reducing CS doses.

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Presence of the Interferon Signature in Anti-Nuclear Antibody Positive Individuals Prior to the Onset of Systemic Autoimmune Rheumatic Disease

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Objectives: Patients with systemic autoimmune rheumatic diseases (SARD) often have a prolonged pre-clinical phase during which they are anti-nuclear antibody (ANA)+ 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. Elevated levels of interferon (IFN)-induced gene expression, termed the IFN signature, are found in several SARD conditions, and IFNs appear to play an important role in disease pathogenesis. Here, we examined whether ANA+ individuals who lack sufficient symptoms for a SARD diagnosis share the IFN-signature.

Methods: ANA+ individuals who: 1) lacked clinical symptoms of SARD (ANA+ no symptoms (ANS)); 2) had at least one clinical symptom of SARD (UCTD); or 3) had a recently diagnosed SARD were recruited from clinics at UHN/MSH hospitals. Healthy controls (HC) were also recruited. RNA was prepared from blood archived in Tempus tubes. Expression of 5 IFN-induced genes was quantified by Nanostring, normalized to expression of housekeeping genes, and summed to generate an IFN5 score. ANAs and levels of specific autoantibodies were measured by the hospital laboratory.

Results: To date we have measured the IFN signature in 60 individuals (16 HC, 12 ANS, 9 UCTD, 20 SjD, 3 SLE/MCTD). There was a trend to higher mean IFN score in all groups as compared to HC (mean ± SD: HC 6,462 ± 6,188; ANS 20,213 ± 30,662; UCTD 27,624 ± 24,827; SjD 52,241 ± 30,060; SLE/MCTD 91,764 ± 38,795), which achieved statistical significance for all but the ANS subset ($p = 0.096$, < 0.0001, 0.003, < 0.0001, respectively). Using a cutoff of 2 SD above the mean of HC as indicative of an elevated IFN5 score, 4/12 ANS, 4/9 UCTD, 16/20 SjD, and 3/3 SLE/MCTD participants had elevated IFN levels. Marked elevations of the IFN5 score were seen in a subset of ANS and UCTD participants, which could not be attributed to recent infection. There was a significant correlation between the number of different ANA specificities present and the IFN5 score for all ANA+ individuals ($p = 0.0008$), and for the UCTD subset ($p = 0.019$). In the ANS subset, all 4 patients with an elevated IFN5 score had anti-Ro antibodies.

Conclusion: An IFN signature is seen in a subset of ANA+ individuals prior to a confirmed diagnosis of SARD and appears to correlate with the type and number of specific ANAs rather than onset of clinical disease.

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Is Rheumatoid Arthritis Cervical Spine Involvement Decreasing Over Time? Results from a Meta-Analysis

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Objectives: Complications in Rheumatoid Arthritis (RA) such as cervical spine involvement seem to be decreasing over time. The prevalence of cervical subluxations in rheumatoid arthritis, including anterior atlanto-axial subluxations (aAAS), vertical subluxations (VS), and subaxial subluxations (SA), over the past 50 years was determined and the progression of cervical subluxations was assessed.

Methods: A literature search was performed in Medline-OVID/EMBASE, PubMed, and Scopus (from 1960 to June 21, 2014). Identified titles/abstracts were reviewed and full reports were obtained if appropriate. Additional studies were retrieved by hand searching relevant references. Studies were included if the sample size was at least 100 and the prevalence of cervical subluxations was reported. Additionally, we also included studies reporting on progression of cervical subluxation. Studies were excluded if they were not published in English. Study quality was assessed using the STROBE checklist. Prevalence of cervical subluxations was calculated for each study. Pearson's correlation and Student's t tests were used to evaluate significance. Trends for prevalence of C-spine involvement over decades was determined.

Results: A total of 12,249 citations were identified with 126 studies for full review, and 58 studies were included with12,808 RA patients from North America, Asia, and Europe. Seventy-five percent were female with a mean age of 57.6 years and 11.5 years of disease. The prevalence of aAAS was 32% in 1970s and prior, 36% in 1980s, 30% in 1990s, and 21% in 2000s (p=0.041). The regional prevalence of aAAS was 27% in North America, 31% in Asia, and 25% in Europe (p=0.132). The overall prevalence of VS was 11% and 13% for SA with no significant temporal changes (p=0.279, p=0.194). Cervical myelopathy occurred in 5% and did not decrease significantly over time (p=0.116). With regards to progression of existing subluxations, aAAS, VS, and SA lesions deteriorated at a rate of 2 lesions, 5 lesions, and 7 lesions per 1000 patients per year, respectively. Cervical myelopathy was found to develop or progress in one person per year per 1000 patients with existing cervical instabilities. There could be publication bias that could over or underestimate the rates of C-spine involvement in RA. **Conclusion:** Rheumatoid arthritis patients have a high rate of cervical spine involvement. Since 1960s, only anterior atlanto-axial subluxations has decreased dramatically. It remains the most common type of cervical instability but it is the least likely to progress comparing to vertical subluxation and subaxial subluxation. Cervical myelopathy continues to be a rare complication.

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Fibrodysplasia Ossificans Progressiva in a Young Girl presenting with Unilateral Neck Swelling
Vinay Shivamurthy (BC Children's Hospital, Vancouver); Kristin Houghton (BC Children's Hospital, Vancouver)
Objective: To describe a young girl who presented with soft tissue swelling of the neck and was subsequently diagnosed to have fibrodysplasia ossificans progressive (FOP)
Methods: Clinical data was collected on retrospective review of the chart.
FOP is a rare disease affecting one in 2 million people. It is inherited in an autosomal dominant pattern although most new cases are attributed to spontaneous mutations. It is characterised by bilateral great toe abnormalities as well as heterotopic bone formation. Children present in their first decade of life with sporadic episodes of painful soft tissue swellings which transform into bone. They may develop flares which may be spontaneous or may be triggered by trauma, intramuscular injections, invasive procedures including surgeries, dental work up or even intense physical activity. Disability is cumulative and average life span is 40 years. Treatment is generally supportive, but, during flare, glucocorticoids can be used at a dose of 2mg/kg starting within 24 hours for 4 days.
Results: 11 year old child presented to ER with 2 weeks history of swelling on the right side of her neck. She had torticollis and swelling of the right sternocleidomastoid (SCM). No other sites of myositis and normal skin and systemic examination. Blood work showed normal CK and CBC. She was initially diagnosed to have focal myositis based on clinical and ultrasound finding. She was treated with oral steroids with follow up in rheumatology. She had initial response to steroids but on subsequent visit her SCM muscle was noted to be firm and was noticed to have bilateral great toe abnormalities as well as limitation of range of motion in elbow and ankles joints. Findings in the ultrasound and MRI of the neck and x rays of the feet were in keeping with FOP.

Conclusion: Fibrodyplasia ossificans progressiva is rare and early diagnosis is critical to ensure optimum outcomes. Recognition of characteristic congenital malformation of the great toes and progressive heterotopic ossification is key to the early diagnosis. There is currently no effective treatment for FOP. Management focuses on treating symptoms and preventing flares.

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Juvenile Idiopathic Arthritis, Intra-articular Corticosteroid Injection and Osteochondritis Dissecans: Is there an Association?

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Objectives: We have observed the occurrence of osteochondritis dissecans (OCD) in our juvenile idiopathic arthritis (JIA) population and sought to look for an association between the two conditions. Our primary objective was to determine if there is an increased incidence of OCD in patients with JIA and our secondary objective was to determine whether the use of intra-articular corticosteroids is related to OCD in JIA patients

Methods: A retrospective chart review was done on patients with JIA currently being followed in a tertiary paediatric rheumatology centre who have clinical and radiographic diagnosis of OCD of the knee. The site of occurrence of OCD was documented as well as use of intra-articular steroids, number of intra-articular injections and management of OCD.

Results: Approximately 450 patients are currently being followed at the BC Children's Hospital paediatric rheumatology centre. Seven patients including four boys with JIA aged 12 to 17 years were diagnosed to have symptomatic OCD with 8 knees affected (4 medial femoral condyle, 3 lateral femoral condyle, 1 both medial and lateral femoral condyles). The prevalence of OCD in our current JIA patients is 1.5% which is 50 times the estimated prevalence of 15-30/100,000 in the general population. Six patients had history of arthritis in the affected knee and all of them were on anti-inflammatory agents and DMARDS and only one on biologics prior to developing OCD. Six out of eight joints had injections to affected knee (range 1-4) and three required surgery (one bilateral procedures) and one pending. In the general population about 1% of children with OCD require surgery.

Conclusion: 1.5% of children with JIA in our tertiary care clinic population have symptomatic knee OCD and surgery was required in the majority of cases. Although, the true prevalence of OCD in the paediatric population is not known, the prevalence of OCD and the rates of surgery in our JIA population is much higher than reported in healthy populations. Synovitis and steroid exposure are recognized risk factors for osteonecrosis so an association is plausible. However, our numbers are small and it is not possible to draw firm conclusions. If a patient with JIA has non-inflammatory mechanical knee pain, OCD needs to be considered. Radiographs should include tunnel (notch) profile views to view the articular surfaces of the distal femoral condyles and if radiographs are negative, MRI is warranted. Early referral to orthopedics / sport medicine is advised.

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Bacillus Pumilus; A Rare Cause of Paediatric Septic Arthritis

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Objective: To describe a case of septic arthritis in a child caused by Bacillus pumilus.

Methods: Clinical data was collected on retrospective chart review.
Septic arthritis in children most commonly results from haematogenous seeding of the joint space by staphylococcus aureus, Streptococcus pyogenes or Kingella kingae. Septic arthritis due to Bacillus species is rare but has been reported to occur following direct inoculation of the joint with a contaminated object. Bacillus pumilus, like other Bacillus species, is a Gram-positive bacillus that is only rarely reported to cause neonatal sepsis and cutaneous infections in adults. Previous reports of septic arthritis due to Bacillus pumilus are limited to a single case in an elderly patient following knee arthroscopy.

Results: A 6 year old, previously well, fully immunised girl had recently been to Africa with her family. She fell while running and immediately developed painful swelling of her left knee. There was no evidence of fracture and it was conservatively managed. A small abrasion was noted on the knee that healed quickly without evidence of infection. The child was reported to have low grade fever that lasted for less than a week. The pain and swelling persisted, and when evaluated on return from holiday, an MRI showed extensive synovial hypertrophy. She was referred to the pediatric rheumatology team for further evaluation. On examination she was well, afebrile, and had a warm right knee with a moderate effusion and flexion deformity. ESR was 68, CRP was 28. A joint aspiration was performed, and the synovial fluid grew Bacillus pumilus. She was started on oral antibiotics, but her knee symptoms worsened. On arthroscopy, the knee had a large pus collection and exuberant inflammation. This fluid again grew Bacillus pumilus. The patient has since received 4 weeks of intravenous antibiotics followed by prolonged course of oral antibiotics with gradual improvement in symptoms and normalisation of inflammatory markers.

Conclusion: Persistent monoarthritis without systemic illness in a young child would often suggest juvenile idiopathic arthritis. However, this case underscores the importance of conducting a careful history and work-up to rule out infection or other cause of arthritis, particularly when associated with high inflammatory markers. We speculate that B.pumilus may have been inoculated by a thorn prick or similar injury at the time of trauma, resulting in a relatively indolent septic arthritis.

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Feasibility of Applying the Flare Definition using the ACR Core Set Variables in Juvenile Idiopathic Arthritis in Routine Practice: Results from the ReACCh-Out Cohort

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Objectives: To determine the feasibility of using the American College of Rheumatology (ACR) core set variables for identification of flare in children with juvenile idiopathic arthritis (JIA) enrolled in a prospective cohort study.

Methods: We studied children in the Research in Arthritis in Canadian Children emphasising outcomes (ReACCh-Out) prospective cohort. The study protocol design aimed to emulate routine clinical practice. Newly diagnosed patients in 16 pediatric rheumatology centres between 2005 and 2010 were recruited. All six ACR core set variables were required at full study visits (0, 6, 12, 18, 24, 36, 48 and 60 months) and active joint counts and physician's global assessment (PGA) at interim visits. Using the full study visits, flare was defined as worsening of at least 3/6 core set variables by at least 30% without concomitant improvement of more than one variable by $\geq 30\%$, after the patient had improved as per ACR Ped 30 criteria. The risk of flare was estimated with Kaplan-Meier survival analysis.

Results: The primary difficulty in applying the ACR core set criteria for a flare was missing information which resulted in unexpected findings. To facilitate inclusion of patients, ESR was not required at each visit and it was missing in 42.4% of the 6177 full visits. Parent's global assessment was missing in 20% and the CHAQ score could not be calculated in 22.1%. Physician-reported variables were missing in a minority. Value thresholds were often needed to avoid division by zero in children who had markedly improved (e.g. no involved joints, normal CHAQ). Analysing the available data from all full visits we observed that, of the 1146 patients in the cohort, 830(72.4%) attained an ACR Ped30 improvement and 290 (25.3%) had one or more flares. The overall risk of flare was 21% at 12 months and 35% at 2 years. Children with psoriatic arthritis and ERA appeared to have a greater risk of flare (40% within 2 years) than children with RF positive polyarthritis (30%) On the contrary, in another study, flare defined as "recurrence of disease manifestations after attaining inactive disease" (using all available visits) reported 626(54.6%) patients with flare and higher risk of flare in those with RF-positive polyarthritis.

Conclusion: A flare definition based on ACR core set variables has been used in JIA controlled clinical trials, but in an observational cohort comprising all JIA subtypes, this definition was difficult to apply and the resulting findings may be unreliable

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Musculoskeletal Complications of Systemic Lupus Erythematosus: Risk Factors and Prevalence for Avascular Necrosis and Osteoporosis
Maeve Gamble (University of Western Ontario, St. Joseph's Health Care, London); Janet Pope (St. Joseph's Health Care, London)

Objectives: Osteoporosis (OP) and avascular necrosis (AVN) are well-recognized musculoskeletal complications of systemic lupus erythematosus (SLE). Steroid therapy and the underlying disease process are the main contributors to these complications. It is unclear however to what degree each of these risk factors contributes to the development of osteoporosis or avascular necrosis. Precise rates of AVN and OP in SLE are unknown but far higher than the general population. The aims of this study were to identify risk factors associated with OP and AVN.

Methods: A comprehensive review of both published articles and unpublished abstracts was conducted using the PubMed, EMBASE, and Cochrane databases. All articles relating to risk factors for avascular necrosis and osteoporosis in patients with SLE were included. Exclusion criteria were: osteoporosis in the pediatric population (pediatric patients with AVN were included), publication with 44 or fewer SLE patients, and studies using the same population of patients.

Results: Ten articles pertaining to avascular necrosis and 13 pertaining to osteoporosis met the inclusion criteria. The prevalence of osteoporosis was 12% (range 5% to 23%) and osteopenia 38% (9% to 50%). Age, cumulative steroid dose, SLE damage, and low BMI were frequently reported risk factors. Other risks in some studies included: limited physical activity, premature ovarian failure, decreased vitamin D exposure, decreased osteocalcin, decreased C4 levels, white or non-African Caribbean ethnicity, positive anti-Sm antibody, and negative anti-Ro antibody. Patients with AVN used more cumulative dose of glucocorticosteroids ($p<0.05$). There was no difference in disease activity in patients who did and did not develop AVN ($p=0.7$). SLE renal involvement had more AVN (OR 2.4, 95% CI 1.5,3.8). Other risks in some studies were: cytotoxic drugs (cyclophosphamide and mycophenolate mofetil), serositis, Raynauds, vasculitis, and seropositivty including Anti-Sm and APLA. There was an insignificant protective effect of antimalarial drugs (OR 0.7, 95% CI 0.4, 1.1).

Conclusion: Several risk factors for OP and AVN were identified, including cumulative steroid dose which was associated with both complications. Given that the prevalence of these complications is higher in SLE patients compared with the general population we sought to identify modifiable risk factors. These may be used to identify patients who are at higher risk with the goal to reduce morbidity and ultimately improve quality of life. The potential protective effect of antimalarials (though not statistically significant in this review) warrants further study.

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A Meta-Analysis of the Effects of Calcium Channel Blockers for the Treatment of Raynaud's Phenomenon

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Objectives: To assess the benefits and harms of calcium channel blockers (CCBs) versus placebo for the treatment of Raynaud's phenomenon (RP) in this Cochrane review.

Methods: The Cochrane library (including CENTRAL), MEDLINE, EMBASE and Clinicaltrials.gov were searched up to June 2014 for randomized controlled trials (RCTs) examining RP. Outcomes of interest were: 1) Frequency of Raynaud's attacks (average/week), 2) Duration of attacks (minutes), 3) Severity of attacks (10 cm Visual analogue scale) 4) Pain, 5) Patient global, 6) Withdrawals and 7) Serious adverse events. Fixed effects models were used to calculate mean differences (MD) or standardized mean differences (SMD) for continuous outcomes and pooled risk ratios (RR) for dichotomous outcomes. Heterogeneity was determined using Chi-squared and I2tests and was considered significant if I2>50%. Subgroup analysis by disease type (primary or secondary), CCB dosage (low, medium or high) and CCB type (mainly Nifedipine and Nicardipine) were performed.

Results: Of the 2337 articles, 939 participants from 36 RCTs investigating the effect of CCBs vs. placebo were included. The majority of these studies were crossover RCTs with low to moderate quality of evidence and used low dose CCBs (i.e. Nifedipine<60mg/day, Nicardipine< 90mg/day). Most trials reported only some of the outcomes of interest. CCBs were significantly more effective in reducing the frequency of attacks in 22 RCTs with 978 participants [(MD -2.6295%CI -3.38,-1.88), $p<0.00001$] and the severity of attacks in 17 trials with 792 participants [(MD -0.73 95% CI -0.99, -0.47), $p<0.00001$].There were no statistically significant differences in duration, pain or withdrawals due to adverse events between CCBs and placebo. Patient global was only reported in one study and serious adverse events were not reported. The presence of significant heterogeneity was addressed by sensitivity and subgroup analyses. Overall, CCBs reduced the frequency and severity of attacks irrespective of dosage, particularly for primary RP. Low dose CCBs reduced the frequency of attacks by 3.3 per week vs. medium dose at 5.6. CCBs reduced frequency of attacks (per week) in primary RP by 3.9 vs. 0.5 in secondary RP. Similar trends were seen in severity of attacks for low dose vs. medium dose CCBs and primary vs. secondary RP. Limitations were identified such as cross over studies with possible carryover effects, low trial quality, missing outcomes of interest and heterogeneity of trials.
Conclusion: CCBs are effective in managing RP, particularly primary RP.

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Predictors of Real-World Treatment Sustainability in RA Patients Treated with Abatacept in Canada: Implications for Routine Care
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Objectives: Treatment sustainability can measure drug effectiveness and encompasses drug effectiveness, safety, and compliance. Recent data suggest that differences in retention may exist between biologic agents even among the same class1-3. However, the majority of data for real-world sustainability of biologics pertains to TNF-inhibitors. This analysis assessed the durability of abatacept in RA patients and evaluated the determinants of treatment sustainability.
Methods: Data on RA patients administered abatacept in routine practice via the Orencia Response Program network, between August 2006 and February 2011 who had at least one follow-up evaluation, were included. Treatment sustainability was assessed with the Kaplan Meier (KM) estimator of the survival function. Parameters associated with treatment sustainability were assessed with multivariate Cox regression using a backwards selection method. Potential predictors considered were: number of previous biologics, monotherapy vs. combination therapy, home vs. clinic infusions, age, sex, severity of disease, presence of comorbidity, and years since diagnosis. The impact of these parameters on HAQ was assessed with mixed models with repeated measures.

Results: A total of 1,771 patients were included with mean (SD) age of 57.6 (13.2) years and duration since diagnosis of 16.5 (11.0). The majority (77.2%) were females. Overall, 672 (37.9%) patients discontinued after a mean (SE) KM-based time to discontinuation of 26.8 (0.5) months. In multivariate survival analysis, increased number of previous biologics [HR1 vs. 0 (95% CI): 1.48 (1.14-1.19, P=0.004; HR≥2 vs. 0 (95% CI): 1.71 (1.34-2.18), P<0.001] and abatacept monotherapy [HRMono vs. Combination (95% CI): 1.23 (1.05-1.45), P=0.011] were associated with shorter duration of treatment while home infusions [HRHome vs. Clinic (95% CI): 0.78 (0.67-0.93), P=0.004] and the presence of a comorbidity HR Yes vs. No (95% CI): 0.68 (0.58-0.80), P<0.001] were associated with increased treatment sustainability. When assessing the impact of these parameters on HAQ, only the number of previous biologics was identified as a significant predictor of lower response (P=0.009) after adjusting for potential confounders, with lower number of biologics being associated with improved response [B0 vs. ≥2 (SE): -0.12 (0.04), P=0.002; B1 vs. ≥2 (SE): -0.05 (0.03), P=0.167].

Conclusion: This real-world analysis identified the number of previous biologics, concomitant DMARD use, infusion location, and presence of comorbidity as independent predictors of abatacept treatment sustainability. The number of previous biologics may be associated with differences in effectiveness as measured by the HAQ whereas the other predictors may be associated with other reasons for discontinuation.

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First Report of Real-World Use of Subcutaneous Abatacept in Canadian RA Patients: The Abatacept Best Care (ABC) Treat-To-Target (T2T) Study

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Objectives: Several randomized controlled studies have demonstrated the superiority of a treat-to-target (T2T) approach compared to routine care (RC), in improving clinical and patient reported outcomes in RA patients. Aligned with this concept, the current recommendations of the Canadian Rheumatology Association dictate that the goal of treatment should be remission or, when not possible, low disease activity. The aim of this analysis was to describe the baseline profile of the currently enrolled patients in the Abatacept Best Care (ABC) study, comparing a T2T approach to RC in patients starting (SC) abatacept by their treating rheumatologist.

Methods: ABC is a prospective randomized, multicenter, post-marketing study aimed at assessing the usefulness of T2T in real-life and describing the adherence of Canadian physicians to the recommended T2T treatment guidelines vs. usual care while collecting data on the real-life use of SC abatacept in Canada. Participating physicians are randomized at a 1:1 ratio to the T2T group, which receives training and recommendations on the T2T approach, or the RC group.

Results: A total of 55 patients (71% females) were included with a mean (SD) age of 60.5 (10.2) years and duration since RA diagnosis of 11.8 (4.2) years. Family history of RA was reported for 35% of patients with available information while 57% and 47% were rheumatoid factor and anti-CCP positive, respectively. Prior biologic experience was reported for 25 (456%) of patients. Abatacept was used as combination therapy with traditional DMARDs in 86% of patients (mean methotrexate dose: 21.9 mg/week), while concomitant use of NSAID(s), and steroids (mean prednisone dose=8.3 mg/day) was reported for 42%, and 31% of patients, respectively. A loading dose of intravenous abatacept was used in 14% of patients. Mean (SD) disease parameters at baseline were: VAS pain = 62.7 (20.4) mm, patient global = 65.0 (16.5) mm, morning stiffness = 64.2 (20.0) mm, fatigue = 62.0 (24.6) mm, physician global = 59.2 (15.5) mm, ESR = 23.0 (20.4) mm/hr, CRP = 27.4 (44.3) mg/L, TJC28 = 9.9 (6.5), SJC28 = 8.8 (5.2), HAQ = 1.44 (0.57), RAPID3 = 19.0 (4.3), DAS28-CRP = 5.2 (1.2), CDAI = 31.4 (11.2), and SDAI = 34.5 (13.3).

Conclusion: More than half of RA patients enrolled in this real-life study initiated SC abatacept as an initial biologic. Overall, the baseline patient characteristics are comparable to those reported from observational studies with intravenous abatacept1,2. Further analysis will evaluate the impact of T2T on the real-life effectiveness of SC abatacept.

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Active and Structural Lesions on MRI of the Sacroiliac Joints Predict Major Clinical Responses in Patients with Non-Radiographic Axial SpA Treated with Etanercept

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Objectives: To assess the predictive capacity of active and structural lesions on MRI of the sacroiliac joints (SIJ) in a cohort of patients selected according to objective measures of inflammation and limited duration of disease.

Methods: Patients had non-radiographic axial SpA per the Assessment of SpondyloArthritis (ASAS) classification criteria, but did not meet modified NY radiographic criteria. Patients had symptoms for >3 months and <5 years, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4, and failed ≥2 NSAIDs. Patients were randomly assigned to etanercept 50 mg/week or placebo, then after 12 weeks, all patients received open-label etanercept 50 mg/week. Clinical and health outcomes were assessed throughout the study, and MRI of the SIJ and spine was performed by two central readers at baseline, weeks 12 and 48 to assess bone marrow edema (BME) using the Spondyloarthritis Research Consortium of Canada (SPARCC) score. Additionally, a post-hoc analysis was conducted to score structural lesions using the SPARCC SIJ structural method (SSS), which assesses fat metaplasia, erosion, backfill, and ankylosis on T1-weighted spin echo (T1WSE) MRI. Two independent readers scored baseline and 48 week T1WSE MRI scans from 187 cases blinded to patients and short tau inversion recovery (STIR) MRI scans. Mean scores of the readers were used. Baseline high sensitivity CRP (hsCRP) levels, SPARCC MRI inflammation and SSS erosion scores were analyzed using logistic models of week 48 ASAS40 and ASDAS major improvement (ASDAS MI change ≥2.0), adjusted for treatment.

Results: Mean (SD) age was 32 (7.8) years, 60.5% were male, and mean (SD) duration of disease symptoms was 2.5 (1.8) years. A total of 73% of patients were HLA-B27 positive and 81% met the ASAS MRI imaging criteria at baseline. Baseline CRP, SPARCC SIJ inflammation, and SSS erosion scores were significant predictors of both ASAS40 and ASDAS MI responses at week 48 in last observation carried forward as well as observed case analyses. The adjusted odds ratios (95% CI) of ASAS40 response for baseline predictors ranged from 1.05 to 1.09 (1.00, 1.19) and ranged from 1.07 to 1.17 (1.03, 1.24) for ASDAS MI; all p-values <0.05. The higher the baseline value the greater the likelihood of response. Fat metaplasia, backfill, and ankylosis were not significant predictors of response.

Conclusion: The presence of objective manifestations of active disease as indicated by CRP and inflammatory or erosive lesions on MRI prior to the start of anti-TNF therapy has predictive capacity for major treatment responses.

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Fat Metaplasia on MRI of the Sacroiliac Joints is a Lead Indicator of Radiographic Progression in the Spine of Patients with Ankylosing Spondylitis

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Objectives: Fat metaplasia in the SIJ on MRI is an early feature of sacroiliitis and occurs both in subchondral bone marrow and also in the excavated area caused by erosion, when it is called backfill. Recent data has shown that these lesions are key intermediaries in the development of SIJ ankylosis. We aimed to test the hypothesis that these lesions may also be lead indicators of new bone formation in the spine of patients with axial SpA. This could provide an important target for therapeutic intervention.

Methods: Bone marrow fat metaplasia and backfill were scored using the SPARCC MRI SIJ structural score (SSS) by two readers and an adjudicator using pre-specified rules for adjudication. 137 pairs of MRI scans blinded to time point (baseline, 2 years) were assessed from a prospective cohort of AS patients (mean age 40.5years, mean symptom duration16.9 years, 53% on anti-TNF) followed for mean 2.3 years. Two readers and an adjudicator independently scored pairs of radiographs (baseline, 2 years) from the same patients using the mSASSS. Radiographic progression was compared in patients with and without positive SIJ MRI for fat metaplasia (SSS score ≥2 or <2) and the degree of SIJ fat metaplasia at baseline (absolute SSS score) was compared in patients with and without radiographic progression (mSASSS >0 or =0) using Mann-Whitney and cumulative probability. Multivariate regression analyses included variables significant in univariate analyses (age, sex, symptom duration, CRP, baseline mSASSS) and treatment.

Results: Radiographic progression was significantly greater in those with positive SIJ fat metaplasia (p=0.015), and especially in patients who only received non-biologic therapy (p=0.023). Baseline SSS SIJ fat metaplasia scores were significantly higher in those who developed radiographic progression compared to those without (1.58 vs 0.65, p=0.008). Both positive SIJ MRI for fat metaplasia and the degree of fat metaplasia were significantly associated with radiographic progression in multivariate analyses (β=0.38 (p=0.005) and β=0.06 (p<0.0001) respectively). SSS score for backfill was also significantly associated with radiographic progression in multivariate analysis (β=0.04 (p=0.019)).

Conclusion: The appearance of fat metaplasia in SIJ subchondral bone marrow and/or at sites of erosion in the SIJ may identify AS patients at increased risk of radiographic progression in the spine.

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Autoantibodies to 14-3-3eta are Novel Biomarkers Associated with Inflammation and Radiographic Progression in Ankylosing Spondylitis

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Objectives: 14-3-3η is a ubiquitous intracellular chaperone protein that is expressed extracellularly in rheumatoid arthritis. An autoantibody response (AAb) is elicited to a range of epitopes on the native protein both within and outside the ligand-binding groove. We aimed to determine whether autoantibodies to the native protein were generated in AS and which specific autoantibody might be associated with inflammation and have diagnostic and prognostic properties.

Methods: Sera from 116 patients with AS followed prospectively and 106 healthy controls were screened against ten 14-3-3η peptides (Pan 1-10). Inflammation was assessed by CRP and MRI of the sacroiliac joint (SIJ) and spine. Radiographic progression over 2 years was assessed using the modified Stoke AS Spine Score (mSASSS). Patients had mean age of 39.7 years, 73% male, mean symptom duration 16.9 years, and 51 (44%) received TNF blocker therapy. Mean (SD) baseline mSASSS was 13.8 (17.6), mean change in mSASSS was 1.8 (2.7), and 52.5% had mSASSS change > 0. Mann-Whitney U-test was used to determine group differences and ROC analysis (AUC) was used to assess diagnostic utility. Potential associations were assessed by Pearson correlation. Multivariate regression analyses were used to examine associations significant in univariate analyses.

Results: Discrimination by AUC ranged from 0.81-0.89 for all 10 autoantibodies ($p<0.0001$ for all). For example, median (SD) expression of the Pan-1 14-3-3η autoantibody was significantly higher in SpA than in healthy controls (838 U/ml (605-1287) vs. 456 U/ml (346-568), $p=0.0001$) and area under the ROC curve was 0.86, 95%CI (0.82-0.91). A cut-off of 803 U/ml delivered 95% specificity and 53% sensitivity (LR+ 11.2, LR- 0.5). For inflammation parameters, Pan-1 and Pan-5 correlated significantly with CRP ($r=0.23, p=0.02$; $r=0.27, p=0.005$) and Pan-1 correlated with SPARCC SIJ MRI score ($r=0.21, p=0.04$). For radiographic progression measured by change in mSASSS, significant correlations were observed with all 10 Pan specificities, notably, Pan-2 ($r=0.39, p<0.0001$), Pan-3 ($r=0.34, p=0.0004$), and Pan-10 ($r=0.35, p=0.0003$). Independent predictors of MRI inflammation were sex ($p=0.006$) and Pan 1 autoantibody ($p=0.008$) (adjusted for age, sex, symptom duration, CRP). Controlling for baseline mSASSS CRP, age, sex, symptom duration, and treatment, Pan antibodies were the only significant predictors of the change in mSASSS at 2 years in multivariate regression analysis: Pan composite score ($p=0.001$), Pan-1 ($p=0.0008$), Pan-2 ($p=0.0001$), Pan-3 (0.0005), Pan-10 ($p=0.0003$).

Conclusion: 14-3-3η autoantibodies are novel serum markers that are differentially expressed in AS versus healthy controls. They are significantly associated with MRI inflammation and baseline expression of several autoantibody specificities predicts radiographic progression.

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Non-adherence to Treat-to-Target of Rheumatoid Arthritis in The International RA BIODAM Program: What Defines this Population?

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Objectives: Adherence to T2T is associated with improved RA outcomes. Previous data from the RA BIODAM program has shown that there remains a substantial gap in implementation even in protocol-specified clinical settings. We aimed to assess patient factors that define the non-adherent population across 10 countries participating in the RA BIODAM program.

Methods: RA BIODAM is an international multicenter (35 sites, 620 patients) 2-year program aimed at the clinical validation of biomarkers reflecting structural damage endpoints in RA. Active RA patients are enrolled and systematically assessed for disease activity with a prompt to make major treatment changes (standard DMARD and/or anti-TNF) in order to achieve a DAS target of ≤2.4. Patients with RA are evaluated every 3 months for outcomes, and serum/urine biosamples, and every 6 months with radiography to determine which RA biomarkers consistently reflect change in damage. An internet-based data entry and management system (IDEMS) was custom designed to automate calculation of the DAS and alert sites to the requirement for treatment change. IDEMS also automates calculation of RA outcomes and attainment of remission (DAS, CDAI, SDAI, ACR Boolean). We assessed a range of patient factors in the T2T adhered and non-adhered populations.

Results: As of September 2014, 538 patients have been recruited of whom 240 have completed at least 15 months follow-up. Non-adherence to T2T was 21%, 10%, 11% for 1, 2, and 3 or more study visits, respectively. Remission at 15 months follow up was more frequent in T2T adhered patients at 74% (DAS), 38% (CDAI), 43% (SDAI), 41% (ACR Boolean) compared to non-adhered patients at 31% (DAS), 11% (CDAI), 13% (SDAI), 13% (ACR Boolean) irrespective of therapy (standard DMARD, anti-TNF). Median data for DAS components at the first T2T non-adherence visit was 9 and 4 for TJC and SJC, 5 for patient global, and 16 for ESR (39.3% with ESR >20). At the subsequent visit, there was still no change in treatment in 32% despite DAS > 2.4: median was 10 and 4 for TJC and SJC, 5 for patient global, and 26 for ESR (58.0% with ESR >20). Non-adhered patients were more frequently female, receiving anti-TNF versus standard DMARDs, and less likely to have experienced adverse events with prior DMARDs. No differences were observed for baseline disease status, number of prior DMARDs, or comorbidities.

Conclusion: Non-adherence to T2T and failure to achieve optimal outcomes is observed despite evidence of persisting disease activity, especially in patients receiving anti-TNF therapy.

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Cardiovascular Morbidity and Mortality of Cutaneous Psoriasis (PsC) and Psoriatic Arthritis (PsA) are well Documented, with Increased Risks of Myocardial Infarction, Ischemic Heart Disease, and the Metabolic Syndrome in these Patients

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Objectives: Cardiovascular morbidity and mortality of cutaneous psoriasis (PsC) and Psoriatic Arthritis (PsA) are well documented, with increased risks of myocardial infarction, ischemic heart disease, and the metabolic syndrome in these patients. However, comparison of subclinical carotid atherosclerosis, a prognostic indicator of vascular risk and coronary events, between the general population and those with PsA or PsC remain lacking. The objective of this study was to evaluate subclinical carotid atherosclerosis between patients with psoriatic disease and the general population.

Methods: Patients were recruited from the Psoriatic arthritis (PsA) and psoriasis (PsC) clinics. Patients with PsA fulfilled CASPAR criteria, and patients with PsC had their psoriasis confirmed by a dermatologist, and had been reviewed by a rheumatologist to assure absence of inflammatory arthritis. Controls were recruited from among hospital personnel, as well as friends and spouses of patients. Controls completed a questionnaire to rule out chronic inflammatory conditions. The presence of traditional cardiovascular risk factors was assessed in all subjects. The extent of subclinical atherosclerosis was assessed using carotid artery ultrasound with measures of intimal media thickness (cIMT) and total plaque area (TPA). Cochrane-Armitage trend test and t tests were used to compare categorical and continuous variables, respectively. The extent of atherosclerosis, as assessed by cIMT and TPA categories, was compared across the 3 groups using multivariate regression analysis adjusting for age and sex.

Results: 343 PsA patients,180 PsC patients and 119 controls were studied. Univariate analysis revealed more severe atherosclerosis as assessed by TPA in PsA patients compared to controls (p=0.002) and to PsC patients (p=0.01). cIMT was also elevated in the PsA cohort compared to controls (p=0.003), but difference in cIMT between PsA and PsC were not significant. Multivariate logistic regression controlling for age and gender demonstrated no differences in TPA or cMIT between PsA compared to PsC or control cohort. Subgroup analysis, however, revealed statistically significant difference of TPA categories in female PsA patients compared to controls (Odds Ratio 1.85, 95% Confidence Interval 1.09, 3.02, p=0.02). It is likely that the differences in age and gender distributions accounted for the lack of difference in TPA or cIMT in multivariate analysis.

Conclusion: This study demonstrated the possible elevated burden of carotid artery plaques and subclinical atherosclerosis in patients with PsA compared to PsC alone or general population.

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Profiles of Switches in Patient with Ankylosing Spondylitis: Comparing Adalimumab, Etanercept, Infliximab, Golimumab and Certolizumab

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Objectives: As much a 40% of patients with ankylosing spondylitis will fail (BASDAI≥ 4) different non-steroidal anti-inflammatory agents and will eventually be treated with an anti-TNF agents. Response is usually satisfactory but retention on drug may vary from one agent to the other and from one patient to the other. Reasons for stopping ad/or switching are either inefficacy, intolerance or spontaneous improvement of the disease activity in a given individual. The goal of this analysis is to explore the first 6, 12 and 18 month period after first exposure to an initial agent and assess the cycling incidence from different anti-TNF agents namely adalimumab (ADA), etanercept (ETA), infliximab (INF), golimumab(GOL) or certolizumab (CERTO).

Methods: Patients with ankylosing spondylitis as diagnosed by their treating rheumatologists and exposed to either adalimumab, etanercept, infliximab, golimumab or certolizumab in first intention after failing two different non-steroidal anti-inflammatory agents for a minimum of 3 months each were extracted from the Quebec inflammatory database Rhumadata®. Demographics and baseline characteristics includes age, gender, disease duration, Hla-B27, BASDAI, BASFI, patient global (vas) and ASDAS (crp). Cycling from one agent to another was then explore at 6, 12 and 18 month time point. Proportion of patients switching vs not switching at each time point are assessed. Reason for switching at each time point (Inefficacy, AEs infections, surgery or death) are expressed in percentages.

Results: The data from 296 patients with ankylosing spondylitis and prescribed either adalimumab (114=39%), etanercept (61=21%), golimumab (31=10%) or infliximab (90=30%) as first biologic agent were extracted. These patients were treated for a period ranging from 0.4 to 173.2 months with a mean treatment duration of 44.0 (StD=36.3) months. At 6, 12 and 18 months, 11.8%, 25.7% and 35.8% of patients had either stopped or switched their medication. The reported reasons for stopping or switching medication were inefficacy (76.4%), adverse events (5.7%), surgery (14.2%) and lost to follow-up (3.6%).

Conclusion: Switches at the 6 month time point vary from 4.4% (ADA) to 9.8% (ETA). The percentage of switches increase with time for all agents except golimumab (9.7% at 12 and 18 months). A significantly higher proportion of patient stops golimumab and do not switches to another agent (51.6%). Main reason for stopping or cycling to another agent is inefficacy.

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Does Combining Methotrexate to Etanercept Improves its Retention Rate in Patients with Early Rheumatoid Arthritis: Analysis of a Subgroup with Less than Three Years Disease Duration

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Objectives: Etanercept (ETA) has demonstrated good retention in both mono and combination therapy in clinical trials conducted over short observation periods (less than 2 years). In unselected patient populations, studies evaluating the efficacy of anti-TNF have demonstrated better results when it is used with methotrexate compared to monotherapy. Similar results have been observed in data generated from patient registries. Our objective is to explore the effectiveness of etanercept with and without MTX in a homogeneous population of recently diagnosed RA patients

Methods: RA patients prescribed ETA as a first biologic agent after January 1st 2004 were included in the present analysis. Patients were kept for analysis if they had a disease duration of at most three years since diagnosis. Baseline demographics for both cohorts included age, disease duration, HAQ-DI, fatigue and pain visual analog scale evaluation (VAS), TJC, SJC, DAS 28 ESR, SDAI, RF and anti-CCP status. The drug retention rate of subjects on ETA monotherapy (n=14) were estimated and compared to the retention rate of subjects also receiving a DMARD (n=72) using Kaplan-Meier survival estimates. Yearly estimates (up to 6 years) were obtained. Statistical analysis was performed using SAS version 9.3. RHUMADATA® is a clinical database and registry used in daily clinical practice at the IRM and CORQ.

Results: At one year, drug retention for ETA monotherapy therapy was estimated at 71% and remained constant at 56% from year 2 to year 6. Estimates for subjects on combination therapy with methotrexate ranged from 75% at year one to 50% at year 6. No statistically significant differences were identified for each the time point..

Conclusion: In a population of RA patients with shorter disease duration (less than 3 years), etanercept with and without methotrexate discloses statistically similar retention rates from 1 up to 6 years. In selected patients with RA and contra-indication to methotrexate ETA monotherapy is an acceptable alternative.

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Prediction of Non-adherence in Patients with Rheumatoid Arthritis

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Objectives: Rheumatoid arthritis (RA) is a very prevalent autoimmune disease affecting close to 1% of the adult population. Adherence to prescribed drug is important to prevent irreversible joint damage. Unfortunately, adherence in this population is low, estimated to 60-70%. As a result, an clinical approach to screen for propension to non-adherence would be valuable. Although a number of self-reported medication adherence questionnaires exist, only the «Compliance Questionnaire on Rheumatology» (CQR) has been validated in patients with inflammatory arthropathies. The primary objective of this study is to evaluate the validity of a Quebec French version of the CQR and assess its possible use as an adherence screening tool in its extended form. A secondary objective would be to evaluate a possible short form, 5 questions or less, of the CQR.

Methods: We first validated the proposed Quebec French by the usual methods. Then, we conducted a longitudinal descriptive study. The inclusion criteria were: RA diagnosis, age over 18 years, RA duration≥ 1 year, and RA treatment for at least the previous six months (DMARD and/or biologic agent) prior to entering in the study. Adherence was measured by two different methods: 1) patients completed the Quebec French version of the CQR questionnaire during a medical visit at the «Institut de Rhumatologie de Montréal» between November 11th and December 17th, 2013 and 2) the pharmaceutical profile for the six months preceding to the medical visit was obtained by contacting the individual pharmacist. The medical possession ratio (MPR) was then calculated for each patient, and compared to the result of the CQR questionnaire.

Results: 160 patients with rheumatoid arthritis were included in this study. All of them gave written informed consent. The preliminary results show an adherence rate to DMARDs of 79.1%, which is slightly higher than the rate found in the literature. The rate of adherence to hydroxychloroquine (HCQ) and methotrexate (MTX) are similar (80.6% vs 80.0%) despite the higher incidence of side effects associated to MTX. The participants seem to be more adherent to oral medication compared to subcutaneous (83.8% vs 71.9%). Adherence calculated by the medical possession ratio (MPR) show that non-adherent patients correlate with a poorer result to their CQR questionnaire.

Conclusion: The Quebec French version of the CQR questionnaire could become an useful tool to evaluate adherence in Quebec patients with rheumatoid arthritis. Further analysis and results are pending.

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Predictors of Clinical Response to Biologics in Rheumatoid Arthritis: Experience from a Canadian Clinic

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Objectives: The purpose of this study was to explore the predictors of clinical response in rheumatoid arthritis (RA) patients followed at a Canadian clinic.

Methods: In this prospective cohort study, adult patients included in the RHUMADATA database with a diagnosis of RA and treated with at least one biologic since 2003 were selected. Patients were followed for three years after therapy initiation or until treatment discontinuation. Patients reaching remission or low disease activity (LDA) according to the Disease Activity Score (DAS)-28 or the Chronic Disease Activity Index (CDAI) score were considered to have demonstrated a clinical response. The association between baseline variables and clinical response to the first biologic at 6, 12, 24 and 36 months was assessed separately using logistic regression models.

Results: In all, 623 eligible patients were treated with at least one biologic (mean age 53.2 years, 77% women, mean disease duration 7.7 years). Because of missing DAS-28 and CDAI values, clinical response to biologic therapy after 6, 12, 24, and 36 months could be determined for 108 (17%), 100 (16%), 59 (9%), and 29 (5%) patients, respectively. In univariate analyses, baseline HAQ score [odds ratio (OR): 0.31; 95% confidence interval (CI): 0.13-0.72] was associated with remission at 6 months, while gender (women vs men; OR: 0.25; 0.07-0.90), employment status [unemployed vs full time (OR: 0.21; 0.05-0.86) and on sick leave vs full time (OR: 0.08; 0.01-0.91)], patient assessment of fatigue (OR: 0.83; 0.71-0.98), and patient global assessment (OR: 0.78; 0.63-0.91) were associated with LDA. ESR values were associated with remission at 12 months (OR: 0.96; 0.94-0.99). Variables associated with LDA at 12 months were physician global assessment of disease (OR: 1.28; 1.06-1.57) and use of methotrexate (OR: 0.28; 0.09-0.88). At 24 months, the number of DMARDs used (OR: 0.28; 0.09-0.84) and use of methotrexate and hydroxychloroquine (0.12; 0.03-0.56) were associated with LDA while only use of methotrexate and hydroxychloroquine (OR: 0.25; 0.07-0.82) was associated with remission. At 36 months, CRP (OR: 0.08; 0.01-0.83) and positive rheumatoid factor (OR: 0.02; 0.002-0.30) were associated with remission while no variables were found to be associated with LDA.

Conclusion: The results of this real-world study suggest that many clinical, laboratory and socioeconomic characteristics may predict response to biologics in RA patients. However, these variables were inconsistent between the different time points assessed. Better understanding of those predictors could help optimize the treatment of RA patients.

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Profile of Joint Involvement over Time in Rheumatoid Arthritis and Psoriatic Arthritis Patients Treated with Anti-TNF

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Objectives: To describe the most commonly affected joints in RA and psoriatic arthritis (PsA) patients at baseline and after 6 months of treatment with infliximab in a real-world, Canadian, clinical practice setting.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with infliximab or golimumab. In this analysis, RA patients treated with IFX between 2002-2012 and PsA patients treated with infliximab between 2005-2012 were included. Based on the 28-joint involvement seven groups were created: shoulder(s), elbow(s), metacarpophalangeal (MCP(s)), wrist(s), proximal interphalangeal (PIP(s)), knee(s), and thumb(s). The impact of treatment on joint swelling/tenderness was assessed with the McNemar test while the Chi-square test was used to compare the affected joints between disease groups.

Results: 832 RA patients (mean age of 55.8 years and disease duration of 10.2 years) and 92 PsA patients (age: 48.7 years; disease duration: 6.8 years) were included. At baseline, mean DAS28, SJC28 and TJC28 in RA vs. PsA patients were 5.8 vs. 4.1 (P<0.001), 10.7 vs. 4.0 (P<0.001), and 12.6 vs. 5.9 (<0.001), respectively. Among RA patients, the joints most commonly swollen at baseline were MCPs (86.8% of patients), wrists (70.5%), and PIPs (53.2%). Knees, thumbs, elbows and shoulders were swollen in 42.3%, 33.7%, 30.5%, and 16.7% of patients, respectively. With respect to tenderness, MCPs were tender in 83.8% of patients, wrists in 75.3%, shoulders in 57.8%, knees in 54.8%, PIPs in 55.3%, thumbs in 38.8%, and elbows in 41.0%. Statistically significant (P<0.05) differences were observed between RA and PsA patients both in the frequency of joint swelling/ tenderness, which were lower in PsA, and the profile of affected joints. Among PsA patients, MCPs, wrists, and knees were the joints most commonly swollen, affected in 57.6%, 34.8%, and 31.5% of patients, respectively; MCPs, knees, and wrists were the joints most commonly tender (63.0%, 43.5%, and 42.4% of patients, respectively). Upon 6 months of treatment, significant improvement in swelling and tenderness in all the most commonly affected joints was observed. The joints most resistant to treatment were MCPs in both RA and PsA patients.
Conclusion: Differences exist in both the frequency and the profile of swollen and tender joints in RA and PsA patients Both diseases shared the MCPs as the joint most commonly affected and most resistant to treatment. Treatment with infliximab for 6 months resulted in a significant reduction in the 28-swollen and tender joint counts in both RA and PsA patients.

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Predictors of Response in Patients with Psoriatic Arthritis Treated with Anti-TNF in a Real-World Setting
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Objectives: Recent studies have suggested that early and aggressive treatment of spondyloarthritis, including ankylosing spondylitis (AS) and psoriatic arthritis (PsA), may be associated with favorable patient outcomes, reducing synovial inflammation, delaying joint damage, and maintaining functional status. The objective of this analysis was to determine the predictive factors of early DAS28 improvement in PsA patients treated with infliximab (IFX) or golimumab (GLM) in a Canadian routine clinical care setting.
Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM. The analysis was based on PsA patients treated with IFX or GLM between 2005 and 2014. Variables associated with improved response were examined using general linear models and those showing a statistical trend (P<0.150) were considered in multivariate analysis to identify independent predictors.

Results: A total of 176 patients were included in the analysis with a mean (SD) age of 49.4 (11.4) years and a disease duration of 5.2 (7.2) years. The majority of patients were male (54.1%). Upon 6 months of treatment statistically significant and clinically meaningful improvements were observed in DAS28 (4.1 vs. 2.9; P<0.001), HAQ (1.05 vs. 0.78; P<0.001), TJC (5.0 vs. 2.6; P<0.001), SJC (3.7 vs. 1.6; P<0.001), pain (46.8 vs. 30.7 mm; P<0.001), PtGA (48.6 vs. 29.7 mm; P<0.001), MDGA (5.3 vs. 2.3 cm; P<0.001), and morning stiffness (65.8 vs. 45.0 min; P<0.001). In univariate analysis, male gender (male vs. female: B=-0.806; P=0.029), not smoking (smokers vs. non-smokers: B=0.984; P=0.131), no previous use of a biologic (naïve vs. experienced: B=-1.995; P<0.001), presence of dactylitis (no vs. yes: B=0.746; P=0.073), and higher disease activity (DAS28 B=-0.525; P<0.001) were associated with greater improvements in DAS28 at six months of treatment. Age, disease duration, number of prior DMARDs, ongoing DMARD use, ongoing steroid use, ongoing NSAID use, presence of enthesitis, presence of nail pitting, and number of peri-articular manifestations did not show any effect on the change in DAS28. Multivariate analysis showed that, upon adjusting for baseline disease severity, male gender (B=-0.838; P=0.056) and no prior exposure to a biologic (B=-2.693; P=0.001) were significant predictors of improved response.
Conclusion: Six-month treatment with IFX or GLM in a real-world setting was associated with significant improvements in all disease parameters studied. Upon adjusting for potential confounders, no prior exposure to a biologic and male gender were identified as independent predictors of greater DAS28 improvement.

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Exploring the DAS: What is the Level of Agreement in the Classification of Remission and Low Disease Activity among the Various Versions of the Disease Activity Score (DAS) and their Correlation? An Analysis from a Prospective, Observational Registry

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Objectives: Two versions of DAS28 are available, DAS28-4 comprising 4 variables [tender and swollen joint counts, acute phase reactant (APR), and patient global assessment] and DAS28-3 where patient global has been omitted. Despite the difference between DAS28-4 and DAS28-3 thresholds for remission and low disease activity (LDA) are the same. The APR used to calculate DAS may be either ESR or CRP. This analysis describes the agreement between these four possible indices, DAS28-4-ESR, DAS28-4-CRP, DAS28-3-ESR and DAS28-3-CRP and compares them in terms of classifying remission and LDA in a real-world, routine clinical care setting.

Methods: BioTRAC is a prospective registry of patients initiating treatment with infliximab or golimumab. In this analysis, data from RA patients who were treated with infliximab between 2002-2014 or with golimumab between 2010-2014 and had available information in all indices were used. The definitions for remission were: DAS28-3/4 <2.6; LDA was defined as: DAS28-3/4 <3.2. Correlation between different indices was assessed with Pearson's correlation coefficient (r) and classification agreement was assessed with Cronbach's alpha (CA) and the kappa statistic.

Results: 869 RA patients who had 3,517 complete assessments were included in the analysis. Non-remission was classified by all indices in 61.4% of cases, while remission was achieved in one (5.9%), two (10.3%), three (5.3%), or all four (17.2%) indices. Similarly, non-LDA was classified by all indices in 46.1% of cases, while LDA was achieved in one (6.2%), two (10.9%), three (5.4%), or all four (31.3%) indices. Overall, a strong linear positive correlation (r>0.8) was observed between all indices. When looking at the internal consistency in terms of classifying disease state, the CA was 0.905 for remission and 0.923 for LDA suggesting an overall high internal consistency. However, when looking at individual inter-item correlations, agreement between indices was variable with DAS28-3CRP and DAS28-4CRP showing highest correlation and DAS28-3-ESR and DAS28-4-CRP showing lowest correlation. When comparing DAS28-4-ESR with DAS28-3-ESR, the latter categorized 16.5% of DAS28-4-ESR remission cases as non-remission and 3.0% of DAS28-4-ESR non-remission cases as remission. With respect to LDA, DAS28-3-ESR categorized 9.1% of DAS28-4-ESR LDA cases as non-LDA and 4.7% of DAS28-4-ESR non-LDA cases as LDA. Similar results were observed with DAS28CRP.

Conclusion: The results of this analysis show that, despite being highly correlated, variability exists in the classification of remission and LDA by the various DAS indices. Decision making based on disease state achieved may vary significantly based on type of APR used in the DAS index.

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Does Treatment Improve HAQ or Do Patients Adjust How They Do Things? An Exploration of the HAQ-DI vs the HAQ-ADI over Time

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Objectives: People with rheumatoid arthritis (RA) and other chronic diseases adjust their lifestyle to accommodate symptoms and limitations. The aim of the current analysis was to assess the utilization of aids/devices or help over time and to determine whether development of self-management behavior is responsible for HAQ improvement in RA patients on anti-TNF treatment in a real-world clinical practice setting.

Methods: BioTRAC is an ongoing, prospective registry of patients initiating treatment for RA, AS, or PsA with IFX or GLM. Data were used from RA patients treated with infliximab (IFX) between 2002-2014 or with golimumab (GLM) between 2010-2014. The correlation between the standard HAQ disability index (HAQ-DI) and the alternative disability index (HAQ-ADI), incorporating or not the use of aids/devices/help, respectively, was assessed with the Pearson's correlation coefficient. Changes in HAQ-DI, HAQ-ADI, the individual HAQ domain scores, or the difference between HAQ-DI and HAQ-ADI over time, were assessed with general linear models. The slope of HAQ-DI and HAQ-ADI improvement in each patient was assessed with the paired-samples t-test.

Results: 1030 RA patients were included with a mean (SD) age of 56.1 (13.5) years and time since diagnosis of 8.5 (9.1) years. Mean (SD) DAS28, CDAI, HAQ-DI and HAQ-ADI scores at baseline were 5.6 (1.5), 34.3 (16.6), 1.59 (0.71), 1.47 (0.73), respectively. At baseline, highest HAQ domain scores included 'Activities', 'Reach', 'Hygiene', and 'Grip'. The use of aids/devices/help was highest for these activities (49.2%, 47.5%, 38.0%, 73.1% of patients, respectively), with females requesting significantly more aids/devices/help than males. Treatment for 60 months resulted in statistically significant and clinically meaningful improvements in HAQ-DI and HAQ-ADI, and in significantly lower utilization of aids/devices/help. A statistically significant difference (P=0.001) was observed in the slope of HAQ-DI (Δ=-0.034/month) and HAQ-ADI (Δ=-0.038/month) improvement over time which could be attributed to the differential rate of use of aids/devices/help over time resulting in the inflation of HAQ-DI. The duration of follow-up was significantly (P<0.001) associated with a greater difference between HAQ-DI and HAQ-ADI changing from 0.12 at baseline to 0.18 at 60 months.

Conclusion: Our results have shown that problems with 'Activities', 'Reaching', 'Hygiene', and 'Gripping' represent primary challenges in RA. Anti-TNF treatment resulted in significant improvements in all HAQ domains. Significant differences were observed over time, however, between HAQ-DI and HAQ-ADI suggesting that RA patients may also adjust their lifestyle to accommodate their symptoms. These findings highlight the importance of educational programs focused on self-management behaviors in RA.