CANADIAN RHEUMATOLOGY ASSOCIATION MEETING

The 67th Annual Meeting of The Canadian Rheumatology Association (CRA) was held at the Fairmont Empress Hotel, Victoria, British Columbia, Canada, March 28–31, 2012. The program consisted of presentations covering original research, symposia, the Dunlop-Dottridge lecture, workshops, the Great Debate, and a special spotlight on Canadian excellence in rheumatology by the CRA Distinguished Rheumatologist, Distinguished Investigator, Teacher-Educator, and Young Investigator. The contributions presented at the meeting are reflected in the abstracts of the meeting, which we are pleased to publish in this issue.

Podium

1

Inflammation and Socioeconomic Status in SLE

Mai Nguyen (University of Manitoba, Winnipeg); John McVagh (University of Manitoba, Winnipeg); Carol Hitchon (University of Manitoba, Winnipeg); David Robinson (University of Manitoba, Winnipeg); Navjot Dhindsa (University of Manitoba, Winnipeg); Hani El-Gabalawy (University of Manitoba, Winnipeg); Christine Peschken (University of Manitoba, Winnipeg)

Objective: Worse outcomes in systemic lupus erythematosus (SLE) patients from lower socioeconomic strata (SES) have been well documented. Low SES is associated with higher chronic stress, which in turn may result in increased inflammation and immune dysfunction. We examined the relationship between SES, autoantibody frequency, and inflammation in SLE patients.

Methods: Adult incident and prevalent SLE patients were enrolled in a prospective cohort at a single centre. Sociodemographic variables, data on health-related habits, diagnostic criteria, disease activity, autoantibodies, treatment, and damage were collected annually using standardized tools. SES was measured as educational level achieved and annual household income. Disease activity was evaluated using the Systemic Lupus Activity Measure (SLAM). Organ damage was measured using the SLICC/ACR Damage Index (SDI). Autoantibodies measured included antinuclear antibody, dsDNA antibody, extractable nuclear antigens and anti-phospholipid antibodies. Inflammation was measured using the erythrocyte sedimentation rate (ESR) score from the SLAM. Baseline data was analyzed, testing for differences in ESR score and total number of autoantibodies positive between income and education groups. Significant variables from univariate analyses were then included in multivariate regression models examining for predictors of total autoantibody frequency, ESR score, and organ damage.

Results: Two hundred seventy-three patients were enrolled in the cohort, mean disease duration was 13.7 years, and mean age was 48.5 years. Ninety percent were female, 14% had incomes below the poverty line, while 51% had annual incomes >\$50,000. Seventy-seven percent had completed high school. No associations were found between SES and autoantibody frequency. Less education and low income were associated with increased ESR scores ($p < 0.001$, $p = 0.035$ respectively) in univariate analysis. Both income and education were predictors of higher ESR scores in linear regression ($p = 0.025$ and $p = 0.047$ respectively). Higher ESR score and lack of high school completion ($p = 0.032$ and $p = 0.04$ respectively) were predictors of SDI scores when total ACR score, age, and income were included in the regression model.

Conclusion: In our cohort, low SES was a predictor of increased inflammation. Both increased inflammation and lower educational attainment were independent predictors of organ damage. Thus inflammation may be a mediating factor between low SES and poor disease outcomes in SLE.

2

An Evaluation of the Validity of Cardiovascular Diagnoses in Administrative Data: A Systematic Review

Natalie McCormick (University of British Columbia, Vancouver); Jamie

Thomas (Arthritis Research Centre, Centre for Health Evaluation and Outcome Sciences, Vancouver); Diane Lacaille (Arthritis Research Centre, University of British Columbia, Vancouver); Juan Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Vancouver)

Objective: To conduct a systematic review of studies reporting on the validation of diagnostic codes for identifying cardiovascular conditions in administrative health data and to compare the validity of the codes.

Methods: A comprehensive literature search was conducted using Medline and EMBASE, from inception to November 2010, using two strategies: (1) all studies where administrative data was used to identify cardiovascular conditions, and (2) all studies reporting on the validation of administrative data to identify these conditions. From a title and abstract screen relevant articles were selected for thorough review for inclusion by two investigators working independently; discrepancies were resolved by consensus. Additional studies were located through hand-searching. A predesigned data abstraction form was used to extract pertinent data, including sensitivity, specificity, positive (PPV) and negative (NPV) predictive values, and kappa, and the study quality was evaluated using the QUADAS tool.

Results: A total of 76 articles were included in the final review. Two cardiovascular events, acute myocardial infarct (AMI) and cerebrovascular accidents (CVA), were selected because of their frequent selection as outcomes of interest in cardiovascular studies; the diagnosis of congestive heart failure (CHF) was also evaluated. PPV was the most commonly reported statistic, followed by sensitivity, whereas NPV and kappa were rarely reported; most data pertained to hospitalizations. While some variability in results was observed, mainly relating to the selection of gold standard with studies using stricter criteria, such as the MONICA criteria for AMI, finding lower sensitivity and PPV values, overall the sensitivity and specificity of hospitalization data was high (>80%) in most studies for identifying AMI (sensitivity ranging from 16-100%, specificity from 80-100%) and CVA (sensitivity >80% in most, range 25-100%; specificity 92-97%). In contrast, validation studies of CHF found less accurate results, with low sensitivity (< 70% in most studies, range 0-87%), highly variable but often low PPV, but acceptable specificity (>70% in most, range 69-100%). The results support the use of hospitalization data for identifying AMI and CVA, but not CHF. It was noted that the accuracy of AMI as a cause of death on death certificates was limited.

Conclusion: Hospitalization data can be used to identify AMI and CVA as a covariate or outcome. Authors should take into consideration that hospitalization data to identify CHF has significant limitations due its relatively low sensitivity and specificity. When using vital statistics data, authors need to acknowledge that the accuracy of AMI as a cause of death is limited.

3

Shared Risk for Chronic Inflammatory Diseases in the Family Members of First Nations Rheumatoid Arthritis Patients

Konstantin Jilkine (University of Manitoba, Winnipeg); Keng Wong (University of Manitoba, Winnipeg); Hani El-Gabalawy (University of Manitoba, Winnipeg)

Objective: RA is prevalent and severe in First Nations (FN). As our previous studies have shown that RA is familial in FN, we have studied the disease-free first-degree relatives (FDR) of FN RA patients to better understand risk in FN. Our studies have shown that compared to FN controls,

FDR have a high prevalence of RA autoantibodies and their cytokine profile resembles that of the RA patients. Because of a high prevalence of other chronic diseases such as obesity, diabetes, and cardiovascular disease in FN and the role that adipokines play in chronic inflammation, we studied the serum concentrations of four adipokines (adiponectin, leptin, resistin, and retinol binding protein 4 [RBP4]) in RA patients, their FDR, and FN controls with no family history of autoimmunity.

Methods: Using commercially available ELISA for adiponectin, leptin, RBP4, and resistin, MCP-1, and hsCRP, we tested banked sera from four cohorts: RA (n=104), FDR (n=273), FN controls (FNC, n=200), and Caucasian controls (CC, n=150). Body mass index data were available for most of the FDR. SPSS 19 was used for analysis.

Results: Serum adiponectin levels were highest in FDR (FDR=9.1 vs RA=8.0 p=0.108, FNC=7.6 p=0.002, CC=6.1 µg/mL p<0.000). In contrast, leptin levels were highest in RA (RA=9.8 vs FDR=6.8, NAN=6.7, CC=6.1 pg/mL, p<0.000), as were resistin (RA=66.5 vs FDR=58.5, FNC=56.0, CC=55.6 ng/mL, p<0.000) and RBP4 (RA=10.9 vs. FDR=10.0, FNC=10.0 ng/mL, p=0.443). MCP-1 levels were comparable in RA vs. FDR (594 vs. 536 pg/mL, p=0.256), and both were dramatically higher than levels in controls (FNC=219, CC=190, p<0.000). Similarly, hsCRP levels were highest in RA (9.1 mcg/mL) but levels in FDR were higher than control groups (FDR=4.9 vs. FNC=1.6, CC=2.2 p<0.000). Adiponectin levels correlated positively with MCP-1 (r=0.113 p=0.003) and inversely with leptin (r=-0.112 p=0.005). There was a strong correlation between the proinflammatory adipokines leptin, resistin and hsCRP, MCP-1 (leptin vs. resistin r=0.316, hsCRP r=0.266, hsCRP r=0.227; resistin vs. hsCRP r=0.227, MCP r=0.137; hsCRP vs MCP1 r=0.340; p<0.000). In FDR, BMI correlated with adiponectin, leptin and hsCRP (r=-0.209, 0.566, 0.293, p<0.001).

Conclusion: We demonstrate that FDR of RA patients exhibit a proinflammatory cytokine and adipokine profile, although the high levels of the anti-inflammatory adipokine, adiponectin, are unexplained. The levels of the proinflammatory adipokines leptin, resistin, the cytokine MCP-1, and hsCRP were all associated with high BMI in the FDR. We hypothesize that this proinflammatory phenotype predisposes these individuals not only to RA, but to a spectrum of other chronic inflammatory diseases, particularly accelerated atherosclerosis and cardiovascular disease.

4

An Evaluation of Comorbidity Indices Derived from Administrative Health Data: A Systematic Review

Marko Yurkovich (Arthritis Research Centre, University of British Columbia, Vancouver); Juan Antonio Avina-Zubieta (Arthritis Research Centre, University of British Columbia, Vancouver); Jamie Thomas (Arthritis Research Centre, Centre for Health Evaluation and Outcome Sciences, Vancouver); Diane Lacaille (Arthritis Research Centre, University of British Columbia, Vancouver)

Objective: To conduct a systematic review of studies reporting on the development or validation of comorbidity indices using administrative health data, and to compare the validity of the indices.

Methods: A comprehensive literature search of Medline and EMBASE, until June 2011, was conducted in a two-step process. We identified: (1) all comorbidity indices used in administrative data studies, and (2) all validation studies of these indices. From a title and abstract screen, relevant articles were selected for review by two independent investigators; discrepancies were resolved by consensus. Inclusion criteria included: English, full-length articles, of studies which developed, adapted, validated or compared the validity of comorbidity indices derived from administrative health data. A standardized data abstraction form was used. Predictive validity and model fit were measured by the c-statistic for dichotomous outcomes, and R² for continuous outcomes.

Results: A total of 81 articles were included in the final review. Two categories of comorbidity indices were identified: 1) those identifying comorbidities based on diagnoses, using ICD codes from hospitalization or out-patient data and 2) those based on medications, using pharmacy claims

data. Articles included 40 diagnosis-based studies, 36 related to the Charlson Comorbidity Index (CCI) and its adaptations, 2 to the Elixhauser Index (EI), and 2 to study-specific indices. An additional 14 studies investigated medication-based indices, such as the Chronic Disease Score (CDS) and the RxRisk-V. The remaining 27 articles compared predictive ability or validity across the above-mentioned indices. The predictive ability of the indices studied ranged from poor (c-stat<0.7) to excellent (c-stat>0.8) depending on the specific index, outcome measured, and study population. Diagnosis-based measures typically resulted in higher predictive ability for short- and long-term mortality outcomes, whereas medication-based indices demonstrated better performance for predicting healthcare utilization or cost. The Deyo and Romano adaptations of the CCI were the most commonly used diagnosis-based indices. In 3 studies directly comparing the Deyo and Romano adaptations, the Romano-CCI consistently demonstrated superior ability to predict mortality outcomes. A total of 11 studies demonstrated superior performance of the EI compared to CCI adaptations in predicting mortality outcomes. Of the Medication-based indices, the RxRisk-V demonstrated superior performance over the CDS.

Conclusion: A number of comorbidity indices derived from administrative data are available. Some demonstrate excellent predictive ability. Selection of an appropriate comorbidity index should consider predictive ability, as well as the type of data available and the outcome of comorbidity one wishes to capture.

5

Frequency and Characteristics of Prolonged Remission in Systemic Lupus Erythematosus (SLE)

Anjali Papneja (University of Toronto, Toronto); Amanda Steiman (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

Objective: SLE is a chronic autoimmune disorder, characterized by a relapsing/remitting course. A small subset of patients experiences prolonged clinical remission, and represents an important group that may provide further insight into SLE pathophysiology. The aim of the study was to characterize the clinical course of SLE patients who achieve prolonged remission.

Methods: Patients followed regularly in the Lupus Clinic between July 1970 and May 2011 were studied. Prolonged remission was defined as SLEDAI-2K =0 (serologically quiescent clinically quiescent (SQCQ)), or =2 or 4 on the basis of active serology only (serologically active clinically quiescent (SACQ)) for at least five consecutive years, with visits ≤ 18 months apart; patients could be taking antimalarials, but not corticosteroids or immunosuppressives. Each patient's pre-remission clinical course was classified as monophasic (single flare followed by remission), relapsing/remitting (≥2 fluctuations in SLEDAI-2K of ≥4 on the basis of clinical activity, with an intervening period of clinical remission (SLEDAI-2K clinical activity=0), or chronic active (persistent clinical activity with SLEDAI fluctuating by ≤3 at each visit). Patients were then matched 1:3 to SLE controls on the basis of sex, age, decade of entry to study, and disease duration at 1st clinic visit, and compared clinically. Descriptive statistics were used. Comparisons were made using t- and McNemar's tests.

Results: 38 of 1613 (2.4%) patients achieved prolonged remission, with one experiencing two discrete remissions. Thus, 39 periods were studied. 32 (84.2%) patients were female. Mean clinic follow up was 21.8±10.3 years, and the average time to remission from clinic entry was 9.2±8.8 years. Mean remission duration was 11.6±6.4 years. 17 remission periods were SQCQ, 11 were SACQ and 11 were mixed SQCQ/SACQ. When subdivided by type, mean remission duration was 9.8±5.7, 9.7±3.5 and 16.5±6.4 years for SQCQ, SACQ and mixed remissions, respectively. Prior to remission, 27 (71.0%) patients had relapsing/remitting disease, 11 (28.9%) had monophasic illness; none was chronically active. Remission patients differed significantly from SLE controls in terms of ethnicity, disease severity and organ manifestations prior to remission

onset and used significantly less corticosteroid and immunosuppressive drugs.

Conclusion: Prolonged remission is an infrequent outcome among SLE patients, lasts approximately a decade, and is preceded by an atypically monophasic course in a significant minority. Remission patients had milder disease and used less corticosteroid and immunosuppressive medication prior to remission compared to controls. These disease patterns may reflect unique pathophysiologic mechanisms, and warrant further investigation.

6

Homology-mediated CNVs Arising from Segmental Duplications in Autoimmune Rheumatic Diseases

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Objective: Recent studies have demonstrated that copy number variations (CNVs) are an important source of genetic variability among patients with rheumatic disease. Our objective was to elucidate the mechanism that mediates the formation of CNVs derived from segmental duplications (SDs) in rheumatoid arthritis (RA) and psoriasis/psoriatic arthritis (PsV/PsA).

Methods: A hierarchical method was employed to fragment SDs into multiple smaller SD units. Combining an end space free pairwise alignment algorithm with a 'seed and extend' approach, an exhaustive search of 409 million alignments was performed to detect complex structural rearrangements within the reference-guided assembly of the NA18507 human genome (18x coverage). We have interrogated every SD unit >100 bp to infer the complexity of duplication blocks within in human genome. Fluorescence in situ hybridization (FISH) was performed to validate the in silico predictions of genomic rearrangements with highly homologous derivatives.

Results: We have identified 1,963 rearrangement hotspots within the duplicated regions which overlap 166 genes. Among these hotspots, we have identified non-allelic homologous recombination (NAHR) regions that are associated with autoimmune/rheumatic disease. Further analysis of these regions have revealed: 1) five breakpoints within the human chemokine ligand (CCL) gene cluster; a gene which is associated with RA; 2) extreme rearrangement within SD blocks in close proximity to the VPEB1 gene; a gene which is associated with RA; 3) four SD breakpoints with complex intra- and inter-chromosomal rearrangements in the beta-defensin gene cluster; a gene which is associated with PsV/PsA. We have also demonstrated that different breakpoints within the same gene are responsible for mediating CNV formation for different autoimmune diseases.

Conclusion: Our study suggests that critical regions which are prone to rearrangement are important targets for the identification of CNVs associated with autoimmune/rheumatic disease. These CNV's likely account for a significant proportion of the missing heritability in autoimmune/rheumatic disease.

7

Is Enthesitis in Psoriasis a Predictor for the Development of Psoriatic Arthritis in Psoriasis?

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Objective: Psoriasis (PsC) is an immune mediated skin disease affecting 2-3% of the population, and Psoriatic arthritis (PsA) is an inflammatory arthritis that affects 30% of people with PsC. One of the hallmark features of PsA is enthesitis, inflammation at the sites where tendons attach to bone. It has been suggested that subclinical enthesitis, as identified by ultrasound, commonly occurs in PsC patients and may precede the devel-

opment of PsA. However, ultrasonographic enthesal abnormalities also occur in the general population, being associated with age, injuries and obesity. Our objectives in this study were twofold: 1. To assess the prevalence of ultrasonographic enthesal abnormalities in patients with PsA, PsC, and healthy controls. 2. To correlate the presence and site of ultrasonographic enthesal abnormalities with age, gender, obesity and occupation in the three groups.

Methods: In this cross-sectional study, PsA patients were studied during their visits to the Toronto PsA clinic, PsC patients were recruited from the University of Toronto Psoriasis cohort, and controls were healthy volunteers. All participants were clinically evaluated for enthesitis bilaterally at calcaneus, knee, and olecranon sites, and underwent ultrasonographic evaluation of these sites. Ultrasound recorded the presence of enthesophytes, bony erosions, tendon thickness, bursitis, calcifications, and doppler signal within the tendon. These abnormalities were then scored using two validated ultrasonographic enthesitis indices, the GUESS and MASEI. Univariate analyses included ANOVA for continuous variables and chi-squared tests for dichotomous variables. Multivariate analyses were performed using stepwise logistic regression models.

Results: We assessed 60 controls, 79 PsC, and 59 PsA patients in total. Demographically, the PsA and PsC groups were older, obese, and had more males than the control group. Univariate analyses revealed that the number of sites with ultrasonographic enthesal abnormalities, GUESS scores, and MASEI scores were significantly higher in the PsA group than the PsC group, with controls having the lowest scores ($p < 0.001$). Multivariate analyses revealed the same relationship (PsA > PsC > controls) for these three variables in study groups under age 50 ($p < 0.05$).

Conclusion: Our results show that the prevalence of ultrasonographic enthesal abnormalities and indices of ultrasonographic enthesitis burden are significantly higher in PsA patients compared to PsC patients, with both these groups being higher than controls. Furthermore, our results suggest that age may modulate the effect of disease status on enthesitis. These findings strengthen the plausibility of enthesitis being a predictor for the development of PsA in PsC, warranting future cohort studies to investigate this in depth.

8

CCN2 is Required for the Fibrosis Observed in Two Models of Systemic Sclerosis

Andrew Leask (University of Western Ontario, London); Shangxi Liu (University of Western Ontario, London)

Objective: CCN2 (CTGF) is overexpressed in scleroderma (systemic sclerosis, SSs) fibroblasts and may represent a good target for anti-fibrotic drug intervention in this disease. However, this hypothesis has yet to be thoroughly investigated. Our aim was to assess whether CCN2 was essential for fibrogenesis.

Methods: We used two models of skin fibrosis. In one, we used the bleomycin-induced model of skin scleroderma. In the other, we used the PTEN-deficient model of skin and lung scleroderma, which we recently developed. We used mice deleted specifically for CCN2 in fibroblasts to assess if loss of CCN2 resulted in resistance to fibrosis that developed in response to bleomycin or in response to loss of PTEN expression. Fibrosis was ascertained by histological measurement of skin thickness, collagen protein expression, myofibroblast formation (using an anti- α -SMA antibody), pericyte recruitment (using an anti-NG2 antibody) and proliferation (using an anti-PCNA antibody).

Results: Loss of CCN2 expression resulted in resistance to both models of fibrosis, as visualized by skin thickness, collagen production, myofibroblast and pericyte recruitment ($N=6$, $p < 0.05$). All myofibroblasts that appeared in response to the fibrotic stimulus were NG2-positive, indicating a pericyte origin ($N=6$, $p < 0.05$). However, proliferation was not affected by loss of CCN2 ($N=6$, $p < 0.05$).

Conclusion: CCN2 is required for fibrosis in two models of scleroderma, but not for cell proliferation. CCN2 may represent a good target for anti-fibrotic drug intervention in SSs.

Serum 25 OH Vitamin D Levels are Low in Early Inflammatory Arthritis but do not Correlate with Immune Responses to Pathogens nor Clinical Activity or Outcome

Carol Hitchon (University of Manitoba, Winnipeg); Neeloffer Mookerjee (University of Manitoba, Winnipeg); Marianna Newkirk (McGill University, Montreal); Christine Peschken (University of Manitoba, Winnipeg); Hani El-Gabalawy (University of Manitoba, Winnipeg)

Objective: Gene-environment interactions, (shared epitope, smoking, infection), have been implicated in Rheumatoid Arthritis pathogenesis. Vitamin D has immunoregulatory function of relevance to autoimmunity and host response to infection. Low 25 OH vitamin D (VitD) levels are associated with inflammatory arthritis and altered responses to pathogens. We determined the prevalence of VitD deficiency in a cohort of early inflammatory arthritis (EIA), its contribution to disease severity and outcome, and the association of vitamin D deficiency with altered immune responses to common pathogens and shared epitope alleles in EIA.

Methods: Early inflammatory arthritis (< 12 months symptoms, 1+ active joint) subjects were followed for one year and clinical outcomes (remission, EULAR treatment response) determined. Treatment was at the discretion of the attending rheumatologist. Shared epitope was determined by DNA sequencing. 25 OH vitamin D (VitD) levels were measured in baseline serum by ELISA and categorized as deficient (< 25 nmol/L), insufficient (25- < 75 nmol/L), optimal (75-250 nmol/L) or toxic (>250 nmol/L). Antibody titers (IgG, IgA and IgM) to *Proteus mirabilis* and *E coli* were measured by ELISA. Smoking was by self report and confirmed with serum cotinine levels. Statistical significance was considered as $p < 0.05$ using non-parametric Mann Whitney U and Chi2 tests and multivariate regression models.

Results: At baseline, 77% of EIA had insufficient (61%) or deficient (16%) levels of vitD. Baseline VitD levels were lower in North American Natives compared to Caucasian even after correcting for season of first visit (49 (32) vs 59 (30) nmol/L $p=0.008$). No associations with gender, serology (RF and/or ACPA), shared epitope, baseline disease activity (DAS28(3variable)/CRP, individual components, or ESR) or smoking status were seen. Baseline vitD levels were not associated with clinical outcomes of remission or treatment response in univariate or multivariate models. Repeated VitD levels were available at 6 months ($n=50$) and 12 months ($n=164$) on selected subjects without adjustment of vitD supplementation. At one year, the majority had vitD levels similar to their baseline vitD category, 33 (20%) improved and 28 (12%) worsened. No significant seasonal variability was seen. Change in VitD correlated with DAS28(3variable CRP) at one year ($r = -0.215$ $p=0.01$) but not with change in DAS28(3variable CRP) $p=NS$. Serum VitD correlated with cotinine levels ($p < 0.05$) but not with antibody titers to pathogens.

Conclusion: The prevalence of VitD deficiency is high in this Canadian cohort of EIA. However, serum levels do not correlate with disease activity or outcome or antibody titers to pathogens. VitD may be more important in predisposing individuals to future inflammatory arthritis.

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Rheumatoid Arthritis Patients Have Anti-Homocitrullinated Fibrinogen Antibodies

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Objective: Homocitrulline is generated by the chemical modification of lysine and is structurally similar to citrulline; the latter has been detected in the joints of RA patients using antibodies to modified citrulline (AMC). A recent study indicates that AMC cannot distinguish citrulline from homocitrulline. Antibodies to citrullinated peptides (ACPA), including citrullinated fibrinogen, are thought to be specific to RA and strongly linked to the Shared Epitope (SE), the major genetic risk factor for this disease.

However, it is unclear whether RA patients also have antibodies to homocitrullinated peptides. Our specific objective was to determine the presence of anti-homocitrullinated fibrinogen antibodies (AHFA) in the sera of patients with RA and other rheumatic conditions and whether homocitrullinated peptides of fibrinogen are predicted to bind to the SE.

Methods: A commercial preparation of human fibrinogen (CalBiochemTM) was homocitrullinated via a reaction with potassium isocyanate and confirmed by mass spectrometry. It was used in ELISA to detect AHFA and anti-citrullinated fibrinogen antibodies (ACFA) from patient serum (RA, Systemic Lupus Erythematosus (SLE) and Psoriatic Arthritis (PsA) meeting ACR criteria). The cutoff value for positive samples was determined using the average reactivity of normal patients + 2 SD ($n=27$). All RA patients were anti-CCP2 positive.

Results: 85/103 lysines showed evidence of homocitrullination present in all three chains of fibrinogen, comprising 34 peptides predicted to bind to the SE using a modified algorithm by Hammer et al. Of these 34 peptides, 5 homocitrullinated peptides were previously shown to be capable of being citrullinated. Using this in vitro homocitrullinated fibrinogen as antigen, 41/84 RA patients tested positive for AHFA and the average reactivity among these positive individuals was 18.403 RU/mL. No normal subjects tested positive for AHFA and only 1/37 psoriatic arthritis patients and 2/37 systemic lupus erythematosus patients tested positive for AHFA (mean reactivities among positive patients were 7.2 and 3.7 0.2 RU/mL, respectively); $p < 0.0001$ for RA compared to others. 53/74 RA patients were positive for anti-citrullinated fibrinogen antibodies (ACFA) and of these 35/53 were also AHFA positive. Four ACFA negative patients tested positive for AHFA.

Conclusion: Fibrinogen can be extensively homocitrullinated and citrullinated. Both citrullinated and homocitrullinated fibrinogen appear to be autoantigens specific to RA.

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Reduced Resource Use and Increased Engagement in Activities of Daily Living and Employment in Patients Attaining Remission in the First Year of Biologic Therapy

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Objective: To compare resource use, engagement in activities of daily living, and employment status by treatment response to biologic therapy in rheumatoid arthritis.

Methods: In addition to the prospective collection of clinical efficacy and safety data in an inception cohort of biologic treated patients with rheumatoid arthritis, we collect data on self-reported resource use (hospital services, community services, out-of-pocket costs), activities of daily living, and changes in employment status. We compared differences in resource use reported in the first year of treatment between patients achieving any definition of remission (2011 ACR/EULAR Boolean definition, SDAI ≤ 3.3 , CDAI ≤ 2.8 , 1981 ACR Remission Definition or DAS28 ≤ 2.6), minimal disease activity (0 tender or swollen joints and ESR < 10 mm/hr, DAS28 < 2.85, ACR core set definition, SDAI < 11 or CDAI < 10) and those not achieving remission.

Results: A total of 1,777 patients (70% female, disease duration 12 years, median DMARD exposure 3) initiated a new biologic therapy between July 2000 and March 2010. Baseline disease activity scores were: HAQ 1.15 (SD 0.76), DAS28 4.36 (SD 1.90), tender joint count 7.1 (SD 8.2), swollen joint count 4.7 (SD 5.5), patient global 4.6 (SD 2.8), and mean morning stiffness duration 70 minutes (SD 143.3). Over the first year of biologic therapy, 556 individuals met remission criteria (31.3%), and an additional 393 met minimal disease activity criteria (22.1%), with the remainder ($n=828$) remaining in moderate or high disease activity. Patients attaining remission (relative to those in moderate or high disease activity) had decreased hospitalizations (5.2% vs 7.1%, $p=0.0329$), fewer over-the-counter drug purchases for arthri-

tis symptoms (32.5% vs 40.0%, $p < 0.001$), fewer days lost due to arthritis symptoms (2.5 (SD 6.5) vs 3.1 (SD 7.1), $p = 0.007$), fewer required help from others for activities of daily living (26.8% vs 36.7%, $p < 0.001$), and fewer reduced their working hours (11.6% vs 16.6%, $p = 0.011$). Patients only achieving minimal disease activity had similar resource use, impairments in activities of daily living and employment status compared to patients in moderate or high disease activity.

Conclusion: Achieving remission, relative to minimal, moderate or high disease activity, results in significantly less resource use, increased independence to complete activities of daily living, and remain in usual work activities in the first year of biologic treatment.

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Barriers to Paediatric Rheumatology Subspecialty Care in British Columbia

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Objective: We conducted a survey of family physicians to assess perceived barriers to paediatric rheumatology subspecialty services.

Methods: We surveyed a stratified random sample of family physicians from all 5 geographic Health Regions in British Columbia. We followed Dillman's modified tailored design method using paper (mail and fax) and web-based questionnaires that included personalized letters, incentives, and reminders to maximize response rates.

Results: 428 out of 2286 eligible participants responded (19%); 31% practiced within 50 km of BC Children's Hospital where most paediatric rheumatologist services are provided, while 39% practiced ≥ 300 km from this centre. 59% of respondents had had a paediatric patient with a rheumatic disease in their practice, yet only 40% of all respondents had ever referred to a paediatric rheumatologist. Practitioners consulted instead of referring to a paediatric rheumatologist included adult rheumatology (11% of respondents), adult orthopaedic surgeon (9%), paediatric orthopaedic surgeon (7%), paediatrician (49%), other specialist (2%), chiropractor (1%), physiotherapist (5%). Approximately 60% of respondents indicated that wait time, distance, ease of transportation, and cost of travel would affect their likelihood to refer to paediatric rheumatology. The local availability of related services was also a factor; for example 38% of respondents reported that the availability of a local adult rheumatologist would affect their likelihood of referring to paediatric rheumatology. Other local resources reported to have this effect included: local paediatric orthopaedic surgeon (31% of respondents), local paediatrician (75%), local chiropractor (11%), and local physiotherapist (18%). Although 66% of respondents reported routinely performing a screening paediatric musculoskeletal exam and 74% stated they were at least somewhat comfortable doing this, 90% could not name a screening tool for this exam and only 1% identified the Paediatric Gait Arms Legs Spine (pGALS) as an appropriate tool for this purpose.

Conclusion: Despite the high percentage of respondents who have followed a paediatric patient with a rheumatic disease in their practice, less than half had ever referred to a paediatric rheumatologist in BC. While initial referral to a paediatrician may be appropriate in many cases, referral to other practitioners instead of a paediatric rheumatologist was common practice. Limited access to paediatric rheumatology services and local availability of alternative practitioners were cited as the main factors. Most respondents were unaware of the availability of simple validated paediatric screening musculoskeletal examination tools.

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Patient Reported Co-Morbidities Predict Risk of Infection in an Inception Cohort of Rheumatoid Arthritis Patients Receiving Anti-Tumor Necrosis Factor Therapy

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Objective: To evaluate the frequency of serious infections in Rheumatoid Arthritis (RA) patients treated with anti-Tumor Necrosis Factor (anti-TNF) therapy.

Methods: RA patients treated with anti-TNF therapy between January 2004 and March 2009 were followed prospectively in our biologics program to assess treatment efficacy and adverse events. Clinical and self-reported data were linked with provincial health care administrative databases. Infections were identified by using ICD 9 and 10 diagnosis codes and categorized as serious if there was an associated hospitalization. We used multivariate Cox-regression to assess independent predictors of the risk of infection.

Results: The cohort consists of 1,086 patients (70% female, mean age of 54 years) with a mean follow-up time of 2.3 years. Seventy percent of patients ($n = 764$) reported an infection during follow-up, while 4% ($n = 42$) suffered a serious infection, for an incidence density rate of 1.67 per 100 patient years of follow up. The most common infections were bronchitis, cellulitis, sinusitis, cystitis and upper respiratory infections. Compared to patients who remained on their first anti-TNF agent ($n = 731$), patients who switched to another anti-TNF ($n = 212$), patients on DMARD alone ($n = 75$), and patients switched from DMARD to anti-TNF therapy ($n = 68$) had similar Hazard Ratios (HR) ($p > 0.05$) for both any and serious infections. In the cohort of patients on their first anti-TNF agent, the specific drug did not predict risk of infection. Pre-existing lung disease ($HR = 1.99$, $p = 0.001$), underlying anemia ($HR = 3.31$, $p = 0.030$) and diabetes ($HR = 1.57$, $p = 0.034$) were associated with increased infection risk, while male sex was protective ($HR 0.81$, $p = 0.039$). There was a trend for greater risk of infection in those patients with a higher baseline DAS score ($HR = 3.89$, $p = 0.072$).

Conclusion: Certain self reported co-morbidities, such as lung disease, diabetes, and underlying anemia significantly increased the risk of infection. The incidence density rate of serious infections was low (1.67 serious infections per 100 patient years), especially in patients who remained on their first anti-TNF agent (1.35 per 100 patient years) and is lower than reported in other cohorts. The risk of any or serious infection did not differ significantly between specific anti-TNF agents.

Posters

1

Development of a Factor VIII Inhibitor in Association with Giant Cell Arteritis: A Case Report

Thirza Carpenter (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

Objective: We describe the case of an unusual presentation of acquired hemophilia, an uncommon autoimmune disorder caused by the production of autoantibodies against coagulation factor VIII. While most often idiopathic, it may present as part of an underlying systemic disorder, including many rheumatologic disorders, rarely giant cell arteritis (GCA).

Methods: Case: A 56 year old woman initially presented with recurrent headaches, jaw claudication and tender, palpable temporal arteries.

Results: Inflammatory markers were elevated (ESR 89, CRP 137.9); GCA was confirmed on temporal artery biopsy. She was started on high-dose prednisone with resolution of her symptoms. However, 6 months into her prednisone taper, while on a dose of 9-mg daily, she re-presented with widespread, spontaneous bruising. On further evaluation, she was found to have extensive ecchymosis on her extremities; diagnostic imaging revealed a rectus sheath hematoma. Investigations revealed a normal platelet count and INR with an elevated PTT of 84. A mixing study was performed which showed failure of the PTT to correct, suggesting the presence of a factor inhibitor. Acquired hemophilia was confirmed with a low Factor VIII level of 0.08 and an elevated FVIII inhibitor level of 20.6. Immune suppressive therapy was initiated with high dose prednisone, oral cyclophosphamide and IVIG. No bleeding episodes requiring the use of recombinant factor

VIII or anti-inhibitor coagulant complex occurred. Prior to her presentation and throughout the course of her illness, her GCA remained asymptomatic; she did not have recurrence of her headache or visual symptoms. Repeat inflammatory markers (ESR 36, CRP 11.4) were minimally elevated at the time of her presentation.

Conclusion: This case is an extremely unusual presentation of an extremely rare disease. It may be idiopathic, approximately 50%, or present as part of an underlying systemic disorder, including many rheumatologic disorders or malignancy. This is the first reported case of an association between an apparently well-controlled underlying vasculitis and acquired hemophilia. When associated with rheumatologic disorders, previous reports have only documented active or undiagnosed conditions. Conclusion: Acquired hemophilia has a known association with undiagnosed systemic diseases and malignancies. We demonstrate that rheumatic diseases, such as giant cell arteritis, can now be shown to cause production of anti-factor VIII antibodies, even when appropriately treated and seemingly quiescent. Acquired hemophilia should therefore remain on the differential diagnosis of patients with well-controlled rheumatologic disorders who present with spontaneous bruising or bleeding.

2

Edmonton Rheumatology Triage System: Etiological Review of Inaccurate Triage for Inflammatory Arthritis Patients

Thirza Carpenter (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

Objective: To review the accuracy of the rheumatology triage system at the University of Alberta for correctly identifying inflammatory arthritis patients within the triage process and to search for factors that may improve the system accuracy.

Methods: The triage rheumatologist, typically using only the information provided in the referring letter and any included investigations, screens all incoming referral letters to identify possible diagnoses and urgency of assessment. After the initial patient visit, the consulting rheumatologist records a post-visit diagnosis and if they agree with the assigned urgency status. The system was devised so patients triaged as “soon”, such as those with possible inflammatory arthritis, could be seen within 6 weeks. We reviewed a 20-month database to identify all newly referred inflammatory arthritis patients who were incorrectly screened at the time of triage as a non-inflammatory process. We reviewed these charts to identify patient characteristics that may have negatively influenced appropriate triage, including ESR, CRP, RF, anti-CCP and imaging studies, as well as presence of morning stiffness, joint swelling and location of joint involvement included in the referral letter.

Results: Since implementation of the triage system, 343 newly referred patients were diagnosed with inflammatory arthritis. 31 patients (9.0%) were incorrectly screened as a non-inflammatory process. The average age was 51.2 years and 23 patients were female (71.9%). 24 patients (75.0%) had one or more inflammatory markers available, with only 3 patients (9.4%) having an abnormally elevated value. 2 patients (6.3%) were RF positive, and 1 was anti-CCP-antibody positive from testing performed post-initial visit. Imaging changes consistent with an inflammatory arthritis were seen in 4 patients (12.5%). 4 patients' referral letters specifically included ‘morning stiffness’ or ‘swollen joints’ in a typical inflammatory distribution, while the remaining referrals (84.4%) did not comment on joint stiffness or swelling, specify the swelling distribution, or described an atypical distribution for synovitis. In total, these findings represent 10 patients.

Conclusion: The triage system correctly identified patients with inflammatory arthritis with an accuracy of 91.0%. This system appears cost-effective because it does not require any specific screening investigations to be performed or reviewed prior to assessment. In fact, it remains unclear if investigations would improve the system accuracy.

3

The Risk of Developing Cardiovascular Diseases among Osteoarthritis Patients: A Prospective Study

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Objective: To determine the risk of developing cardiovascular diseases (CVD) among osteoarthritis (OA) patients using population-based administrative data.

Methods: A random sample from Population Data British Columbia from years 1991 to 2004 was analyzed. OA patients were identified using the case definition of at least two visits to a health professional in two years or at least one discharge from the hospital with an ICD-9 code of 715, and similarly, CVD cases were identified from the hospital admission records using the ICD-9 code for ischemic heart disease, congestive heart failure and stroke. All incident and prevalent OA cases in the random sample from 1991 to 1996 were identified after deleting prevalent CVD cases. This gave between 1 to 3 matched by age, sex, and baseline year, a sample of 13,406 OA patients and 38,901 non-OA individuals. Cox proportional hazards regression model was used to estimate the relative risks after adjusting for patients' administrative history of hypertension, hyperlipidemia, diabetes, obesity, chronic obstructive pulmonary disease, Charlson comorbidity, and socio-economic status (SES).

Results: With mean follow up of 6.8 years, we documented 7,988 new CVD cases with an incidence rate of 2.2 per 100 person years. At baseline, the mean age of OA patients was 62 years and 60% were women. A statistically significant increased risk of developing CVD was observed among OA compared with non-OA individuals. The adjusted relative risk (RR) for CVD was 1.15 (95% CI 1.10-1.21). A statistically significant interaction was observed between age and gender. Among men aged 20-64 years, the RR for CVD was 1.20 (95% CI 1.05-1.37) and among men aged ≥ 65 years, the RR for CVD was 1.11 (95% CI 1.01-1.21). Among women aged 20-64 years, the RR was 1.31 (95% CI 1.13-1.52) and among women aged ≥ 65 years, the RR was 1.12 (95% CI 1.04-1.20). Patients' obesity, hypertension, diabetes, a high comorbidity score, and low SES also showed a significantly higher RR of developing CVD among men and women.

Conclusion: Younger men with osteoarthritis had a 20% increased risk of developing CVD and younger women with osteoarthritis had a 31% increased risk of developing CVD relative to non-OA individuals. Older male and female osteoarthritis patients had similar increased risk of developing CVD. Patients with obesity, diabetes, other conditions, and patients with a low SES had an increased risk of developing CVD among both men and women.

4

Rapid Reductions in Fatigue and Sleep Problems and Correlation with Improvements in Patient-Reported Outcomes in Patients with Active RA Treated with Certolizumab Pegol in the REALISTIC 12 Week Phase IIIB Randomized Controlled Study

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Objective: To determine the impact of certolizumab pegol (CZP) on fatigue, sleep problems and other PROs in the REALISTIC (RA Evaluation In Subjects receiving TNF Inhibitor Certolizumab pegol) 12-wk, Phase IIIB study evaluating CZP in a broad population of patients (pts) with active RA.

Methods: 1,063 pts with active RA and an inadequate response to ≥ 1 DMARD were randomised 4:1 to CZP 400mg (n=851) at Wks 0, 2 and 4 followed by 200mg every 2 wks or placebo injection (control, n=212) every 2 wks added to current therapy. PROs included fatigue (Fatigue Assessment Scale [FAS; 0-10 numeric rating scale]), sleep quantity and quality (Sleep

Problem Index II domain of the Medical Outcomes Study sleep scale [MOS-SPI]), pain (0-100mm visual analogue scale [VAS]), and patient's global assessment of disease activity (PtGA, 0-100mm VAS). The minimal clinically important difference (MCID) is a clinically relevant change in a patient's status. The % of patients reporting MCIDs were determined: ≥ 1 for FAS, ≥ 6 for MOS-SPI, and ≥ 10 mm for pain-VAS and PtGA. Correlations between PRO and DAS28 were also assessed (Pearson correlations ρ , CZP group only).

Results: Baseline characteristics were similar for CZP pts vs controls (FAS: 6.2 vs 6.4, MOS-SPI: 47.6 vs 48.1, pain VAS: 58.8 vs 62.3; PtGA: 59.2 vs 61.6). Statistically significant, meaningful improvements in fatigue were reported with CZP vs control from the first time point at Wk 2 to Wk 12. Sleep problems were significantly reduced in the CZP group vs controls from the first assessment at Wk 6 to Wk 12. CZP was associated with significant reductions in pain and PtGA from Wk 2. At Wk 12, more CZP pts had improvements $\geq$ MCID in FAS (56.4% vs 46.2%, $p < 0.01$), MOS-SPI (49.7% vs 42.5%, $p = 0.058$), pain VAS (59.0% vs 42.0%, $p < 0.001$) and PtGA (59.5% vs 42.5%, $p < 0.001$). Correlations between PROs and DAS28 were moderate (0.3).

Conclusion: CZP treatment was associated with clinically meaningful reductions in fatigue and sleep problems, as well as improvements in pain and PtGA, in a diverse group of RA pts reflecting those seen in daily clinical practice. The % of patients reporting MCIDs in PROs can easily differentiate CZP vs standard treatment even in a short-term trial. Correlation analyses showed that measurement of different PROs consistently demonstrate the benefit of CZP in this patient population.

5 Association of Gastroesophageal Factors and Progression of Interstitial Lung Disease in the Canadian Scleroderma Research Group (CSRG), a Large, Multi-Center Database

Xuli Zhang (University of Western Ontario, London); Ashley Bonner (McMaster University, Hamilton); Marie Hudson (McGill University and Jewish General Hospital, Montreal); Murray Baron (McGill University and Jewish General Hospital, Montreal); Janet Pope (University of Western Ontario, London)

Objective: Restrictive interstitial lung disease (ILD) is a common complication of systemic sclerosis (SSc) and is a leading contributor to mortality in SSc patients. Once lung fibrosis occurs, lung function disease course may become stable or progressively decline. While some demographic and SSc-related factors have been associated with development of ILD, little is known about what contributes to progression. We studied the clinical manifestations of SSc-gastroesophageal (GE) involvement in relation to ILD status to determine associations between GE involvement and ILD progression in SSc.

Methods: The Canadian Scleroderma Research Group (CSRG), a multi-center database of adult SSc patients, annually evaluates and collects patient information including demographics, skin manifestations, internal organ involvement and function assessment data. Using indicators of GE involvement and annual pulmonary function test results from the CSRG database, comparisons were made between no ILD, stable ILD and progressive ILD groups based on FVC% predicted. Univariate and multivariate analyses were used to determine associations between GE factors and ILD development and progression.

Results: The study included data from 1043 SSc patients with a mean age of 55.7 years and mean disease duration of 10.8 years. Among the variables of interest, physician indicators such as esophageal dysmotility ($P = 0.009$) and post-esophageal dilatation ($P = 0.041$), along with patient indicators such as difficulty swallowing ($P = 0.016$) and waking up choking ($P = 0.026$) appeared to significantly increase risk of developing ILD. In comparing progressive vs. stable ILD patients, early satiety ($p = 0.018$) and a combination of post-dilatation and choking ($p = 0.042$) increased risk of ILD progression.

Conclusion: Esophageal dysmotility and GERD appear to be associated with ILD in SSc, with some factors specifically related to progressive ILD.

The presence of both dysmotility and GERD had a far higher risk of progressive ILD which illustrates a potential dose-response phenomenon. These results hold important implications for management of ILD in SSc, where aspiration risk should be minimized via treatment of GERD and dysphagia.

6 Factors Predicting Increasing Treatment in Early Rheumatoid Arthritis (ERA): Results from the CATCH Study. It is not the DAS but the Physician Global Assessment and the Swollen Joint Count that are Strongly Associated with Increasing Treatment

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Objective: The disease activity score (DAS) was developed in rheumatoid arthritis (RA) to guide therapeutic decisions. The aim of this study was to determine factors most strongly associated with an increase in therapy in early rheumatoid arthritis (ERA) including DAS and non-DAS parameters. **Methods:** Data were collected from the Canadian Early Arthritis Cohort (CATCH); patients were included if they had > 2 visits, and baseline and 6 months data. A regression analysis was done to determine factors associated with treatment intensification.

Results: Of the 1,145 ERA patients, 790 met inclusion criteria. Mean age was 53.4 (SD 14.7), disease duration was 6.1 months (SD 2.8), 75% were female, and DAS28 at baseline and 6 months was 4.7 (SD 1.8) and 2.9 (SD 1.8), respectively. The factors most strongly associated with intensifying treatment in univariate analyses were physician global assessment (OR = 7.8 at 3 months and OR = 7.4 at 6 months, respectively, $P < 0.0005$) and SJC (OR = 4.7 and OR = 7.3 at 3 and 6 months, respectively, $P < 0.0005$). DAS did not affect treatment intensification as strongly in univariate analyses (OR = 3.0 at 3 months and OR = 4.6 at 6 months, $P < 0.0005$). In the logistic regression model only physician global assessment was strongly and consistently associated with treatment intensification (OR = 1.5 and OR = 1.2 at 3 and 6 months, respectively, $P < 0.0005$). DAS28 was not a consistent predictor of treatment intensification (OR = 1.0, $P = 0.987$ at 3 months and OR = 1.2, $P = 0.023$ at 6 months). When treatment was intensified, only 2.3% of physicians listed DAS28 as a reason for the treatment change compared to 51.7%, 49.9% and 23.8% for SJC, TJC and global assessment, respectively. For the same SJC, larger joint involvement was more likely to influence treatment than small joint involvement at 3 months (OR = 1.4, $P = 0.027$).

Conclusion: Physician global assessment was independently associated with an increase in treatment at 3 and 6 months in ERA, whereas DAS28 was not. Physicians rarely stated that DAS28 was the reason for increasing treatment. At 3 months at the same joint count, involvement of larger joints was more associated with increasing therapy.

7 Patient Reported Disease Activity including Joint Assessment: A Comparison of RADAI (Rheumatoid Arthritis Disease Activity Index) and RAPID3 (Routine Assessment of Patient Index Data 3) in Patients Treated with Certolizumab Pegol Over 12 Weeks

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Objective: Self-reported disease activity (DA) indices such as RAPID3 and RADAI offer a patient focused approach to clinical management. RAPID3 is an index without joint counts, whereas RADAI includes a

self-assessment of tenderness in 16 joint areas. This post hoc analysis of the REALISTIC study assessed the performance of RAPID3 and RADAI to measure impact of treatment with certolizumab pegol (CZP) in a broad population of RA pts closely resembling routine clinical practice.

Methods: During the 12-week (wk), double-blind phase of the REALISTIC study 1063 pts with inadequate response to ≥ 1 DMARD were randomized 4:1 to CZP 400 mg at Wks 0, 2, and 4, followed by 200 mg at Wks 6, 8, and 10, or placebo (PBO), added to their current treatment. The RADAI (summarized as a joint tenderness score [JS] or the total score [TS], both ranging 0 to 10, with 10 indicating highest DA) was administered at 0, 2, 6, and 12 wks. Mean change from baseline in RADAI-TS was assessed using ANCOVA applying LOCF (CZP vs PBO). The percentage of patients achieving a minimum clinically important difference (MCID) for the RADAI-TS was evaluated (defined as a 1-point decrease). Correlations between RADAI-TS, RADAI-JS, RAPID3, and clinical DA measures (including DAS28[ESR] and total and swollen joint counts [TJC, SJC]) were examined using Pearson coefficients.

Results: Mean baseline RAPID3 and RADAI-TS were similar between groups (CZP vs PBO: RAPID3 14.75 vs 15.50, RADAI-TS 5.56 vs 5.68). Statistically significant improvements in RAPID3 and RADAI-TS were reported with CZP vs PBO from as early as Wk 2 up to Wk 12. Significantly more CZP pts had improvements $\geq$ MCID in RADAI and achieved RAPID3 low DA or remission from Wk 2 onward. Correlations between RADAI (TS and JS) or RAPID3 and DAS28(ESR) were high, while correlations between RADAI-TS and RAPID3 were very high. Patient reported scoring of the joint for tenderness in the RADAI highly correlated with physician-reported TJC and moderately with SJC. Responsiveness of RADAI and RAPID3 was good, especially in patients with moderate or high number of affected joints at baseline.

Conclusion: Rapid and significant improvements in RAPID3 and RADAI were observed within the first 3 months of CZP treatment in a broad population of RA patients. RADAI and RAPID3 may represent reliable patient reported measures of disease activity in RA patients

8

Differences in Autoantibodies, Activity (SLEDAI) and Damage (SDI) Scores between Childhood-Onset and Adult-Onset Lupus: A Meta-Analysis

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Objective: In systemic lupus erythematosus (SLE), autoantibodies and other laboratory tests are used for diagnosis, correlate with clinical manifestations, and provide prognostic information. Age at SLE onset may impact autoantibodies, and disease activity and damage, as measured by SLEDAI and SDI, respectively. We previously described American College of Rheumatology (ACR) criteria differences between childhood-onset lupus (cSLE) and adult-onset lupus (aSLE). A meta-analysis of all studies that directly compared cSLE to aSLE was performed to determine: (1) which autoantibodies, and (2) whether activity and damage scores, vary with age at disease onset.

Methods: A literature search of the MEDLINE/PubMed, EMBASE, CINAHL, and SCOPUS databases (until January 2011) was conducted to identify relevant articles. Study quality was assessed using the STROBE checklist. Two independent reviewers determined eligibility criteria. Pooled odds ratios and mean differences were calculated assuming random effects, and heterogeneity was estimated and presented as OR; 95%CI.

Results: Of the 484 studies identified, 19 were eligible. The total number of patients was 7519. Mean trial quality was 18/32, ranging from 8 to 29. Several statistically significant differences were found: anti-dsDNA antibody (1.97; 1.31-2.96) and IgG/IgM anticardiolipin antibody (1.66; 1.20-2.28) levels, and mean disease activity scores (SLEDAI) (4.73; 2.13-7.32), were higher in cSLE. Disease damage (SDI) was lower in cSLE, but not significantly (0.50; -0.13-1.14). Rheumatoid factor (RF) was increased in

adults (.53; 0.32-0.87). Other autoantibodies and labs were not different between the groups (ANA, anti-Smith, anti-RNP, anti-U1RNP, anti-Ro and anti-La, antiphospholipid, lupus anticoagulant, complements, ssDNA and Coomb's test).

Conclusion: The results of this meta-analysis suggest that cSLE may have different autoantibody profiles (increased anti-dsDNA and anticardiolipin antibody, less RF), and more disease activity than aSLE. Damage may be less in children, but larger studies are needed.

9

Rates and Causes of Hospitalizations in Systemic Lupus Erythematosus in London, Ontario over 3.5 Years

June Lee (University of Western Ontario, London); Janet Pope (University of Western Ontario, London)

Objective: We wanted to determine the rate and reasons for hospitalizations in patients with SLE (systemic lupus erythematosus) in a regional center.

Methods: A chart review was performed for all patients admitted to the three hospitals in one teaching centre (London, Ontario), which services approximately 1 million people. All patients with SLE admitted to any London hospital between January 2006 and June 2009 had full chart audits. Patients were excluded if a diagnosis of SLE could not be confirmed.

Results: Of 147 patients hospitalized, 102 patients met the inclusion criteria with a combined total of 160 hospitalizations; 5 were newly diagnosed with SLE during hospitalization. Of those with established SLE, the average age at diagnosis was 33 years and 66 of 93 (71%) had a rheumatologist. The most common reason for admission was disease flare (21%), followed by infection (15%), adverse drug reactions (9%), acute coronary syndrome (2.5%) and venous thromboembolic event (1.9%). Combining disease flares and SLE complications, 71 (44%) hospitalizations were due to SLE; 14% were ICU admissions. Of the remaining admissions not primarily attributed to SLE, 5 were complicated by SLE during hospitalization. Patients hospitalized for SLE disease flare had a shorter disease duration ($p=0.001$), had seen their rheumatologist more recently ($p=0.016$) and were on a higher dose of prednisone on admission ($p=0.003$) compared to those hospitalized for other reasons. There was no significant difference in age, length of hospital stay, ICU requirement, or rate of death between these two groups. The average length of hospitalization was 8.5 (± 11.0) days. The average number of hospitalizations for each patient was 1.6 (± 1.1). Patients who were subsequently hospitalized more than once had a significantly higher Charlson co-morbidity score ($p=0.004$), and were more likely to have a history of SLE cerebritis ($p=0.031$) and higher admission dose of prednisone ($p=0.009$) at their first admission. There was no relationship between multiple hospital admissions and age, disease duration, having a GP or rheumatologist, or any SLE medications.

Conclusion: There was an average of 46 hospitalizations for SLE per year in London, ON. If SLE is 0.1% of the population and the referral population is from 400,000 to 1 million, the SLE hospitalization rate would be from 11.5% to as low as 4.6% per year and vascular events were rare (but some may not have been hospitalized) and infections still accounted for 15% of hospitalizations. Disease flares were the most common cause of hospitalization.

10

Interleukin-6 (IL-6) as an Important Mediator in Systemic Sclerosis (SSc): A Cumulative Analysis and Conceptual Model

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Objective: To critically analyze published literature on the potential importance of IL-6 in systemic sclerosis (SSc), as it has been postulated that IL-6 may be a target for SSc treatment.

Methods: PubMed and Scopus databases, ACR abstracts (from 2009-10) and EULAR abstracts (from 2009-2011) were searched by 2 reviewers until May 30, 2011 for English language original articles and abstracts studying

IL-6 in SSc, using keywords “scleroderma; SSc; adult; cytokines; interleukins and interleukin-6”. Data were extracted from selected articles to construct a cell interaction model of IL-6 effects in SSc where each interaction was from a publication. Negative articles were also included. Data were excluded if they were irrelevant to IL-6 in SSc mechanisms.

Results: 412 reports were found (PubMed N=80; Scopus N=329; 3 abstracts), and 370 were excluded (irrelevant), leaving 39 publications and 3 abstracts (37 from PubMed, 16 from Scopus but 14 were repeated from PubMed search), where 38 suggested IL-6 was important in SSc and 4 did not. A model of feedback from IL-6 between cells in SSc was constructed.

Conclusion: Of the 42 publications, 38 suggested that IL-6 may be important in SSc allowing for a conceptual framework within SSc including effects on macrophages, fibroblasts, plasma cells, monocytes and extracellular matrix.

11

C-Reactive Protein (CRP) is Associated with High Disease Activity in SSc. Results from the Canadian Scleroderma Research Group (CSRG)

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Objective: Elevated ESR in SSc is associated with morbidity yet little is known about the predictive value of C-reactive protein (CRP) in SSc. This study was done to determine the associations of CRP in SSc subsets.

Methods: The CSRG is a large multi-site dataset comprised of patients with SSc, where patient and physician reported measures and lab tests are performed annually. The frequency of elevated CRP and ESR and their relationships to clinical parameters, scleroderma disease activity score (SDAS), scleroderma disease severity score (SDSS), health assessment and changes between annual follow up were studied. Statistical comparisons were made for CRP in early (< 3 years from 1st non-RP symptom) vs. late SSc, and diffuse cutaneous SSc (dcSSc) vs. limited cutaneous (lcSSc).

Results: 1,043 patients with a mean $\pm$ SD age of 55.4 ± 12.1 years, predominantly female (86.1%), and having a mean disease duration of 11.0 ± 9.5 years were analyzed, of whom 38% had dcSSc, 62% had lcSSc and 10.6% had early dcSSc. Elevation of CRP and ESR occurred in 25.7% and 38.2%, respectively. Baseline CRP in dcSSc (11.98 ± 25.41 mg/L) was higher than in lcSSc (8.15 ± 16.09 mg/L); $p = 0.016$. SSc patients with disease duration ≤ 3 years had higher CRP (12.89 ± 28.13 mg/L) than those with disease duration > 3 years (8.60 ± 17.06 mg/L); $p = 0.041$. Though not consistent in all subsets, CRP was significantly associated ($p < 0.01$) in the overall group with: ESR, mRSS, worse TLC $< 80\%$, FVC $< 80\%$, DLCO $< 75\%$, disease activity (SDAS), damage (SDSS), and HAQ. In early dcSSc, the frequency of elevated CRP and ESR was 41.5% and 44.2%, respectively. CRP seemed to normalize in many SSc patients over time. Adding or withdrawing prednisone did not significantly change CRP.

Conclusion: CRP is elevated in approximately one quarter of SSc patients, especially in early disease. It is correlated with disease activity, severity and poor pulmonary function.

12

Clinical and Polysomnographic Characteristics Associated with Excess Sleepiness in Rheumatoid Arthritis Patients

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Objective: Subjective reports of sleep dysfunction are common in rheumatoid arthritis (RA) patients. Our objective was to determine whether excess sleepiness in RA is associated with objective polysomnographic (PSG) abnormalities.

Methods: RA patients with abnormal sleep scores were identified in clin-

ic and age/gender matched to RA patients with normal Epworth Sleepiness Scale (ESS) scores. All patients underwent overnight PSG studies. Questionnaire instruments including several sleep and RA assessments were re-applied on the PSG study night.

Results: Seven men and 18 women participated. Ten patients had abnormal and fifteen normal ESS scores on the PSG night. PSG data revealed 68% of patients had abnormal apnea hypopnea index (AHI ≥ 5). Abnormal ESS (> 10) had 80% positive predictive value (PPV) for abnormal AHI; negative predictive value (NPV) of normal ESS was 40%. In contrast, high risk categorization for obstructive sleep apnea (OSA) by Berlin questionnaire had PPV of 77.8%, and for low risk status, NPV of 37.5%. Examining genders separately, an abnormal ESS was associated with significantly higher AHI in men ($p = 0.030$). Conversely, in women, an abnormal ESS was associated with higher fatigue ($p = 0.031$), modified Health Assessment Questionnaire (mHAQ) ($p = 0.002$), and depression ($p = 0.010$) scores.

Conclusion: In this population there was a high prevalence of abnormal AHI consistent with OSA. An abnormal ESS had high PPV for abnormal AHI. Our findings suggest the ESS may be more closely associated with PSG characteristics in men. Careful evaluation for gender equivalency of sleep disorder screening tools would be relevant in the female predominant RA population.

13

Oral Apremilast is Effective in the Treatment of Subjects with Active Psoriatic Arthritis with and without Concomitant Methotrexate Therapy

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Objective: Evaluate the efficacy and safety of apremilast (APR), a novel, orally available small molecule that specifically targets phosphodiesterase-4, for the treatment of active psoriatic arthritis (PsA) with and without concomitant methotrexate (MTX).

Methods: In a phase 2 randomized, double-blind, placebo-controlled, multicenter study, subjects with active PsA (joint involvement ≥ 6 months; ≥ 3 tender joints; ≥ 3 swollen joints) were randomized to placebo ($n = 68$), APR 20 mg BID (APR20; $n = 69$), or APR 40 mg QD (APR40; $n = 67$) and treated for 12 weeks. At week 12, placebo subjects were re-randomized to APR20 (P/APR20; $n = 20$) or APR40 (P/APR40; $n = 20$) until week 24. Stable doses of NSAIDs, corticosteroids, and MTX (≥ 56 days before screening; dose range 1.5-30 mg/week) were allowed; randomization was stratified by baseline MTX use (MTX, $n = 115$; no MTX, $n = 89$). Last observation carried forward was used for missing data. The Breslow-Day statistic was used to test the null hypothesis of homogenous odds ratio (APR versus placebo) among subjects treated and not treated with MTX.

Results: At week 12, 43.5% (30/69) of subjects receiving APR20 ($P < 0.001$) and 35.8% (24/67) receiving APR40 ($P = 0.002$) achieved an ACR20 versus 11.8% (8/68) receiving placebo. No differences were noted in ACR20 in subjects taking MTX versus not taking MTX: placebo, 10.3% versus 12.8%; APR20, 46.7% versus 41.0%; and APR40, 36.7% versus 35.1%. There was no evidence that APR treatment response (APR versus placebo) differed among subjects treated and not treated with MTX. At the end of the treatment-extension phase, $> 40\%$ of subjects in each group achieved an ACR20 (APR20, 42.5%; APR40, 43.5%; P/APR20, 40.0%; P/APR40, 45.0%). The most frequently reported adverse events (AEs) during double-blind treatment were diarrhea (8.8-26.9%), headache (16.2-22.4%), nausea (17.4-22.4%), fatigue (7.2-16.4%), and nasopharyngitis (11.6-17.6%); most AEs were mild or moderate ($> 90\%$). Fourteen subjects experienced ≥ 1 serious AE; 2 were suspected to be treatment-related. No opportunistic infections were reported, and no deaths occurred. Gastrointestinal AEs, particularly diarrhea and vomiting, tended to occur in more subjects treated with MTX versus without MTX regardless of randomization assignment. Overall, there was no strong evidence for increasing AEs with concomitant APR/MTX versus APR monotherapy.

Conclusion: APR20 and APR40 demonstrated efficacy versus placebo in

active PsA with an acceptable tolerability profile. APR worked effectively with and without concomitant MTX therapy. Further studies are ongoing to explore APR efficacy for the treatment of PsA, psoriasis, ankylosing spondylitis, and rheumatoid arthritis.

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Occupational Risk and Osteoarthritis Disease: A Population-Based Study in the United States Adult Population

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Objective: Previous studies on occupational risk for osteoarthritis have been limited in the range of occupations. There has not been a population-based study on a nationally representative sample that investigates the association between a comprehensive list of occupations and risk of osteoarthritis in the United States. This study is to examine the relative risk for the occurrence of osteoarthritis between different occupations in the U.S. adult population. Design: Population-based complex survey study.

Methods: This is a population-based complex survey study in the setting of National Health Interview Survey between 2005 through 2009. The participants were Randomly sampled non-institutionalized adults of the United States. The main outcome measures was Self-reported osteoarthritis defined as 'Ever been told you had arthritis' by a physician; occupation categories were based on US census bureau coding of Standard Occupation Classification.

Results: A total of 88,202 participants were interviewed during this five year period. Osteoarthritis was reported in 17,237 (19.5%) participants. After applying appropriate weights, controlling for age, sex, ethnicity, obesity, and using Computer and Mathematical Occupations as a reference group, the likelihood of developing osteoarthritis was 2.04 times higher in respondents working in Military Specific Occupations (95% CI: 1.36, 3.05), 1.54 times higher in Installation, Maintenance, and Repair Occupations (95%CI: 1.25,1.89), 1.54 times higher in Healthcare Support Occupations (95%CI: 1.23,1.94), 1.51 times higher Construction and Extraction Occupations (95%CI: 1.22,1.87), 1.51 times higher in Protective Service Occupations (95%CI: 1.2,1.9), 1.47 times higher in Production Occupations (95%CI: 1.21,1.79), 1.41 times higher in Food Preparation and Serving Related Occupations (95%CI: 1.14,1.74), 1.38 times higher in Transportation and Material Moving Occupations (95%CI: 1.13,1.69), 1.37 times higher in Building and Grounds Cleaning and Maintenance Occupations (95%CI: 1.11,1.7), 1.28 times higher in Sales and Related Occupations (95%CI: 1.06,1.56), 1.24 times higher in Office and Administrative Support Occupations (95%CI: 1.03,1.5).

Conclusion: This study identifies occupation groups in US adult population with high risk for osteoarthritis. Additional research on characteristics of the high risk occupations is needed for guiding prevention in US adult job settings.

15

Comparison of Work Disability in Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis Patients from a Single Centre

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Objective: Few studies directly compare work disability (WD) and the loss of work productivity in patients with different forms of inflammatory arthritis (IA). We measured the prevalence of WD and work productivity loss in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) at a single centre. We also examined the relationship between WD and patient-reported measures of disease activity.

Methods: Ethics approval was obtained. Data were collected from 1303 patients visiting the Rheumatology Clinic at St. Joseph Health Centre in London, Ontario, Canada. Each patient was given a questionnaire package asking about work status. WD was defined as the inability to work or early

retirement due to arthritis. The package included the Work Limitations Questionnaire (WLQ) which measures the degree of loss in work productivity caused by health problems. In addition, the Health Assessment Questionnaire (HAQ), Patient Global Assessment of disease activity (PGA) and Functional Comorbidity Index (FCI) were collected. These data were cross-referenced with doctors' charts to ensure accuracy. Non-responders were compared with responders through chart review. Relationships between the WLQ scores, demographic information, and the results of the HAQ, PGA and FCI were analyzed.

Results: Out of 1303 patients, 846 (332 RA, 88 PsA, 58 AS; 65% response rate) completed the questionnaires, of whom 289 completed the WLQ (139 RA, 51 PsA, 35 AS). The mean age was 51.7 (SD 14.5), 74.3% female and 11.3 years of disease duration, and this was similar except for AS where there were more men and younger patients. The non-responders tended to be male and older (by 3.1 years), but did not significantly differ in other demographic characteristics. The proportion of patients with WD due to arthritis was 22.8% (RA), 29.9% (PsA), and 27.6% (AS). The average loss of the productivity, as measured with WLQ, was 4.45%, 4.71% and 5.63% for RA, PsA and AS, respectively. The WLQ score was significantly correlated with HAQ score, PGA fatigue score, PGA pain score, PGA sleep score, PGA general health score, and with increasing number of comorbid conditions for all three IA conditions.

Conclusion: WD and productivity loss were apparent in all three IA conditions. WLQ scores showed close associations with HAQ and PGA scores. Work limitations were presumably high even in early disease as the disease duration was not correlated with WLQ scores or absence from work. This suggests that early intensive interventions may be appropriate to reduce productivity loss.

16

Smoking and Ankylosing Spondylitis: A Systematic Review

Alison Kydd (University of British Columbia, Roberts Creek); Lyn March (University of Sydney, Sydney)

Objective: Smoking is known to influence a number of autoimmune conditions such as Rheumatoid Arthritis, Psoriasis, and Crohn's disease. This systematic literature review is designed to examine the influence of smoking on Ankylosing Spondylitis (AS) with three primary objectives: 1. Is smoking a risk factor for the development of AS? 2. Is smoking associated with poorer function in AS patients? 3. Is smoking associated with a reduced response to biologic therapy in AS?

Methods: An article search was conducted in Medline, EMBASE and the Cochrane Library utilizing a detailed search strategy for AS and smoking. The search resulted in 283 articles which were reviewed by the two authors for exclusion and inclusion based on pre-specified criteria. A hand search of article reference lists, as well as a search of the abstract databases from last two ACR (2009,2010) and EULAR (2010, 2011) meetings were also conducted.

Results: Fifteen studies were included in the analysis. Five studies were cohort studies, two were case-control studies and an additional eight studies were cross-sectional in nature. Two cross-sectional studies addressed AS disease onset with respect to smoking status. An early spondyloarthritis cohort of 654 patients found that smoking was associated with earlier onset of inflammatory back pain symptoms while a smaller study of established AS patients failed to find a similar association. There were eleven papers addressing function in AS with respect to smoking. One cohort of 212 AS patients found that smoking was associated with more rapid progression in functional disability (HAQ-S score) over a median follow-up of 5 years. With the exception of some smaller studies, most studies supported the negative impact of smoking on AS with higher disease activity, poorer function, more impaired quality of life and more rapid radiographic progression in AS patients who smoked. Finally, four cohort studies had mixed results with respect to smoking and response to biologic therapy in AS.

Conclusion: There is insufficient evidence to determine whether smoking is a risk factor for the development of AS. Smoking appears to be associated with worse disease activity, function, and quality of life in established

AS. The current literature also supports an association between smoking and more severe radiographic changes, data which may be of benefit in patient education. There is a paucity of literature regarding the impact of smoking on the response to biologic therapy in AS. Prospective follow-up of well-documented AS cohorts would make a significant contribution to current knowledge.

17

Development and Assessment of User Satisfaction of the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) Responder Index-50 (SRI-50) Website with Computer-Adaptive Training and Examination Modules

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Objective: SRI-50 is a novel, valid and reliable index able to measure $\geq 50\%$ improvement in disease activity in lupus patients. We aimed to describe the development of SRI-50 website, www.sri-50.com, and to assess user satisfaction with its training and examination modules among rheumatologists and rheumatology fellows.

Methods: The first phase included the development of www.sri-50.com including: SRI-50 training manual, computer-adaptive training modules and a data-bank for examination of cases. In this phase 3 rheumatologists, a web designer and a coordinator participated. The second phase involved rheumatologists and rheumatology fellows from different academic centers most of whom were unfamiliar with SRI-50. Participants were requested to review the training modules and to complete 5 randomly assigned case scenarios in the examination module. The third phase of this study included the evaluation of the training and examination modules, and the overall performance of the website. For this purpose an online satisfaction survey with 15 questions was developed to assess: 1) feasibility: download and switch speed, ease of use, and the time required to complete the training and examination modules, 2) content: presentation of the website and overall impression, usefulness of the website to familiarize rheumatologists with SRI-50 and prepare them to use SRI-50 in clinical trials. Participants were encouraged to provide comments to improve the website.

Results: The first phase was accomplished by the development of the website. 10 rheumatologists and 4 rheumatology fellows evaluated the website in the second phase. Rheumatologists were from Canada, USA, Ireland, Argentina, Australia, Israel, Sweden, Brazil, and China. The results of the third phase, the satisfaction survey of the website, showed that participants strongly to somewhat agreed on the website design and presentation, ease of use, and usefulness to familiarize them with SRI-50. The mean time needed to complete the training and examinations modules was 26 ± 15 and 50 ± 21 minutes, respectively. After completion of the training and examination modules, participants reported a suitable level of preparation to implement the SRI-50 in clinical trials. Participants provided beneficial suggestions and further modifications to the site were made based on this evaluation. Fellows found the website very helpful in preparing them for use of SLEDAI-2K and SRI-50.

Conclusion: A dedicated website for SRI-50, (www.sri-50.com), was developed and includes training and examination modules. The website has

good overall acceptance among rheumatologists. Participants confirm that the website is very helpful in preparing them for use of SRI-50.

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Clinical and Radiographic Implications of Time to Treatment Response in Early Rheumatoid Arthritis Patients Treated with Methotrexate: Clinical Trials Reflect Clinical Practice Despite Substantial Differences in Baseline Disease Activity

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Objective: Retrospective analysis of the PREMIER trial demonstrated that, in early RA patients on methotrexate (MTX), timing and magnitude of clinical response determines long-term outcomes. Baseline (BL) disease activity of clinical trial patients is often more severe than that in clinical practice. This study evaluates the association of clinical responses by 12- or 24-weeks with long-term outcomes in MTX-treated patients from PREMIER who had BL levels of disease activity resembling those observed in "real world" practice.

Methods: In this post hoc analysis, observed data from MTX patients in PREMIER with BL DAS28(CRP) ≤ 6.0 were evaluated [total MTX population mean DAS28(CRP) = 6.3]. Patients were categorized as early- or delayed-responders (R) based on clinical measures [ACR50/70, or improvement in DAS28(CRP) > 1.2] at 12- and 24-weeks: early-R achieved clinical target by week 12 and maintained it at week 24; delayed-R didn't achieve the target until week 24. Long-term outcomes for early- and delayed-R were percentage in DAS28(CRP) remission (< 2.6) or with rapid radiographic progression (RRP, $\Delta mTSS > 3$) at week 52; odds ratios (OR, 95% CI) were used to compare outcomes of early- and delayed-R.

Results: 72 of 199 evaluable MTX-patients had BL DAS28(CRP) ≤ 6.0 [mean (SD) DAS28(CRP) = 5.5 (0.4)]. Percentages of early-R/delayed-R were 29.2%/27.8% for ACR50, 13.9%/18.1% for ACR70, and 58.8%/22.1% for DAS28(CRP) improvement > 1.2 ; all percentages were comparable with those in the total MTX population. Long-term outcomes were somewhat better for patients with lower DAS28(CRP) at BL, although the trends observed in the overall population remained: early-R, irrespective of the magnitude of the response, had better clinical and radiographic outcomes at week 52. Delayed-R with ACR50 or improvement in DAS28(CRP) > 1.2 had significantly reduced odds of achieving remission at week 52 [OR (95%CI): 7.33 (1.63-33.08), 7.14 (1.72-29.68), respectively]. In fact, delayed-R needed to reach ACR70 by week 24 to have comparable odds of reaching remission at week 52. Delayed-R, regardless of response magnitude, also had a high proportion of RRP at week 52; ACR70 delayed-R had an RRP prevalence $> 30\%$.

Conclusion: MTX patients with lower BL DAS28(CRP) achieved somewhat better clinical and radiographic outcomes at week 52 than the overall MTX population. Patients not achieving strong clinical response by week 12 had a lower likelihood of achieving remission and were at increased risk of developing RRP compared with early-R. Therefore, these data lend support to the applicability of the findings in PREMIER to patients with lower BL disease activity, a population possibly more reflective of RA patients typically seen in rheumatology clinics.

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Crowned Dens Syndrome: A Rare Cause of Acute Neck Pain

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Objective: To report a case of crowned dens syndrome (CDS) which presented with acute neck pain mimicking meningitis or deep pharyngeal infection.

Methods: We reviewed the case of a previously healthy 59 year old woman

who presented to hospital with acute neck pain and features of severe infection, eventually diagnosed with CDS. The medical literature was reviewed for presentation, pathophysiology, clinical and radiological features, and treatment of CDS.

Results: Crowned dens syndrome is a rare and underrecognized cause of severe neck pain in the middle-aged and elderly. It is characterized by the acute onset of severe pain and stiffness in the cervical spine. Accompanying fever and elevated inflammatory markers often lead to a delay in the proper diagnosis. CDS is most often associated with calcium pyrophosphate deposition disease or hydroxyapatite crystals, and occasionally seen in other inflammatory conditions. Peri-odontoid calcification is required for diagnosis: it is seen on cervical CT scan but is not usually visible on plain radiographs. Treatment consists of anti-inflammatories and steroids. Our patient presented with severe and progressive CDS. She had severe neck pain, inability to swallow her saliva due to pharyngeal pain, markedly elevated inflammatory markers, and rapid evolution in the CT appearance of calcification around the dens. She had no clinical or radiological evidence of peripheral chondrocalcinosis. Her symptoms dramatically responded to oral corticosteroids.

Conclusion: Our case demonstrates the typical clinical and radiological features of CDS as well as challenges in diagnosis due to its mimicry of other causes of pharyngeal and neck pain and stiffness. CDS is an under-recognized condition which should be included in the differential diagnosis of severe neck pain, as delayed diagnosis can lead to prolonged suffering and potentially severe complications with erosion of structures at C1-C2. The correct diagnosis can lead to the initiation of appropriate therapy and prompt relief of symptoms.

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Long-Term Cost-Effectiveness of Adalimumab Therapy in Juvenile Idiopathic Arthritis: From a Canadian Perspective

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Objective: As the long-term impact of treatment on the course of juvenile idiopathic arthritis (JIA) remains unknown, long-term outcomes of children with JIA treated with DMARDs and adalimumab were analyzed from a Canadian healthcare system and societal perspective.

Methods: A Markov model was structured on an analysis of the DE038 clinical trial of adalimumab in JIA. Children transitioned between 5 health states consisting of mild, moderate, and severe active symptoms and remission with and without joint limitations. Quality-of-life weights were derived from trial Childhood Health Assessment Questionnaire and symptom responses, while outcomes were incorporated as cost weights from reports of medical care costs. The time horizons were of 7 years and of a lifetime. Costs and outcomes were discounted at 5% per year.

Results: The cohort of 100 children with JIA is estimated to have 472 quality-adjusted life years (QALYs) under placebo with DMARDs versus 558 QALYs when treated with adalimumab over the 7-year time period. Total cohort costs are \$4,544,100 for placebo and \$9,558,422 for adalimumab for the healthcare system, and \$6,127,013 and \$10,094,297, respectively, for the societal perspective. The associated incremental cost-effectiveness ratios (ICERs) of treating with adalimumab are \$58,392 and \$46,199 per QALY gained for the Canadian healthcare system and societal perspectives, respectively. The lifetime analysis, which includes the expected costs for joint replacement procedures required in adulthood, improves the ICERs to \$24,931 and \$18,872 for the Canadian healthcare system and societal perspectives, respectively. The lifetime cohort including children and adults has 1,716 and 1,889 QALYs for placebo and adalimumab, respectively. Joint replacement procedures are responsible for \$894,958 under placebo and \$188,576 when treated with adalimumab. Sensitivity analyses demonstrate lower ICERs when the mean age is changed to 7 years and the children are observed until age 18 years (an 11-year time horizon).

Conclusion: Adalimumab has a considerable therapeutic value for chil-

dren with JIA and is cost-effective even over a relatively short time horizon. Using the lifetime analysis that accounts for joint replacement significantly improves the ICERs, indicating that treatment benefits persist over a lifetime.

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Indirect Comparison of Biologics in Rheumatology; Cost per Responder and Number Needed to Treat

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Objective: An indirect comparison of the biologics used in the treatment of rheumatoid arthritis was undertaken in a Canadian setting. In order to distinguish them, annual drug cost and therapeutic efficacy based on ACR50 responses were used.

Methods: Two different methods assessed the cost per responder (CPR). The first compared best response rates recorded in randomized, double-blind, placebo-controlled trials. The absolute risk reduction provided a number needed to treat (NNT) for the second method, from which a second CPR estimate was derived.

Results: In rheumatoid arthritis, the most common rheumatoid affliction, adalimumab shows the best therapeutic response with a NNT of 2.1 and a CPR of \$15,546 (best response methodology) and \$18,197 (NNT methodology), based on ACR50 response at 24 weeks. Etanercept follows with a NNT of 2.8 and a CPR of \$22,702 and \$24,835 for the best response and NNT methodology, respectively. Certolizumab and tocilizumab have NNTs ranging from 3.0 to 4.8 depending on dosage, with associated NNT CPRs varying from \$20,806 to \$49,128. Golimumab, abatacept and infliximab generate NNT estimates of 4.2, 4.3 and 4.6, with NNT CPRs of \$36,874, \$40,071 and \$64,845, respectively. The highest NNT was 10.0 for rituximab, generating a CPR as high as \$90,620 when calculating from the NNT estimate.

Conclusion: Results of the indirect comparison outline considerable differences in cost and efficacy of biologics. Adalimumab is associated with the lowest number needed to treat and a low cost per responder, demonstrating an increased value for rheumatoid arthritis patients as well as for payers and the Canadian healthcare system.

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Ascites and Splenomegaly in a Woman with Limited Systemic Sclerosis: Unmasking a Diagnosis of Nodular Regenerative Hyperplasia of the Liver

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Objective: To describe a presentation Nodular Regenerative Hyperplasia of the liver in a woman with limited scleroderma and pulmonary arterial hypertension.

Methods: Case: A 57-year old Caucasian female with a 30-year history of limited scleroderma was admitted to hospital with RUQ pain, protuberant abdomen, early satiety, and weight gain of 10 lbs over the last 3 months.

Results: Her CREST syndrome had previously been stable. Her moderate-severe pulmonary arterial hypertension (PAH) secondary to scleroderma was managed with continuous IV prostacyclin infusion and sildenafil. The patient had complained of intermittent episodes of dull and diffuse RUQ pain and abdominal fullness beginning five years prior. However, repeated laboratory tests and imaging of the liver and abdomen remained normal. An upper GI endoscopy performed in 2008 also showed no abnormalities. At the time of admission, abdominal ultrasound showed ascites, splenomegaly and bilateral pleural effusions. AST and ALP were only mildly elevated, with normal albumin and INR. Marked portal hypertensive gastropathy with nodularity was visualized on endoscopy, with no significant varices noted. Her cardio-respiratory function was stable from previous, with a functional NYAH class of III and a cardiac RVSP of 96 mmHg. Diagnostic alternatives considered in this patient included right heart fail-

ure secondary to PAH, hepatoportal sclerosis, or an intrinsic liver disease. A transjugular needle biopsy revealed Nodular Regenerative Hyperplasia (NRH) of the liver. The patient was treated with gentle diuresis and supportive management, and was discharged upon demonstrating clinical improvement of her ascites.

Conclusion: NRH is a rare diagnosis of unclear etiology that has been associated with rheumatologic disorders and PAH. Unfortunately, a diagnosis may only be made after the onset of symptomatic portal hypertension, a potentially life-threatening condition. In this patient, subtle and non-specific symptoms might have represented early manifestations of NRH, but normal liver function tests and negative imaging studies precluded further investigation. Treatment alternatives for ascites are limited in the context of PAH, a common complication of scleroderma; aggressive diuresis or paracentesis could drastically compromise cardiac output in a patient with altered hemodynamics from right heart dysfunction. Further research is needed to better understand the pathogenesis of NRH, and its relationship to connective tissue diseases and PAH.

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Comparison of the 1987 American College of Rheumatology Criteria and the 2010 American College of Rheumatology/European League against Rheumatism Criteria in Patients with Established Rheumatoid Arthritis

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Objective: The new 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria were developed to improve the ability to classify patients with early rheumatoid arthritis (RA). However, the ability of these criteria to classify patients with established RA has not been evaluated widely. In this study we evaluated the diagnostic properties and agreement between the 1987 and 2010 criteria in a cohort with established RA.

Methods: Participants were recruited from a longitudinal study of care for RA. Prevalent RA cases, initially identified using administrative data, agreed to participate in yearly surveys. Medical records were obtained from their rheumatologist, internist or family physician (if not followed by a rheumatologist). Medical records were reviewed by a rheumatologist (MVG) who evaluated whether cases met 1987 ACR criteria, using "traditional" (4/7 criteria) and "classification tree" schema, and 2010 ACR/EULAR criteria and also recorded her clinical impression from reviewing the chart. Sensitivity, specificity, positive predictive value (PPV) of both criteria compared to study rheumatologist's impression (gold standard) were calculated. Agreement between RA diagnosis using 1987 and 2010 criteria was calculated using kappa statistic and percent perfect agreement.

Results: Of the 409 participants in the longitudinal study, 330 gave permission to access their medical records, 316 records were successfully obtained, but only 235 had sufficient information to assess criteria and were included in the analysis (163 from rheumatologists; 66 family physicians; 5 internists and 1 orthopedic surgeon). The sample included 73% female; mean (SD) age: 66 (12) years; mean RA duration: 12.2 years. Using study rheumatologist impression as the "gold standard", RA diagnosis according to 1987 criteria had a sensitivity of 92% (when people met either traditional or tree criteria) and was 90% (when using only traditional criteria), PPV of 89% and specificity of 77% (whether "either" criteria or "traditional" criteria were used). Using the 2010 criteria, sensitivity was 82%, PPV 91% and specificity 81%. Agreement in RA diagnosis between the 2010 criteria and 1987 criteria was high with 86% perfect agreement and kappa = 0.69 (95% CI: 0.59-0.78).

Conclusion: This study provides useful information on the performance of the 2010 ACR/EULAR diagnostic criteria in established RA. Our study revealed a high level of agreement between both sets of criteria, and that the 2010 ACR/EULAR criteria can be used in patients with established RA

with a slightly lower, but nonetheless acceptable, sensitivity and comparable PPV and specificity to the 1987 criteria.

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"Shrinking Lung Syndrome" Masked by Pleuropericarditis: A Case Report and Review of Literature

Iman Hemmati (Department of Medicine, University of British Columbia, Vancouver); Kenneth Blocka (The University of British Columbia, Vancouver)

Objective: To present an unusual case of shrinking lung syndrome (SLS) masked by pleuropericarditis with a review of the literature.

Methods: We report a case of SLS in a 44 year old woman in which the diagnosis was initially confounded by concurrent pleuropericarditis. The English medical literature was comprehensively reviewed for SLS for its presentation, clinical findings, diagnosis, treatment, with specific focus on its pathogenesis.

Results: SLS is a rare respiratory complication associated with systemic lupus erythematosus (SLE). The main manifestation of the disease is unexplained dyspnea, chest pain and orthopnea. Lung volume reduction without parenchymal abnormalities along with restrictive ventilatory defect on pulmonary function test (PFT) are the hallmarks of this condition. Pathogenesis, treatment and prognosis of SLS are not well described due to the small number of reported cases. The diagnosis of SLS was made based on imaging, PFT, and the exclusion of other respiratory diseases associated with SLE. Treatment with corticosteroid and intravenous cyclophosphamide was initiated due to simultaneously diagnosed renal involvement.

Conclusion: Our case demonstrates the salient features of SLS. It emphasizes that although SLS is a rare disease limited to small subset of patients with SLE, it should be considered in patients with SLE with unexplained dyspnea. Moreover, symptoms of pleuropericarditis can mask and delay the diagnosis of SLS. The prompt diagnosis and treatment can lead to decrease in morbidity and stabilization of PFT.

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Residronate Associated Scleritis: A Case Report and Review of the Literature

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Objective: Presentation of the first reported case of residronate associated scleritis. Review of bisphosphonates and inflammatory eye diseases.

Methods: A case of scleritis associated with risidronate use in a 73-year-old Chinese woman is reported. The English medical literature was reviewed for bisphosphonates and their association with inflammatory eye diseases.

Results: Bisphosphonates are increasingly being prescribed in patients with chronic inflammatory conditions for the prevention and/or treatment of osteoporosis. Cases of ocular inflammation in patients taking bisphosphonates have been reported since the early 1990s. Reported cases include both nitrogen and non-nitrogen containing bisphosphonates and with both intravenous and oral use. We report the first case of risidronate induced scleritis. The case involves a 73 year old woman who developed scleritis following exposure to risidronate in 2007 with recurrence of scleritis upon risidronate exposure again in 2009. Discontinuation of risidronate and treatment with intravenous and topical corticosteroid resulted in both clinical and radiological improvement within 24 hours. Applying the Naranjo's adverse drug reaction probability scale, a causality assessment was made which categorized this reaction as definite with a score of 9.

Conclusion: In our case there was a strong causal relationship between the use of risidronate and scleritis. Although rare, ocular adverse effects of bisphosphonates may be serious and should be known to prescribing physicians. This is important in rheumatology practice as many of our patients

are prescribed this class of medication for either prevention or treatment of osteoporosis. Moreover, ocular inflammation can be a sign of systemic disease and such patients may be referred to a rheumatologist. As such we should bear this in mind with respect to our differential diagnosis.

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Time to Consultation and DMARD Treatment of Patients with Rheumatoid Arthritis in Edmonton

Niall Jones (University of Alberta, Edmonton); Vince Choi (Edmonton); Anthony Russell (University of Alberta, Edmonton)

Objective: A role for triage?

Methods: This audit reviewed the charts of new rheumatoid arthritis patients first seen by one of three Edmonton rheumatologists in the decade beginning July 2000. Two of these rheumatologists were in an academic setting and one in community practice. The results were compared to a similar audit of a practice in Calgary, with the one physician not participating in a triage process.

Results: A total of 482 charts were reviewed from the indexes but only 151 had the required documentation to allow inclusion. Patients were first referred by their family doctor a mean of 9.8 months (median four months, range 0 to 128 months), after their first symptoms. They were then referred and seen by a rheumatologist at a mean of 1.2 months (median 0.8 range 0-8). These data are in keeping with similar numbers collected by VC from an in-progress study in Calgary. There, the mean wait time for the same interval (from symptom onset to rheumatologist visit) is 12.5 months with 87.1% of patients having been seen within 12 months. Of the 151 patients reviewed in our study, 149 (98.6%) received a prescription for DMARDs at the time of the initial consultation for RA. The remaining patients received DMARDs within one week of the initial consultation.

Conclusion: This study shows that in Northern Alberta, patients with suspected RA wait a median of 11 months from symptom onset to first consultation visit with their rheumatologist, and these data were similar for the overall delay for the Calgary rheumatologist studied. It appears that in Edmonton these patients are referred and seen by rheumatologists in a timely manner once they present with symptoms suggestive of RA. Furthermore, these patients are started on appropriate DMARD therapy once seen by a rheumatologist. This is a trend noted in similar study data from Toronto but contrasts with those in studies from other Canadian centres, where it has been reported that DMARD use by a rheumatologist ranges from 58-84%. Our results suggest that a delay in presentation may not necessarily be due to the consultation process but rather with the initial presentation to primary care. The reasons patients might delay presenting with arthritic symptoms to their primary care doctor are likely multiple, including in some areas the lack of a primary care physician.

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Efficacy with Abatacept in Patients with Earlier Versus More Long-standing Disease: Insights from the AIM Trial

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Objective: To investigate whether disease duration affects achievement of disease activity targets (as assessed by the DAS28 and SDAI) in patients treated with abatacept in the AIM trial.

Methods: In the Phase III double-blind AIM trial¹, patients with active rheumatoid arthritis (RA) refractory to MTX were randomized and treated with abatacept or placebo, plus background MTX. SDAI and DAS28 treatment targets of LDAS (≤ 11.0 and ≤ 3.2) and remission (≤ 3.3 and < 2.6) were evaluated at Month 12, according to baseline disease duration: ≤ 2 ver-

sus >10 years. Post-hoc analyses were based on as-observed data for patients with available data at visit of interest.

Results: At baseline, 22.9 (99/433) and 20.5% (45/219) of patients randomized and treated with abatacept and placebo, respectively, had disease duration ≤ 2 years, and 31.2 (135/433) and 33.8% (74/219) had disease duration >10 years. For abatacept versus placebo-treated patients with ≤ 2 and >10 years disease duration, LDAS and remission rates (95% CI) at Month 12 are presented: • SDAI remission: 16.5% (8.6, 24.4; $m=85$) versus 7.1% (0.9, 23.5; $m=28$) and 7.7% (2.9, 12.5; $m=117$) versus 0% ($m=52$) of patients (estimates of difference, 9.3 [-7.9, 26.6] and 7.7 [-1.0, 16.4]) • SDAI LDAS: 56.5% (45.9, 67.0; $m=85$) versus 21.4% (6.2, 36.6; $m=28$) and 41.9% (32.9, 50.8; $m=117$) versus 15.4% (5.6, 25.2; $m=52$) of patients (estimates of difference, 35.0 [11.3, 58.7] and 26.5 [9.7, 43.3]) • DAS28 remission: 35.3% (25.1, 45.5; $m=85$) versus 7.1% (0.9, 23.5; $m=28$) and 22.9% (15.3, 30.5; $m=118$) versus 1.9% (0.0, 10.3; $m=52$) of patients (estimates of difference, 28.2 [6.5, 49.8] and 21.0 [7.5, 34.4]) • DAS28 LDAS: 50.6% (40.0, 61.2; $m=85$) versus 21.4% (6.2, 36.6; $m=28$) and 39.0% (30.2, 47.8; $m=118$) versus 13.5% (4.2, 22.7; $m=52$) of patients (estimates of difference, 29.2 [5.6, 52.7] and 25.5 [9.0, 42.0]).

Conclusion: Abatacept plus MTX confers clinical efficacy in patients with both earlier and more long-standing RA even when using more stringent remission criteria. SDAI- and DAS28-defined LDAS and remission rates were numerically greater for abatacept-treated patients with ≤ 2 versus >10 years disease duration, suggesting that patients with shorter disease duration appear to have a greater chance of achieving disease activity targets. These data extend previous findings on ACR response², and support the use of abatacept in earlier disease in patients with active RA. References: 1 Kremer J, et al. *Ann Intern Med* 2006;144:865-76; 2. Yazici Y, et al. *Clin Exp Rheum* 2011;29:494-499

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Abatacept plus MTX Treatment Confers Similar Clinical Efficacy Regardless of Baseline Rheumatoid Factor or CRP Status in the AIM Trial

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Objective: To assess clinical efficacy with abatacept + methotrexate (MTX) according to baseline rheumatoid factor (RF) and CRP status.

Methods: Patients with active RA refractory to MTX were randomized and treated with abatacept or placebo, plus background MTX in the double-blind AIM trial. Proportions of patients (95% CI) achieving remission and LDAS (defined by DAS28 [< 2.6 and ≤ 3.2] and SDAI [≤ 3.3 and ≤ 11]) were evaluated at Month 12 according to baseline RF status (positive [RF+] and negative [RF-]) and baseline CRP quartile; < 1.2 , $1.2- < 2.1$; $2.1- < 4.0$ and ≥ 4.0 mg/dL. Post-hoc analyses are based on as-observed data.

Results: At baseline, 81.8% (354/433) and 78.5% (172/219) abatacept- and placebo-treated patients, respectively, were RF+, versus 12.0% (52/433) and 14.2% (31/219) who were RF-. Similar proportions of RF+ and RF- patients achieved DAS28-remission (79/307 [25.7%, 95% CI: 20.8, 30.6] and 11/41 [26.8%: 13.3, 40.4]) or LDAS (134/307 [43.6%: 38.1, 49.2] and 18/41 [43.9%: 28.7, 59.1]) following 12 months of abatacept treatment. Estimate of difference versus placebo was similar regardless of RF status. Similar proportions of RF+ and RF- patients achieved SDAI-remission (34/306 [11.1%: 7.6, 14.6]) and 3/41 [7.3%: 1.5, 19.9]) and LDAS (144/306 [47.1%: 41.5, 52.7] and 24/41 [51.2%: 35.9, 66.5]) following 12 months of abatacept treatment. 95% CI for the estimate of difference between abatacept and placebo did not cross zero in RF+ patients. Remission rates are presented for abatacept and placebo and the corresponding estimate of difference (95% CI) versus placebo for the lowest and the highest baseline CRP quartiles. DAS28 remission: • < 1.2 mg/dL:

Abatacept=37% (27, 48; m=83); Placebo=4% (1, 15) Estimate of difference: 33% (16, 50) • ≥ 4.0 mg/dL: Abatacept=20% (13, 28; m=104); Placebo=3% (0, 16); Estimate of difference: 17% (0, 34) SDAI remission: • < 1.2 mg/dL: Abatacept=21% (12, 29; m=83); Placebo=2% (0.1, 12); Estimate of difference: 18% (4, 33) • ≥ 4.0 mg/dL: Abatacept=5% (0.7, 9; m=103); Placebo=3% (0, 16) Estimate of difference: 2% (-9, 12) Higher proportions of abatacept patients achieved remission according to DAS28 and SDAI compared with placebo across all baseline CRP quartiles (data not shown for intermediate quartiles), although outcomes appeared numerically better in the lowest quartile. Across all CRP quartiles, 95% CI for the estimates of difference versus placebo did not cross zero, except for the most stringent outcomes.

Conclusion: Abatacept has consistent efficacy over 12 months in RA patients from the AIM trial regardless of baseline RF or CRP status.

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RAPID3 (Routine Assessment of Patient Index Data 3) at Week 12 Predicts Progression of Joint Damage at Year 1 in Rheumatoid Arthritis Patients Treated with Certolizumab Pegol Plus Methotrexate Edward Keystone (University of Toronto, Toronto); Owen Davies (UCB Belgium, Brussels); Kristel Luijckens (UCB, Braine-l'Alleud); Jerry Syrotuik (UCB Canada Inc., Oakville)

Objective: The RAPID3 patient derived assessment of disease activity has been demonstrated to correlate with DAS28 in patients treated with certolizumab pegol (CZP). The objective of this post-hoc analysis was to investigate if RAPID3 or EULAR response criteria predict structural joint damage in RA patients treated with CZP + methotrexate (MTX) or placebo (PBO) + MTX.

Methods: Data from patients treated with CZP 200 mg + MTX or PBO + MTX in RAPID 1 were analyzed. At Wk 12, patients were categorized according to good, moderate or poor RAPID3 or EULAR DAS28(ESR) criteria. Data were pooled for patients in each group achieving a good or moderate RAPID3 or EULAR response, and progression of joint damage was evaluated in good/moderate vs poor RAPID3 or EULAR responders. Radiographic non-progression was defined as a change of ≤ 0.5 units from baseline in mTSS.

Results: At Wk 12, the majority of CZP + MTX pts had good/moderate RAPID3 or EULAR responses (CZP 200 mg + MTX vs PBO + MTX: RAPID3, 66.8% vs 23.5%; EULAR, 77.6% vs 29.1%). Mean RAPID3 scores at baseline were similar between Wk 12 response groups for RAPID3 (range: 15.10-16.99) and EULAR (range: 15.62-16.93) criteria. At baseline, mean and median mTSS were similar between Wk 12 response groups (RAPID 3: mean = 35.29-45.14, median = 19.75-24.50; EULAR: mean = 35.94-47.65, median = 20.00-21.50). At Wk 52, patients with a poor RAPID3 or EULAR response at Wk 12 had a greater increase in mTSS from baseline than those patients with a good/moderate response. Furthermore, fewer patients with a poor RAPID3 or EULAR response at Wk 12 were mTSS non-progressors vs patients with a good/moderate RAPID3 or EULAR response at Wk 12. There was greater inhibition of radiographic progression with CZP + MTX vs PBO + MTX irrespective of the level of response at Wk 12 (good/moderate or poor) and how response was determined (RAPID3 or DAS28).

Conclusion: In this post-hoc analysis, RAPID3 or EULAR responses at Wk 12 predicted progression of structural joint damage at Wk 52. These results suggest that both RAPID3 or EULAR response criteria can be used as predictors, offering the physician the choice of clinical or patient focused prediction tools. For RA patients receiving MTX, assessing RAPID3 response at Wk 12 could be used to aid treatment decision making.

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Baseline Tender Joint Count Scores Predict Long-term Household Productivity in Patients with Rheumatoid Arthritis Treated with Certolizumab Pegol Plus Methotrexate

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Objective: This analysis evaluated if baseline tender/swollen joint counts (TJC/SJC) are associated with and predict household productivity in patients with active rheumatoid arthritis (RA) receiving certolizumab pegol (CZP) plus methotrexate (MTX).

Methods: Pooled data at 1 year for CZP 200 and 400 mg completers from RAPID 1 and RAPID 2 and its open-label extension were used. Household productivity (missed days of household work, days with reduced household productivity, days with outside help hired, missed days of family/social/leisure activities) was assessed using the Work Productivity Survey (WPS-RA). Frequency distribution of WPS-RA scores over time was summarized by TJC/SJC baseline 25% and 75% quartiles. Hand, large upper extremity (shoulder, elbow, hand), large lower extremity (hip [tenderness], knee, ankle), or total joint count were assessed. Analyses were conducted on observed data.

Results: At baseline higher disease activity was associated with higher impairment in household duties and social activities. Patients receiving CZP had rapid, sustained improvements in household productivity over time in all TJC/SJC quartiles. Over 1 year, fewer days of household work were missed per month in patients with lower ($\leq 25\%$ quartile) vs higher ($> 75\%$ quartile) TJC baseline scores in large lower extremity joints: by Week 4 (Wk) 69.2% vs 57.0% of patients missed ≤ 4 days of household work per month, increasing to 82.4% vs 72.7% by Wk 12 and by Wk 48, to 89.0% vs 82.6%. Although improvements in household productivity were reported by patients with higher baseline TJC scores in the lower extremities, these were consistently smaller vs patients with lower baseline TJC scores. Similarly patients with lower TJC baseline scores in large lower extremity joints had greater reductions in days with reduced productivity and in days with outside help hired vs patients with higher baseline scores. Fewer days of family/social/leisure activities were missed per month in patients with lower vs higher hand/total TJC baseline scores. Patients with higher vs lower SJC baseline scores had similar improvements in household productivity over time; there were no differences between the 2 groups at Wk 48.

Conclusion: At baseline higher TJC/SJC scores were associated with increased impairment in household productivity. Improvements in household productivity were seen with CZP treatment in both patients with lower vs higher baseline TJC scores, with greater improvements in patients with lowest baseline TJC scores.

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Real - Life Effectiveness of Infliximab in the Treatment of Rheumatoid Arthritis over 4 Years: The Canadian Experience

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Objective: In recent years, the efficacy of anti-TNF in the management of Rheumatoid Arthritis (RA) has been demonstrated in numerous controlled clinical trials. Longitudinal observational studies assessing the real-life effectiveness of anti-TNF agents are essential in order to demonstrate the true benefits. The objective of this study was to assess in Canadian clinical practice the 48-month outcomes in patients with RA treated with Infliximab.

Methods: The data for this analysis were obtained from BioTRAC, an observational prospective registry of adult RA patients initiated on treatment with Infliximab since 2002 and managed as per routine care. Patients enrolled were biologic-naïve or had initiated treatment with a biologic for a

period of < 6 months prior to enrolment. This analysis included 111 patients with rheumatoid arthritis who had completed 48 months of treatment.

Results: Mean age of the patient cohort was 56 years and mean duration since diagnosis was 10.2 years. At initiation of treatment, 95% were treated with DMARDS and 78% with Methotrexate. Mean (SD) patient parameters at baseline were: C-reactive protein (CRP) = 19.8 (26.6) mg/L, erythrocyte sedimentation rate (ESR) = 36 (25.4) mm/hr, morning stiffness = 71.4 (41.5), tender joint count (TJC) = 14.9 (7.1), swollen joint count (SJC) = 12.7 (6.9), health assessment questionnaire (HAQ) = 1.7 (0.8), patient global assessment of disease activity (SGA) = 65.5 (20.9), physician global assessment of disease activity (PGA) = 67.0 (18.4), and DAS28-CRP = 5.9 (1.1). Upon 6 months of treatment, significant and sustained improvements ($P < 0.05$) were observed in all parameters analyzed, which were maintained over the 48 months of treatment. The proportion of patients achieving ACR20/ACR50/ACR70 by 6 months was 67%/ 54%/ 18%.

Conclusion: The results of this observational study have shown that Infliximab is effective in reducing symptom severity and improving outcomes in patients with rheumatoid arthritis over a four year period in a Canadian longitudinal observational study.

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The Impact of Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program-Trained Extended Role Practitioners on Healthcare Delivery: A Two Year Prospective Study

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Objective: The Advanced Clinician Practitioner in Arthritis Care (ACPAC) training program focuses on the assessment, diagnosis, triage and independent management of selected musculoskeletal and arthritis-related disorders. It is offered to experienced physical and occupational therapists. The objectives of this study were: 1) to examine the clinical performance of ACPAC program-trained Extended Role Practitioners (ERPs) and 2) to evaluate the extent to which these ERPs are delivering integrated and timely healthcare.

Methods: ACPAC ERPs ($n=30$) from 15 healthcare institutions across Ontario (urban, rural, academic, non-academic, adult and paediatric) completed a longitudinal survey each quarter for 2009 and 2010. Indicators were developed via consensus and pilot testing. Analyses were descriptive.

Results: Response rate varied from 83-97% across quarters. ERPs saw 13407 and 14546 patients in 2009 and 2010, respectively. In 2009, the majority of patients were referred by a family physician (43.9%), and 35.8% by a specialist. This shifted in 2010 to 37.3% and 51.5%, respectively. Over the two-year period, combined adult and paediatric caseloads included new consults (24.9%) and follow-ups (55.6%). Remaining patients underwent triage by an ERP. Most common patient diagnoses included: osteoarthritis (51.6%), rheumatoid arthritis (14.7%) and juvenile idiopathic arthritis (11.1%). About 90% of respondents were working in an extended practice role. The longest median wait time from referral to initial assessment by an ERP was 22 days. Approximately half of ERPs participate in each of: education delivery, research and leadership roles, with the majority pursuing professional development. Approximately one third of patients were referred, by an ERP, for x-rays, lab tests and other services (i.e. splints, footwear), followed by referral to allied health services and specialists, and communication via dictated letters. As many as 79% of ERPs acted under the auspices of medical directives, ordering x-rays (over 80%), lab tests (over 60%) and diagnostic ultrasounds (over 40%). Approximately 70% recommended medication/dosage changes (up to 14% made these changes independently). Approximately 90% recommended joint injections (up to 18% performed them).

Conclusion: ACPAC program-trained therapists are primarily seeing patients with osteoarthritis or rheumatoid arthritis in a follow-up capacity,

with most patients referred by a family physician or specialist. Most ERPs are utilizing medical directives to support their extended practice roles. This new human health resource may be an effective way to address the progressive decline in arthritis care specialists. Future evaluations should monitor the evolution of ERPs' extended roles and assess the impact of ERP-based care on patient outcomes.

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Serological Analysis of Patients with Positive ANA/ENA and Antibodies Directed to DFS70/LEDGF Referred through a Rheumatology Triage System

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Objective: Since referral of patients with a positive anti-nuclear antibody (ANA) or extractable nuclear antigen (ENA) tests to rheumatologists has been criticized as an inappropriate use of tertiary care resources and because an accurate and timely diagnosis can improve health outcomes while reducing health care costs, we studied the serological profiles of patients referred to rheumatologists through a regional triage system because of a positive ANA or ENA. As an approach to informing an evidence based approach to triage, the primary objectives were to determine the most common ANA/ENA specificities and the presence of anti-dense fine speckled (DFS70) antibodies.

Methods: Cases that met three criteria were included in the study: 1) referred to Rheumatology Central Triage from 2009-2010 ($n=10,230$); 2) reason for referral was a "positive ANA or ENA" ($n=392$); 3) were evaluated by specialists at Foothills Medical Center ($n=153$). The Central Triage clinical database was used to segregate cases and to obtain demographic and baseline clinical information. An administrative serological database was used to retrieve specific ANA and/or ENA test results. Where serological information was absent from the initial referral (i.e. anti-DFS70), serological tests were retrospectively performed on sera retrieved from storage.

Results: The referral autoantibody (aab) profile showed that the three most common primary ANA patterns were nuclear speckled [$n=44$; 28.8%], homogeneous speckled [$n=27$; 17.6%], and nucleolar [$n=14$; 9.2%] with titers ranging from 1/160-1/5120. Sixty patients [39.2%] had a positive ENA with the four most common specificities being anti-Ro52 [$n=22$; 36.7%], anti-SS-A/Ro60 [$n=16$; 26.7%], anti-chromatin [$n=15$; 25.0%], and anti-topo I (Scl-70) [$n=11$; 18.3%]. Of note, 5 [8.3%] tested positive for anti-dsDNA. Of 101 available sera, 19 [18.8%] were anti-DFS70 positive and was the only aab detected in 13 patients (68.4%). Other aab that coexisted with DFS70 included anti-topoisomerase I (Scl-70) (3), Ro52 (2), chromatin (1) and Jo-1 (1).

Conclusion: This is the first known study to evaluate serological parameters of patients referred to rheumatologists via a central triage system because of a positive ANA/ENA. The spectrum of aab specificities was wide with anti-Ro52, which has been established as a sensitive but not a specific biomarker for SARD, being the most common aab detected. In addition, ~19% of the patients referred had only antibodies to DFS70, which in isolation have been negatively correlated with the diagnosis of SARD. If these findings are clinically validated, testing for anti-DFS70 or anti-Ro52 will have important implications for the urgency of these referrals through a triage system.

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Effect of Shock Absorbing Insoles on Biomechanical and Clinical Aspects of Knee Osteoarthritis

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Objective: To examine the immediate and short-term (1 month) changes in knee joint loading, pain, and function following the insertion of shock absorbing insoles (SAIs) into the shoes of patients with knee OA.

Methods: Sixteen individuals (6M, 10F, age: 66.9 ± 12.5 years), with radiographically-confirmed knee OA underwent testing on two separate occasions (baseline and follow-up). Participants completed the Western Ontario and McMaster Universities Index (WOMAC) to assess self-reported pain. Objective physical function was assessed as the time to ascend 12 stairs. 3-dimensional gait analyses at a self-selected walking speed were performed under two different randomly-presented conditions: 1) shoes only, 2) insertion of $\frac{3}{4}$ length SAIs. Reflective markers were placed on the participants' skin over specific lower limb anatomical landmarks, and their positions were tracked using 8 high-speed, digital cameras sampling at 120 Hz. Ground reaction force data were sampled at 1200 Hz using 2 force platforms. A biaxial accelerometer was placed on the tibial tuberosity to measure vertical tibial acceleration upon impact. A total of 5 walking trials with and without the SAIs were completed at both sessions. Participants were sent home with the SAIs and documented total wear time. The primary outcome measures were: the peak external knee adduction moment (KAM), the KAM impulse (area under the KAM curve), and peak tibial acceleration. Secondary outcomes were: WOMAC pain and total scores, and timed stair climb. Within- and between-session differences in the primary outcomes were evaluated using a 2-factor repeated measures analysis of variance, while between-session differences in the secondary outcomes were evaluated using paired t-tests.

Results: Participants wore their SAIs an average of 213.4 ± 98.1 hours over the one month trial. No significant within- or between-session knee joint loading differences were observed for any biomechanical variable ($p > 0.05$). Conversely, significant improvements were found for the WOMAC pain subscale (4.4 ± 3.1 vs. 6.4 ± 2.9 ; $p=0.02$), and the total WOMAC score (25.3 ± 13.5 vs. 30.7 ± 14.8 ; $p=0.04$). Finally, the time to ascend 12 stairs was significantly ($p=0.01$) shorter at the follow-up assessment (6.1 ± 2.7 seconds) compared to baseline (6.5 ± 3.1 seconds).

Conclusion: Although there were no joint load reductions, pain and function were found to be significantly improved with the use of the SAIs for one month. Therefore, although the SAIs can improve clinical symptoms, their effect on disease progression is less clear.

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A Systematic Review to Determine the Validity of Diagnoses of Osteoporosis and Fragility Fractures in Administrative Data

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Objective: Conduct a systematic review of the literature to determine the validity of diagnoses of osteoporosis and fragility fractures in administrative data.

Methods: A comprehensive search was conducted in November 2010 using Medline and EMBASE to identify original research studies reporting the validity of diagnoses of osteoporosis and fragility fractures in administrative data. The search was augmented by consulting with experts in the field and reviewing references from selected studies. Title and abstracts and selected studies were reviewed by two independent investigators working by consensus. A pre-determined data abstraction form was used to extract relevant data from selected studies.

Results: Eleven full-length studies were included in the final review, of which 8 were primary validation studies (N=2 osteoporosis, N=6 fractures) and 3 reported validation of fracture diagnoses as part of a larger study. The validity of the diagnosis of osteoporosis in administrative data was fair when at least three years of data from hospital and physician visits claims were used (area under the curve (AUC)=0.700) or when pharmacy data was available (with or without the use of hospital and physician visit claims data, AUC > 0.700). Nonetheless, the positive predictive values (PPV) of

the diagnostic algorithms were low (< 0.60). There was significant heterogeneity among studies that examined the validity of diagnoses of fragility fractures in administrative data. There was good evidence to support the use of hospital data to identify hip fractures (sensitivity 69-97% and PPV 63-96%) and the addition of physician claims data and procedural codes to hospitalization data improved these characteristics (sensitivity 83-97% and PPV 86-98%). Vertebral fractures were difficult to identify using administrative data, even when using outpatient physician visits and procedures data. There was some evidence to support the use of administrative data to define other fractures that do not require hospitalization (eg. radius/ulna, humerus) if physician visit claims and procedure codes were available.

Conclusion: Administrative data can be used to identify hip fractures, especially when physician claims and procedural codes, in addition to hospitalization data, are available. Algorithms to accurately identify osteoporosis and vertebral fractures in administrative data are still suboptimal.

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Rheumatoid Arthritis Quality Indicators Compliance Study

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Objective: The purpose of the study is to assess adherence to each of the Arthritis Foundation's (AF) 27 rheumatoid arthritis (RA) quality indicators (QIs) assessing 17 areas of care at Canadian rheumatology clinics that are based in university teaching hospitals to determine areas in need of improvement.

Methods: Retrospective chart audits were conducted on patients with RA who were diagnosed between January 2007 and May 2010 and under the care of a single rheumatologist for at least 1 year. The chart audits were conducted at 4 Canadian rheumatology clinics based at: Sunnybrook Health Sciences Centre, Kingston General Hospital, Toronto Western Hospital, and Mount Sinai Hospital. Descriptive statistics were calculated for site adherence for each patient chart audited and aggregated adherence for each QI from all applicable charts. Site adherence was compared using one-way ANOVA.

Results: 74 charts were audited. Adherence to QIs was significantly different among sites evaluated ($p < 0.0001$). Some QIs were generally well adhered to (100% - 83%): regular follow-up, radiographs of hands & feet, glucocorticoids, methotrexate transaminitis monitoring, DMARDs, folic acid, surgery, time to referral, baseline & follow-up studies, osteoporosis prophylaxis, and assistive devices. QIs in need of improvement in terms of adherence (75% - 10%) were: reproductive issues, history and examination, radiographs of cervical spine, exercise, informing patient about risks, and vaccines.

Conclusion: Overall adherence to the 27 AF RA QIs requires improvement. Some non-adherence may be attributed to lack of documentation of clinic encounters (such as exercise and informing patient about risks), and failure to receive consult notes from other physicians in a timely manner (such as surgery consults and vaccine updates). Future studies exploring reasons for non-adherence and methods to increase adherence are needed to improve the quality of rheumatology care. Areas in need of improvement may inform practice-based performance improvement projects and provide needs analysis for designing multifaceted continuing education interventions.

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Peer to Peer Mentoring for Individuals with Early Inflammatory Arthritis: Feasibility Pilot

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Objective: The goal of this research is to examine the potential benefit of early peer support to improve the health and quality of life of individuals with early inflammatory arthritis (EIA). This poster presents preliminary findings of a pilot study, as part of a complex healthcare intervention, to assess acceptability and feasibility of a peer support intervention for individuals with EIA.

Methods: Qualitative and quantitative methods were used to evaluate a feasibility pilot of a peer mentoring intervention for individuals with EIA. Individuals with IA (diagnosed at least 2 years and managing well) were recruited through a rheumatology clinic, The Arthritis Society, and research team to be trained as peer mentors. A peer mentor training model was developed consisting of 18 hours of didactic and interactive sessions over 4 non-consecutive days. Individuals with EIA (mentees; disease duration 6-52 weeks) were recruited through 2 rheumatology clinics. Trained peer mentors were paired with an individual with EIA to provide support (face-to-face or telephone) up to once a week over 12 week period. Peer mentor self-efficacy was assessed at baseline, immediate post-training, immediate post-peer mentoring program and 3-months follow-up. Mentees were assessed at baseline, immediate post-program and 3-months follow-up re: disease modifying anti-rheumatic drugs (DMARDs)/biologic treatment use, self-efficacy, self-management, health-related quality of life, anxiety, coping-efficacy, social support and disease activity. Results were compared from baseline using paired t-tests. One-on-one interviews with participants were also conducted to examine acceptability and feasibility of study procedures and outcome measures and to gain perspectives on the value of peer support. Key themes were identified through constant comparison.

Results: Nine pairs participated. The training was well-received by mentors. Mentees perceived emotional, informational, appraisal, and instrumental support, while mentors themselves reported benefits (e.g., new self-management techniques, lifestyle changes), and learned from mentees' fortitude and self-management skills. Participants' experience of peer support was informed by the unique relationship they forged with their peer partner. All participants were unequivocal about the need for peer support for the newly diagnosed. Quantitatively analysis is ongoing. Mentors' self-efficacy increased, and it is anticipated that mentees will experience improvements in outcomes.

Conclusion: Early peer support is proposed as a way to augment current care in rheumatology. The intervention was well-received. The training process, peer support program, and outcome measurements were demonstrated to be feasible with modifications. This intervention has been expanded to a small pilot RCT study to demonstrate effectiveness of peer support in EIA management.

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The Effect of In-Utero Smoking Exposure on the Risk of Developing Rheumatoid Arthritis: A Proof of Concept Study

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Objective: To determine whether in-utero exposure to maternal smoking may influence the later development of rheumatoid arthritis (RA) and warrants further investigation.

Methods: A postal survey was sent to 723 RA and 156 OA patients from the existing database of 9 rheumatologists at the University of Alberta in Edmonton, Canada. Data collected in the anonymous survey included age, gender, BMI, education, arthritis severity (VAS), medication exposures, smoking status, and the smoking status of both parents during pregnancy

and before the age of 18. Descriptive statistics were calculated using standard statistical software. The study was approved by the University of Alberta Health Ethics Research Board.

Results: 292 RA patients (40% response rate; M:F 79:205; BMI 27) and 59 OA patients (38% response rate; M:F 10:48; BMI 28) completed the survey. The OA group was slightly older than the RA group (66 vs 60, $P=0.002$), had longer disease duration (17 vs 14 years, $p=0.65$), and similar disease severity (VAS 5/10). RA patients had significantly higher pack years of smoking than OA patients (43.1 vs 29.6, $p=0.019$). While the rate of smoking was higher in pregnant mothers of RA patients than OA patients, (21.5% vs 14%), there was no statistical difference. A similar pattern is noted if including only non-smoking patients, with a trend of more in-utero smoking exposure for RA than OA (19% vs 11%, $p=0.57$). Nineteen (90%) of the pregnant smoking females continued smoking throughout the RA patient's childhood compared with 3 (100%) of OA patients. Sixteen (76%) of the smoking pregnant mother's partners continued smoking throughout pregnancy compared with 3 (100%) of the OA patients' fathers. A comparison could not be made to the population at-large as this was not yet tracked in the 1940s.

Conclusion: Despite no clear demonstration of an in-utero smoking association with RA and the presence of several confounders including second-hand smoke exposure in childhood, this proof of concept study suggests the need for further review given the trend to greater in utero smoking exposure in RA compared to OA patients. Future considerations include a larger cohort of RA and OA patients to allow for complete age- and gender-disease matching, or a younger cohort to allow for a comparison the general population.

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Availability of Pediatric Rheumatology Training within Pediatric Residency Programs in Canada - A Complete Report

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Objective: The aim of this study was to survey all pediatric residency programs in Canada to determine the availability of pediatric rheumatology training.

Methods: Program directors of all 17 pediatric residencies in Canada were contacted via email and asked to fill out a questionnaire assessing availability and content of formal pediatric rheumatology teaching in their program.

Results: Response was received from 15/17 programs (88%). There was no formal pediatric rheumatology teaching available on-site at 3 centers as there was no rheumatologist on staff. However, all 3 centers offered an off-site rotation at another university. Overall, 11 centers offered an elective rotation in pediatric rheumatology, while 4 centers had a mandatory rotation. The length of rotation at each centre was 4 weeks and was usually done in PGY 2 or PGY 3. In one institution the elective 4week Rheumatology block was combined together with Gastroenterology. When an elective rotation was available, it was chosen in vast majority of centers by < 50% of residents. No university reported higher residents' demand than could be accommodated. Formal large group lectures on rheumatologic disorders were offered at all centers except one, on average 3 hours per year. Small group lectures (case based learning, problem assisted learning etc) were available at 7 centers, on average 3 hours per year. A formal lecture on MSK exam was a part of the postgraduate training at 10 institutions.

Conclusion: There is excellent availability of pediatric rheumatology training for pediatric residents at surveyed pediatric programs. However, at the majority of programs, rheumatology rotations are elective and are chosen by less than half of the residents in each program. Mandatory large and small group lectures on pediatric rheumatology topics combined account for only 5-6 hours of teaching per year. This indicates a need for development of strategies to ensure adequate training in pediatric rheumatology for pediatric residents.

A Comparison of Systemic Lupus Erythematosus (SLE) Patients Achieving Prolonged Clinical Quiescence (PCQ) On and Off Corticosteroids and/or Immunosuppressive Medications

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Objective: Some patients with SLE achieve PCQ. We previously described patients achieving corticosteroid- and immunosuppressive-free PCQ. As physicians attempt to minimize patients' exposure to these medications given their associated morbidities, this study's aims were to describe patients who achieve PCQ maintained on these medications and to compare them to those maintaining medication-free PCQ.

Methods: Patients followed regularly in the Lupus Clinic from July 1970 - October 2011 were identified. PCQ was defined as SLEDAI-2K=0 or =2 or 4 from active serology for ≥ 5 consecutive years, with visits ≤ 18 months apart, in patients consistently maintained on corticosteroids and/or immunosuppressives ("MED"). Charts were reviewed to characterize the PCQ period. MED demographics and clinical course before and during PCQ were then compared to patients who achieved PCQ, defined above, but without the use of corticosteroids or immunosuppressives for its duration ("NO MED"). Descriptive statistics were used. Comparisons were made using t- and McNemar's tests.

Results: 34/1613 (2.1%) MED patients were identified. Mean MED PCQ duration was 8.5 ± 2.9 (range 5.1-16.3) years, and ended with flare in 12 patients (35.3%). In the 22 (64.7%) patients whose PCQ did not end in flare, medications were successfully discontinued in five (14.7%), being tapered in 6 (17.6%), and maintained in two (5.9%) with organ transplants necessitating ongoing immunosuppression; six (17.6%) patients were maintained on a stable regimen, with no standardized drug withdrawal algorithm specified; three patients (8.8%) were lost to follow up. 38/1613 (2.4%) NO MED patients were identified, with mean PCQ duration 11.6 ± 6.4 (range 5.1-29.4) years. When the groups were compared, MED patients were younger at diagnosis (27.9 ± 11.7 versus 36.1 ± 15.2 ; $p=0.01$) and required more immunosuppressives (52.9% versus 23.7%; $p=0.01$) and corticosteroid (100% versus 57.9%; $p<0.0001$) at higher cumulative doses (42.9 ± 39.7 versus 20.7 ± 17.2 grams (among those requiring corticosteroids; $n=22$); $p=0.006$) prior to PCQ. There was no between-group difference in ethnicity, SLEDAI-2K at presentation, antimalarial use, time to PCQ, organ manifestations, autoantibody profile, or SLICC damage index prior to, during, or at last PCQ visit.

Conclusion: 2.1% of our cohort achieves PCQ of ≥ 5 years on corticosteroids and/or immunosuppressives; however, this group appears heterogeneous: the minority who flared, representing a group whose disease activity is merely suppressed by ongoing medication use, and the majority who tolerated/were tolerating medication withdrawal, reflective of true PCQ (as in NO MED). Further comparison between these (remission/suppression) subgroups and to the NO MED cohort may be instructive as each may reflect unique pathophysiology.

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The Gait, Arms, Legs & Spine (GALS) Exam: An Effective Screening Tool for Rheumatoid Arthritis When Used by Family Physicians and Nurse Practitioners

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Objective: Background & Purpose: Early referral to a rheumatologist for diagnosis of rheumatoid arthritis (RA) and initiation of appropriate treatment is critical, although recognition of RA signs and symptoms in primary care remains a challenge. The study's purpose was to evaluate the sensitivity and specificity of the GALS (gait, arms, legs & spine) examination when used by family physicians and nurse practitioners to screen for RA signs and symptoms.

Methods: Participating healthcare professionals (HCP), including 2 rheumatologists, 3 family doctors (FDs) and 3 nurse practitioners (NPs), were trained to perform the GALS exam and by viewing an instructional DVD and attending a hands-on workshop. One week after training, HCP performed the GALS on 41 study participants recruited through local rheumatology practices. Twenty participants had previously been diagnosed with RA. The remaining 21 participants did not have RA. Study participants were divided into two groups (A & B) such that approximately half of the participants in each group had RA. Group A participants were assessed by 1 rheumatologist, 1 FD and 2 NPs while Group B participants were assessed by 1 rheumatologist, 2 FDs and 1 NP. HCPs recorded abnormalities of the gait, arms, legs and spine and whether a diagnosis of RA was suspected. HCP were blinded to participants' medical history and were unaware that any of the study participants had previously been diagnosed with RA. HCP were told that the primary objective of the study was to investigate their level of agreement with rheumatologists. Sensitivity and specificity were calculated for each HCP to determine the ability of the FDs and NPs to screen for RA signs and symptoms using the GALS when compared to the rheumatologists' screen on the study day.

Results: Findings of the FDs and NPs were compared with the rheumatologists' findings in their respective groups. When compared to the rheumatologists' GALS exam findings on the study day, sensitivity for each of the 3 FDs was 60%, 80% and 100%, and for the 3 NPs was 60%, 80% and 90%. Specificity for each of the 3 FDs was 82%, 82% and 70%, and for the 3 NPs was 100%, 80% and 73%.

Conclusion: These results suggest that the GALS exam may be a useful screening tool for RA when used by FDs and NPs working in the primary care setting. Differences in level and type of clinical experience may contribute to the variations observed. The merits of introducing the GALS exam into primary care curricula should be explored.

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Outcomes of Infliximab Treatment in Canadian Rheumatoid Arthritis Patients of Different Age Groups

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Objective: Rheumatoid Arthritis (RA) is a chronic inflammatory disease with an average age of onset of ~55 years. Given that aging affects many biological processes, including immunological, the patient profile and response to anti-TNF treatment may differ with age. The objective of this real-life observational Canadian study was to assess the influence of age on baseline characteristics as well as on response to treatment with Infliximab.

Methods: Data for this analysis were obtained from BioTRAC, an observational prospective registry of adult RA patients initiated on treatment with Infliximab since 2002 and managed as per routine care. Patients enrolled were biologic-naïve or had initiated treatment with a biologic for a period of < 6 months prior to enrolment. In this analysis, 545 RA patients were included who were enrolled by June, 2011 and had at least one follow-up assessment. Patients were divided into 5 subgroups based on age at time of enrollment: ≤ 40 , 41-50, 51-60, 61-70, and > 70 years.

Results: Among the 545 patients comprising the study cohort, 14% were ≤ 40 years of age, 18% were 41-50 years-old, 31% were 51-60 years of age, while 23%, and 14% of patients belonged to the 61-70, > 70 age subgroups, respectively. At baseline, a significantly higher proportion in the older subgroups were RF+ (60%, 68%, 79%, 77%, and 79% of patients, respectively) and of female gender (74%, 69%, 71%, 83%, 84% of patients, respectively). Furthermore, significant between-group differences were observed in disease duration ($P<0.001$), HAQ ($P<0.001$), ESR ($P<0.001$), CRP ($P=0.021$), and DAS28-ESR ($P=0.003$) with disease duration and severity increasing with age. However, morning stiffness, TJC, SJC, SGA, PGA and DAS28-CRP were comparable between-groups. Upon 6-months of treatment, remission achievement was significantly higher in younger sub-

groups with 41%/27%/15%/17%/13% of patients achieving DAS28-ESR remission, 31%/36%/16%/17%/17% achieving DAS28-CRP remission, 20%/27%/5.4%/11%/13% achieving SDAI remission, and 15%/13%/4%/6%/5% of patients achieving ACR/EULAR remission in the ≤40, 41-50, 51-60, 61-70, and >70 patient subgroups, respectively. However, regardless of age group, all parameters studied (morning stiffness, HAQ, ESR, CRP, TJC, SJC, SGA, PGA, SDAI, DAS28-ESR, and DAS28-CRP) significantly ($P < 0.05$) improved over time upon treatment with Infliximab for 36-months, with the exception of ESR in the >70 years-of-age subgroup.

Conclusion: The results of this observational study have shown that Infliximab is effective in improving outcomes in rheumatoid arthritis over a three year period, regardless of age. However, significant variation in patient baseline characteristics and remission rates within various age groups is observed.

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Cannabinoid Use in Fibromyalgia is Associated with Male Gender, Opioid Use and Drug Seeking Behaviour

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Objective: Without an ideal treatment and with only three drugs having FDA approval, fibromyalgia (FM) patients may seek treatments outside mainstream medicine. Although the endocannabinoid system plays a role in pain mechanisms, there is limited information of effect of cannabinoids in chronic pain or FM. Although not currently recommended for treatment of FM, it is possible that patients may be using cannabinoids, with prevalence of use unknown and requiring examination.

Methods: We have examined cannabinoid use, licit and illicit, in FM labeled patients attending a tertiary care pain clinic, between January 2005 and December 2010, by chart review. Demographic and clinical information, mental health status as assessed by a psychologist, and medication use were documented. Univariate comparisons of continuous variables were made using Student's t-tests, and for categorical variables chi-squared tests were used.

Results: 457 patients, mean age 47 ± 11 years, 40 males, 308 (67%) unemployed and 165 (36%) on disability were evaluated. Three hundred and two (66%) retained the diagnosis of FM, and 155 (34%) were assigned some other primary diagnosis (140 other medical diagnosis, 65 current serious mental health disorder, 51 with both). FM patients had a mean pain VAS of 6.4 and a Fibromyalgia Impact Questionnaire score of 65.7, and were using an average of 1.9 prescription medications for treatment of symptoms. Cannabinoids were used by 59 (13%) patients, 46 (78%) used illicit marijuana, 14 (24%) used prescription cannabinoids (13 nabilone, 1 dronabinol) and 1 used both. Cannabinoid users vs. non users were more likely to be male 22% vs. 7% ($p=0.0006$), be taking opioids 47% vs. 29% ($p=0.007$) and demonstrate drug-seeking behaviours 32% vs. 4% ($p=0.009$). There was a tendency for cannabinoid users to suffer from more unstable current mental illness and also to be unemployed.

Conclusion: Cannabinoids were used by 13% of all patients labeled FM, and 1/3 of all males. Illicit marijuana was the most used cannabinoid. Concomitant opioid use and drug seeking behaviour raises concerns regarding the underlying motive for use. Although cannabinoids may possibly offer a therapeutic effect for pain relief, caution regarding any recommendation for use should be exercised until there is more evidence regarding psychological health and association with substance abuse.

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The Care Gap in Management of Fibromyalgia: A Needs Assessment Prompting the Development of Clinically Relevant Guidelines for the Diagnosis, Management and Follow-up of Patients

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Objective: Clinicians remain challenged regarding the clinical care of fibromyalgia (FM) patients. New criteria with the elimination of the tender point examination, the absence of a positive diagnostic test and lack of an ideal treatment nurtures insecurity. There is a need for direction in the diagnosis and care of FM patients. Our objective was to perform a needs assessment regarding challenges in the management of these patients and formulate these needs into questions that could drive a literature search as the first step towards development of clinically useful and applicable guidelines.

Methods: 139 healthcare professionals treating patients with FM from various disciplines including physicians (rheumatologists, family physicians, pain specialists, neurologists, psychiatrists and physiatrists), pharmacists, nurses, and psychologists convened in workshop settings in eight regions of Canada. Following a formal presentation of current concepts in FM, open discussion followed with recording of commentary. Following review of all recorded discussions, a needs assessment was formulated as a series of questions and is presented as a descriptive analysis.

Results: Four major domains of clinical challenge were identified: 1. Insecurity in confirming a diagnosis, often requiring confirmation by a specialist which might be patient or payer driven. Concerns exist regarding misdiagnosis with resulting excessive investigation. 2. A poor understanding of pain mechanisms and a perception of knowledge gap especially in primary care. 3. Treatment choices are confusing in the context of multiple symptoms, voluminous anecdotal literature and the perception that pharmacologic recommendations may be largely industry driven. Non-pharmacologic treatments, although recommended, are often poorly accessible and costly, with limited direction regarding treatment combinations. 4. Ideal follow-up is unknown without guidance regarding ideal outcome measures and frequency of follow-up. Physician biases are emphasized with the perception that FM patients are "difficult", requiring prolonged clinical time, and often demonstrate suboptimal treatment responses.

Conclusion: There exists considerable uncertainty and an important care gap in the understanding, diagnosis and management of FM. Updated clinically applicable and comprehensive guidelines that address these issues are required to provide better care for patients with FM.

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Preliminary Results for the Development of Clinically Applicable Canadian Guidelines for the Care of Patients with Fibromyalgia

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Objective: To develop Canadian evidence-based guidelines for the evaluation, diagnosis and management of persons with fibromyalgia (FM), taking into account advances in the understanding of the pathogenesis of FM and new diagnostic criteria.

Methods: A needs assessment generated key questions regarding the diagnosis and management of FM following structured consultation with 139 healthcare professionals from different disciplines across Canada. Each question was used to drive a literature search to identify evidence, graded according to the classification system of the Oxford Centre for Evidence Based Medicine, supporting a recommendation. Recommendations were reviewed by an expert panel to determine applicability to clinical practice.

Results: Sixty recommendations pertaining to the identification, evalua-

tion and management of persons with FM, incorporating new clinical concepts of FM were drafted. The essence of the recommendations are as follows: FM represents a composite of symptoms, with body pain present as the pivotal symptom. There is a spectrum of severity which associates with functional outcome, with variability of symptoms over time. The diagnosis of FM is clinical, does not need specialist confirmation, and requires only limited laboratory testing. A physical examination will exclude some other condition as a cause for body pain, but does not confirm the diagnosis of FM. There is no confirmatory clinical or laboratory test and excessive testing is strongly discouraged. Treatments should be multimodal with incorporation of non-pharmacologic and pharmacologic strategies, with focus towards reduction of symptoms and functional maintenance. Patients should be active participants in health care. In the absence of an ideal pharmacologic treatment, agents that affect more than one symptom are desirable. Lower doses of medications than those used in clinical trials, as well as combination of medications may facilitate adherence to treatment recommendations by reducing the frequency of side effects related to drugs. Emphasis on proper lifestyle practices, periodic assessment of the need for continued medication and evaluation of efficacy and side effect of ongoing treatments is recommended. New symptoms should be evaluated according to good clinical practice to exclude a new illness without summarily attributing all symptoms to FM.

Conclusion: These new Canadian guidelines for care of patients with FM should provide the health community with more confidence in the global care of these patients and should improve patient outcome.

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Late Versus Early Development of Lupus Nephritis

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Objective: A recent longitudinal observational study of an inception cohort, showed that of 107 patients who developed lupus nephritis, 48(45%) did so after the first three years. 9% of these patients developed lupus nephritis after 10 years. In this study we compare the baseline characteristics of patients who developed early nephritis (within 3 years of entry into the clinic) with those who developed late nephritis (after 3 years) to determine predictors of late development of lupus nephritis.

Methods: Inception patients seen in clinic within one year of diagnosis of SLE were selected from a single centre cohort followed in an observational cohort study. Lupus nephritis was defined as sterile hematuria and/or pyuria, granular casts, proteinuria ($>500\text{mg}/24\text{hr}$), or elevated serum creatinine (defined as greater than $120\mu\text{mol}/\text{l}$) on two or more consecutive visits, or dialysis, transplant or WHO renal biopsy $\geq$ class 2. We identified patients who developed lupus nephritis after entry into the cohort. Early lupus nephritis was defined as those developing nephritis in the first 3 years. Patients developing lupus nephritis after three years were defined as having late lupus nephritis. The comparisons were done using T-test and chi-square test. Included in the model were sex, age at SLE diagnosis, race, SLEDAI-2K, steroids, antimalarial, immunosuppressant, complement and DsDNA at inclusion.

Results: 107 patients were identified from an inception group as having developed lupus nephritis in the course of their follow-up. This group was comprised of 89% female, 80% Caucasian. Mean (SD) age at SLE diagnosis was 34(13.9), mean (SD) SLEDAI -2K was 8.1 (7.4) and mean (SD) SCR was 73.8(16.9). 51.0% had low complement and 49.5 % had DsDNA. From this group, 59(55%) developed lupus nephritis within the first three years (early), while 48(45%) developed nephritis after three years. (Late). Comparison between early and late groups at first clinic visit showed that age at SLE diagnosis was younger in the early group Mean(SD) =30.9(12.2) compared to the late group.

Conclusion: Among patients who developed Lupus Nephritis after three years, age at diagnosis was the only significant contributor. Thus ongoing observation regarding renal involvement in SLE is important in all patients.

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Comparative Performance of Autoantibody Immunoassays in the Screening and Diagnosis of Systemic Autoimmune Rheumatic Disease (SARD) - Experience of a Tertiary Hospital Laboratory

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Objective: We evaluated the comparative performance and diagnostic accuracies of several diagnostic testing approaches and algorithms (I-VI) for the screening and diagnosis of SARDS in a large tertiary hospital laboratory: 1. Universal testing strategy: (I) ANA-IF only, (II) ENA (ELISA), (III) ENA (MPBA). 2. Sequential Testing strategy: ANA-IF (+) with reflex ENA/DNA (IV) All cases, (V) ANA Titre ≥ 160 , (VI) titre ≥ 320 .

Methods: 373 eligible patients had autoimmune tests performed (12/2009 - 8/2010) with identifiable clinical information for disease categorization and residual frozen blood samples for the completion of all autoimmune assays evaluated in the study.

Results: Screening Tests for SARDS: Test sensitivity, specificity, PPV and NPV (%) respectively for (I) ANA-IF (85.6 $\pm$ 3.5, 21.2 $\pm$ 3.0, 33.4 $\pm$ 3.5, 76.1 $\pm$ 5.6), (II) ENA-ELISA (91.5 $\pm$ 3.0, 50.5 $\pm$ 3.1, 46.2 $\pm$ 4.1, 92.8 $\pm$ 2.6); (III), ENA/DNA-MPBA (83.1 $\pm$ 3.7, 58.4 $\pm$ 3.6, 48.0 $\pm$ 3.4, 88.2 $\pm$ 2.6). ANA+ with reflex ENA/DNA (IV) All cases (80.5 $\pm$ 3.7, 62.7 $\pm$ 3.0, 50.0 $\pm$ 3.7, 87.4 $\pm$ 2.4), (V) ANA Titre ≥ 160 (28.0 $\pm$ 4.0, 84.3 $\pm$ 2.2, 45.2 $\pm$ 5.6, 71.7 $\pm$ 2.7) (VI) ANA Titre ≥ 320 (22.0 $\pm$ 3.8, 90.2 $\pm$ 2.0, 51.0 $\pm$ 7.0, 71.4 $\pm$ 2.6). Supplementary Test for SARDS: Comparative performance for ENA-ELISA and ENA/DNA-MPBA (AUC) respectively: (A1) SLE (78%,79%), (A2) Sjogren Syndrome (83%,74%), (A3) Dermatomyositis/Polymyositis (75%,64%), (A4) Scleroderma (60%,73%), (A5) MCTD (74%,71%).

Conclusion: To consider alternative universal screening strategy to replace ANA-IF, clinical laboratories should evaluate the discriminating performance of ENA assays. Key discriminate power of ENA is driven by specific ENA components seen in SARD subtypes and is kit/reagent dependant. A more sensitive ENA (ELISA) method can safely replace ANA (IF) as a screening method and offers more optimal test specificity (less false positivity). This is of particular importance in a hospital testing environment because of the high prevalence of non-SARD immune diseases. Sequential testing strategy (ANA+ with reflex ENA/DNA testing) will result in poor performance, i.e. may increase diagnostic yield in some, but will create diagnostic inaccuracy in many. Salvaging strategies for this approach include: (1) Adoption of a universal ENA/DNA tests strategy for ANA positive cases. (2) Consider low titre with ENA/DNA positivity as true positive cases.

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Demonstration of the Use of Electronic Medical Records to Study Drug Survival Analysis of Anti-TNF- α Therapies in Patients with Rheumatoid Arthritis in a Community-based Rheumatology Practice

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Objective: Biological therapies are commonly used in the treatment of Rheumatoid Arthritis (RA). In recent years, drug survival rates have become useful measures of the effectiveness and safety of these therapies. Survival analyses have found widespread application to rheumatologic drug studies. The survival analysis serves to examine the duration of a particular therapy before its side effects or lack of efficacy require switching to a different treatment. The purpose of this study is to demonstrate how to design and carry out a survival analysis, of anti-TNF agents in patients with RA, in a community rheumatology practice by extracting database information from an electronic medical record.

Methods: All patients with RA, as defined by the 1987 American Rheumatism Association criteria, started on any biologic therapy including infliximab, etanercept, adalimumab, tocilizumab, abatacept, golimumab, anakinra, certolizumab or rituximab before July 15, 2011, at two community rheumatology practices at Credit Valley Rheumatology were included. Patient electronic medical records (EMR) were accessed using PS Suite by Practice Solutions Software Inc. The parametric search function within PS Suite was used to identify patients who met the inclusion criteria. Specifically, patients with ICD-9 code 714.0 and/or "rheumatoid arthritis" and/or RA listed in their EMR current problems field were identified. In addition, the electronic search term identified which of these EMR included any of the biologics being studied in the patient's current medications. For these identified patients, more detailed demographic data was extracted from EMR regarding age, gender, disease duration, rheumatoid factor status, length of each therapy, the number of previous DMARDs tried and the date and reason for termination of any therapies. Drug survival of each biologic agent was calculated by Kaplan-Meier survival analysis and the factors associated with longer/shorter drug survival were identified.

Results: Of the 5274 patients in the practice, 2321 patients with RA were identified according to the search parameters specified above, with 162 receiving etanercept, 44 adalimumab, 37 infliximab, 26 tocilizumab, 20 abatacept, 10 golimumab, 3 anakinra, 7 certolizumab, and 9 rituximab. Drug survival analysis data and prognostic indicators are reported in the attached graphs.

Conclusion: This study demonstrates that drug survival information for RA patients on biologic therapies can be easily extracted from electronic medical records, in a community practice. This data can be modeled to analyze patient populations and medical interventions. The results can be used to help maximize clinical outcomes and achieve the longest drug survival for each biologic therapy.

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Au Coeur de L'Arthrite Psoriasique: A Study On The Cardiovascular Comorbidities Of Psoriatic Arthritis

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Objective: 1: To evaluate the prevalence of traditional cardiovascular risk factors among Psoriatic Arthritis (PsA) patients in the rheumatology outpatient clinic at Hôpital Maisonneuve Rosemont (HMR). 2: To evaluate whether cardiovascular risk factors are assessed upon diagnosis of PsA and whether these risk factors are followed-up by the rheumatologists.

Methods: The SPARCC database from 2008 to 2011 was used to identify "High Risk" patients with Psoriatic Arthritis on the basis of the 10-year general cardiovascular Framingham risk score Cox logarithm. BMI was used in the case of patients for whom the lipid-based Framingham risk score could not be calculated. Patients' charts were then reviewed to document the rheumatologists' follow-up for cardiovascular risk factors. A consultation referral to cardiology, internal medicine or the lipid clinic, or a prescription for antihypertensive or lipid lowering drugs, the patient's BMI or the order for a lipid screening lab were searched.

Results: The cohort studied was outpatients with a PsA diagnosis from the Rheumatology division at HMR. Sixty-eight patients were eligible for the purpose of this study. Amongst those 68 patients, 39 had a FRS of 20% or more resulting in 57.4% of the patients being at "High Risk" for cardiovascular disease during the following 10 years (C.I.: 45.6-69.1%). The overall management of the risk factors by any physician, identified by searching the SPARCC database for the patient's medications revealed that 19 "high risk" patients were taking lipid lowering drugs, as recommended by the Canadian Guidelines. The remaining 20 "high risk" patients were either treated for hypertension only or not managed at all.

Conclusion: The present study indicates that many psoriatic arthritis patients in this cohort were at high risk for general cardiovascular events and that less than half of these patients were appropriately managed.

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Depression in Psoriatic Disease: Prevalence and Associated Factors

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Objective: A high rate of depression is reported in several studies of psoriasis patients, ranging from 19.2 to 62%. Psoriatic arthritis (PsA) affects approximately 30% of patients with psoriasis and has the potential to cause severe joint damage. Research into the prevalence of depression in PsA patients, and the contribution of joint disease to depression in psoriatic disease, is limited. The objectives were: 1) To determine the prevalence of depression in PsA patients and identify associated demographic and disease-related factors. 2) To determine if there is a difference between patients with PsA and those with psoriasis without PsA (PsC).

Methods: Consecutive patients attending PsA and PsC clinics were assessed for depression through administration of the Hospital Anxiety and Depression Scale (HADS). Patients with PsA satisfied CASPAR criteria and those with PsC had dermatologist confirmed psoriasis and PsA excluded by a rheumatologist. The severity of skin manifestations was assessed by the Psoriasis Area and Severity Index (PASI) and the severity of arthritis through active and damaged joint counts. Patients were also asked to complete a number of questionnaires assessing their health and quality of life. ANOVA, T-tests, and Chi-squared tests were used to compare the prevalence of depression between patient cohorts and determine factors associated with depression.

Results: To date, 289 patients have completed the HADS (207 PsA, 82 PsC). The prevalence of depression among PsA and PsC patients is 20.4% and 8.5% respectively ($P=0.02$). Factors associated with depression include unemployment ($P=0.01$), active joint count ($P=0.04$), and all patient-reported quality of life measures. These measures include the Health Assessment Questionnaire ($P\leq 0.0001$), Patient Global Assessment ($P\leq 0.0001$), Fatigue Severity Scale ($P\leq 0.0001$), and the Dermatology Quality of Life Index ($P=0.03$). A higher PASI was not associated with an increase in depression and was similar among the depressed and non-depressed groups ($P=0.58$).

Conclusion: The rate of depression in PsA patients is higher than previously reported and more common than in patients with PsC. Of the two objective measures of disease severity analyzed, active joint count and PASI, only the active joint count was associated with an increase in depression. Patient-reported pain, disability, fatigue, and reduced overall health, were strongly associated with increased depression. These results indicate the importance of active joint disease, and the importance of the patients' perceptions of their own health and functioning, when attempting to address depression in patients with PsA.

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Prevalence of Malignancy in a Cohort of Patients with Psoriatic Arthritis

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Objective: The risk of developing malignancy and its progression to cancer significantly increase with arthritis severity and progression (5-7) or possibly the treatment with immunosuppressives (8-10). The aim of this analysis was to compare the prevalence of different malignancies in patients with Early (EPsA) and Established PsA, defined as < 2 and ≥ 2 years from diagnosis, respectively.

Methods: Patients were recruited prospectively from a rheumatology clin-

ic specializing in PsA. Disease severity was assessed using CRP, ESR, DAS28, PASQ, and the PASI score. The association of the treatment modalities with the prevalence of cancers was also analyzed.

Results: Eighty four patients with EPsA and 112 patients with Established PsA were included in this analysis with mean PsA duration of 1.0 and 5.6 years, respectively ($P < 0.001$). Mean age (48.0 vs. 49.7 years) and gender distribution (52.4% vs. 48.2% females) were comparable in both cohorts. However, patients with Established PsA were significantly younger at the onset of Psoriasis (38.7 vs. 34.1 years; $P = 0.030$) and PsA (47.9 vs. 44.3 years; $P = 0.037$). Among the 196 patients, 19 (9.7%) had a malignancy, of whom 14 (12.5%) belonged to the Established cohort and 5 (6.0%) to the Early cohort (OR (95%CI) Established vs. EPsA = 1.70 (0.79,3.66); $P = 0.148$). Three patients had two malignancies. The most frequently observed cancers were cervical (OR (95%CI) Established vs. EPsA = 6.4 (0.8,52.1); $P = 0.083$), bowel and lung (OR (95%CI) Established vs. EPsA = 0.24 (0.03,2.38); $P = 0.225$) cancer, occurring in 9 (4.6%), 4 (2.0%), and 4 (2.0%) patients, respectively. Multivariate logistic regression adjusting for the age of PSO diagnosis showed that the incidence of malignancy was significantly different between the two cohorts (OR (95%CI) Established vs. EPsA = 3.3 (1.1,10.0); $P = 0.039$). Baseline age, DAS28, PASI, duration of PsA symptoms, and age of PsA diagnosis were not significantly associated with cancer incidence. No treatment type was significantly associated with an increased rate of malignancy.

Conclusion: Overall, an increased prevalence rate of malignancies was observed in patients with Established vs. Early PsA. The total incidence of malignancies observed in our study was comparable to the one reported in patients from Toronto (11.2% vs. 10.2%), although with a different distribution of the most frequently seen cancer types.

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Parametric Survival Analysis as Well as Multi-State Analysis Confirms the Association between Human Leukocyte Antigen Alleles and the Development of Arthritis Mutilans in Patients with Psoriatic Arthritis
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Objective: Genetic factors may influence development of Arthritis Mutilans (AM), the most severe form of psoriatic arthritis (PsA). We conducted a case-only study to identify HLA alleles associated with development of AM in patients with PsA.

Methods: Data on the presence of AM were obtained from a large cohort. In this cohort plain radiographs of the hands, feet and spine are obtained at baseline and at 2-yearly intervals. The radiographs are scored using the modified Steinbrocker method. AM was defined as ≥ 5 joints with grade 4 damage. Data on the time when joints with grade 4 damage was first observed was obtained on 610 Caucasian subjects satisfying CASPAR criteria. HLA typing was performed by PCR-SSO. First, parametric survival analyses with interval censoring using a Weibull model adjusted for age at diagnosis of PsA and sex were conducted to identify HLA alleles associated with time to development of AM. This analysis however ignores the information provided by time of development of grade 4 damage in the first 4 joints. Therefore, a multi-state analysis that models the transition from no grade 4 damage to 1, 2, 3, 4 and finally ≥ 5 joints with grade 4 damage was conducted.

Results: The 610 subjects (58% males, mean age at diagnosis 36 years, duration of PsA 7 years at first visit) had a median of 3 radiographic assessments during a median follow up of 6.3 years. 97 (16%) subjects developed AM. The median time to development of AM was 1.3 years. Univariate survival analyses showed that HLA-B*27 and HLA-DQB1*02 alleles are associated with an increased hazard of developing AM whereas HLA-A*11 and -C*04 are associated with a reduced hazard. Multivariate analysis showed that HLA-B*27 (HR 2.14, $p < 0.01$) and -DQB1*02 (HR 1.80, $p < 0.01$) are independently associated with increased hazard whereas

HLA-A*11 (HR 0.36, $p = 0.03$) and -A*29 (HR 0.22, $p = 0.04$) are independently associated with reduced hazard of developing AM. Univariate multi-state transition analyses showed that HLA-C*01, -B*08, -B*27, -DQB1*02 increases risk of transition through each state whereas HLA-A*11, -C*03, -C*04 and -B*60 decreases risk. Multivariate multi-state transition analysis using a reduced common effects model confirmed that HLA-B*27 (RR 1.50, $p = 0.001$) and -DQB1*01 (1.42, $p = 0.001$) increases risk and HLA-C*03 (0.77, $p = 0.013$) decreases risk.

Conclusion: Survival analysis and multistate analysis suggests that HLA-B*27 and -DQB1*02 are associated with increased risk of developing AM in PsA.

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Predicting Progression from Oligoarticular to Polyarticular Juvenile Arthritis

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Objective: To determine whether early wrist or ankle involvement are risk factors for extension to a polyarticular course in a cohort of paediatric patients with an oligoarticular onset of juvenile arthritis (oligoJA).

Methods: This is a retrospective cohort study of children with oligoJA presenting to paediatric rheumatology clinics at the Universities of Saskatchewan and Manitoba from 1981 to 2010. OligoJA was defined as ≤ 4 joints at the first and 6 month visits. Risk factors for extension from oligoJA to polyarthritis (> 5 joints) by 2 and 5 years after diagnosis were modelled using logistic regression while controlling for sex, ANA status, and ever having used DMARDs, systemic corticosteroids, intraarticular corticosteroid injections, or biologic-based therapies. Time to extension was assessed using Cox proportional hazard analysis.

Results: 420 patients met eligibility criteria. 56% were female. The median time from disease onset to diagnosis was 136 days (IQR 56, 365); 15 patients in the logistic regression models extended by 2 years ($n = 280$, of which 5.4% extended) and 27 by 5 years ($n = 339$, of which 8.0% extended). At 2 years after diagnosis the odds of extension was 6.02 times higher (95% CI 1.56, 23.32) in those with initial wrist involvement than in those without, and at 5 years it was 3.43 times higher (95% CI 1.09, 10.81). The OR of extension in those with initial ankle involvement versus those without was 2.21 (95% C.I. 0.61, 8.01) at 2 years and 1.54 (95% C.I. 0.58, 4.10) at 5 years. Cox proportional hazard modelling failed to show a significant difference in time to extension with either early wrist or ankle arthritis.

Conclusion: This study independently confirms previous published findings that wrist arthritis in the first 6 months after diagnosis of oligoJA is a risk factor for extension. Unlike previous reports, we did not find an increased probability of extension in patients with early ankle arthritis. Patients with ankle or wrist arthritis in the first 6 months after diagnosis were not more likely to extend sooner than those without early involvement of these joints.

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Distinct Phenotypical Clusters in Childhood Inflammatory Brain Diseases: Implications for Diagnostic Evaluation

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Objective: The spectrum of childhood Inflammatory Brain Diseases (iBrainD) is rapidly expanding. Overlapping clinical presentations lead to

significant diagnostic uncertainty. However, early diagnosis and treatment are critical to prevent brain damage. The objective of this study was to identify distinct clusters of childhood IBrainD based on clinical, laboratory and imaging features at presentation in order to guide the diagnostic approach.

Methods: A single centre cohort study was performed with consecutive children up to 18 years of age who were diagnosed with an IBrainD from June 1989 to December 2010 and were enrolled in the BrainWorks cohort at The Hospital for Sick Children. Demographic, clinical, laboratory, neuroimaging and histologic data at diagnosis were collected. Latent class analysis was performed to identify clusters of patients based on key presenting features. Associations between the clusters and variables including demographic characteristics, diagnostic tests and diagnosis were determined.

Results: A total of 165 children (51% females, median age 8.3 years) with IBrainD were identified: 123 primary angiitis of the CNS (cPACNS), 11 secondary CNS vasculitis, 7 neuronal antibody syndromes, 6 post-infectious IBrainD and 18 other IBrainD (e.g. neurosarcoidosis). Three distinct clusters of children with IBrainD were identified based on key clinical and imaging features at diagnosis. Children in cluster 1 were significantly more likely to present with seizures, behaviour changes and cognitive dysfunction ($p < 0.0001$), while those in cluster 2 experienced vision abnormalities and ataxia ($p < 0.0001$). Paresis was the most common presenting feature in cluster 3 ($p < 0.0001$). Predominant MRI findings in clusters 1 and 2 were bilateral T2/FLAIR lesions ($p = 0.001$) and in cluster 3 were unilateral ischemic lesions ($p < 0.0001$). The clusters were associated with specific diagnoses and diagnostic test results: for example, children in cluster 3 were likely to have positive findings on angiography ($p < 0.0001$).

Conclusion: Children with IBrainD presented with distinct phenotypical patterns that are associated with specific diagnoses. This information should inform the development of a diagnostic classification for childhood IBrainD in the future. Based on the identified clusters, specific pathways of diagnostic evaluation are warranted.

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Best Practices for the Use of Administrative Health Data for Rheumatic Disease Research and Surveillance

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Objective: Administrative databases represent a tremendous resource for rheumatic disease surveillance and research; we aimed to develop best practice, consensus statements for their use in this regard.

Methods: 52 individuals with diverse expertise in the use of administrative data participated in a two-day workshop. Eight months prior, participants were organized into three working groups and conducted literature reviews on the following: case definitions; methods; and co-morbidity/outcomes. At the workshop, consensus techniques were used to create endorsed statements.

Results: Thirteen consensus statements were endorsed. Case definitions: Case definitions for rheumatic disease should be justified based on purpose, validity, and feasibility; validation studies should adhere to published guidelines on their conduct and reporting; and limitations of administrative data for case ascertainment should be acknowledged. Methods: Confounding by indication must be addressed; appropriate methods to address other common sources of confounding and bias should be used; exposure risk windows should be clearly defined and justified; and limitations of administrative data should be acknowledged. Comorbidity/outcomes: For osteoporosis, diagnostic codes should not be used alone because of low sensitivity. Hip fractures can be accurately identified using hospital discharge data, while fractures not requiring hospitalization can be identified by combining physician billing diagnoses and procedure codes. For vertebral fractures, additional research is needed. For cancer, exclusive of cancer registries, an algorithm with good sensitivity and excellent specificity should be chosen in a comparable population. Implications of an imperfect case definition should be discussed. For infections, hospitalization diagnoses can be used to ascertain serious bacterial infections. Current data

is not sufficient to recommend administrative data to identify opportunistic infections. For cardiovascular disease, hospitalization data can be used to ascertain acute myocardial infarction, but there are significant limitations for congestive heart failure. Administrative data can be used to identify kidney disease requiring dialysis. Current data do not support using hospitalization data to identify kidney disease as a co-morbidity or outcome.

Conclusion: Our recommendations are consistent with other recent guidelines including the ISPOR report and the EULAR Points paper to address specific needs of rheumatic disease biologics registries. Our standards address additional issues, including Canada-specific details. Ongoing work involves the dissemination of these statements, whose usefulness and implications extend beyond Canada's borders.

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Clinical and Serological Correlates of Systemic Sclerosis Sine Scleroderma: Findings from a Canadian Cohort

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Objective: Systemic sclerosis sine scleroderma (ssSSc) is a subtype of scleroderma without skin involvement. The objective of this study was to describe the clinical and serological features of a large cohort of ssSSc patients and compare them to those of patients with limited scleroderma (lSSc) and diffuse scleroderma (dSSc).

Methods: Data from the Canadian Scleroderma Research Group (CSRG) cohort database were extracted for comparative analysis. Subjects with ssSSc were defined as patients diagnosed with scleroderma by an expert rheumatologist but without any skin thickening or tightening. Descriptive statistics were used to describe the study subjects and to make comparisons between the ssSSc, lSSc and dSSc groups.

Results: There were 1291 patients in the CSRG registry at the time of analysis, of which 47 (3.6%) had ssSSc, 767 (59%) lSSc and 477 (37%) dSSc. Demographics - Mean age at disease onset and mean disease duration of the ssSSc group did not differ significantly from that of the lSSc and dSSc groups. However, the proportion of females in the 3 groups (96% ssSSc, 90% lSSc, 79% dSSc) was significantly different. Similarities of clinical features - The rates of Raynaud's phenomenon, telangiectasias and esophageal dysmotility were similar to those in the other 2 groups. The number and severity of gastrointestinal symptoms were slightly lower but not significantly different from those with lSSc and dSSc. The proportion of subjects with pulmonary hypertension was also similar in all 3 groups. Differences with lSSc and dSSc - In addition to modified Rodnan skin scores that were significantly different between the 3 groups (0 in ssSSc, 5 in lSSc and 18 in dSSc), ssSSc subjects were significantly less likely to have fingertip ulcers, compared to both lSSc and dSSc. As well, there were lower rates of interstitial lung disease in ssSSc than in lSSc and dSSc. Serology - The serological profile of ssSSc patients was closest to that of lSSc patients and different from that of dSSc patients. In particular, 50% of the ssSSc group was anti-centromere antibody positive, 7% were anti-topoisomerase antibody positive and 4% were anti-RNA polymerase III antibody positive.

Conclusion: This is one of the largest datasets of ssSSc reported to date. Overall, subjects with ssSSc were similar to other SSc patients with respect to vascular disease and serology. However, they appeared to have less extensive tissue fibrosis, in particular involving the skin and the lungs.

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Understanding Rural Rehabilitation Practice: Perspectives from Occupational Therapists and Physical Therapists in Rural and Remote British Columbia

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Objective: The health disparity between rural and urban residents, including higher rates of arthritis and other chronic diseases, combined with a shortage of health professionals requires innovative strategies to optimize the provision of health care services in rural regions. We aimed to understand the barriers and facilitators to rural rehabilitation practice from the perspectives of occupational therapists (OTs) and physical therapists (PTs) working in rural British Columbia (BC).

Methods: This study employed a purposive sample of OTs and PTs who lived and worked in rural (population < 15,000) BC. Participants were purposively selected according to practice type, role, and experience to obtain a range of perspectives. Using a semi-structured interview guide, participants were asked to identify what skills, knowledge and rehabilitation practices they considered unique to rural, barriers to primary health care, and educational preparation necessary for rural practice. Interviews were transcribed and analysed inductively using the methodological approach of interpretive description (ID) to extrapolate rural practice paradigms, develop a conceptual understanding of practice, construct interpretations and consider implications for education, practice and policy. Consistent with the ID methodology, we held a webcast with participants to review the findings and ensure our interpretations were grounded in the realities of rural practice.

Results: Of the 43 eligible therapists, 22 responded, and 19 were included in the purposive sample (13 PTs and 6 OTs). Rurality, or the features of the rural context including geography and access to resources/ services, had a substantial influence on participants' definition of health. Participants considered 'rural general practice' as a specialty and described 'stretching their roles' to their full scope of practice and building partnerships with individuals and community as strategies to mitigate resource shortages and meet patients' needs. Skills in reflective practice, self-directed learning, networking and collaboration were deemed essential to maintaining competency. Improving access to continuing education, mentoring and support from professional organizations were regarded as critical to recruitment and retention. Strategies for delivering care to residents with arthritis included group medical visits with visiting rheumatologists and culturally-sensitive community-based approaches to self-management.

Conclusion: This research illuminates the influence of the rurality on rehabilitation practice through the innovative ways rehabilitation services are delivered in rural areas. Understanding the context and the support necessary for rural OTs and PTs has the potential to assist recruitment and retention and inform training programs, ultimately enhancing arthritis care in rural communities and addressing health disparities.

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Rheumatoid Arthritis Patients and Their Unaffected First Degree Relative have a High Prevalence of Periodontal Disease

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Objective: Rheumatoid Arthritis (RA) and Periodontal Disease (PD) are chronic inflammatory conditions that share many pathogenic mechanisms. Both are associated with the HLA-DRB1 gene and cigarette smoking. Studies suggest an increased prevalence of PD in RA patients, particularly RA patients positive for Anti-Citrullinated Peptide Antibodies (ACPA). Unaffected First Degree Relatives (FDR) of RA patients may share genetic and environmental risk factors for RA and therefore they may represent a pre-RA state. The objective of this study was to determine the prevalence of PD in unaffected FDR of RA patients.

Methods: Patients were recruited from an outpatient tertiary care centre if

they met ACR criteria for RA. FDRs were deemed unaffected by RA after assessment by a rheumatologist. All subjects were interviewed using a questionnaire including joint symptoms, smoking history, alcohol consumption, medical history, family history of RA, and dental hygiene. Surrogate markers for PD included bleeding gums and tooth loss. ACPA were measured using Anti-CCP2 ELISA (Euroimmune™).

Results: 75 RA patients (mean age 59.41, 73.3% female) and 35 FDR (mean age 54.13, 68.6%) were recruited ($p>0.05$). Both RA patients and FDR had high rates of smoking (61.1% and 55.6% respectively, $p>0.05$). There were also no differences found in dental hygiene practices (brushing and flossing). Prevalence of tooth loss was high in both groups: 60% in RA patients and 50% in FDR ($p=0.4245$). There was no difference in prevalence of bleeding gums (27% in RA patients and 25% in FDR; $p=1.0$). As expected, smokers were more likely to have tooth loss than non-smokers (OR 2.84 [95% CI: 1.06, 7.60] in RA patients and OR 12.25 [95% CI: 2.54, 59.0] in FDRs). Prevalence of bleeding gums was not different in smokers and non-smokers. None of the FDRs were ACPA positive. The ACPA positive RA patients were not at increased risk of tooth loss (OR 0.45; 95% CI: 0.13, 1.57) nor bleeding gums (OR 0.64; 95% CI: 0.2, 2.06).

Conclusion: RA patients and their unaffected FDRs had a high prevalence of cigarette smoking and PD (>50%). Smokers were at high risk of PD; however, ACPA did not appear to increase the risk of tooth loss or bleeding gums in RA patients.

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Effectiveness of Different Biologic Agents at Improving Physical Function: A Systematic Review and Meta-Analysis

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Objective: Uncontrolled Rheumatoid arthritis (RA) leads to joint damage and long-term disability. The Health Assessment Questionnaire Disability Index (HAQ) is a validated measure of physical function that predicts disability. Biologic drugs improve function in RA patients; however, the magnitude of the effect of the different biologic agents is unclear. The objective of this study is to determine the effectiveness of different biologic drugs at improving physical function as measured by a decrease in HAQ score.

Methods: A systematic review and meta-analysis of randomized, double-blind trials of biologic agents for the treatment of RA (by ACR criteria) was conducted. Trials were included if patients were HAQ scores between subgroups. $\Delta > 15$ years old and HAQ scores were reported at baseline, 6 and/or 12 months. We searched PubMed, EMBASE and the Cochrane Library. Quality of trials was assessed by the Cochrane bias assessment tool and the Jadad score. The effect measure was the difference from baseline in the mean change in HAQ (Δ HAQ) at 6 or 12 months in the biologic group compared to the control group (placebo, disease modifying anti-rheumatic agent and/or other biologic). HAQ scores ranged from 0 to 3 and the minimal clinically important difference (MCID) was considered 0.22. Meta-analyses were analyzed via the random effects model and ANOVA tests were performed to assess similarities in the HAQ scores between subgroups.

Results: Twenty-seven trials were included in the meta-analysis comprising 12,998 patients and 10 different biologic agents (adalimumab, certolizumab, etanercept, golimumab, infliximab, abatacept, rituximab, tocilizumab, anakinra and fostamatinib). Biologics had a 0.251; 95% CI (0.291, 0.212) greater decrease in HAQ scores compared to controls, which met MCID. Subgroup analysis revealed that the difference in Δ HAQ was -0.266 (-0.325, -0.207) for anti-Tumour Necrosis Factor- α (anti-TNF) agents. This was significantly higher than the non-Anti-TNF subgroup ($p < 0.0001$), where the difference was -0.224 (-0.276, -0.173). Adalimumab, certolizumab and rituximab also had greater differences in Δ HAQ compared to the other biologic agents.

Conclusion: Biologic agents are effective at lowering HAQ by the minimal clinically important difference. Anti-TNF agents were found to be

more effective than non-anti-TNF agents, but the magnitude of the effect may not be clinically significant.

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Real-Life Effectiveness of Infliximab in the Treatment of Ankylosing Spondylitis over 3 Years: The Canadian Experience

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Objective: Ankylosing Spondylitis (AS) is a chronic inflammatory disorder affecting as much as 1% of the general population. The efficacy of Infliximab in the management of AS has been demonstrated in several controlled clinical trials with limited follow-up periods. Longitudinal observational studies assessing real-life effectiveness of anti-TNF agents are essential in order to demonstrate the true benefits. The objective of this study was to assess in Canadian clinical practice the 36-month outcomes in patients with AS treated with Infliximab.

Methods: The data for this analysis were obtained from BioTRAC, an observational prospective registry of adult AS patients initiated on treatment with Infliximab since 2005 and managed as per routine care. Patients enrolled were biologic-naïve or had initiated treatment with a biologic for a period of < 6 months prior to enrolment.

Results: A total of 204 AS patients who had at least one follow-up assessment were included in this analysis, with a mean age of 46 years and mean disease duration since diagnosis of 10.6 years. Among these, 148, 83, and 46 had a 12-, 24-, and 36-month assessment, respectively. At the time of enrollment in the registry, mean (SD) patient parameters were: C-reactive protein (CRP) = 1.7 (1.9) mg/dL, erythrocyte sedimentation rate (ESR) = 26.9 (20.5) mm/hr, morning stiffness = 75.9 (39.3), health assessment questionnaire (HAQ) = 1.1 (0.6), physician global assessment of disease activity (PGA) = 67.2 (18.1), BASDAI = 6.5 (2.1), BASFI = 6.2 (2.4), and ASDAS = 3.8 (0.9). By 6 months of treatment significant improvements ($P < 0.05$) were observed in all clinical and patient outcome parameters studied, which were sustained over 36 months of treatment. By 6, 12, 24, and 36 months 58%/ 68%/ 76%/ 84% and 30%/ 38%/ 48%/ 45%, achieved Clinically Important Improvement in ASDAS ($\Delta \geq 1.1$) and ASDAS Major Improvement ($\Delta \geq 2.0$), respectively. The proportion of patients with very high disease activity (ASDAS > 3.5) decreased from 64.2% at baseline to 7.9% at 36 months.

Conclusion: The results of this Canadian, longitudinal, real-life observational study demonstrate that treatment with infliximab over three years is effective in reducing symptom severity and improving outcomes in patients with ankylosing spondylitis.

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Vitamin D Receptor Polymorphism rs2228570 (FokI) in North American Natives with Rheumatoid Arthritis and Their Unaffected First Degree Relatives

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Objective: North American Natives (NAN) have high prevalence rates for rheumatoid arthritis. Our previous studies of a Cree/Ojibway population in Central Canada have shown an early age of onset, high prevalence and titers of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) and shared epitope alleles in the background population. 25 OH Vitamin D (VitD) has immune effects of potential importance to RA pathogenesis and low serum levels have been associated with RA and disease activity in other populations. We sought to examine association of the

RS2228570 (FokI) polymorphism of the VitD receptor gene with RA susceptibility in the NAN population.

Methods: We tested NAN RA patients ($n=458$) and unrelated controls without autoimmune disease ($n=715$) were tested for the RS2228570 (FokI) single nucleotide polymorphism of the vitamin D receptor gene. The genotyping data were analyzed using genotypic (DD vs Dd vs dd), allelic (D vs d), dominant (DD, Dd vs dd), and recessive (DD vs Dd, dd) models.

Results: The minor allele frequency in the unaffected control group was 0.43. Significant differences between affected RA patients (90/240/118) and unaffected controls (157/307/241) were found using the genotypic model (ChiSq 11.83; $p=0.0027$). Using an allelic model, there was no significant difference between the RA patients and controls (OR 1.12 $p=NS$, CI 0.95-1.32). Analysis using the dominant model was significant (RA=330/118 vs Controls=464/241 OR 1.45 $p=0.006$ CI 1.12-1.89). No interactions were seen between the presence of ACPA, RF and VitD receptor polymorphisms in the RA population.

Conclusion: The RS2228570 (FokI) VitD receptor polymorphism is associated with RA in the NAN population. Since VitD is important in maintaining dendritic cell tolerance, polymorphisms of the VitD receptor may contribute to loss of self tolerance in RA.

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Synovial Fluid Examination for Crystals. A Quality Assurance Program Which Has Improved Reliability

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Objective: To improve the quality and reliability of synovial fluid (SF) examination for crystals in routine clinical practice. For the patient with possible crystal-induced arthritis, the assessment of their SF is the key investigation which allows establishment of a definitive diagnosis. An incorrect synovial fluid analysis report (particularly a false positive report of urate) could result in life-long inappropriate drug therapy.

Methods: Under the auspices of the Royal College of Pathologists of Australasia Quality Assurance Programs, a SF QAP has been operating for 12 years (ongoing), mainly throughout Australia and New Zealand but also to Singapore and Malaysia. SFs donated by patients are stored at -80°C. After thawing, plastic capillary tips containing 25 microlitres SF are distributed by post/courier in approved safety packs to the laboratories twice per year. Each survey contains 3 different SFs and all laboratories receive the same SFs, allowing valid comparison between laboratories. In addition, a DVD/CD of a microscopic examination of up to 5 SFs is distributed each year, followed by the same DVD/CD with commentary highlighting appropriate methods and potential pitfalls. A yearly workshop is also held at different locations throughout Australasia.

Results: Over the 12 years of the program the number of participating laboratories increased from 121 in 1999 to 134 in 2011. Correct reporting of CPPD crystals showed a trend towards greater accuracy over the 12 years. Because real SFs were used, the difficulty of correct interpretation varied greatly between SFs. In 2011 the sensitivity for detection of crystals, when only one type of crystal was present in each SF, was: urate 95%, CPPD 82%. For SFs containing both urate and CPPD, sensitivity for urate remained high (83% and 99%) but sensitivity for CPPD was low (20% and 33%). The value of the teaching DVDs and workshops was not measurable in terms of diagnostic accuracy but the educational activities were repeatedly rated highly by participants.

Conclusion: Quality assurance of SF examination, using real fluids donated by patients, is feasible across a large region and has resulted in an improvement in test results which hopefully reflects greater accuracy in assessment of routine clinical specimens.

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A Serological Storm

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Objective: 1. To describe a patient with untreated Hepatitis C presenting with a unique autoantibody profile. 2. To highlight the concept of Hepatitis C being a non-specific activator of the immune system and having the potential to cause a “serological storm”. 3. To highlight the importance of Hepatitis C screening in the workup of rheumatic diseases.

Methods: We describe a patient presenting with a sensory polyneuropathy and a flurry of autoantibodies leading to the diagnosis of Hepatitis C. Case: A 56-year-old man was referred to the rheumatology clinic for evaluation of foot paresthesias and constitutional symptoms in the setting of numerous positive autoantibodies.

Results: Review of systems was unremarkable; no sicca, mucocutaneous ulcers, photosensitive rash, Raynaud’s phenomenon, gastroesophageal reflux, chest pain or dyspnea. Physical exam revealed hepatosplenomegaly and a blanchable macular rash over the thenar and hypothenar eminences. There were no mucocutaneous findings consistent with connective tissue disease or vasculitis. There were no swollen joints, but he had tender proximal interphalangeal (PIP) and carpometacarpal (CMC) joints. Neurological examination revealed a wide-based gait and sensory deficit in the toes. Laboratory investigations revealed the following: hemoglobin 102 g/l, lymphocytes $3.6 \times 10^3/\text{mm}^3$. Fasting glucose, liver enzymes, thyroid function, creatinine, and urinalysis were normal. VDRL was negative. Autoantibody analysis: positive antinuclear antibody (ANA) 1:160 (nucleolar pattern). ELISA revealed positive anti-dsDNA, anti-Sm, anti-RNP, anti-Ro/SSA, anti-La/SSB, anti-Jo-1, and anti-Scl-70 autoantibodies. Both cANCA/PR-3 and pANCA/MPO were strongly positive (> 500 AAU/ml; normal < 20 U/ml). Cryoglobulins were less than 1% and repeat testing showed a cryocrit 0%. Rheumatoid factor level was 12 (N <10). Complements and ESR/CRP were normal; there was diffuse hypergammaglobulinemia. Nerve conduction studies (NCS) and electromyography (EMG) showed a sensorimotor polyneuropathy. Hepatitis C antibody was positive, Genotype 1 and RNA PCR was 1.69 E6 IU/mL .

Conclusion: Our patient’s case is unique with respect to his exact autoantibody profile in the absence of clinically significant rheumatic disease. This case illustrates the importance of interpreting autoimmune serology only in the appropriate clinical context. Conversely, if the workup of rheumatic complaints reveals multiple autoantibodies, it is prudent to consider untreated Hepatitis C infection in the differential diagnosis.

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Novel Use of Botulinum Toxin Type A to Improve Active Flexion and Function Post-metacarpophalangeal Joint Arthroplasty in Juvenile Idiopathic Arthritis

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Case Report: Objective: A 50 year-old female with juvenile idiopathic arthritis (JIA) presented with hyperextension and abduction at the 5th metacarpophalangeal (MCP) joint, resulting in loss of normal function. Functional losses persisted after arthroplasty. Standard treatment with physical and occupational therapy at the GF Strong Rehabilitation Centre (Vancouver, BC) also failed to restore functional active flexion at the 5th MCP due to muscle imbalance caused by the hypertrophic abductor digiti minimi (ADM) and atrophied flexor digiti minimi (FDM). Botulinum toxin type A (BTX-A) was therefore used to improve active flexion at the 5th MCP. In other patients, BTX-A has been used to improve pain, tone, and

range of motion post-arthroplasty. Method Used: A trial block of the ADM muscle with local anesthetic injection was performed to estimate the potential response to BTX-A injection. Two BTX-A injections were given, 25 units per injection, 4 months apart. There was continued exercise at the direction of physical and occupational therapy throughout the follow-up period. Serial measurements and videos of passive and active flexion were recorded to document progress. Results Obtained: The initial muscle block was successful. With the first BTX-A injection, there was a maximal gain of 5 degrees of passive flexion and 11 degrees of active flexion. The effect of the first BTX-A injection was lost by 3 months, but there was a reduction in the hypertrophy of the ADM, which persisted throughout the post-injection study period. Repeat injection 4 months later had less benefit. At 5 months, compared with baseline measurements (pre-BTX-A), there was no improvement of passive flexion, but there was a gain of 6 degrees of active flexion. The only recorded side effect was slight numbness in the distal fingertips that improved to baseline after the initial BTX-A injection. Video representation provides dramatic visualization of the improvement in active 5th MCP flexion after the BTX-A injections. Brief

Conclusion: A 50 year-old female with JIA had significant benefit of 6 degrees in active flexion of the 5th MCP, 5 months post-BTX-A injection, after MCP arthroplasty. We could not identify prior case reports of similar use for BTX-A post small-joint hand arthroplasty. BTX-A injection may be a beneficial adjunct to improve small joint range of motion when it does not improve with traditional splinting and exercise alone.

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Persistence of Osteoporotic Patients to Annual Intravenous Zoledronic Acid Infusions

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Objective: While there are numerous efficacious anti-fracture medications currently available for the treatment of osteoporosis in Canada, most have been limited in their effectiveness by poor medication compliance and persistence. Zoledronic acid is an amino-bisphosphonate that is administered via intravenous infusion on an annual basis. This investigation aims to detail the persistence to annual intravenous zoledronic acid infusion over a three-year period in men and women with an elevated risk of fragility fracture.

Methods: All patients seen at the Saskatoon Osteoporosis and Arthritis Infusion Centre who received a zoledronic acid infusion between the dates June 7, 2007 and April 1, 2011 were included in this analysis. Patient charts were collected and data were entered into a standardized collection sheet. Pertinent data collected included date of birth, sex, basic anthropometric information (height, mass, BMI) and zoledronic acid infusion dates, among many other clinical variables. The mean time between successive zoledronic acid infusions was calculated for each individual and the number of patients who returned for repeat infusions was determined to provide an estimate of therapy persistence.

Results: Of the 380 patients that initially received a zoledronic acid infusion, 284 received a second infusion by the end of the data collection period. Since many of the patients had received their first infusion less than a year from the end of the data collection period, these individuals were removed from the pool of possible patients that could have received a second infusion (n=55), leaving a total of 41 (12.6%) of the eligible patients having not received a second infusion. Similarly, 139 patients received a third infusion, with 88 patients not yet eligible for a third infusion, leaving a total of 98 (41.4%) of the eligible patients having not received a third infusion. For those who obtained a second infusion, the mean (standard deviation) time since their initial infusion was 398 (47) days and for those who received a third infusion, there was a mean 386 (46) days between the second and third infusion.

Conclusion: Zoledronic acid had encouraging persistence with 100% of patients persistent for the first year, 87% for the second year, and 59% for the third year. Adherence to therapy was 100% for all years by virtue of the administration method.

Social Work Delivered Using a Self-Management Approach Supports Health Related Quality of Life for Clients with Complex Arthritis: A Pilot Study

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Objective: Social work (SW) support has been shown to benefit individuals who are affected by arthritis through focusing on the practical, social and emotional aspects of life. Social workers with advanced training in arthritis working for a publicly funded community rehabilitation program deliver services to people with complex forms of arthritis using a self-management approach. This pilot study evaluated the impact of the SW intervention on Health Related Quality of Life and the client-centredness of care provided by the social workers.

Methods: Social workers administered the Medical Outcomes Survey Short Form-8 questionnaire (SF-8) at baseline and at $\geq$ six weeks post baseline whether or not the client was discharged. The SF-8 consists of eight items each representing one health domain (general health, physical functioning, role functioning-physical, bodily pain, vitality, social functioning, mental health, role functioning-emotional). Each subscale is scored from 1 to 5 or 6 on a Likert-like scale and then standardized using a scoring algorithm to come up with a score out of 100 with a higher score representing better health. Changes from baseline to follow-up were analyzed using non-parametric tests for paired data. Client-centredness of care was measured at discharge using a modified version of the Client-centred Rehabilitation Questionnaire (CCRQ).

Results: Study participants ($n=48$) were mostly female (81%), with a mean age of 59 years (min: 22; max: 82). Half had inflammatory arthritis. At baseline, all subscales of the SF-8 were worse than the population norm and 70% of respondents were rated at risk for depression. At follow up, there were significant improvements in all domains of the SF-8 (Wilcoxon Signed Rank Test, $P<.01$). Although still worse than the population norm at follow-up, the number of people at risk of depression was reduced to 46%. A subsample of participants completed the CCRQ ($n=26$). Most clients were satisfied with the care they received, however pain control was still an issue for approximately 10% of the clients at discharge.

Conclusion: Clients with complex arthritis receiving self-management support from social workers were generally satisfied with all aspects of their care in the community and reported improved health related quality of life. Results suggest that the risk of depression might be decreased following the program. Although improved, results suggest that a longer follow-up may be required in order to demonstrate maximum benefit of the program, particularly in the area of pain management.

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Efficacy and Safety of Abatacept Treatment for Rheumatoid Arthritis in a Real-life Setting in European and Canadian Populations: A 6-Month Interim Analysis of the ACTION Study

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Objective: Evaluation of retention, efficacy and safety of abatacept in RA patients treated in routine clinical practice in Europe and Canada.

Methods: ACTION (Abatacept In rOutine clinical practice) is a non-interventional, prospective, longitudinal study in abatacept-treated RA

patients. 6-month interim analysis results of abatacept+DMARD-treated patients who received prior anti-TNF treatment are presented. Follow-up was every 3 months. Retention rate (Kaplan-Meier estimation) and disease activity (DAS28 ESR and/or CRP, CDAI, for patients with available data) are reported over 6 months. Serious adverse events (SAEs) were assessed in enrolled patients, and reported up to study cut-off.

Results: Of 546 enrolled patients (Mar 2008-Aug 2010), 526 received IV abatacept (Germany, 374; Canada, 152). Of 455 patients who had prior anti-TNF treatment, 327 (71.9%) subsequently received abatacept+DMARDs and are evaluated here; 128 (28.1%) patients received monotherapy. Not all 327 patients reached Month 6 at time of analysis. Mean (SD) baseline characteristics were: age, 54.4 (12.4) years; disease duration, 11.1 (8.6) years; 82% female; 68.4% RF+; 66.2% anti-CCP+; 73.1% erosions. 45.6%, 42.8% and 11.6% had failed one, two and three anti-TNFs, respectively. At initiation, 56.3%, 11.3%, 32.4% of the 327 patients receiving abatacept+DMARD, and 77.4% of patients across all treatment patterns, were receiving MTX, MTX+DMARD, DMARD and corticosteroids. Reasons for failing prior biologic treatment (available for 314 patients) were: lack of efficacy (primary inefficacy) 95/314 (30.3%), loss of efficacy (secondary inefficacy) 142/314 (45.2%), and intolerance 58/314 (18.5%). Month 6 estimated retention rate was 83.4% (95% CI: 77.6-87.8); 35 patients discontinued within 6 months due to lack of efficacy ($n=21$), intolerance ($n=4$), poor compliance ($n=3$), major improvement ($n=1$), other reasons ($n=6$). Month 6 retention rates according to history of prior anti-TNF therapy were: 1 prior anti-TNF, 82.1% (72.7-88.5); ≥ 2 prior anti-TNFs, 84.41% (76.36-89.90); primary inefficacy, 79.38% (65.86-88.02); secondary inefficacy, 85.75% (77.04-91.34); intolerance, 81.94% (65.69-91.02). At Month 6, rates of remission and LDAS were as follows: DAS28 (ESR), 17.5% and 35.0%; DAS28 (CRP), 18.2% and 40.9%; CDAI, 5.4% and 36.0%, 16 SAEs were reported in 15/546 (2.7%) patients with no events of TB or opportunistic infection reported.

Conclusion: This is the first large-scale, global observational study of abatacept use in a real-life setting, which confirms its clinical effectiveness and safety in anti-TNF refractory RA patients with long-term, erosive disease.

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Evaluation of Parenteral Methotrexate as a First-line Treatment in Early RA: A Nested Case Control Study from a Nationwide Cohort

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Objective: Previously we examined the CATCH (Canadian Early Arthritis) Cohort for outcomes associated with parenteral methotrexate (pMTX)-based treatment in patients presenting with early rheumatoid arthritis (ERA). Findings suggested increased remission in the first year if patients were started on "early optimal" pMTX vs. all other treatment approaches. To account for possible confounders we designed a nested case control study to further assess the possibility that pMTX offers a clinical advantage.

Methods: Cases and controls were selected using the CATCH cohort, a multi-site nationwide prospective observational cohort study looking at practice and outcomes in ERA. Cases were patients receiving pMTX ≥ 20 mg weekly within 3 months of initiation of treatment. For the purposes of this study we limited cases to a single site community practice where it is standard practice to begin with pMTX 25 mg weekly in patients presenting with ERA. Controls were selected from the entire CATCH cohort to match cases on both treatment and demographic variables in a 2:1 ratio. Matched variables included: Gender, Smoking history, Age $\pm 10\%$, baseline DAS28 (low, medium or high disease activity), rheumatoid factor status, and concomitant use of corticosteroids (defined as > 7 days oral prednisone or > 2 separate IM steroid injections in the first year). Cases and controls were compared for achievement of DAS28 remission (DAS28 < 2.6) and DAS28

Low Disease Activity (DAS28 < 3.2) at 6 and 12 months. We further evaluated what proportion of patients achieved these clinical outcomes on monotherapy, combination traditional DMARD therapy, or with Biologics as part of their treatment regimen.

Results: Sixty-nine Cases (n=69) met our criteria. Of these 62 had available clinical outcome data at 6 months and 56 had available data at 1 year. A total of 138 Controls were selected based on our defined criteria. Cases achieved remission 55% of the time by 6 months and 77% of the time by 12 months. They achieved LDAS 71% of the time by 6 months and 84% of the time by 12 months. At the time of abstract submission, clinical outcomes for controls were being evaluated.

Conclusion: Parenteral Methotrexate at early optimal doses may be an effective 1st line treatment in patients presenting with ERA. Confounders inherent to an observational cohort design are addressed by conducting a nested case control study.

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The Comparative Efficacy and Toxicity of Initial DMARD Choices for Patients with Moderate-Severe Early Rheumatoid Arthritis: A Bayesian Network Meta-Analysis

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Objective: The objective was to compare the relative efficacy and toxicity of initial DMARD treatment options for patients with moderate-severe RA, recommended in the 2011 CRA Recommendations for the Management of RA: oral methotrexate (MTX) monotherapy, subcutaneous (sc) MTX monotherapy, combination therapy with MTX + other DMARDs, or MTX + anti-TNF therapy (TNF).

Methods: A systematic review of MEDLINE, EMBASE, Cochrane Central and 2009-2010 ACR/EULAR abstracts was performed to identify any randomized controlled trial that compared at least 2 of the 4 treatment choices in adult patients with RA. Trials without an active comparator arm were excluded (i.e., trials comparing the continuation of a failed DMARD to the addition of another DMARD). The primary efficacy and toxicity outcomes were ACR50 response and withdrawal (WD) due to toxicity. Secondary outcomes included WD due to inefficacy, total WD, ACR20 and ACR70 responses. Treatment effects relative to oral MTX were calculated through a Bayesian random-effects network meta-analysis, incorporating both direct and indirect treatment comparisons. Comparisons were made to estimates from Bayesian direct effect (non-network) meta-analyses.

Results: 16 trials were identified with the following treatment arms: oral MTX, sc MTX, combination therapy with MTX [MTX+hydroxychloroquine/chloroquine (HCQ/CQ); MTX+sulphasalazine (SSZ); MTX+SSZ+HCQ] and MTX+TNF. There was a 99% and 100% probability that MTX+SSZ+HCQ and MTX+TNF respectively were superior to oral MTX monotherapy for ACR50 responses [MTX+SSZ+HCQ: OR 1.8 (95% Credible Interval (CrI): 1.1-3.0); MTX+TNF: OR 1.9 (95%CrI:1.4-2.7)]. Other DMARD combinations and scMTX monotherapy were not more effective than oral MTX. Similar results were found for ACR20 and ACR70 responses, although the ACR70 response for MTX+SSZ+HCQ showed only a trend towards superiority [OR: 1.6 (95%CrI: 0.8-3.7)]. MTX+SSZ+HCQ and MTX+TNF were associated with 64% and 92% probabilities respectively that treatment was associated with more withdrawals due to toxicity than oral MTX. No treatment was superior to oral MTX for total WD. Results were similar in analyses of direct treatment comparisons, however credible intervals were wider and an evaluation of ACR responses for MTX+SSZ+HCQ and MTX+HCQ relative to oral MTX was not possible due to a lack of studies directly comparing these treatment options.

Conclusion: Amongst currently recommended treatment choices for initial DMARD therapy in RA, there is a high probability that both MTX+SSZ+HCQ and MTX+TNF are more effective than oral MTX for clinically relevant outcomes. The incorporation of indirect treatment com-

parisons through the network meta-analysis permits inferences about ACR responses for MTX+SSZ+HCQ that are not possible through a traditional meta-analysis.

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Body Mass Index and its Relationship to Disease Activity and Response to Anti-TNF Therapy in Rheumatoid Arthritis

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Objective: The purpose of this study was to determine whether body mass index (BMI), as an estimate for body fat, is related to a) disease activity in rheumatoid arthritis (RA) and b) response to and survival on initial anti-TNF therapy.

Methods: The patients in this study were drawn from our biologic therapy monitoring database. Patients, in whom BMI could be calculated, treated with an anti-TNF therapy from 4/2002-3/2011 were included. BMI was calculated using patients' height and weight. Disease activity (DAS28), health assessment questionnaire (ClinHAQ) and BMI scores were recorded at clinic visits pre- and during treatment with anti-TNF therapies. Patients were grouped based on their initial anti-TNF therapy. Regression analysis was used to determine if a relationship existed between BMI and DAS28 and HAQ scores. EULAR response criteria were used to determine a patient's response to anti-TNF therapy. Survival time was calculated from a patient's record of therapy changes.

Results: A total of 130 patients (93 females and 37 males) were included. The mean baseline BMI of the 130 patients was 26.6 ± 5.4 (overweight). The mean disease duration for these patients when first starting anti-TNF therapy was 8.4 ± 7.0 years. Patients' BMI were categorized by World Health Organization criteria (underweight, normal, overweight and obese). The majority were overweight or obese (60.31%). One patient was underweight. The mean BMI did not change over time. Baseline disease activity scores were high, with DAS28 > 5.1. Initial anti-TNF therapies (%patients) were: etanercept (45%), infliximab (32.1%) and adalimumab (22.9%). BMI and initial RA severity scores were not correlated (r=0.0369). Median survival on any therapy, based on BMI, showed no difference between the normal (1.5 years), overweight (1.9 years), and obese (1.7 years) patients. A significant difference in gender-specific median survival time was found between obese men and women 4.17 v 1.40 years, log rank test (p=0.0440).

Conclusion: This study did not show a relationship between BMI and disease severity in our cohort of RA patients. There was also no relationship found between patients' BMI and overall responsiveness to anti-TNF therapies. However the longevity of anti-TNF therapy in obese males is longer than all female patients and male patients in the other two BMI categories.

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Discrepancy between Patient and Physician Global Assessments of Disease Activity in Early and Established Rheumatoid Arthritis Patients

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Objective: To evaluate the discrepancy between patient global assessment (PTGA) and physician global assessment (MDGA) of Rheumatoid Arthritis (RA) disease activity in patients with early active disease and in patients with established inactive disease. To assess the potential factors influencing the discrepancy between PTGA and MDGA.

Methods: Global assessment scores, patient demographics and clinical

measures were collected from the Canadian Early Arthritis Cohort (CATCH) database for the early RA patients (n=897) and from a retrospective chart review of one physician's practice (EK) for established RA patients who were in DAS28 remission (n=100). All the patients met the 1987 ACR criteria for RA and had only taken conventional DMARDs. Discrepancy was calculated as PTGA minus MDGA. A difference of ≥ 30 mm or ≤ -30 mm was considered clinically meaningful. Positive discrepancy was defined as ≥ 30 mm, negative discrepancy was defined as ≤ -30 mm, and no discrepancy was $< +30$ and > -30 mm. Chi-square and Mann-Whitney U tests were used to compare patients characteristics between positive/negative discrepancy groups and no discrepancy groups.

Results: A discrepancy (positive/negative) between PTGA and MDGA was observed in 324 (36%) early RA patients and 25 (25%) established RA patients. Out of 324 early RA patients with a discrepancy, 213 (66%) had a positive discrepancy. These patients, compared to patients with no discrepancy, had lower swollen (mean) (7.2 vs 8.7, $p=0.006$) and tender joint counts (8.3 vs 9.8, $p=0.03$) and higher pain score (73.3 vs 54.0, $p<0.0001$). Patients with negative discrepancy, compared to patients with no discrepancy, had higher swollen joint count (9.8 vs 8.7, $p=0.02$), higher CRP (19.1 vs 14.3, $p=0.008$) and lower pain score (27.2 vs 55.7, $p<0.0001$). In the established RA cohort, out of 25 patients with discrepancy only one had negative discrepancy. Patients with discrepancy were younger (52 vs 58, $p=0.04$) with higher damaged joint count (22.5 vs 13.3, $p<0.01$), ESR (25.2 vs 17.5, $p=0.03$), CRP (10.3 vs 4.7, $p<0.01$) and pain score (63.9 vs 12.6, $p<0.0001$) compared to those with no discrepancy.

Conclusion: A clinically meaningful discrepancy between PTGA and MDGA exists in a significant proportion of patients with RA. In patients with discrepancy, PTGA is more likely to be higher than MDGA in both early active and established inactive disease. This discrepancy seems to be significantly influenced by pain which appeared to be associated with damage in patients with established disease.

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Patients with Early Rheumatoid Arthritis Determined to be Inadequate Responders after 12 Weeks May Still Have Substantial Improvement in Core Set Measures. Results from an Early Arthritis Cohort

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Objective: ACR or EULAR response criteria have been used in trials and also in routine clinical practice to guide treatment decisions in RA. Patients who fail to achieve DAS28 change ≥ 1.2 or ACR20 are generally considered inadequate responders. The objective of this study was to evaluate clinical improvement in individual core set measures in patients who were considered inadequate responders using DAS28 and ACR composite measures of disease activity.

Methods: Patients with early RA who were enrolled and prospectively followed in the Canadian Early Arthritis Cohort (CATCH) were studied. Patients receiving DMARD therapy for 3 months who failed to achieve DAS28 change ≥ 0.6 , DAS28 change ≥ 1.2 or ACR20 were examined for 20% and 30% improvement in their disease activity core set measures.

Results: 416 patients with mean age 52.5 yr (14.3)(SD), disease duration 6.1 mo (3.0), Tender Joint Count (TJC) 9.2 (7.1), Swollen Joint Count (SJC) 8.2 (6.2) and DAS28 5.1(1.6) at baseline were included in this analysis. At 3 months 197(47%) patients had not achieved ACR20, 304 (73%) had not achieved ACR50 and 348 (84%) had not achieved ACR70. Half of included patients had DAS28 improvement < 1.2 and in 142 (34%) patients

DAS28 improvement was < 0.6 at 3 months. About a third of patients with DAS28 change < 0.6 had 30% improvement in TJC, SJC, patient and physician global. This proportion varied from 30% to 44% in patients with DAS28 change < 1.2 and from 20-41% in patients who did not achieve ACR20. Mean core set measure improvement in patients with DAS28 < 0.6 was found to vary from 18% (patients global) to 26% (SJC). Thirty seven percent of patients with DAS28 change < 0.6 achieved HAQ Minimal Clinically Improvement (MCID)[0.22]. This proportion was 42% for patients with DAS28 change < 1.2 or 35% in patients who failed to achieve ACR20.

Conclusion: A substantial proportion of patients who fail to achieve a significant improvement in composite measures of disease activity frequently used in clinical studies may still exhibit substantial improvement in their individual core set measures. These findings should be considered when making treatment decisions in real world clinical settings and identifying patients with an inadequate clinical response.

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Prophylactic Therapy for Latent Tuberculosis Prior to Anti-Tumor Necrosis Factor Therapy in Patients with Rheumatoid Arthritis: A Decision Analysis

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Objective: Screening for latent tuberculosis infection (LTBI) prior to anti-TNF therapy is recommended, with patients offered prophylactic therapy if they screen positive. The utility of this in low-risk populations is uncertain, given a low absolute risk of TB reactivation in patients who screen positive and risks associated with prophylaxis. The objective was to determine if prophylactic therapy for LTBI should be initiated in patients with rheumatoid arthritis (RA) who screen positive prior to starting anti-TNF therapy.

Methods: A Markov model with a lifetime horizon and monthly cycles was developed to model the decision of whether to initiate prophylaxis with isoniazid (INH) for 6-9 months prior to starting anti-TNF therapy in a hypothetical cohort of patients with RA who screen positive for LTBI. The base case was a 50-year old patient, born in a country with a low TB prevalence with a positive tuberculin skin test of 5-10 mm, who had not been vaccinated with BCG and had no other risk factors for TB reactivation outside of RA and anti-TNF therapy. All model inputs were based on literature reviews. The outcome was quality-adjusted life years, which were discounted at 3%/year. Sensitivity analyses were performed across all variables and for several model assumptions.

Results: No prophylaxis was the favoured approach with a gain of 8.1 quality-adjusted life-days. The decision was robust to the range of plausible values of relative risk (RR) of TB reactivation associated with anti-TNF therapy (RR: 1.3-15.5). Prophylaxis was favoured if the RR of TB reactivation associated with RA alone was > 3.2 or if the utility associated with INH prophylaxis was > 0.98 . For any given baseline probability of TB reactivation, as age increased, prophylaxis was less favoured. This occurred because the risk of hepatotoxicity is accrued initially and increases with age, and because older patients have less lifetime risk of TB reactivation and therefore less potential to benefit from prophylaxis. Prior BCG vaccine or the use of 4 months of rifampin instead of INH did not change the favoured decision.

Conclusion: For RA patients with a low-positive LTBI screen, who are otherwise at low risk of TB reactivation, holding prophylaxis prior to anti-TNF therapy is appropriate. The decision to initiate prophylaxis should be tailored to a patient's age, baseline annual risk of TB reactivation and patient preference for a 9-month course of isoniazid.

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Patterns of Use and Predictors of Initial Disease-Modifying Anti-Rheumatic Drug Therapy in Early Rheumatoid Arthritis: Results From a Multicenter Canadian Early Arthritis Cohort

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Objective: Recently published Canadian Rheumatology Association (CRA) Recommendations for the Management of Rheumatoid Arthritis (RA) suggest DMARDs be started at time of diagnosis of RA with methotrexate (MTX) monotherapy or in combination with other DMARDs. Our objective was to describe current patterns of initial DMARD therapy in patients with early RA (ERA) prior to the dissemination of practice recommendations and identify predictors of initial DMARD choice.

Methods: Patients from a Canadian, multicentre early inflammatory arthritis cohort (CATCH) with new onset RA (1987 ACR Criteria) were studied. Patients with 6-52 weeks of synovitis were followed according to a standard protocol and were treatment naïve or minimally-treated with DMARDs (defined as no DMARDs >1 month prior to first visit). A multi-variable logistic regression model was used to determine which variables were independently associated with the initial DMARD choice. The outcome for the primary analysis was MTX use at the initial visit (Y/N). A secondary analysis was performed for use of combination DMARD therapy (Y/N). The variables of interest were treatment center and patient characteristics: age, gender, RF, DAS28, HAQ-DI and presence/absence of erosions. Both analyses were repeated using DMARD prescribed by 3 months as the outcome.

Results: 565 RA pts were included. Most (82%) were treatment-naïve at first visit. Baseline patient characteristics were (mean (SD) or %): age 52(15) years; 74% female; disease duration 6.0(8.1) months; RF+ 60%; DAS28 5.4(1.4), HAQ-DI 1.0(0.7); erosions 32%. At the initial visit, 57% of patients received MTX and 27% received combination therapy. For 455 patients having at least 3 months of follow-up, 66% were on MTX by 3 months. The strongest predictor of both MTX and combination DMARD use at initial visit was the treatment center ($p < 0.0001$). Patients with a higher DAS28 were more likely to receive MTX (OR: 1.3 (95%CI:1.2-1.5) and combination therapy (OR: 1.2 (95%CI:1.0-1.3)); no other patient characteristics were associated with a higher rate of MTX or combination DMARD use. Similar results were found when the analyses were repeated using DMARD(s) prescribed by 3 months, with only treatment center and DAS28 associated with use of MTX and combination therapy.

Conclusion: In patients with an established diagnosis of RA, MTX prescription starts at the initial visit are low at 57%, although this increases by 3 months to 66%. Treatment center is strongly associated with the choice of initial therapy, which may represent an opportunity for treatment recommendations to help standardize care.

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Prevalence of Pediatric Systemic Autoimmune Rheumatic Disease in First Nation Peoples of Alberta, Canada

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Objective: Systemic autoimmune rheumatic disease (SARD) encompasses a group of conditions that are relatively rare in the pediatric population. One such disease, systemic lupus erythematosus (SLE) is more common among First Nation Peoples (FN) than the general population in adult based studies, and some clinic derived data support this finding. We aimed to provide preliminary prevalence estimates of SARDs in FN and non-FN pediatric populations using provincial administrative data in the province of Alberta, Canada.

Methods: We used province-wide physician billing and hospitalization data from Alberta Health and Wellness from 1994 to 2007 to estimate SARD prevalence. We included the following SARDs: systemic lupus erythematosus (SLE), systemic sclerosis (SSc), unclassified connective tissue disease (UCT), and dermatomyositis/polymyositis (DM/PM). Physician billings were coded according the International Classification of Diseases (ICD) Clinical Modifications 9, as were hospitalizations prior to 2002. After 2002, hospitalization data was coded using ICD 10th revision, Canadian Adaptation. Prevalence was calculated as absolute counts per 100,000 population ≤ 18 years of age. Cases were defined by the presence of any 1 of the following: (a) 1 or more hospitalization diagnostic codes (primary or non-primary); (b) 2 or more billing codes within 2 years but at least 8 weeks apart by any physician; (c) at least 1 billing code by a rheumatologist. Individuals registered with the Department of Indian and Northern Affairs of the Government of Canada are considered to have FN treaty status, and these were identified using methodology derived by Alberta Health and Wellness. Metis and non-treaty individuals of FN descent were excluded from FN prevalence estimates.

Results: Higher prevalence rates were not seen for SLE, DM/PM, SSc, or UCT among FN pediatric populations. The prevalence rate for SLE was 4.0 in FN and 8.7 in non-FN; DM/PM was 2.0 in FN and 6.5 in non-FN; SSc was 2.0 in FN and 2.9 in non-FN, and UCT was 0 in FN and 2.0 in non-FN.

Conclusion: We were unable to establish a higher SARD prevalence in the pediatric FN population of Alberta. The prevalence of SLE in the FN population was surprisingly low. Key limitations include not accounting for the potential roles of geographic disparities in access to care, cultural factors affecting access to care, inability to identify Metis and non-treaty FN, the need for better validation of SARDs case definitions for administrative data, and the small number of FN cases. Further work must address these issues.

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Effectiveness and Safety of Annual Intravenous Zoledronic Acid Infusions for Treatment of Osteoporosis

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Objective: Zoledronic acid has demonstrated efficacy in significantly decreasing the risk of new vertebral, non-vertebral and hip fractures in postmenopausal osteoporotic women. Further, zoledronic acid was demonstrated to be safe in these registrations trials; in fact, overall mortality was significantly lower in the cohorts administered zoledronic acid over a three-year period as compared to the placebo group. However, patients selected for clinical trials differ considerably from those who are treated in the clinical setting. This investigation sought to determine the effectiveness and safety of annual intravenous zoledronic acid infusions in a cohort of osteoporotic patients from a typical clinical setting.

Methods: All patients seen at the Saskatoon Osteoporosis and Arthritis Infusion Centre who received a zoledronic acid infusion between the dates June 7, 2007 and April 1, 2011 were included in this analysis. Patient charts were collected and data were entered into a standardized collection sheet. Information collected included date of birth, sex, basic anthropometric information, current medications, other serious medical conditions, personal history or fracture, zoledronic acid infusion dates, bone mineral density (BMD) assessment dates and results (for lumbar spine, femoral neck and total hip sites), fracture incidence, and adverse event information during and between infusions, among other variables. Effectiveness was reflected in longitudinal BMD measures (at least one BMD measure pre-infusion) and incidence of fracture after infusion. Safety was reflected by adverse event reporting.

Results: There were a total of 804 Aclasta infusions collected from 380 patients (28 men, 352 women). The mean age of the patients was 66.3 years and almost a third (31%) had suffered a previous fragility fracture. BMD increased after infusion at all measured sites. There were a total of 804 zoledronic acid infusions and during these infusions there were 0 reported

adverse events. Between the initial and second infusion 9.9% of patients reported some form of adverse event (29 in 294). Between the second and third infusions 2.8% of patients reported an adverse event (4 in 142). Following the first infusion, only 1.9% (6 of 322) of the cohort experienced a fracture during follow-up.

Conclusion: The increase of BMD at all investigated sites after the initial zoledronic acid infusion corroborates the findings from the phase III regulatory studies. There were no acute infusion-related adverse events recorded over 804 infusions. Lastly, only 1.9% of the patients that received a zoledronic acid infusion experienced a fracture after infusion.

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Five-year Incident Fracture Risk Assessed by Quantitative Multisite Ultrasound: The Canadian Multicentre Osteoporosis Study

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Objective: To assess the ability of Beam-Med Multisite quantitative ultrasound (QUS) to predict fracture risk over a five-year follow-up period.

Methods: The participants included for these analyses were a subset of the Canadian Multicentre Osteoporosis Study (CaMOS). QUS was used to estimate bone strength (speed of sound in m/s) at three anatomical sites: the distal radius, the tibia and the phalanx. After QUS assessment, all participants were prospectively followed for a five-year period during which incident fractures were recorded in detail. Further, extensive questionnaires were employed at the time of QUS measurement. Two survival analyses (proportional hazards regression) were completed for each skeletal site - an uncontrolled univariate analysis and an adjusted multivariate analysis controlling for age, anti-resorptive use, femoral neck BMD, number of diseases, previous fractures, BMI, sex (in combined model), parental history of hip fracture, current smoking, current alcoholic drinks >3 per day, current use of glucocorticoids, and diagnosis of rheumatoid arthritis. Many of these control variables were selected because they are used in the FRAX fracture stratification tool used world-wide. The unit of change for all regression analyses was 150 m/s, approximately one standard deviation for all measurement sites. Analyses were completed for the group as a whole and by sex. Lastly, separate analyses were completed for all clinical fractures, non-vertebral fractures and hip fractures.

Results: There were a total of 2633 (70.4%) women and 1108 (29.6%) men included in these analyses (total sample of 3741). A total of 204 incident fractures occurred over five years of observation (5.5% fractured). When stratified by sex, incident fractures occurred in 177 women (4.8%) and in 27 men (0.7%). Hip fracture events occurred in 35 individuals (30 in women and 5 in men) and non-vertebral fracture events occurred in 160 individuals (139 in women and 21 in men). Univariate models revealed statistically significant predictive ability for all three measurement sites in the combined group and for women alone for all three fracture types, but not for the men's group. The adjusted model found that measures at the distal radius and tibia in the combined and women's groups could significantly predict all clinical fractures and non-vertebral fracture within the next five years.

Conclusion: The Beam-Med MultiSite QUS provides significant five-year fracture prediction, independent of bone mineral density and other significant risk factors for fracture, when measured at the distal radius and tibia sites.

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Treatment of SSc including Organ Involvement: What to Use when First-Line Treatment Fails - A Consensus Report

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Objective: There is a need for standardization in systemic sclerosis (SSc) management, particularly after usual (1st-line) treatment.

Methods: SSc experts (n=118) were sent 4 surveys to gain consensus for SSc management. Cases were given for mild and severe organ involvement in order to construct treatment algorithms. Experts were surveyed to determine the rate of agreement with each algorithm. Good agreement (consensus) was considered >70%.

Results: 55 responded to all surveys (47% response rate). After ACEi use for mild scleroderma renal crisis (SRC) {97%}, 2nd-line was to add either a CCB {37%} or ARB {35%}, then an alpha blocker (20%) in severe SRC. Treatment of mild and severe SRC was similar (75% agreement). ERAs were 1st-line in mild PAH (72%) and proceeded by adding PDE5i (77%) and then a prostanoid (73%). For severe PAH, initial treatment was any of: prostanoid (49%), combination of ERA and PDE5i (19%) or ERA and prostanoid (16%) {71% agreed}. For mild Raynaud's (RP), CCB (92%) were followed by adding a PDE5i (35%), then an ARB (32%) and finally a prostanoid (23%). For more severe RP, 54% agreed on adding a PDE5i or a prostanoid (32%). For prevention of digital ulcers (mild history) treatment was a CCB (73%), then to add a PDE5i (57%) then an ERA (47%), and a prostanoid (38%) {50% agreed}. A severe history was similar. For ILD, induction was usually IV cyclophosphamide (65%) or occasionally oral (64%) or mycophenylate mofetil (MMF) (48%) or azathioprine (45%). For maintenance, MMF was chosen by ¾ (56% agreed). For skin involvement after methotrexate, MMF was usually chosen (38% agreed). For GERD, half would exceed the maximum recommended PPI dose if required (72% agreed). For joint involvement after methotrexate (60%), corticosteroids (37%) or hydroxychloroquine (31%), then biologics (20%) should be considered (62% agreed).

Conclusion: Discrepancies in drug choices occurred after 1st-line treatment in SSc. Not all algorithms had good agreement. This study provides some guidance for SSc management.

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Correlations between Changes in Biomarkers and Clinical Outcomes for Early Phase (Proof of Concept) Trials in Active Diffuse Systemic Sclerosis Using Data from an Imatinib Study

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Objective: Imatinib has been studied in the treatment of systemic sclerosis (SSc) and data from one study were used to determine if biomarker changes were related to changes in clinical parameters (as some patients improved, others worsened or were stable).

Methods: A small, blinded placebo controlled study with imatinib in SSc obtained serum samples and skin biopsies at baseline and 6 months; analyzing samples for fibrotic and inflammatory cytokines. Correlations between changes in cytokines and clinical outcomes (modified Rodnan skin score [mRSS], physician and patient global assessments and HAQ) were performed.

Results: In serum, only VCAM-1 ($p < 0.001$) decreased significantly after 6 months of imatinib treatment but the medication was not well tolerated so half did not receive the recommended dose. In tissue homogenates, soluble intercellular adhesion molecule-1 (sICAM-1) ($p = 0.009$) was significantly different with an increase after 6 months. There were strong correlations for: fold-changes in some serum biomarkers and in changes in clinical parameters: patient global and IL-13 ($p=0.000$, $r=0.964$), physician global and PDGF ($p=0.041$, $r=0.774$), IFN-gamma ($p=0.022$, $r=-0.825$), sCD40L ($p=0.002$, $r=0.937$) and TGF-beta1 ($p=0.021$, $r=0.830$), and HAQ with IL-17 ($p=0.045$, $r=0.764$). Fold-change correlations in tissue were mRSS and VEGF ($p=0.020$, $r=0.831$), patient global and E-selectin ($p=0.004$, $r=0.913$), and physician global with CD40L ($p=0.008$, $r=-0.883$).

Conclusion: Biomarkers may have a role in early phase clinical trials of SSc as some changes correlate strongly with changes in clinical parameters.

Factors Affecting Glucocorticoid Use in Early Rheumatoid Arthritis. Results from an Early Arthritis Cohort

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Objective: Recent guidelines recommend early, short-term use of Glucocorticoids (GC) in patients with recently diagnosed active RA. Concerns over side effects, however have limited the use of these therapeutic agents. The pattern of GC therapy in real world setting may vary based on patients' clinical status, availability of other therapeutic agents, physician and patient preference. The objective was to determine the prevalence of GC use in patients with early RA and to identify the effect of baseline characteristics of patients and treatment center on GC use.

Methods: Patients with early RA were studied in the Canadian Early Arthritis Cohort (CATCH), a prospective cohort where data was collected according to a standardized protocol from 19 participating centers. For the present analysis we included any patient who had at least 3 months follow up. The primary outcome was any form of systemic GC (oral or parenteral) use during the first 3 months. Disease activity, using DAS28, was assessed at baseline and then every 3 months in each group. Univariate analysis compared baseline characteristics in two groups and a multivariable logistic regression analysis was used to model the use of GCs.

Results: 455 patients were included in the analysis who had at least 3 month follow up and were not treated prior to enrolment. 74% were women with a mean age of 52 (SD)(15) years, DAS28 5.5(1.4) and disease duration of 183(270) days. Rheumatoid factor (RF) was positive in 61%. 92 patients (20%) had received systemic GC (PO or IM) during the first 3 months. In univariate analysis two groups were not significantly different in their baseline DAS28 or HAQ. Steroid users were older ($p=0.00018$), had higher ESR ($p=0.0006$), CRP ($p=0.0003$) and erosion ($p=0.045$) but lower rheumatoid factor +ve ($p=0.004$). Multivariate regression analysis showed that patients' higher age and treatment center were associated with steroid use.

Conclusion: Despite recent guidelines recommending short-term use of GCs as part of initial management in patients with active recently diagnosed RA, most of these patients did not receive GC in this real world clinical setting. GC use was strongly influenced by the treating center. Younger patients were less likely to receive GC. The heterogeneity in practice patterns may represent a potential role for clinical practice guidelines to inform treatment decision making.

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Improving Clinical Trial Recruitment in a Real World Practice. Results from the Canadian Early Arthritis Cohort

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Objective: Current clinical trials are not representative of characteristics of patients in clinical practice. A minority of patients in clinical practice meet current entry criteria for most trials. The objective was to evaluate whether using more liberal clinical trial entry criteria in a real world clinical

setting will generate clinical outcomes comparable to the use of 'standard' entry criteria and will improve clinical trial recruitment.

Methods: Patients with early RA enrolled in the Canadian early Arthritis Cohort (CATCH), were evaluated. Patients were included in present study if: Age ≥ 18 , met ACR 1987 criteria, initiating MTX at baseline, had ≥ 6 -month follow up, did not receive biologics and had available ACR responses. Disease activity was assessed at baseline and 24 weeks. Two "standard" enrolment criteria were defined: 1) ≥ 6 TJC68 and ≥ 6 SJC66 with either an ESR >28 or CRP >1.5 mg/dl, 2) ≥ 6 TJC28 and ≥ 6 SJC28 with either an ESR >28 or CRP >1.5 mg/dl. Five "liberal" criteria were defined as: 1) SDAI >11 , 2) DAS28 >3.2 , 3) ≥ 6 TJC28 and ≥ 6 SJC28 + elevated ESR or CRP (ESR >20 or CRP >1), 4) ≥ 4 TJC28 and ≥ 4 SJC28 + ESR >28 or CRP >1.5 mg/dl, 5) ≥ 4 TJC28 and ≥ 4 SJC28 + elevated ESR or CRP (ESR >20 or CRP >1). Proportion of patients eligible for enrolment based on each criteria were compared, their baseline characteristics, ACR and EULAR responses were compared.

Results: 312 patients were eligible for analysis. Percentages of patients who met each inclusion criteria were as: Standard 1, 33%; Standard 2, 28%; Liberal 1, 90%; Liberal 2, 88%; Liberal 3, 32%; Liberal 4, 33% and Liberal 5, 40%. Patients in the first two liberal groups had the lowest proportion of elevated ESR/CRP (41% and 42% compared to $>70\%$ in other groups). ACR50 response rate was 56-57% in standard groups and 53-55% in liberal groups (except group 3). EULAR response rate was comparable among various groups.

Conclusion: Liberal trial entry criteria may improve recruitment from real world practice settings. Patients with a reduced joint count at entry (4 versus 6) and a greater than normal acute phase reactant were more likely to achieve the entry criteria with a significant proportion of patients having an elevated CRP. Entry criteria with 4 TJC28 and SJC28 with greater than normal acute phase reactant should be considered for future trials.

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Analysis of TNF-inhibitor Switchers in Clinical Practice

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Objective: Switching of TNF inhibitors (TNFi) is a common strategy in rheumatoid arthritis (RA) treatment. Few studies define criteria for primary/secondary failure or provide information regarding optimization of TNFi prior to switching thus making the reasons for switching difficult to interpret. This retrospective study evaluated reasons for TNFi switching using pre-defined criteria for primary/secondary TNFi failure when optimization of TNFi was ensured before switching.

Methods: A retrospective chart review was completed on RA patients initiating TNFi, etanercept (EN), adalimumab (ADA), infliximab (IFX), from 1998-2010(Sept) in the clinical practice of one rheumatologist (EK). Patients had their TNFi optimized for dose/duration of use defined as a trial of EN 50mg 2x/week and ADA 40mg q2wks both for ≥ 3 months or IFX q6-8weeks (≥ 4.5 mg/kg, ≥ 16 weeks). Primary failure was defined as $<20\%$ improvement in SJC. Secondary failure was defined as an improvement of $\geq 50\%$ in SJC at 6-10 months followed by loss of improvement to 20% of baseline SJC.

Results: In total, 340 patients received EN, 114 IFX, and 96 ADA. 86(16%) were TNFi switchers. Of the 86 patients who were TNFi switchers, 52(60%) initiated EN, 24(28%) initiated IFX and 10(12%) initiated ADA as the first TNFi. Baseline group demographics for switchers were: Age (mean $\pm$ sd) 52.5 $\pm$ 15.0 yrs and disease duration 15.5 $\pm$ 9.8 yrs, SJC 11.5 $\pm$ 6.4, ESR 34.9 $\pm$ 27.8mm/hour, MD global 7.0 $\pm$ 2.6. Patients had failed mean of 4.3 (± 2.1) DMARDs prior to TNFi. Differences in baseline characteristics (mean) were observed in three TNFi treatment groups as following: age 53.2, 52.5, 47.8yrs, disease duration 13.8, 18.5, 14.5yrs, ESR 40.4, 30.0, 12.4mm/hour; SJC 11.2, 12.0, 11.8, number of DMARDs failed 4.2, 4.6, 4.0, MD Global 6.8, 7.5, 6.8 in EN, IFX, ADA treated groups respectively. With respect to reason for failure, EN was switched mainly due to

secondary failure; ADA mainly due to primary failure. IFX was switched equally as primary/secondary failure.

Conclusion: Results of this retrospective study show that 16% of patients may experience TNFi treatment failure and this proportion appears slightly greater in IFX treated patients. However, patients initiating IFX had longer disease duration, higher SJC and MD global and failed more DMARDs than EN or ADA patients indicating that IFX patients had more active and potentially refractory disease. Although treatment arms are small, trends toward differences in reasons for switching emerged. Further analyses with larger populations and controlling for disease severity, treatment optimization and defined criteria for failure are needed.

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Alberta's First Nations Community is Not at Increased Risk of Inflammatory Myopathy: Population-based Prevalence Estimates Using Administrative Databases

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Objective: To provide population-based prevalence estimates for inflammatory myopathies in Alberta's First Nations (FN) and non-First Nations (non-FN) communities. In addition, we examined the effect of demographic factors which may affect our estimates, given that they influence access to health services and thus identification of affected individuals in administrative healthcare databases.

Methods: Physician billing claims and hospitalization data (years 1994-2007), coded according to the International Classification of Diseases (ICD) system, were used to ascertain cases of polymyositis and dermatomyositis, using three case definitions: i) ≥ 1 billing code by a rheumatologist; ii) ≥ 2 billing codes by any physician, ≥ 8 weeks apart but within 2 years; or iii) one hospitalization diagnosis. A latent class Bayesian hierarchical regression model was employed to account for the imperfect sensitivity and specificity of these data sources in case ascertainment. We accounted for demographic factors, estimating prevalence for FN and non-FN populations by sex, age group, and location of residence (urban versus rural). FN status was determined by methodology derived by the provincial steward for health data to identify individuals registered with the Department of Indian and Northern Affairs of the Government of Canada.

Results: Contrary to other rheumatic diseases, the overall prevalence point estimate for myositis was lower in the FN population, at 25.0/100,000 persons, with a relatively wide credible interval (CrI) (95% CrI 13.4-49.0), compared to 33.8/100,000 (95% CrI 28.9-39.6) in the non-FN population. Except for rural FN females < 45 years of age, all prevalence point estimates were higher in the non-FN population although the credible intervals overlapped. In non-FN we demonstrated higher prevalence estimates for females and older individuals, with similar trends in FN individuals. Trends were seen for higher myositis prevalence in rural locations.

Conclusion: Female sex and older age were associated with higher myositis prevalence. We did not find higher myositis prevalence estimates in FN individuals, but our estimates are limited by the inability to capture Métis and non-treaty individuals of FN descent. There was an interesting trend for higher prevalence in rural areas, which raises potential hypotheses about genetic risk pools and/or environmental factors that might be triggers for autoimmune disease (e.g. pesticides, zoonotic pathogens, respirable silica etc.) as well as physician diagnosis and referral patterns.

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Health System Costs are Reduced by Patients Attaining Remission or Low Disease Activity

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Objective: To compare healthcare costs across levels and duration of treatment response.

Methods: We determined healthcare utilization (physician visits, outpatient department visits, and hospitalizations) from a provincial administrative database (years 2004-2009) for a prospective cohort of anti-TNF treated patients ($n=1,086$, mean age 54 years). Remission status was classified according to the DAS28 score by the following categories: i) sustained remission (DAS28 score ≤ 2.6 for ≥ 2 years); ii) brief remission (DAS28 score ≤ 2.6 for < 2 years); iii) low disease activity period (DAS28 2.6-3.2 for < 2 years); and iv) persistent disease activity (never achieving remission or low disease activity (DAS28 > 3.2)). We examined both total healthcare costs and costs directly attributable to RA per patient per year for each category of clinical response, standardized to 2008 Canadian dollars. A propensity score matching technique was used to compare the costs between the categories accounting for confounding by individual variables affecting healthcare utilization, including specific therapy received, baseline function, smoking, age, sex, disease duration and medical comorbidities.

Results: Statistically significant reductions in cost were observed for patients in sustained remission (average difference \$2590, 95%CI 1093-4440), brief remission (average difference \$1451, 95%CI 325-2635) and a period of low disease activity (average difference \$1997, 95%CI 458-3652) compared to patients who had persistent moderate or high disease activity. A significant reduction in cost was also observed between patients in sustained remission and patients with only a brief remission (average difference \$1063, 95%CI 267-1983). Costs directly attributable to RA were constant in all categories of response at approximately 31%.

Conclusion: Healthcare system savings are achieved when RA patients attain remission or a low disease activity state, and in particular if that response can be maintained for longer periods of time. RA-attributable costs are constant across response categories. Ongoing longitudinal observation of anti-TNF treated patients may identify more significant cost savings associated with a reduction in long-term morbidity.

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Identified Predictors for Remission in Rheumatoid Arthritis Depend on Remission Definition

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Objective: To identify if baseline predictors for remission vary by the definition of remission used.

Methods: Our pharmacovigilance protocol captures clinical data on treatment efficacy and safety for patients treated with biologic therapies since July 2000. We calculated the proportion of patients achieving remission within the first year of initiating a new biologic agent, using the following definitions: i) 2011 ACR/EULAR Boolean Definition; ii) SDAI ≤ 3.3 ; iii) CDAI ≤ 2.8 ; iv) 1981 ACR Remission Definition; v) DAS28 ≤ 2.6 . Predictors for remission were assessed first in univariate analysis for each remission definition. All significant predictors were then assessed in multivariate models.

Results: Our analysis includes 1,583 patients (70% female, mean disease duration 12 years, mean prior DMARDs=3) with a total of 4,532 visits during the first year of treatment. Remission was identified in 8.4% of the cohort using the 2011 ACR/EULAR Boolean definition, 14.6% using the

SDAI score, 12.3% using the CDAI score, 5.2% using the 1981 ACR definition, and 34.5% using the DAS28 score. Highly correlated definitions were the SDAI and CDAI ($r=0.87$), SDAI and Boolean definition ($r=0.78$) and CDAI and Boolean definition ($r=0.76$). Less correlated definitions were DAS28 and SDAI ($r=0.52$), DAS28 and CDAI ($r=0.50$), DAS28 and Boolean definition ($r=0.51$), and the 1981 ACR and Boolean definitions ($r=0.55$). In univariate analysis, male sex, seropositivity, and lower baseline values for DAS28 score, HAQ score and inflammatory markers predicted remission for all definitions. The number of prior DMARDs was a significant predictor in all definitions except DAS28 remission. Short disease duration at inception was a predictor for remission in the DAS28 definition only. Obesity, smoking status and biologic naïve status did not predict remission by any definition. In multivariate models, a baseline DAS28 score < 3.2 was a predictor for remission for all definitions. A lower baseline HAQ score was a predictor for remission for all definitions except DAS28 remission, and normal inflammatory markers at baseline was a predictor for remission using the 2011 ACR/EULAR Boolean, SDAI and DAS28 definitions. Additional predictors in the multivariate model for DAS28 remission but not the other definitions were male sex and seropositivity.

Conclusion: In general, predictors for remission are constant across remission definitions. Additional predictors are identified in less stringent definitions. Similar analysis performed in additional cohorts will help clarify the effect of remission definition on the identification of predictors for remission.

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Improved Reproducibility of Joint Space Width Measurements Acquired with High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) Using a 3D Joint Space Thickness Analysis

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Objective: Prior methodology used to determine the minimum joint space width of metacarpal (MCP) joints based on Region Growing Analysis (Image Processing Language) had poor reproducibility and was not robust to changes in joint position, thus limiting applicability in longitudinal studies. We propose a 3D joint space thickness measurement to decrease measurement error associated with repositioning.

Methods: The 2nd and 3rd MCPs of the dominant hand of early rheumatoid arthritis and control subjects was imaged using HR-pQCT (Scanco Medical AG, Brüttisellen, Switzerland). This novel peripheral CT instrument is capable of accurately and reproducibly imaging bone microstructure at a nominal isotropic voxel dimension of 82 micrometres. Precise measures of 3D microstructural morphometric parameters and volumetric density of the cortical and trabecular components of bone are possible. For this analysis, grayscale data obtained from HR-pQCT was binarized using Scanco Medical's standard patient analysis method to extract bone from the surrounding soft tissue. A series of analysis steps creates dilated and eroded images of the metacarpal and proximal phalange bones to smooth the periosteal contours. The masks of the smoothed bones are subtracted from the final image to yield a mask of the joint space. The joint space is measured in 3D using the 'direct' method (i.e. fitting maximal spheres) which provides a measure and distribution of joint space thickness.

Results: Ten joints were imaged twice, with repositioning of the patients' hands between series. The mean joint space width of the 2nd MCP was 2.13 mm (SD 0.15) and of the 3rd MCP was 2.20 mm (SD 0.21). Reproducibility with repositioning was excellent, with overlapping filtered histograms (data not shown), and a root square mean coefficient of variance of 2.4%.

Conclusion: We have devised an analytical method to provide precise measurements of joint space width, robust to changes in joint position. This method will be superior for analyzing joint space width measurements in longitudinal studies, where repositioning error is of concern.

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Hydroxychloroquine Retinopathy in Inflammatory Arthritis: A Retrospective Analysis in Canadian Patients

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Objective: Antimalarial agents such as hydroxychloroquine (HCQ, Plaquenil®) have been linked to toxic ocular changes after prolonged use. The incidence of toxic changes is unclear for patients with inflammatory conditions, although prior studies show a low incidence. The objective of this study was to examine the frequency of HCQ retinopathy in patients treated for various inflammatory conditions, with an abnormal mfERG.

Methods: Seven hundred eighty two patients (age range 26 - 90 years) treated with HCQ between 2004 and 2010 were identified in a qualitative retrospective study. Sixty seven patients with potential retinopathy were identified after an abnormal multifocal electroretinogram (mfERG). Follow-up serial studies and complete ophthalmic assessments (visual acuity, dilated fundoscopy, automated Humphrey visual field (HVF)) six months to a year apart were conducted to distinguish patients with HCQ retinopathy, from those with abnormal mfERG stemming from non-antimalarial toxic changes or a false positive mfERG result.

Results: Of the total number of patients identified with an abnormal mfERG, four female patients (age range 59-72 y.o.) were identified with probable retinal toxicity (5.88 %) after 2.2, 4, 6 and 8 years of treatment with HCQ (median dose 400 mg/d). None of these patients had ocular symptoms. Both patients using HCQ for more than 5 years developed Bull's eye maculopathy and an abnormal HVF, while the other two were identified with serial mfERG and ophthalmic assessments. Eighteen patients (age range 29-75 y.o.) initially thought to have an abnormal mfERG had no evidence of ocular toxicity. Twenty-nine patients (age range 36-90 y.o.) had a persistently abnormal mfERG with no evidence of toxicity (42.6 %). Many of them (21 patients) had other ocular diseases (glaucoma, macular degeneration, diabetic retinopathy, cataracts, retinal pigment epithelial changes).

Conclusion: We report a much higher rate of HCQ retinal toxicity than previously described in this select population. Of the sixty-seven patients, none of the patients with ocular toxicity were symptomatic and one of them developed ocular disease after 2.2 years of treatment. Patients who have risk factors for potential toxicity, including duration of HCQ use, age, and other ocular diseases may benefit from mfERG screening, even in the absence of ocular symptoms. Our study highlights the important role mfERG may play in the early detection of patients at risk for developing antimalarial toxicity.

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Long-term Radiographic Outcome in Psoriatic Arthritis Patients Treated with Golimumab: 104 Week Results from the GO-REVEAL Study

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Objective: Golimumab (GLM), a human monoclonal anti-TNF α antibody administered as every 4 weeks subcutaneous injections demonstrated long-term clinical efficacy and acceptable safety through wk104. The effect of GLM on inhibition of progression of structural damage PsA pts has been shown through wk52. Week 104 radiographic results are being reported now.

Methods: Adult PsA pts with ≥ 3 swollen & 3 tender joints (SJC/TJC) were randomized to receive SC placebo (PBO) or GLM 50 mg or 100 mg q4 wks. At wk16, pts with < 10% improvement in SJC/TJC's entered early escape (EE) in a double-blinded manner to GLM 50 mg (PBO pts) or GLM 100 mg (GLM 50 mg pts). All pts randomized to PBO received GLM 50 mg from wk24 through wk104. Pts on GLM 50 mg could be dose-escalated based on the investigator's judgment to GLM 100 mg after unblinding at wk52. Radiographs of the hands and feet were read at wks 0, 52, and 104. Erosions and joint space narrowing were evaluated by two independent readers unaware of treatment and image time sequence using the van der Heijde-Sharp (vdH-S) method modified for PsA. Data was analyzed based on randomized groups (analyses for PBO group includes pts who qualified for EE, crossed-over to GLM 50mg and pts were dose-escalated from GLM 50 mg to GLM 100 mg; GLM 50 mg group includes pts who qualified for EE and pts who were dose-escalated to GLM 100mg; GLM 100 mg group includes pts who qualified for EE). Due to lack of adequate control arm, no statistical comparisons were performed at wk52 or wk104.

Results: 405 pts were enrolled. Mean age was 46-48 yrs, median SJC/TJC's were 12-14/22-24, HAQ scores were 1.0-1.1, CRP levels were 0.6 mg/dL, and mean (median) total vdH-S scores were 16.34-22.99 (9.00-10.50). Change from baseline to wk52 in total scores were [mean+SD (median, IQR)]: 0.10 ± 1.88 (0.00[0.00,0.50]), -0.30 ± 1.65 (0.00[-0.50,0.00]), and -0.35 ± 1.70 (0.00[0.00,0.00]) for the PBO, GLM50mg, and GLM100mg groups, respectively. Change from wk52 to wk104 in total score were: -0.03 ± 1.59 (0.00[0.00,0.00]), -0.10 ± 1.0 (0.00[0.00,0.00]), and 0.02 ± 0.71 (0.00[0.00,0.00]), respectively. Change from baseline to wk104 in total score were: 0.08 ± 3.19 (0.00[-0.50,0.50]), -0.39 ± 2.04 (0.00[-0.90,0.00]), and -0.32 ± 1.873 (0.00[-0.50,0.00]), respectively.

Conclusion: GLM 50 mg and 100 mg treated patients with active PsA showed no to minimal evidence of radiographic disease progression through wk104.

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Early and Sustained Remission Associated with Normalized Physical Function, Health-Related Quality of Life & Significantly Improved Productivity in Patients with Active Psoriatic Arthritis Treated with Golimumab: 2-Year Data from Phase III GO-REVEAL Trial

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Objective: To evaluate the impact of golimumab(GLM) on disease remission, physical function, work productivity and healthcare utilization in patients with psoriatic arthritis (PsA) over 2yrs.

Methods: GO-REVEAL was a multicenter, randomized, placebo-controlled study. Adult patients with active PsA (n=405) were randomized to GLM(50 or 100 mg) q4wks or placebo. At wk16, patients with inadequate response entered early escape. All placebo-treated patients received GLM50mg from wk24. Clinical responses were analyzed using 20% improvement by the American College of Rheumatology criteria(ACR20) and 75% improvement by Psoriasis Area and Severity Index(PASI75); remission was measured by disease activity score (DAS28 < 2.6). Patient reported outcomes included health assessment questionnaire(HAQ), self-reported productivity and medical visits. Comparisons between GLM and placebo-treated patients before wk24 were performed using ANOVA on van der Waerden normal scores for continuous outcomes or Chi-square test.

Results: At baseline, mean age was 47.0 yrs and 63% of patients were male. Baseline HAQ was 1.02 and PASI score was 7.8. Compared to placebo, a greater proportion of patients treated with GLM achieved DAS28 remission as early as wk4(16.3% vs. 3.6%, $p < 0.001$) and wk14 (30.6% vs. 1.9%, $p < 0.001$). Increased remission was observed over time with over 50% of patients treated with GLM achieving remission at wk104. A greater proportion of GLM-treated patients achieved ACR20 and PASI75 response, a normalized physical function (HAQ ≤ 0.5) or quality of life, or had significantly improved work productivity compared to placebo-treated patients at wk14 (all p-values < 0.01). These improvements were sustained over time through wks52 and 104. A greater proportion of patients in DAS28 remission also achieved normal physical function, or had significantly improved work productivity from baseline at wks52 and 104, when compared to those not in remission. Improvement in employability, reduced time lost from work by patients and care-givers and reduced healthcare utilization were observed at wks52 and 104, especially among those who achieved DAS28 remission. The overall safety profile of GLM through wk 104 was similar to other anti-TNF α agents used for the treatment of PsA.

Conclusion: GLM treatment induced early and sustained remission (DAS28 < 2.6), resulting in long-term improvements in physical function, health-related quality of life, work productivity and reduction in healthcare utilization in PsA patients.

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Golimumab Treatment Inhibits Progression in Joint Damage in Patients with Psoriatic Arthritis Regardless of Baseline Disease Severity

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Objective: To identify variables associated with radiographic joint damage in pts with PsA treated with golimumab(GLM) or placebo(PBO) (standard therapy with MTX or/and NSAIDs) in a Ph3 randomized, PBO-controlled study(GO-REVEAL).

Methods: Adult PsA pts with ≥ 3 swollen & ≥ 3 tender joints were randomized to subcutaneous placebo (PBO) or GLM (50 or 100mg) q4wks. At wk16, pts with < 10% improvement in swollen and tender joint counts entered early escape in a blinded fashion to GLM50mg (PBO pts) or GLM100mg (GLM50mg pts). Starting at wk 24, pts remaining on PBO were crossed over to GLM50mg. Changes from baseline in PsA modified vdH-S scores of hands and feet were compared at wk24 and wk 52 by stratification of baseline disease activity (DAS28>5.1 vs. ≤ 5.1) or CRP level (> 0.6 vs. ≤ 0.6 mg/dL). Logistic regression model was used to adjust for covariates (age, gender, disease duration, body weight, baseline MTX use) when examining association of baseline DAS28 with joint progression from baseline to wk 24 or from wk 24-52. In logistic regression model, only pts who had no missing X-ray data were evaluated.

Results: 405 pts were enrolled with mean (SD) total PsA modified vdH-S scores of 18.15 (27.76) to 23.85 (35.41) and baseline DAS28 score of 4.9 (1.0) to 5.0 (1.1). At wk24, GLM-treated pts had significantly less radiographic damage than PBO (mean change from baseline -0.09 ± 1.32 vs. 0.27 ± 1.26 , $p = 0.015$) or had no progression (change ≤ 0) than PBO-treated pts (77.7% vs. 62.7%, $p = 0.003$). These differences were greater among pts with high disease activity (DAS28>5.1) ($p < 0.01$) or elevated CRP (CRP>0.6 mg/dL) ($p = 0.01$) than pts with moderate disease activity or normal CRP. After adjusting for baseline characteristics using a regression model, higher baseline disease activity was significantly associated with radiographic progression at wk24 in the PBO group ($p < 0.01$), but baseline disease activity was not associated with radiographic progression in the GLM group. Similarly, disease activity at wk24 in all pts randomized to GLM or switched to GLM at wk24 was not associated with radiographic progression from wk24 to 54, suggesting that irrespective of disease activity at wk24, there was absent or nominal progression in joint damage at wk52.

Conclusion: PsA pts with high arthritis disease activity or CRP level at baseline experience more joint damage if treated with standard therapy only. Adding GLM provides additional benefit in inhibiting radiographic progression, especially for pts with more severe disease activity. The beneficial effect of GLM on joint damage was also observed in pts with baseline DAS28 < 5.1 or CRP < 0.6 mg/dl but to a lesser degree than in pts with high disease activity.

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The Effectiveness of Abatacept in a Large RA Real World Practice: Changes in the HAQ Over Time and Durability of Response

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Objective: A large Canadian database was used to determine effectiveness of abatacept in real world RA patients by examining changes in health assessment questionnaire (HAQ), and the proportion of patients continuing abatacept over time.

Methods: RA patients administered abatacept in routine practice via the Oencia Response Program network, between Aug. 2006 and Feb. 2011 who received clinic or home infusions and had at least one follow-up evaluation were included. The number needed to treat (NNT) to improve HAQ by at least the minimally important difference (MID > 0.22) and abatacept survival until last follow up were calculated overall, and for those post DMARD and post TNFi.

Results: Among the 2,929 patients enrolled, 1,771 (60.5%) were eligible for the study (mean age 57.6 years; disease duration 16.5 years (SD 11.0), 77% female, 79.2% had past TNFi) with a mean (SD) follow up of 13.8 (12.3) months. Mean (SE) durability of treatment was 26.8 (0.53) months; where 66% were still on abatacept at 12 and 53% at 24 months. The survival was longer where abatacept was the first biologic vs. post TNFi ($P=0.0001$). In abatacept as 1st biologic, 70% achieved MID in HAQ vs. 71% if post TNFi ($P=0.65$) with $NNT=1.4$ in each group and there were also no differences in % achieving MID comparing no past biologic to 2, 3 or 4 previous biologics. For those staying on abatacept, the mean improvement in HAQ increased over time; changing at 6, 12, 18 and 24 months by -0.29, -0.41, -0.45 and -0.51 respectively with no difference between abatacept as first biologic vs. post TNFi. Increased baseline HAQ (OR 2.13 (1.89, 2.39)) and less years of RA (OR 0.98 (0.97, 0.99)) were significant predictors of achieving the MID for HAQ.

Conclusion: The results demonstrate that abatacept is effective in improving function in RA despite long disease duration. For those still on abatacept, HAQ continued to improve over the first 2 years. The real world durability of abatacept is better as first biologic; however the overall survival in this large study seems similar to other biologics despite 79% having previous TNFi exposure.

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A Novel Program for Young Rheumatologists: Description of the Future Leaders in Rheumatology Program (FLIRT)

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Objective: Specific programs aimed at development of junior faculty as future leaders may be lacking at many institutions and academic programs. The Future Leaders in Rheumatology (FLIRT) program was developed to address this need.

Methods: FLIRT is a competitive program sponsored by pharmaceutical companies and approved by The Canadian Rheumatology Association (CRA). CRA members, program directors and division heads were con-

tacted to nominate potential future leaders in academic or community practice who were early in their careers. Criteria for entry were based on scoring the CV, candidate's statement of future leadership roles and letters of support. Candidate selection criteria included completion of core rheumatology training and affiliation with a Canadian university or being considered to be tomorrow's leaders in the community. Candidates required at least one of: 1) demonstrating commitment to a higher level of education and expertise in rheumatology and showing promise of becoming a future thought leader (this could be with an academic appointment or a community 'rising star'), 2) actively involved with clinical or basic research and / or 3) actively involved in education. Peer review of applicants was performed by members of the CRA representing a broad spectrum of experiences (regional representation, academic, community).

Results: Twenty-two of 28 applicants were accepted into the program. The program was developed based on a comprehensive needs' assessment completed by candidates. Program objectives were to: 1) provide aspiring young Canadian rheumatologists with the opportunity to participate in a high-quality, innovative multi-faceted program; 2) build personal and professional contacts with thought leaders both nationally and internationally; and 3) develop insights into career building, publications, promotion and advocacy. Faculty have a broad expertise in research, education, and leadership. The needs' assessment identified understanding promotion, mentoring, maintaining work life balance, presentation skills and relations with other agencies and pharmaceutical industry as high needs. Two face-to-face one day meetings were conducted as this was the preferred method of interacting. To date, content has included: presentation skills with feedback to presenters, update on promotion pathways, maintaining work life balance, mentorship, self-promotion, learning and teaching skills, critiquing CVs, workshops on education pathways, research and interactions with organizations, advocacy at various levels and grant writing. Program evaluations have demonstrated high scores >5.5 out of 7.

Conclusion: Junior faculty have identified a need for leadership training. The FLIRT program may be a model for identifying and promoting leadership development in rheumatologists early in their career.

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Function and Disease Activity Vary by Rheumatoid Factor Status in Early Inflammatory Arthritis with Stronger Associations in RF Positive Patients: Results from the CATCH Cohort

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Objective: Our goal was to investigate the relationship between functional capacity and disease activity in early inflammatory arthritis (EIA) in a contemporary cohort and to determine if the correlations changed over time.

Methods: Data from patients ($n=1,143$) were collected from the Canadian Early Arthritis Cohort (CATCH), a multi-site observational cohort of EIA. HAQ and DAS28 were assessed at each visit. Correlations were done between HAQ and DAS every 3 months for the first year and then at 18 and 24 months. The relationship between HAQ and DAS in older and younger subjects (< 65 versus ≥ 65) and in those who were RF positive or negative was studied.

Results: Mean symptom duration at first visit was 6.3 months. Mean HAQ and DAS scores were highest at the initial visit. HAQ scores decreased over time from a baseline of 0.94 to 0.40 at 24 months. Mean DAS28 scores also decreased over time from a baseline of 4.54 to 2.29 at 24 months. Correlations between HAQ and DAS were significant at all time points ($p<$

0.01) and varied over time. The strongest correlation between HAQ and DAS in the first 12 months occurred at the first visit ($r=0.53$, $n=1,143$), at which point many of the patients were untreated. At 6, 9, and 12 months the correlation was weaker ($r=0.41$, $r=0.30$, and $r=0.40$, respectively). Strong correlations were again noted at 18 months ($r=0.57$, $n=321$) and 24 months ($r=0.59$, $n=214$). The baseline correlation between HAQ and DAS was significantly different than correlations obtained at 3, 6, and 12 months ($p=0.02$, 0.01 , and 0.01 , respectively). Age did not change the association between HAQ and DAS {< 65 years old ($r=0.50$, $n=868$) versus ≥ 65 ($r=0.48$, $n=254$)}, but RF status did: RF+ relationship was stronger than RF negative ($r=0.63$, $n=636$ versus $r=0.47$, $n=477$).

Conclusion: Function and disease activity both improved after initiation of treatment; HAQ and DAS were related, but in the first year they were most strongly linked at the first visit. Those with positive RF status had stronger associations over the two-year period.

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Improving Outcomes in Early Rheumatoid Arthritis by Determining Best Practices: Does Site Size Matter OR is it Best Treatment Early? An Analysis of the Canadian ERA Cohort

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Objective: To investigate whether site differences occur and have an effect on disease outcome, and if so, to determine whether site differences in treatment are the reason for this effect.

Methods: Sites from the CATCH database with at least 40 patients at 6 and 12 months after enrolment were studied and randomly renumbered with investigators blinded to site. Remission was calculated (using DAS28 < 2.6, SDAI $\leq$ 3.3, CDAI $\leq$ 2.8) to determine differences between sites including treatment. Regression models included site as a variable and confounding baseline characteristics that had a p -value < 0.10 in univariate analyses.

Results: Of the 1138 baseline (8 sites ranged from 58 to 255 patients), 798 and 640 patients had data at 6 and 12 months. Baseline descriptive statistics (mean (SD) or %) were: age 52(17) years; 72% female; 23% had erosions; 54% were current or ever smokers; 37% anti-CCP positive; 51% RF positive; disease duration 187(203) days; number of comorbidities 2(2); HAQ 0.9(0.7); DAS28 4.5(1.4). Increasing site size was not related to symptom duration, age, number of comorbidities, % with RF and % meeting criteria for RA. Combination DMARDs varied from 18.5% to 74.6% and mean number of DMARDs was 1.2 to 2.3. The site with the most combination therapy at baseline and throughout follow up (2nd largest site) had more patients in remission, the largest change in DAS at 6 months and the least amount of treatment intensifications over the year. At 12 months, the two largest sites had the best changes in DAS and one strategy was initial onset of combination DMARDs (3/4 of patients at onset) and the other site strategy was initial use of sc methotrexate in 62%. The two largest sites had least changes of DMARDs over the first year. The smallest site had worst outcomes and most treatment changes. Regression analyses showed that site was an important predictor for mean changes in DAS28 ($p \leq 0.000$), increase in DAS28 ($p \leq 0.004$), DAS28 remission ($p \leq 0.000$), CDAI remission ($p \leq 0.000$), and SDAI remission ($p \leq 0.022$). Medication increase over time was a strong predictor of poor outcome ($p < 0.05$).

Conclusion: Site is a major predictor for ERA outcome at 6 and 12 months with successful treatment methods (initial combination therapy) for best change in DAS and remission at 6 months and initial combination therapy or starting with sc methotrexate for outcomes at 12 months.

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Adherence to Rheumatoid Arthritis Treatment Recommendations

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Objective: Assess adherence to the 2008 American College of Rheumatology recommendations for the treatment of rheumatoid arthritis, in order to evaluate quality of care provided at a tertiary care centre.

Methods: A retrospective chart review was performed to identify clinical parameters (patient demographics, prognostic features, disease duration, disease activity), and treatment parameters (prescribed therapies, investigations) for patients with rheumatoid arthritis seen at our centre since January 2009. Using these parameters, we assessed adherence to treatment recommendations for the following categories: i) appropriate therapy for level of disease activity, ii) baseline investigations for initiation of new therapeutic agents, iii) frequency of laboratory monitoring, iv) vaccinations, v) tuberculosis screening, and vi) discontinuation of therapeutic agents if a contraindication to that therapy exists or develops.

Results: A sample of 100 randomly selected charts representing 310 visits with 4 tertiary care rheumatologists was analyzed. Patient demographics were representative of typical rheumatoid arthritis patients (78% female, average age 54 years). The chart audit identified adherence to treatment recommendations based on disease activity levels in 89.7% of visits. Inappropriate continuation of anti-malarial monotherapy (based on moderate or high disease activity, or poor prognostic factors) occurred at 20 of the 23 visits where non-adherence to treatment recommendations was identified. Adherence to recommendations for biochemical investigations and tuberculosis screening at initiation of a new therapy was excellent, as was the frequency of laboratory monitoring. However only 68.9% of patients had a documented ophthalmologic examination in the first year of anti-malarial therapy, and only 2.1% of charts contained information on vaccination status. Appropriate discontinuation of therapy was observed in peri-operative management, cases of acute infection, elevation of liver enzymes, pre-existing lung disease and parturition.

Conclusion: We have demonstrated that the majority of patients with rheumatoid arthritis receiving care at our centre are treated to current therapeutic targets and receive appropriate investigations. Two main areas for improvement relate to ophthalmologic testing recommendations and verification of vaccination status.

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Development of the OA GO AWAY Tool: A Self-management Aid for Patients with Knee or Hip Osteoarthritis

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Objective: To develop a self-management tool that enables patients to keep track of their exercise and eating habits as well as the ways OA is affecting their lives in order to promote exercise adherence and healthy eating

Methods: A review of the literature identified valuable properties of interventions to improve exercise adherence and healthy eating. Based on these findings, a tentative self-management tool for monitoring exercise and eating behaviours as well as relevant OA outcomes was created by a team of experts in rheumatology and graphic design. Ten patients with OA of the hip or knee used it in clinical practice for up to two months and reviewed the items for clarity and relevance.

Results: The "OA GO AWAY" self-management tool comprises 2 parts: a monthly self-evaluation journal and a daily exercise log, which may be used for tracking health behaviours and outcomes over time as well as establishing personal goals. The monthly self-evaluation journal helps

patients to assess several health outcomes relevant to OA including individualized functional challenges, sleep, mood, energy, pain, measures of body weight and fitness as well as other symptoms. The journal also evaluates treatments being used for their OA (including medication and alternate treatments) and eating habits. The exercise log allows patients to monitor the frequency, time and intensity of their exercise and physical activities and their OA treatments on a daily basis. Patients found the tool easy to use and felt that documenting personally meaningful challenges helped them to understand the impact of OA on their life and the importance of being active and eating well.

Conclusion: The OA GO AWAY tool is now ready for psychometric and feasibility testing. It may be an innovative tool to support patients with OA of the hip or knee to actively self-manage their disease. It is hoped that, by self-monitoring personally meaningful outcomes, patients will in turn be motivated to improve their adherence to exercise and healthy eating.

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Patient-Driven On-Line Survey on Granulomatosis with Polyangiitis

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Objective: Granulomatosis with polyangiitis (Wegener's; GPA) is a rare small-sized vessel vasculitis with a low prevalence. These numbers make it difficult to recruit large numbers of patients for cross-sectional studies. In recent years internet-based forums and weblogs (blogs) have emerged as a means for patients with rare diseases to connect and share experiences. Recently, one of our patients with GPA posted a link on her blog, requesting GPA patients worldwide to complete a SurveyMonkey® questionnaire on their disease. The objective was to determine results of a patient blog on GPA.

Methods: The survey was devised by our GPA patient, who placed it online in November 2010 on her blog. The survey targeted patients with GPA, as a self-reported diagnosis, and included 10 questions to anonymously assess country of residence, gender, age at diagnosis, selected comorbidities, presenting symptoms, specialty of the physician who eventually provided the diagnosis, diagnostic delay and initial treatments.

Results: After 7.5 months data collection, 369 respondents completed the survey. Six of them were excluded because of other reported conditions. After reviewing the remaining forms, 345 respondents with consistent evidence for GPA and who filled in >80% of the questionnaire were retained for analysis. 61.9% were women and 62.3% were aged between 30 and 60 years at diagnosis. Of the 316 who answered the question where they were living at diagnosis, most patients were from North America (74.7%), 16.8% from Europe, and 8.5% from elsewhere. The main self-reported signs at diagnosis were fatigue (67.8%), sinus symptoms (67.2%), arthralgias, night sweats, earache, weight loss, cough, loss of appetite, headaches, cutaneous symptoms, ocular manifestations or bloody sputum. Prior history of allergy was reported by 30.5% patients. GPA diagnoses were established by rheumatologists (for 40% of the respondents), but also ENT surgeons, respirologists or nephrologists (for 15.4, 13.0 and 12.2%, respectively). The delay between first symptoms attributed to GPA and diagnosis was 15.1 ± 26.0 months. Only 3 patients reported not having received corticosteroids as their initial treatment (cotrimoxazole instead), whereas 61.3% were given cyclophosphamide.

Conclusion: Patient-driven surveys and reported outcome studies represent novel and powerful methods to study rare diseases such as GPA. The high response rate to this original patient-driven online survey strongly supports such initiatives. Even though its design did not allow us to confirm GPA diagnosis, its findings are close to those previously reported on diagnostic delay and initial GPA manifestations.

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Quantification of Hand Temperatures using Thermography in a Healthy Patient Cohort

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Objective: Thermography is a novel and potentially useful tool for evaluating patients with inflammatory arthritis. Objective was to explore the range of temperature values in normal individuals using a thermography camera, and to calculate the precision of temperature measurements in the same individuals in the absence of inflammatory arthritis.

Methods: 1) Thermographic examination was performed using a thermography camera "FLIR T300 Shortwave Thermovision System" and following the International Academy of Clinical Thermology guidelines. All subjects rested for a 15 minute acclimation period prior to the thermal image. The camera was maintained at a fixed distance (0.5 m) over the hands, and the subjects positioned their hand in a resting hand splint to ensure consistency. Both a thermography image and digital image were performed. The patients were imaged on two occasions, in the morning and in the afternoon. 2) A group of 29 healthy volunteers from the University of Alberta were analyzed. Subjects with history of inflammatory or symptomatic joint disease or exclusionary criteria were excluded from the study. 3) The lowest temperature between MCPs and PIPs of each subject was considered as the temperature parameter. The difference in temperature between a joint and this fixed reference was designated the delta spot temperature.

Results: Results of 29 patients were: 18 female, 11 male; mean age of 33.5 years. Descriptive statistics were completed on the results. The lowest absolute MCP temperature was 25.1°C, while the highest was 35.5°C. The lowest absolute PIP temperature was 24.1°C, while the highest was 34.8°C. The greatest temperature parameter difference was 3.8°C, with the mean difference 0.74°C. The warmest joint, most consistently was the first MCP.

Conclusion: The assessment of hand temperature using thermography in a healthy patient cohort is necessary to determine the abilities of the thermography camera. This data provides the first assessment of healthy patients, and the quantitative temperatures assessed. The data provides support that the absolute temperature varies between individuals, however the change between joints is important. Thermography is able to detect quantitative differences between joint temperatures.

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Evaluation of Interprofessional Patient-Centred Collaborative Practice Behaviour and Perceptions following an Intensive Continuing Education Development Initiative in Arthritis Care

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Objective: The purpose of this study was to evaluate the practice behaviour and perceptions amongst Advanced Clinician Practitioner in Arthritis Care (ACPAC) program-trained extended role practitioners and relevant members of their teams at one year and beyond completion of training in order to determine the extent to which this new human health resource in arthritis care is perceived to function in the context of Interprofessional Patient-centred Collaborative (IPC) practice in Ontario.

Methods: This study used a mixed-method approach. Qualitative: Focus groups (n=3) for ACPAC practitioners (n=20 participated); Interviews (n=18) for their clinical colleagues and administrators. These were digitally audio-recorded for verbatim transcription, entered into HyperResearch software for textual data analysis. Transcripts were coded for anticipated and emergent themes using the method of constant comparison including searches for disconfirming evidence. Themes related to IPC were identified using components of Barr et al (2005) evaluation of interprofessional edu-

cation (IPE) initiatives framework to evaluate behavior and modification of attitudes and perceptions, change in organizational practice and benefit to patient. Quantitative survey completed by ACPAC practitioners (n=24): Bruyère Clinical Team Self-Assessment on Interprofessional Practice and a single-item rating of team's readiness for IPC practice. Descriptive statistics were used.

Results: Interviews and focus groups with ACPAC graduates and their clinical colleagues or administrators suggest these practitioners are generally effective at promoting and contributing to IPC within arthritis care settings. Varying degrees of IPC exist within their arthritis care teams. Barriers such as institution-specific lack of medical directives, remuneration conflicts, and role recognition issues were identified to impede role implementation. Quantitative survey: Seventy percent felt their team was actively working in an IPC practice model; 25% felt it was in the precontemplation or contemplation phase; 5% were prepared for action (making plans). Mean Bruyère subjective subscale scores were high (all >3, scale range 1-5=better perception of teams IPC practice) and lower (mean 4.6, scale range 0-9=more team practices associated with IPC) on the objective scale.

Conclusion: ACPAC graduates are effective participants of, and contributors to IPC care at select sites. Their presence appears to both promote organizational change and impart general benefit to the collaborative care of patients with arthritis. However, ACPAC graduates are working on teams that are at varying stages of readiness for IPC practice. They appear to understand what is needed for IPC while fewer actual IPC team practices are in place. Intensive IPC components were recently added to the ACPAC curriculum to address this gap.

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Annual Golimumab Utilization for Psoriatic Arthritis Patients Enrolled in United States Managed Care Plans

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Objective: Golimumab (GLM) has recommended dosing of 50 mg once monthly in psoriatic arthritis (PsA). GLM managed care utilization data in the United States (U.S.), published thus far, have reported less than one year of utilization data and have not been specific to a population of patients with PsA. This study assessed the observed one-year GLM dosing patterns within a U.S. managed care population of PsA patients.

Methods: The IMS LifeLink™ Health Plan Claims database was utilized to identify patients who had/were: index golimumab pharmacy claim started 4/24/2009-01/06/2010; aged ≥18 years at index; ≥1 PsA ICD-9 diagnosis code (696.0); and 12 months pre- and ≥12 months post-index continuous enrollment. Biologic experience was defined as ≥1 medical or pharmacy claims for abatacept, adalimumab, certolizumab, etanercept, or infliximab at anytime during the 12 month period prior to the first GLM prescription. GLM utilization was reported as the proportion of patients and prescriptions at the recommended 50 mg dose, and intervals between fills, for the 12 month post-index period.

Results: A total of 127 PsA patients receiving GLM (n=914 prescriptions) were identified; 59.8% were female; mean±SD age was 49±10 years. The majority (78.7%) of patients had pre-index biologic experience. Among the biologic-experienced, 73.0% received 1 unique biologic, 24.0% received 2 unique biologics, and 3.0% received 3+ unique biologics before GLM. A 50 mg GLM dose was dispensed in 95.3% of all PsA patients upon initiation and 96.6% of all prescriptions. The GLM dose at each of the first 12 prescription fills was 50 mg for 95.2%-97.9% of patients. A 50 mg GLM dose was dispensed upon initiation in 94.0% and 100.0% of biologic-experienced and non-biologic-experienced PsA patients, respectively. The overall mean±SD interval between GLM prescriptions was 32±14 days; the median was 30 days. Based upon the observed GLM prescription intervals, a mean of 11.4 GLM doses per year would be realized.

Conclusion: In this nationally representative managed care population, the majority of PsA patients receiving GLM was biologic-experienced and received a 50 mg dose on a monthly basis. Despite the history of biologic

use, the majority of PsA patients using GLM did not have an apparent increased dose requirement upon initiation.

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Golimumab Dosing Patterns and Patients Characteristics, Real-life Data from the BioAdvance® Canadian Patient Support Program

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Objective: Background: Golimumab (GLM) is a monthly, subcutaneous, anti-TNF-α agent that is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) in adults. This study evaluates the baseline characteristics and dosing patterns of patients who received golimumab in Canada as reported in the database of the BioAdvance® patient support program (PSP). We assessed GLM dosing patterns within a Canadian population of RA, AS and PsA patients in the BioAdvance® patient support program.

Methods: The BioAdvance® Patient support program of Janssen Inc. is a set of patient services designed to support infliximab, golimumab and ustekinumab patients throughout their treatment. Part of this program includes the management of prescription lifecycle and/or changes in dosing. The database was utilized to identify golimumab patient baseline characteristics and dosing patterns. The following parameters were evaluated: Indication (RA, AS or PsA), most recent physician prescribed frequency of dosing, status of participation in the PSP (Discontinued yes/no), biologic experience (≥1 prior biologic) & type of drug reimbursement plan (Public or Private).

Results: A total of 2248 patients receiving GLM were identified between 2009 and 2011. 1158 had a diagnosis of RA, 544 of AS and 546 of PsA. The majority (62.8%) of patients had no prior biologic experience. The latest recorded prescription of GLM was 50 mg once monthly in 98.7% of the patients irrespective of their participation status (16.3% of GLM patients were no longer part of the PSP at the time of analysis). In patients no longer part of the PSP, the last prescribed dose was 50 mg once monthly in 100% of the cases. Among the 1.3% (29/2248) of patients not prescribed 50 mg once monthly dosing 8/2248 were on 50 mg Q4wks (0.36%), 17/2248 on 50 mg Q3wks (0.76%) and 4/2248 on 50 mg Q2wks (0.18%). Of these 29 patients out of 2248 not prescribed a 50 mg once monthly dose of GLM, 55.17% (16/29) were previously exposed to a biologic treatment prior to GLM initiation (7 etanercept, 7 adalimumab and 2 remicade).

Conclusion: In this Canadian BioAdvance® support program, 98.7% (2219/2248) of Canadian GLM patients were continuously prescribed a 50 mg dose on a once monthly basis.

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Characteristics of Golimumab Utilization and Compliance in a Large National Payer Database

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Objective: Golimumab is a once-monthly, subcutaneous, anti-TNF-α agent that is indicated for the treatment of moderately to severely active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) in adults. This study evaluates the baseline characteristics, utilization patterns and dosing compliance of patients who received golimumab in a large healthcare payer database.

Methods: We performed a retrospective analysis of the IMS LifeLink™ Health Plan database from 1/1/1995 through 10/31/2010. This paid-claims database is a systematic sample of commercial health plan information obtained from managed care plans throughout the United States. A total of 65,937 patients in this database had a diagnosis of either RA, PsA, or AS, had at least one biologic on record started after diagnosis, were ≥18 years of age at the time of the first diagnosis. Of these patients, 182 had continuous enrollment, ≥6 months pre- and post index of golimumab use, at least two records of golimumab use, no other biologics during the golimumab treatment window, and once a month fill patterns. Monthly was defined as an interval of 28-31 days.

Results: Of the 182 patients that received at least two golimumab doses, 130 had a diagnosis of RA, 32 of PsA, and 20 AS. The mean age at diagnosis was 48.5 yrs and 74% of the sample was female. A total of 109 (59.9%) patients were bio-experienced and 73 (40.1%) were bio-naïve before initiating golimumab. Of these patients, the median and mean dosing interval was 29 days and 32.6 days. When looking at biologic-naïve patients, dosing intervals were similar for biologic-experienced patients. 84% of the refills were within the monthly (± 7) day compliance window. A 50 mg dose was observed in 97.6% of fills.

Conclusion: In this healthcare payer database, the majority of patients with at least 2 fills of golimumab were female, > 40 years of age, and had prior biologic experience. Golimumab patients showed consistent dosing intervals and high compliance with a majority of fills at 50mg.

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Direct Medical Costs in Patients with Systemic Autoimmune Rheumatic Diseases

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Objective: To estimate the direct medical costs in a population-based cohort of Systemic Autoimmune Rheumatic Diseases (SARDs)-including the connective tissue (CTD) disorders systemic lupus erythematosus, systemic sclerosis, Sjögren's disease, and poly/dermatomyositis, and systemic vasculitides (VD)- from the province of British Columbia (BC), Canada.

Methods: Data sources: Our administrative data captured all health services (outpatient visits, investigations and hospitalizations) and all prescriptions from 1996-2007 (regardless of funding source). Study population: A population-based cohort of SARDs cases was identified using the following algorithm: (a) ≥ 2 ICD codes for SARDs ≥ 2 months apart but within a 2-year period by any non-rheumatologist physician (b) ≥ 1 ICD code for SARDs by a rheumatologist, or (c) ≥ 1 hospitalization diagnostic code of SARDs. To improve specificity, we excluded individuals with at least 2 visits ≥ 2 months apart subsequent to the 1st SARD visit (2nd for a non-rheumatologist) with diagnoses of other non-SARDs inflammatory arthritides, and those where a SARDs diagnosis by a non-rheumatologist was unconfirmed when seen by a rheumatologist. Cost calculation: Costs for medical services and prescriptions were summed directly from paid claims. Case-mix methodology was used for hospitalizations. Costs are reported in 2007 Canadian dollars.

Results: We identified 18,741 total SARDs cases, including 16,773 CTD and 1680 VD diagnoses, contributing 82,140, 76,052, and 4763 patient-years (PY) respectively. Direct medical costs over 12 years totalled \$571,216,779 for all-SARDs with \$154,580,562 (27%) from outpatient costs, \$291,664,950 (51%) from hospitalizations, and \$124,971,266 (22%) from medications. % by-component was nearly identical for CTD but VD cases incurred proportionally greater hospital costs (67%), with double the hospitalization rate (overall mean/PY=0.59 and 0.53 for SARDs and CTD vs. 1.31 for VD), while outpatient costs accounted for 20% and prescriptions only 13%. Overall, after inflation adjustments, mean annual per-PY utilization and expenditures for two components decreased over 12 years: hospital expenditures decreased ~50% (from \$5579, \$4540, and \$15,596 to \$2776, \$2425, and \$6179) and outpatient $\geq 25\%$ (from \$2205, \$2075, and \$3687 to \$1641, \$1561, and \$2513, for the all-SARDs, CTD, and VD groups respectively). Conversely, medications had a mean per-PY cost increase of ~50% (from \$1116, \$1085, and \$1426 in 1996 to \$1670, \$1617, and \$2272 in 2007).

Conclusion: The costs of SARDs at the population level represent a substantial economic burden at \$81,670,492 in 2007. The direct medical costs for Canadian SARDs patients have increased substantially over 12 years,

with medications responsible for the largest cost increase, both per-patient and overall.

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Baseline Levels of the Inflammatory Biomarker CRP are Significantly Correlated with MRI Measures of Synovitis at Baseline and after 26 Weeks of Treatment in Patients with Early Rheumatoid Arthritis

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Objective: Early detection of joint inflammation and destruction in rheumatoid arthritis (RA) by MRI is a sensitive predictor of disease progression.^{1,2} This subanalysis assessed MRI scores after 26 weeks of treatment with adalimumab+methotrexate (ADA+MTX) or MTX alone, and the correlation of baseline disease characteristics with MRI scores at baseline, week 26, and change over 26 weeks.

Methods: OPTIMA was a phase 4 trial of MTX-naïve patients ≥ 18 years old with RA < 1 year and active disease (DAS28 > 3.2, ESR ≥ 28 mm/h or CRP ≥ 1.5 mg/dL, and either >1 erosions, RF+, or anti-CCP+) randomized to ADA+MTX (N=515) or placebo (PBO)+MTX (N=517) for 26 weeks. High-field 1.5-Tesla MRI was conducted on metacarpophalangeal and wrist joints of the most clinically severe extremity per patient before and after i.v. gadolinium-based contrast. Synovitis, osteitis, and erosions were scored by 2 independent blinded radiologists using a modified OMER-ACT-RAMRIS system. Changes in observed MRI measurements were compared using an ANCOVA model adjusted for baseline. The relationship between MRI and baseline disease traits was assessed for CRP, TJC68, SJC66, DAS28, and HAQ using Pearson correlation.

Results: The MRI substudy included 70 patients with at least 1 MRI; 59 patients (27 ADA+MTX, 32 PBO+MTX) completed both baseline and week 26 MRI. Mean baseline MRI values were similar between treatment groups: 6.22/6.77 (synovitis), 5.37/3.33 (osteitis), and 6.13/4.14 (erosion) for ADA+MTX and PBO+MTX, respectively. ADA+MTX patients showed significantly greater mean decreases in MRI scores for synovitis ($-3.61/-2.03$, $P=.003$), osteitis ($-3.98/0.00$, $P=.006$), and erosion ($-0.78/1.41$, $P=.004$) compared with PBO+MTX. MRI scores were highly correlated with one another ($P < 0.001$) at baseline, week 26, and changes from baseline. Baseline CRP was significantly correlated with MRI synovitis at baseline ($P=.001$) and week 26 ($P=.02$), change in MRI synovitis ($P=.009$), and absolute erosion score at week 26 ($P=.03$), while baseline osteitis demonstrated a significant correlation with baseline TJC68 ($P=.04$).

Conclusion: ADA+MTX resulted in greater reductions in synovitis, bone erosion, and osteitis MRI scores at 26 weeks compared with PBO+MTX in early RA patients. Particularly striking was the lack of effect of MTX alone on osteitis. The strong correlation between changes in osteitis and erosion corroborates current views that osteitis precedes erosion. Baseline CRP correlation with responsiveness of MRI synovitis to treatment supports utilization of CRP in patient selection. 1 Benton N, et al. Ann Rheum Dis 2004;63:555-61. 2 Hodgson RJ, et al. Rheumatology 2008;47:13-21.

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CRRC-IRD: Cardiovascular Risk Reduction Clinic for Inflammatory Rheumatic Diseases: First Year Data of a Prospective, Observational Cohort

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Objective: The CRRC-IRD is a pilot clinic evaluating and managing cardiovascular (CV) risk of patients with inflammatory arthritis (IA). This

study evaluates the CV risk of patients with moderate to severe IA through application of CV risk scores. The carotid intima media thickness measurement (cIMT) will be evaluated to determine its utility in measuring blood vessel wall thickness as a surrogate marker of CV risk.

Methods: Patients with moderate to severe IA were invited to attend the CRRC-IRD as part of a biologics surveillance program in northern Alberta. After initial postal screening of traditional CV risk factors & fasting labs (lipid panel, glucose), clinic attendees were evaluated with pre-specified case report forms including IA activity and traditional CV risk factors. Framingham & Reynold's risk scores were calculated & the European League Against Rheumatism (EULAR) CV risk multiplicative factor of 1.5 applied when criteria were met. CIMT measurements were made on consenting patients at a later date. Risk factor modification was performed where appropriate.

Results: Thirty-four patients (M:F 12:22) attended the clinic to date, mean age 59.9 ($\pm$ 13.6) years, with the following diagnoses: 27 (79%) RA; 2 (6%) juvenile idiopathic arthritis; 5 (15%) psoriatic arthritis. Twenty-one (62%) patients were RF+, 21 (62%) anti-CCP+, and 18 (53%) were RF+/anti-CCP+. Mean disease duration was 19 $\pm$ 14 years, ESR 17 $\pm$ 17 mm/hr, CRP 7 $\pm$ 12 mg/l & DAS28 2.4 $\pm$ 1.5. Traditional CV risk assessment showed 6 (18%) active smokers, 11 (32%) with high cholesterol (LDL > 3.5 mmol/L), 3 (9%) with diabetes, 10 (29%) with untreated systolic hypertension, 16 (47%) with a family history of premature CVD & 9 (27%) with personal history of CVD. The mean Framingham and Reynold's risk score of a CV event in the next 10-years was 13.2% and 3.4% & the mean Framingham risk score applying EULAR multiplicative factor of 1.5 was 22% (21 patients). Mean CIMT measurement for any observed carotid artery was 0.71 $\pm$ 0.27 mm (118 arteries), with 45 arteries having a thickness of > 0.75 mm. Plaques were noted in 14 patients.

Conclusion: The CRRC-IRD model demonstrates the importance of evaluating CV risk given the large number of patients with abnormalities in traditional CV risk factors. The utility of existing risk scores and application of EULAR factor requires further evaluation given the discrepancy in projected rates of CV risk between risk scores. Utility of CIMT for CV risk assessment requires further validation.

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Mortality in ANCA-associated Vasculitis. A Meta-analysis of Observational Studies

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Objective: ANCA-associated vasculitis including Wegener's granulomatosis, microscopic polyangiitis and Churg-Strauss syndrome are rare disorders associated with an increased risk of early mortality when compared to the general population. Our objective was to determine the magnitude of the risk of overall mortality in patients with ANCA-associated vasculitis compared to the general population through a meta-analysis of observational studies.

Methods: A literature search was performed using MEDLINE and EMBASE databases from their inception to September 2011 by an experienced librarian to find all primary references and published reviews. Keywords included systemic vasculitis, mortality, ANCA-associated vasculitis (AAV), Wegener's granulomatosis (WG), Churg-Strauss syndrome (CSS), microscopic polyangiitis (MPA), survival rate, and standardized mortality ratio (SMR). Observational studies that met the following criteria were assessed by two researchers: 1) the individual syndromes identified by either the American College of Rheumatology classification criteria 1990 or the Chapel Hill Consensus Conference on disease definitions and 2) reported standardized SMRs and 95% confidence intervals (95% CIs) or data to calculate them. We calculated weighted-pooled summary estimates of SMRs (meta-SMRs) for overall mortality using the random effects model and tested for heterogeneity using the Q statistic. Robustness of the

results was evaluated using a jackknife sensitivity analysis; i.e. the analysis was repeated multiples times, each time with the removal of a single study from the baseline group.

Results: We identified seven studies with eight cohorts with 2,808 patients who were enrolled from 1966-2005. From these, four studies reported data by gender. Overall, the mortality risk was similar between males and females [meta-SMR = 3.3 (95% CI 2.3 - 4.8 and 3.4 (95% CI 1.9 - 6.1) respectively). Four studies assessed only WG (n= 2,079), two studies included WG and MPA (n=292) and one included WG, MPA and CSS (n= 99). Overall, there was a 300% increased risk of mortality for all AAV when compared to the general population (meta-SMR= 3.1 (95% CI 2.5 - 3.9). The meta-SMR for WG was 3.3 (95% CI 2.6 - 4.3). The jackknife sensitivity analysis showed that the meta-SMR remained significantly increased, with the point estimates ranging from 2.9 to 3.5 and the corresponding 95% CI remaining higher than 1. As expected, we identified significant heterogeneity among studies ($Q = < 0.0001$).

Conclusion: This is the first meta-analysis assessing mortality in AAV using SMRs. Overall, patients with AAV have a three-fold increased risk of mortality when compared to the general population with no significant difference between genders.

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A Meta-Analysis of Randomized Trials in the Treatment and Prevention of Digital Ulcers (DU) in Systemic Sclerosis (SSc)

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Objective: Digital ulcers (DU) in SSc occur in 50% and may be quite severe. Assessing data from DU trials in SSc may provide guidance for treatment.

Methods: The objective of this meta-analysis was to assess the efficacy of various pharmacologic therapies in treating and preventing DU in SSc including DU trials and Raynaud's Phenomenon (RP) SSc trials which recorded DU. MEDLINE, EMBASE (to November, 2010) and ACR and EULAR abstracts (2009-10) were searched for trials dealing with DU. Randomized trials comparing pharmacologic therapy with placebo or another agent were eligible. Inclusion criteria and trial quality were assessed by 2 reviewers. Quality was scored based on randomization, blinding, statistical methods, intention to treat analysis, and method of randomization. RevMan 5 software was used for analyses.

Results: 40 studies were found, and 19 excluded. Main reasons for exclusion were non-randomisation (7), no DU outcome (8) or insufficient data (4). Quality score for trials was moderate (mean 2.9/5). Prostacyclins overall when combined were not effective, but intravenous (IV) iloprost was associated with significant prevention (reduction in new DU by standardized mean difference {SMD} of -0.77; 95% CI -1.46 to -0.08; $P=0.03$); oral prostaglandins were ineffective. Atorvastatin decreased the number of new DU (SMD -0.85; 95% CI -1.32 to -0.38; $P=0.0004$). Nifedipine was associated with an insignificant decrease in the number of patients developing new DU (RR 0.50; 95% CI 0.17 to 1.46) and no significant differences in overall number of DU and mean number of new DU. Sildenafil was not significant in complete DU healing but for improvement of DU in two trials ($P=0.03$) and tadalafil had healing and prevention of DU in one trial. In a head to head trial, iloprost was not superior to nifedipine for healing or prevention of DU. Two large bosentan trials were associated with a reduction in the number of new DU (SMD -0.36; 95% CI -0.59, -0.13, $P=0.0002$) but no difference in the proportion of people with DU healing ($P=0.6$). Antiplatelet treatment, heparin, dimethyl sulfoxide, ketanserin, prazosin, PGE1, beraprost, cicaprost, and cyclofenil were not statistically different from placebo

Conclusion: Small sample size, secondary data from RP trials, variable definitions of improvement and prevention and few comparative trials limit the conclusions. The results suggest that there is evidence to support the use of IV iloprost in healing DU in SSc. Bosentan can decrease the number of new DU (prevention). PDE5 inhibitors may have benefit.

Long-term Outcome of Early Neuropsychiatric Events due to Active Disease in Systemic Lupus Erythematosus

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Objective: Neuropsychiatric (NP) manifestations attributable to active disease affects up to 30% of individuals with systemic lupus erythematosus (SLE). The short-term impact of neuropsychiatric events includes increased organ damage, fatigue, mortality, and lower health-related quality-of-life. The current study investigated the impact of NP events attributable to active SLE on long-term disease activity, organ damage and health-related quality-of-life.

Methods: Seventy-two NP cases and 144 matched controls from the Toronto Lupus Cohort, enrolled between 1970 and 2005, were included in the study. NP cases had at least one NP event attributable to active SLE at first clinic visit. Controls did not have NP events at first clinic visit, and were matched to cases on age, sex, disease duration and decade. Paired case-control analyses were performed on measures of disease activity (SLEDAI-2K), disease damage (SDI) and health-related quality-of-life (SF-36), at 1-year, 3-years and 5-years after first clinic visit.

Results: NP cases showed greater disease activity than controls at first clinic visit ($p < 0.0001$) and greater cumulative organ damage at 1-year follow-up ($p = 0.01$). No statistically significant differences were found on 3-year or 5-year outcomes. Mean scores showed a decreasing trend of disease activity, increasing organ damage and persistent low quality-of-life for both cases and controls.

Conclusion:

This study shows that early neuropsychiatric events due to active SLE are not major contributors to long-term disease activity, accumulation of damage or health-related quality-of-life. The long-term prognosis and patterns of disease in SLE patients with early NP events is similar to those of SLE patients without these symptoms.

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Occupational Exposure and Knee Osteoarthritis: A Review of Evidence

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Objective: To examine the relationship between occupational exposure and knee osteoarthritis (OA).

Methods: A literature search was conducted on EMBASE (1982-April 2011) and MEDLINE (1946-April 2011) using the terms 'knee osteoarthritis', 'occupational exposure', and 'occupational diseases'. A study was eligible if it: 1) included adults reporting on a current or previous occupation; 2) measured individuals' exposure to work-related activities including heavy lifting, kneeling, squatting, and stair climbing; 3) measured the presence of radiographic or MRI-identified knee OA, or joint replacement surgery. Heterogeneity of reported measures of association prevented a meta-analysis. Results were synthesized by sex and exposure subgroups: 1) heavy lifting, 2) kneeling and knee bending, 3) heavy lifting and kneeling, 4) climbing stairs, and 5) job title. Study quality was also assessed.

Results: The initial search uncovered 331 articles, of which 33 met the inclusion criteria. The majority of studies in each subgroup showed a statistically significant association between the exposure and the presence of knee OA, after adjusting for confounding variables. Most eligible studies examined the role of heavy lifting at work ($n = 18$); among those 13 found a significant association with the presence of OA, with odds ratio (OR) varying from 1.4 to 7.3. Ten studies achieved high methodological quality, suggesting a moderate-level of evidence that heavy lifting is a risk factor for knee OA. In studies involving occupational exposure in men, 23 of 25 showed a statistically significant positive association

with OA. Among the high quality studies ($n = 15$), all showed a significant association between work-related activities and the presence of OA (OR between 1.1-7.9). The findings suggest moderate-level evidence that occupational activities are a risk factor for knee OA in men. In contrast, studies examining occupational exposure for women, 11 of 16 found a statistically significant association between work-related activities and the presence of OA (OR between 1.4 - 6.1). 11 studies were rated as high quality; of those 8 showed a statistically significant relationship. There remains some ambiguity in what is defined as occupational in women.

Conclusion: There is moderate evidence that occupational tasks that involve heavy lifting and kneeling are risk factors for knee OA, especially in men. This concurs with previous reviews from 1997 and 2008. There is a need for further research to evaluate the role of occupational risks in knee OA in women. Particularly, there is a need to further define what is occupational (e.g., home makers) in women.

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Perceptions of Pain: Experiences of First Nations Women with Inflammatory Arthritis

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Objective: Arthritis disproportionately affects First Nations peoples as compared to non-Aboriginal Canadians, especially women. Our pilot study aimed to understand the experiences of inflammatory arthritis (IA) pain and pain coping among on-reserve First Nations women.

Methods: Five women living in an on-reserve First Nations community on Vancouver Island were mailed study introduction letters. All women had previously participated in an arthritis household survey and had consented to future contact. Three women agreed to participate and were interviewed in a semi-structured format about their experiences living with IA pain. Interviews lasted 60-90 minutes and were transcribed verbatim. Two researchers independently coded the transcripts, using grounded theory to identify dominant themes.

Results: Participants included one person with psoriatic arthritis and two with rheumatoid arthritis. All women were married or in common-law relationships, had children (two had grandchildren), and had been diagnosed with IA for one to five years. Central challenges identified by all participants in coping with IA pain included difficulty meeting family obligations; two of three participants noted lengthy wait lists to see health professionals, lack of rheumatologists, and expense of medications. Three dominant themes emerged regarding pain coping strategies. The most common strategy identified by participants was persevering through the pain. Women reported working through the pain and "pushing through it" to meet their obligations to family, work and community. The second major theme was receiving support from and being connected to family, friends and community. Family members motivated them to take care of their bodies by encouraging them to attend social events and to exercise. The third theme was empowerment and taking control of one's health. As one participant stated "I have to manage my own health and it's taken me a long time to realize that, no it doesn't belong to my doctor, it doesn't belong to a nurse, it belongs to me." Participants made efforts to listen to their bodies, facilitating use of non-pharmacological pain management modalities such as energy healing and visualization exercises, resting, hot baths, and hand waxing.

Conclusion: Persevering through the pain, being connected to community, and being empowered to take control of one's health were central IA pain coping strategies among these First Nations women. Further investigation of pain coping approaches among other First Nations peoples is required to inform culturally relevant, patient or community-centred approaches to arthritis pain management.

Impact of a Rheumatology Consultation Service in Hospitalized Patients

Shirley Chow (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Heather McDonald-Blumer (Mount Sinai Hospital, Toronto)

Objective: 1) To describe the nature of the hospital rheumatology consultations 10 years apart for educational merit 2) To determine whether a hospital rheumatology consultation service alters diagnostic accuracy, changes or expedites treatment, and whether treatment recommendations was adopted by the primary service. 3) To evaluate if needs are met by assessing the complexity of the rheumatology consult service referrals

Methods: Consecutive patients seen on the consultation service at the University Health Network/ Mount Sinai Hospital from July 1 2010 to December 31 2010 were recorded in a logbook. Using a standardized case form, the charts were reviewed and the patient's demographic information, admitting diagnosis, reason for consultation, referring service, final rheumatologic diagnosis, duration of hospital stay, treatment implemented and outcome were recorded.

Results: 268 patients were recorded in the log books over this 6 month period. These included 163 females and 105 males with a mean age of 55 years (range 19 to 92 years). This is more than the 238 consults seen over a 10 month period in 1999. The most common diagnoses seen were 62 connective tissue diseases, 59 crystal induced arthropathy, 25 vasculitis, 22 poly-arthritis; 15 osteoarthritis; 14 regional syndromes; 14 infections; 10 spondyloarthritis, and 8 others. The remaining 38 had non-rheumatologic conditions. This is similar in breadth as 1999. The consults were requested from different medical services, but most commonly internal medicine at 104. There were 82 emergency referrals, 158 urgent referrals, and 28 non-urgent referrals. The rheumatology team helped establish the diagnosis in 177 patients, confirmed the diagnosis in 57 consults, and did not change the diagnosis in 34 patients. 74 of 80 patients with swollen joints had their joints aspirated or injected. 94 patients had steroids or disease modifying therapy initiated or adjusted. 126 patients had follow-up with a rheumatologist.

Conclusion: The rheumatology hospital consultation service provides consultation from various specialties for a variety of rheumatic diseases, thus providing an excellent educational experience. Most referrals were for emergent or urgent rheumatic diseases. The service helped establish or confirm the diagnosis and helped initiate treatment. In general the suggestions were adopted by the team. In conclusion, the rheumatology consult service is needed and provides expert care. The retrospective and qualitative nature of this study preclude definitive conclusions. This study provides the groundwork for further research.

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Increasing Rheumatology Exposure to Internal Medicine Residents in the Setting of Limited Resources: Evaluation of A Web-Based Image of the Month

Steven Katz (University of Alberta, Edmonton)

Objective: Previous studies have demonstrated poor musculoskeletal abilities of internal medicine residents when compared to other medical subspecialties. Further, a lack of rheumatology exposure is associated with this ability, with increased exposure being linked with improved ability. However, rheumatology manpower and resources remain limited to facilitate this. The internet may provide a solution to improve rheumatology exposure while using available resources efficiently.

Methods: An Image of the Month webpage was established in July 2010 on the www.EdmontonRheumatology.com website, a site representing rheumatologists in Edmonton, Alberta, Canada. Each month, a rheumatologist was responsible for posting a new image with a question which could be answered and submitted online by University of Alberta Internal Medicine residents. At the end of each month, a token book prize was awarded randomly to a correctly submitted respondent. One year data was analyzed to determine the change in rheumatology exposure for internal medicine residents and the resources required to implement this program.

Results: The Image of the Month webpage has posted images monthly for 12 months. There was no cost to implement the program as the website already existed and there was pre-existing funding for the book prize. The rheumatologist required no more than 15 minutes monthly to administer the contest. The webpage had over 700 unique visits. Out of 80 internal medicine residents, 46 participated at least once out of 12 possible images, with 34 having multiple entries. The average participation per resident was 3.6 times (range 1-11). 25 residents completed a rheumatology rotation over this time, of which 13 submitted an answer at least once. This means 33 residents received rheumatology exposure over the twelve months that may not have otherwise.

Conclusion: The Image of the Month webpage successfully improves rheumatology exposure with minimal resources required. Further study is necessary to determine the impact this exposure may have on MSK abilities of internal medicine residents.

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Case Report: Inclusion Body Myositis Presenting as Clinical Dermatomyositis

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Objective: To describe an interesting case of clinical dermatomyositis with pathological features of inclusion body myositis.

Methods: We describe the case of a 53 year-old Indian male with a history of type II diabetes with an eight month history of progressive weakness, fatigue, and arthralgia. He had a two year history of intermittent shortness of breath and dry cough. He had wasting of the intrinsic muscles of the hands and synovitis in the MCPs and PIPs. Respiratory exam revealed expiratory crackles. He had weakness of both proximally and distally, with the lower extremity more affected. He was unable to rise from a chair without assistance. On initial exam he had no skin features of dermatomyositis but at a subsequent visit he developed erythematous macules of the extensor surface of the hands.

Results: He had a creatinine kinase of 1668 U/L (normal < 250U/L), AST 97 U/L (normal < 40U/L), and hemoglobin 104g/L. Chest x-ray showed interstitial markings bilaterally. CT scan chest revealed fibrosis and early honeycombing. Antibody testing for anti-Jo was positive 385 MFU (normal < 120). He was anti SSa positive 534 MFU (normal < 120), and anti SSb positive 407 MFU (normal < 120), a low positive rheumatoid factor of 26 kU/L (normal < 20) and negative anti-CCP. HIV testing was negative. A vastus lateralis muscle biopsy showed chronic inflammation, mainly CD8+ T-cells invading myofibers with occasional rimmed vacuoles with neurogenic features. Staining for amyloid was negative. Immunohistochemistry was positive for occasional Tau deposition within vacuoles. This was consistent with inclusion body myositis. He was treated with prednisone 40mg daily and plaquenil 200mg daily with moderate improvement in weakness and did have complete normalization of his creatinine kinase and AST. Prednisone was tapered to 10mg per month. After eight weeks of prednisone therapy, he developed hemoptysis, fever and worsening shortness of breath. He had new infiltrates on chest x-ray and was diagnosed with pulmonary tuberculosis.

Conclusion: This patient had myositis, interstitial lung disease, skin findings of dermatomyositis and was anti-Jo positive. On muscle biopsy, the pathologic features were not consistent with dermatomyositis, but rather inclusion body myositis. Our patient had a moderate response to steroid therapy. There is a previous case report of biopsy findings of IBM in a patient with clinical dermatomyositis who responded to steroids. This is an interesting case of a patient with clinical dermatomyositis with biopsy features of IBM who was steroid responsive.

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Treatment of Carcinoma in Situ of the Bladder while on a TNF Antagonist as the Cause of an Iatrogenic Mycobacterium Infection: A Case Report

Derrick Chan (Royal College of Surgeons in Ireland, Edmonton); Peter Chiu (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

Case Report: It is well known there is an increased risk for tuberculosis for patients being treated with a TNF antagonist. We report a case of TB caused by treatment of bladder cancer. Mr. M is a 75 year old gentleman formally diagnosed with rheumatoid arthritis (RA) in 2006. His past history is significant for transitional cell carcinoma of the bladder treated surgically in 2008. His initial DMARD regimen did not adequately control his RA, and therefore a TNF antagonist, adalimumab, was introduced in July 2009. At that time, a Mantoux test was negative for previous TB exposure, as was a chest x-ray. He responded well to adalimumab, with improvement of his disease activity. In June 2010, as part of routine surveillance, he had a repeat cystoscopy which was suspicious for cancer recurrence. He was given intravesicular BCG (Bacillus of Calmette-Guerin) treatments over the latter half of 2010. Cystoscopy was again performed in February 2011, demonstrating cystitis despite treatment. Urine cytology was sent, which returned positive for acid fast staining. Subsequent typing was positive for *Mycobacterium bovis*. The patient was evaluated by the TB service, who successfully treated him with a 1 month course of levofloxacin, isoniazid and Vitamin B6. Further investigation revealed no disease dissemination outside the bladder. The risk of BCG therapy rarely needs consideration for patients on TNF antagonists. As a vaccine given for TB prevention, it is uncommonly used in an adult population. However, it is a common treatment for bladder carcinoma in situ. The risk of BCG cystitis and true sepsis is quite low, reported at 0.4%, however, a TNF antagonist would likely increase this risk as BCG is a live-attenuated treatment. We present a rare case of BCG cystitis in a patient on a TNF antagonist. This case demonstrates the need for increased vigilance for patients on TNF antagonists and ongoing education with our colleagues who may not be as familiar with this therapeutic modality.

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Predictors of Reduced Leisure Activity in a Symptomatic Population-based Cohort: Results from the Knee Osteoarthritis Progression Study

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Objective: 1) Determine the extent of leisure activity (LA) reduction in a population-based cohort of subjects with knee pain; 2) identify risk factors for LA reduction.

Methods: A population-based cohort of subjects, aged 40-79, with knee pain were evaluated comprehensively for knee osteoarthritis (OA) at baseline and 3-year follow-up (n=163). LA reduction was determined at follow-up based on the questions 'Have you reduced (or stopped) any of your regular leisure activities in the past 3 years because of your knee pain?' (yes, no). Predictor variables included baseline measures of age, gender, body mass index, marital status, education, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain, stiffness, and function (normalized scores 0-100), smoking status, physician diagnosis of OA, history of severe injury (defined by the use of a walking aid for >1 week or not), proportion of years of regular sports activity after age 20, medication use, comorbidities, depression, and OA severity. OA severity was based on x-ray and magnetic resonance imaging (MRI) and categorized as radiographic OA (ROA) (abnormal MRI cartilage, abnormal x-ray), pre-ROA (abnormal MRI cartilage, normal x-ray) and no OA (normal MRI cartilage, normal x-ray). Backwards elimination logistic regression modelling was performed to determine the association of predictor variables with LA

reduction.

Results: Of 163 subjects, 77 (47.2%) had reduced regular LA at follow-up. Worse WOMAC function and greater proportion of years performing regular sports activity after the age of 20 (controlling for each other) were significantly associated with a reduction in LA. Compared to a WOMAC function score of 0-9.9, an increased risk of LA reduction was seen for WOMAC function of 10-19.9 (OR 1.7; 95% CI 0.7-3.9); for WOMAC function 20-29.9 (OR 3.5; 95% CI 1.3-9.4); for WOMAC function 30-39.9 (OR 15.5; 95% CI 2.4-98.4); and for WOMAC function 40-100 (OR 7.1; 95% CI 2.1-23.2). Increasing proportion of regular sport activity after the age of 20 was associated with an increased risk of reduction of LA (for a full unit increase from 0 to 1, OR=2.8, CI 1.2-6.5). Other predictors were not significantly associated with LA reduction.

Conclusion: WOMAC function was a strong predictor of LA reduction. Risk of LA reduction also increased with the proportion of years spent in sport since the age of 20. The reduction in LA with increased sport experience needs to be examined further. Management of knee pain should focus on improving function to promote future maintenance of LA.

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A Case Report of Hemophagocytic Syndrome in a Patient with Dermatomyositis

Kimberly Legault (McMaster University, Hamilton); Alfred Cividino (McMaster University, Hamilton)

Case Report: Hemophagocytic syndrome (HS) secondary to rheumatological disease is a relatively common phenomenon in the pediatric population, but is rare in adults. We present a case of HS arising in a 58-year old woman with active dermatomyositis with concomitant inflammatory arthritis, sicca syndrome, and cardiomyopathy. HS manifestations included fever, encephalopathy, elevated transaminases, cytopenias, ferritin level of 14,000, hypofibrinogenemia, hypertriglyceridemia, and hemophagocytosis on bone marrow examination. Therapy was initiated with high-dose corticosteroids, IVIG, and cyclosporine. Unfortunately she deteriorated and died of multi-organ failure. HS has been described in case series of patients with a variety of rheumatological and hematological disorders, although only rarely associated with dermatomyositis. Mortality rate overall ranges from 20-70% between studies. Pathogenesis is related to dysregulated activation of macrophages and T-cells with defects in T- and NK-cell cytotoxicity. Therapies used in HS in this population have included high-dose glucocorticoids, cyclosporine, cyclophosphamide, IVIG, and etoposide, among others, although no controlled studies have been performed. Our case highlights the difficulties in treating HS in patients with complex autoimmune disease, who are often already managed with immunosuppressive therapies and who have pre-existing organ compromise secondary to their underlying disease.

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The Incidence of Infection in Psoriatic Arthritis - Results from a Longitudinal Observational Cohort

Amir Haddad (Toronto Western Hospital, Toronto); Arane Thavaneswaran (Toronto Western Hospital, Toronto); Vinod Chandran (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

Objective: Many patients with psoriatic arthritis (PsA) are treated with biologic agents. The main adverse event is infection. However, the rate of infection among patients with psoriatic disease is unknown. The purpose of this study was to investigate the rate, type and characteristics of illness in patients with PsA in contrast to a control group of patients with psoriasis without arthritis (PsC).

Methods: The PsA cohort was initiated in 1978. Patients are followed at 6-12 month intervals according to a standard protocol which includes history, physical examination laboratory evaluation and radiographic assessment. It collects documentation of the presence, site and type of infection at each visit. In 2006, the PsC was initiated. Patients are assessed by a rheumatologist to exclude the presence of inflammatory arthritis, and are

followed at yearly intervals according to the same standard protocol. Data are tracked in a computerized database and infections after 2006 were included. Descriptive analyses were conducted using t tests and chi-square tests.

Results: 695 patients with PsA and 511 patients with PsC and were followed up since 2006. 607 infections were detected among 318 patients with PsA, and 176 observed infections among 144 patients with PsC. The incidence rate of infection was similar in both groups with 0.33 (95% CI 0.31, 0.36) per patient-year in the PsA cohort and 0.29 (95% CI 0.25, 0.30) per patient-year in the PsC cohort ($p=0.15$). The incidence rate of infection for patients on biologics was higher at 0.44 (95% CI 0.39-0.50) and 0.66 (95% CI 0.39-1.04) in the PsA and PsC cohorts respectively. Patients with PsA were more likely to have 4 or more infections during the course of follow-up compared to patients with PsC ($p=0.0001$). Among patients with PsA the most common infections were lung, sinus, skin and genitourinary whereas among PsC patients, skin, genitourinary and lung were most prevalent. Patients with PsA had less bacterial infections compared to PsC (62% vs. 77.1% $p=0.005$), and were less likely to have been treated with antibiotics than patients with PsC (73.6% vs. 87.1% $p=0.0003$).

Conclusion: The incidence rate of infection was similar in PsC and PsA cohorts. Patients with PsA suffered from recurrent infections more commonly than patients with PsC. Patients in both cohorts were more likely to have a bacterial etiology for infection and to require antibiotic treatment. The most commonly reported infection was pneumonia in the PsA group and cellulitis in the PsC group.

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The Predictors of Infection in Psoriatic Arthritis - Results from a Longitudinal Observation Cohort

Amir Haddad (Toronto Western Hospital, Toronto); Arane Thavaneswaran (Toronto Western Hospital, Toronto); Vinod Chandran (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

Objective: Many patients with psoriatic arthritis (PsA) are treated with immunosuppressives and biologic agents. Infection is a reported adverse event. The purpose of this study is to identify factors that could predict infection in patients with PsA in contrast to a control group of patients with psoriasis without arthritis (PsC).

Methods: The PsA cohort was initiated in 1978. Patients fulfil the CASPAR criteria and are followed at 6-12 month intervals according to a standard protocol. In 2006 a cohort of patients with PsC was initiated. Patients are assessed by a rheumatologist to exclude the presence of inflammatory arthritis, and are followed at yearly intervals according to the same protocol. Data were tracked in a computerized database and collected prospectively. Multivariate analysis using generalized estimating equations was used to relate the probability of infection to potential predictor variables such as age, sex, PASI score, functional comorbidity index, actively inflamed joint count and treatment with NSAIDs, DMARDs, Biologics and phototherapy. Survival analysis was used to distinguish individual contribution of these predictors to infection.

Results: The PsA cohort included 695 patients with 607 reported infections, the most prevalent infection was pneumonia at 21%. The incidence rate of infection was 0.33 (95% CI 0.31-0.36) per patient-year but was higher among patients treated with biologic agents (0.44 (95% CI 0.39-0.50)). Patients with infections were less likely to be males (OR=0.42 95% CI 0.31-0.55) and more likely to be treated with biologics (OR=1.43 95% CI 1.07-1.91). Patients with pneumonia were more likely to be males (OR=1.73 95% CI 1.02-2.96). Patients with serious infections (that required antibiotics or hospitalization) were more likely to have a higher PASI score (OR=1.1 95% CI 1.04-1.16). The PsC cohort included 511 patients with a total of 176 observed infections, the most commonly reported infection affected the skin at 18.3%, the incidence rate of infection was 0.29 (95% CI 0.25-0.30) per patient-year and was higher (0.66 (95% CI 0.39-1.04)) in patients on biologics. Patients with all infections were more likely to be younger at visit (OR=0.97 95% CI 0.94-0.99), less likely to be males (OR=0.58 95% CI 0.36-0.93) and had a Higher FCI (1.33 95% CI 1.1-1.6), no predictor was found to be associated with skin infections.

Conclusion: The positive predictors for infection in patients with PsA are female gender and treatment with biologics. These data prove the association between infection and biologic treatment in PsA.

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On-line Case Simulation Versus Paper Format: The Ability to Screen for Arthritis Using GALS

Veronica Wadey (University of Toronto, Toronto); Heather Blumer-McDonald (University of Toronto, Toronto); Alfred Cividino (McMaster University, Hamilton); David Levy (McMaster University, Hamilton); Jean Wessel (McMaster University, Hamilton); Deborah Kopansky-Giles (Canadian Memorial Chiropractic College, Toronto); Jodi McIlroy (University of Toronto, Toronto); Douglas Archibald (Department of Family Medicine, University of Ottawa, Ottawa)

Objective: Introduction: The purpose of this study was to determine if groups learning by case simulation using an on-line learning technology (OLT) or paper format (PF) would demonstrate greater improvement in knowledge, skills and satisfaction in learning how to screen for arthritis using the gait, arms, legs, spine (GALS) screening tool for arthritis. The purpose of this study was to determine if medical residents learning by case simulation using an on-line learning technology (OLT) would demonstrate greater improvement in knowledge, skills and satisfaction in learning how to screen for arthritis using the gait, arms, legs, spine (GALS) screening tool for arthritis than residents learning by paper format (PF)

Methods: A randomized control trial (RCT) was conducted with family medicine and rheumatology residents followed by focus group interviews. An orientation session with pre/post test questionnaires and analyses was completed. Thirty-two subjects completed the GALS assessment and were randomized into either the OLT or PF groups. Data was analyzed based on 13 participants in the OLT experimental group and 19 in the PF - control group. Repeated Measures ANOVA was used to assess the extent to which there was an effect of format on learning from Time 1 to Time 2. A separate Repeated Measures ANOVA was run to determine the effect of format on retention from Time 2 to Time 3. Focus groups were completed.

Results: Both groups learned from the module regardless of the method of learning used ($p < .000$). Pre/Post-test analyses after the information session demonstrated no significant difference among family medicine and rheumatology residents in either the online (OLT) and paper format (PF) groups (means of 2.60 out of 4 for the OLT group; 2.76 out of 4 for the PF) and implies that both groups were equal. Both groups suffered some decline in their test scores at follow-up, however there appeared to be no difference in the extent to which the groups did so. Retention was not affected by learning format (OLT versus PF). Both groups had similar level of knowledge about GALS at the end of the module, and at follow-up. Findings from the focus groups suggested that both the family medicine and rheumatology residents found the GALS module to be very informative, especially the examination videos that were perceived as clear concise and effective. FMED residents articulated that they had opportunities to apply the GALS screening assessment to patients during their clinical encounters and made positive identifications for inflammatory arthritis.

Conclusion: All residents learned from both OLT and PF methods and found the GALS module very informative, especially the examination videos. A preference for the online learning resources was expressed by all residents. The successful identification of patients with inflammatory arthritis by these participating residents suggests the possibility of knowledge transfer into clinical practice.

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On-line vs Paper Format Learning: Identifying Inflammatory Arthritis Early: Randomized Control Trial

Veronica Wadey (University of Toronto, Toronto); Heather Blumer-McDonald (University of Toronto, Toronto); Alfred Cividino (McMaster University, Hamilton); David Levy (McMaster University, Hamilton); Jean Wessel (McMaster University, Hamilton); Deborah Kopansky-Giles (Canadian Memorial Chiropractic College, Toronto); Jodi McIlroy

(University of Toronto, Toronto); Douglas Archibald (Department of Family Medicine, University of Ottawa, Ottawa)

Objective: The purpose of this study was to determine whether medical residents learning by case simulation using on-line learning technology (OLT) on “sore hands, sore feet”, would have a greater improvement in knowledge, skills and satisfaction in learning how to identify patients with early-stage inflammatory arthritis than medical residents using a paper format (PF) only.

Methods: A randomized control trial (RCT) was conducted with family medicine and rheumatology residents followed by focus group interviews. An orientation session with pre/post test questionnaires and analyses was completed. Thirty-one subjects completed the “Sore Hands, Sore Feet” (SHSF) learning module and were randomized into either the OLT or PF groups. Twelve residents completed the module online (OLT - experimental group) and 19 completed the paper-based format (PF - control group). Each of these learning methods underwent full content review prior to this trial. Data was analyzed based on: Time 1 (Pre-Module), Time 2 (Post-Module) and Time 3 (3 month Follow-up). The OLT group did not complete the Pre-Module assessment; however 19 in the paper-based group did so. Repeated Measures ANOVA was used to assess the difference between groups.

Results: No significant difference among family medicine and rheumatology residents in either the online (OLT) and paper format (PF) groups (means of 2.60 out of 4 for the OLT group; 2.76 out of 4 for the PF) existed at the beginning of the study. There was a significant increase in scores from Time 1 (11.21/16; SD=2.30) to Time 2 (12.79/16; SD=2.20) for the PF group. At time 2 and time 3, there were no differences in scores between the PF and OLT groups [provide values for the OLT group.] There was a small but statistically significant decrease in scores from Time 2 to Time 3 for BOTH groups (Post-test mean scores equaled 12.58 out of 16; SD=1.78 and Follow-up mean scores equaled 11.97 out of 16; SD=2.09). Findings from the focus group interviews suggested that all residents found the SHSF module to be very informative. Residents learned how to appropriately refer a patient to a rheumatologist and carried out this act during clinical encounters. This may suggest that knowledge transfer was occurring.

Conclusion: Overall, the residents learned from both OLT and PF methods. A preference for the online learning resources was expressed by all residents.

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The Arthritis Program - Interprofessional Training Program (TAP-ITP): An Evaluation of a Successful Interprofessional Curriculum

Lorna Bain (Southlake Regional Health Centre, Newmarket); Carol Kennedy (St. Michael's Hospital, Toronto); Jennifer LePage (Training Pirates, Holland Landing); Douglas Archibald (Department of Family Medicine, University of Ottawa, Ottawa); Sandra Mierdel (Southlake Regional Health Centre, Newmarket); Carter Thorne (Southlake Regional Health Care, The Arthritis Program, Newmarket)

Objective: To evaluate the effectiveness of the TAP Interprofessional Training Program (TAP ITP) in improving interprofessional patient-centred collaboration (IPC) within clinical teams by teaching tools to foster a positive change within the clinical environment.

Methods: A national needs survey on models of care and interprofessional team practice guided program development. The curriculum was developed in a blended, episodic manner using technology, classroom instruction and asynchronous learning. Successful elements of The Arthritis Program (TAP), a patient-centred interprofessional model of care, were used as the bench mark to inform curriculum development. Eligible learner(s) included two cohorts: 1) Health care professionals working within hospital and community-based arthritis programs; 2) Trainees enrolled in the Advanced Clinician Practitioner in Arthritis Care (ACPAC) program 2010/2011 cohort. This was a pre-post single group design. Data were collected at the beginning of program, immediate post-program, and after one year (not yet completed). Outcomes were assessed using the following reliable and valid measures: Demographics; readiness for IPC; W(e)Learn program evaluation;

Interprofessional (IP) Learner and Team Contracts; Interprofessional Collaborative Competencies Attainment Survey (ICCAS); Attitudes Toward Health Care Teams (ATHCT); and Bruyère Clinical Team Self Assessment Scale. Analyses included both descriptive and inferential statistics. Comparative analyses included repeated measures.

Results: 22 learners participated (n=15 professionals from 4 distinct clinical teams across Canada; n=7 ACPAC trainees). Prior to attending TAP-ITP, 60% of learners felt that their team was in the pre-contemplation/contemplation stage of their team's readiness for IPC. Immediate post-program there was a shift to 80% of the learners believing that their team was in the prepared for action/action stage. The W(e) Learn program assessment indicated that participants were very satisfied with TAP-ITP. Mean scores ranged from 6.02 (program content) to 6.6 (program structure), each item scored out of 7=positive learning experience. ICCAS scores revealed statistically significant differences in pre to immediate post-program perceptions of IPC competencies (19 of 20 competencies, $p < 0.05$). These findings may indicate greater team function in the following areas: communication, collaboration, roles and responsibilities, collaborative patient/family centred approach, conflict management/resolution and team functioning. Paired t-tests for each pre to immediate post-program score were all significant ($p < 0.05$) for each of the Bruyère subscale and overall scores, ATHCT Quality of Care/Process and borderline significant for the Physician Centrality scale ($p = 0.06$).

Conclusion: This study provides evidence that the TAP-ITP program improves knowledge, skills and attitudes in interprofessional patient-centred collaboration in both individual learners and teams enrolled in the curriculum.

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Patient Satisfaction with ACPAC Program Trained Extended Role Practitioners: A Multi-Centre Study

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Objective: In an effort to provide more appropriate and timely arthritis care, patients are being presented with new models of care and disease management. An innovative and rigorous education program for licensed physiotherapists and occupational therapists, the Advanced Clinician Practitioner in Arthritis Care (ACPAC) program focuses on the assessment, diagnosis and independent management of selected musculoskeletal and arthritis-related disorders. As stakeholders in their own care, it is important to give patients a voice in determining the value of their care provider. Our objectives were to evaluate patients' satisfaction with the care received from ACPAC Program graduates, referred to here as Extended Role Practitioners (ERPs), and to evaluate the reliability (internal consistency) of our primary outcome measure.

Methods: The patients (n=325) of 27 ERPs were recruited from 15 health-care institutions across Ontario. This cross-sectional study utilized a self-report survey. The primary outcome measure was the Patient-Doctor Interaction Scale, modified to reflect patient-therapist interaction (PTIS). PTIS subscales included: Providing Information (PI), Rapport (R), Meeting Patient Needs (PN). Secondary outcomes included satisfaction with services received; acceptability of wait times; overall satisfaction, and a comparison of ERP-based arthritis care with that received from other healthcare professionals. Analyses were descriptive. Estimate of internal consistency (of PTIS) using Cronbach's alpha.

Results: Respondents' mean age was 54 years (3-75), most were female (72%), adult (82%) and living in urban areas (79%). The majority was not working (51%) and most had an inflammatory (52%) or non-inflammatory (33%) diagnosis. Scores are reported as a mean (sd) (1-5=very satisfied) or percent response. PTIS subscale scores were high. PI: 4.5 (0.6), R: 4.6 (0.5), PN: 4.6 (0.5). Satisfaction with services received: item means ranged

from 4.1-4.6. Wait time was acceptable: from referral (88% agree/strongly agree); in clinic (87% agree/strongly agree). Overall satisfaction was high: 4.4 (0.7). The majority felt the arthritis care they received was comparable to (37%) or better than (61%) that provided by other healthcare professionals. Among patient-generated suggestions and commendations, patients requested shorter wait times and noted graduates' excellent communication skills and compassion, as well as the efficient, yet thorough care provided. The PTIS subscales obtained Cronbach's alpha coefficients ranging from 0.84 to 0.89, indicating moderate to high reliability.

Conclusion: Given patients' consistent satisfaction across outcomes and self-reported appreciation of the type of care received by ERPs, the growth and development of ACPAC ERP-based models of care and the associated policy implications should be explored.

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Current Gout Management Practices in Canada

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Objective: This chart audit program, undertaken in Canada, monitored how hyperuricemia in patients with gout is currently managed within primary care settings. Even though gout is quite prevalent in Canada, it is unclear if physicians have been applying newly developed treatment strategies. The study was designed to identify current care gaps (e.g., monitoring criteria for kidney function, identification of target levels for serum uric acid (sUA) levels, clinical efficacy of urate-lowering therapy (ULT), and use of prophylaxis in conjunction with ULT).

Methods: This online program consisted of a retrospective multicentre observational clinical chart review on gout. Between September 2011 and January 2012, 500 outpatients with gout attending primary care clinics were profiled. General practitioners (GPs)/family physicians ($n \geq 50$) were requested to complete 10 case report forms (CRFs) based on the first 10 consecutive patients who visited their office, had gout, and satisfied the selection criteria requirements. Participating physicians were also initially asked if they recalled the target sUA level needed to initiate ULT treatment. All patients profiled were asked prior to provide their informed patient consent. Current gout treatment practices were benchmarked with EULAR guidelines for the management of gout.

Results: Preliminary analyses indicated that renal function assessment was often overlooked prior to administering ULT. Several triggers (e.g., tophi, number of flare-ups, and high sUA levels) were confirmed as the basis for the initiation of ULT. Physicians typically failed to monitor sUA levels after initiation and to recognize whether the patients with gout were on-target in terms of efficacy for ULT. As expected, many physicians prescribed anti-inflammatory prophylaxis in conjunction with a ULT agent.

Conclusion: This study has demonstrated care gaps in the management of gout by primary care providers in Canada, especially in overlooking the consequences of hyperuricemia as a chronic disease. Because of the transient nature associated with flare-ups, immediate symptoms, such as extreme pain, receive more attention. This situation may be prompted in part by the absence of clear-cut guidelines for the management of gout in Canada. New guidelines should be created or external guidelines should be adapted to the Canadian setting. Educational programs for primary care providers may also improve the application of the latest evidence-based therapies.

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Edmonton Rheumatology Triage System: Review of Initial Implementation and Effect on Wait Times for Inflammatory Arthritis

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Objective: To describe the triage system created and employed by 8 rheumatologists at the University of Alberta and to review 20-month data, including examination of access to care for inflammatory arthritis patients prior and subsequent to the introduction of the triage system.

Methods: The triage rheumatologist, typically using only the information provided in the referring letter and any included investigations, screens all incoming referral letters to identify possible diagnoses and urgency of assessment. After the initial patient visit, the consulting rheumatologist records a post-visit diagnosis and if they agree with the assigned urgency status. The system was devised so patients triaged as "soon", such as those with possible inflammatory arthritis, could be seen within 6 weeks. Triaged patients' wait-times, defined as from time of referral to clinic visit, and pre and post-triage diagnosis were compiled in a database. We report this descriptive data from the triage process, emphasizing the inflammatory arthritis group. The wait-time for inflammatory arthritis was also compared to a random sample of inflammatory arthritis patients from the year preceding the triage system implementation.

Results: A total of 3476 new referrals were seen, with an overall average wait-time of 60.0 days. 2183 referrals were triaged as "routine", with an average wait-time of 94.7 days; 1137 as "soon", with an average wait of 31.4 days; 131 referrals as "urgent" with an average wait of 8.7 days. Of the new referrals, 343 patients had a final diagnosis of inflammatory arthritis with an average wait-time of 58.9 days; 189 were appropriately assigned "soon" with an average wait-time of 31.4 days. The majority of those with an inaccurate urgency status were due to miss-assigned urgency status associated with learning the new triage system, not misdiagnosis. In the year prior to the triage system, the inflammatory arthritis sample group ($N=49$) had an average wait-time of 66.0 days. When comparing the two inflammatory arthritis groups, the overall average wait-time was not significantly reduced ($p=0.1452$), but the average wait-time for inflammatory arthritis appropriately triaged as "soon" was reduced by 34.6 days ($p \leq 0.0001$).

Conclusion: This triage system effectively reduces wait-times for targeted patient groups that require more urgent care, provided they are identified correctly in the triage process. Utilization of a triage system may be universally applicable and effective way to ensure appropriate patient care.

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A Population-Based Study of Rheumatologist and Orthopedic Surgeon Availability, Socioeconomic Inequalities, and Population Characteristics

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Objective: To examine variation in the use of rheumatologist and orthopaedic surgeon services for arthritis in relation to service availability, demographics and geographic characteristics of the population in Ontario.

Methods: Health administrative data for 2007/08 were used to identify individuals accessing rheumatologist and orthopaedic surgeon services in 105 geographic areas, and to develop an index of primary care physician availability. The 2006 Census was used to derive area level indicators of population characteristics: SES (education and income), % of the population > 45 years, % of Aborigines and urban-rural location. Indices of specialist availability that combine full time equivalents with the distance to rheumatologists or orthopaedic surgeons respectively were calculated

incorporating data from surveys of these specialists. Hierarchical Poisson regression models were fitted to examine the contribution of area level indicators and individual age and sex to the use of rheumatologist services and to orthopaedic surgeon office visits and surgery by patients with arthritis. Rate ratios and 95% confidence intervals were calculated.

Results: Overall 5.9 per 1000 population made visits to rheumatologists for arthritis (3.0/1000 for inflammatory arthritis); 23.4 per 1000 population made visits to orthopaedic surgeons and 8.2 per 1000 population had surgery for arthritis. There were substantial variations by area in the availability of rheumatologists and orthopaedic surgeons. Residents of areas in the highest SES quintile were 50% more likely to visit rheumatologists than those in the lowest quintile for both arthritis and inflammatory arthritis, but there was no SES gradient in orthopaedic office visits or surgery for arthritis. Availability of rheumatologists comparing quintiles of highest to lowest availability was associated with visits for arthritis overall (RR=1.26 (95%CI: 1.04-1.52)) but not for inflammatory arthritis. Availability of orthopaedic surgeons was associated with higher rates of office visits, but not surgery. Residents of areas with greater access to primary care physicians were more likely to make visits to rheumatologists and orthopaedic surgeons. Residents of areas with the highest proportion of Aboriginals were more likely to visit rheumatologists for inflammatory arthritis.

Conclusion: SES inequalities exist in the use of rheumatologist services. Lack of availability of primary care physician referral is also a potential barrier to both rheumatology and orthopaedic surgeon services. These findings point to the need for models of care to enhance access particularly for more deprived populations such as those with low SES and/or high proportions of Aboriginals.

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Models and Processes of Care for People with Arthritis

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Objective: The benefits of early diagnosis and treatment of inflammatory arthritis, wait times for joint replacement and limited health human resources have resulted in the development of alternative models of care delivery to address these care gaps. This study identified models of arthritis care and determined how care was organized within the models.

Methods: One-on-one interviews were conducted with program managers and care providers in British Columbia (BC), Alberta (AB) and Ontario (ON), Canada. We also asked about the profession, role and skill set of those providing care. Interviews were transcribed verbatim and analyzed using content analysis.

Results: 53 interviews were conducted, 17 in BC, 11 in AB and 25 in ON representing 40 models. Five overarching models were identified: 1) a community-based model that usually includes a single health professional or multiple health professions working independently with patients; 2) a traditional model where primary care physicians refer to a specialist often working with another professional who has an extended role; 3) a multi-

professional model; 4) an inter-professional model; and, 5) an inter-professional model where care is provided both by individuals and in a group format. Multi-professional models and inter-professional models were developed in the context of specialist care and rarely were situated in primary care. Rarely were models developed and implemented for people with arthritis in general. Additionally, some models had formalized linkages with community providers, particularly related to chronic disease management including exercise programs. None of the models addressed the entire continuum of care. Some models include health professionals working in alternative ways, e.g. enhancement with extended roles or substitution where roles are delegated. Processes to enhance access for specific subgroups of people with arthritis including triage processes for people with suspected inflammatory arthritis for rheumatology consultation and for people who were likely candidates for joint replacement were most common.

Conclusion: Innovative care models have been developed to improve access to care for people with arthritis and these models mainly have focused on inflammatory arthritis and total joint replacement. Most models do not or in only a limited way address conservative management for people with the most common type of arthritis, osteoarthritis. There continues to be a need for the development, implementation and evaluation of innovative models of care for people with arthritis in general across the continuum of care.

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Continued Opioid Use in Fibromyalgia is Associated with Negative Health Related Outcomes

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Objective: Opioids are not recommended for the treatment of fibromyalgia (FM), but are used by up to 1/3 of patients, and were identified by patients as giving best symptom relief in an Internet survey. The effect of opioids needs to be balanced with negative health and psychosocial effects, and similarity between adverse effects of opioids and symptoms of FM need to be appreciated. Long-term risks are also unclear. We have examined the outcome in FM patients followed in a multidisciplinary setting stratified according to opioid use.

Methods: FM patients followed prospectively in a multidisciplinary pain clinic were stratified according to opioid use. Demographic information, work status and history of substance abuse were recorded. Outcome measures included: Patient Global Impression of Change (PGIC), employment and disability status, Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire (HAQ), Pain Disability Index (PDI), patient global status and pain by Visual Analog Scale (VAS), and anxiety and depression by Arthritis Impact Measurement Scale (AIMS). Univariate comparisons of continuous variables were made using Student's t-tests, and for categorical variables using chi-squared tests. Logistic regression was used to model the association between selected variables.

Results: One hundred and thirty one of 159 patients (82%), mean age 50±10, 92% female, had at least one follow up visit at mean (SD) of 26±15months. Opioid use vs. non-use was reported in 43 (33%; Group 1) vs. 88 (67%; Group 2). Twelve patients in Group 2 were given a trial of opioids, followed by discontinuation. Opioid use was significantly associated with poorer outcome for multiple measures including pain report, functional impairment, employment status and disability payments. Change scores from baseline to follow-up only achieved significance for HAQ, with deterioration in group 1 (p=0.011). A logistic hierarchical regression analysis revealed that baseline level of pain was a significant predictor of opioid status at follow-up, even after controlling for demographic and substance abuse-related variables (p=0.007).

Conclusion: In this first study reporting health related outcomes and opioid use in FM, opioid users had poorer symptom, functional and occupational outcome compared to non-users. Although opioids may have been

initiated due to more severe symptoms, we have no evidence that these agents improved function, and rather may have contributed to this less favourable outcome. Only a formal study of opioid use in FM will clarify this issue, but until then physicians must be vigilant regarding the multiple adverse consequences of opioid therapy.

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Supporting Evidence for the Clinical Utility of the Pain Subscale of the American College of Rheumatology 2010 Preliminary Diagnostic Criteria for Fibromyalgia

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Objective: Understanding and recording the patient's experience of chronic pain is challenging, with no single ideal measurement. Evaluation of pain may be by narrative report, measurement by pain scales or completion of pain drawings. As pain is an individual experience, measurements may be variably interpreted and may evaluate different components of pain such as location, intensity or emotional value. We have examined the agreement between the pain subscale of the ACR 2010 preliminary diagnostic criteria for fibromyalgia (FM), the Widespread Pain Index (WPI), completed as a checkbox, and the Body Map (BM), a drawn report of pain on a manikin, in FM patients. The WPI was also correlated with other measures of pain.

Methods: FM patients currently in a cohort study at a tertiary care multi-disciplinary pain centre completed the WPI (total score 19), the BM (total score 50) and other measures of pain including: pain intensity Visual Analog Scale (VAS), McGill Pain Questionnaire (MPQ), Pain Disability Index (PDI) and Pain Catastrophizing Scale (PCS). The manikin was rescored to correspond to the 19 regions used in the WPI. Correlations between the WPI and the newly scored manikin, termed manikin WPI (manWPI), were calculated. Comparisons were made for the total scores as well as for each of the 19 individual regions for the WPI and the manWPI, and both the WPI and manWPI were compared to other pain instruments using Pearson's correlation coefficient.

Results: One hundred and three patients, 97 (94%) females, mean age 50 ± 10 yrs and mean Fibromyalgia Impact Questionnaire 60 ± 21 completed all pain instruments at a single clinic visit. The correlation coefficients for the WPI vs BM, WPI vs manWPI and manWPI vs. BM were .73, .72 and .90 respectively ($p < 0.001$ for all values). Correlation coefficients for each of the 19 individual areas ranged between 0.27 and 0.60, showing overall moderate correlations, with strongest for low back pain and weakest for jaw pain. Other measures of pain similarly showed good correlation with both the WPI and manWPI, with lowest values recorded for PCS.

Conclusion: The WPI component of the ACR 2010 preliminary diagnostic criteria for FM correlates well with a visual representation of pain as portrayed in a manikin drawing, irrespective of the scoring method, as well as with other measures of pain. Taking into account the simplicity of the checkbox format, the WPI can be recommended as a reliable pain measurement for FM.

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The 2010 American College of Rheumatology Fibromyalgia Survey Diagnostic Criteria and Symptom Severity Scale is Valid and Reliable in a French Speaking Fibromyalgia Cohort

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Objective: There is currently no ideal tool to measure symptom severity or change in symptoms over time in fibromyalgia (FM). The Fibromyalgia Survey Diagnostic Criteria and Severity Scale (FSDC) is a patient administered questionnaire, assessing both the diagnosis of FM and symptom severity. The FSDC combines a measurement of pain, the Widespread Pain

Index (WPI), and symptom severity (SS) of fatigue, unrefreshed sleep, cognitive complaints and somatic symptoms. The sum of WPI and SS provides a composite score of FM severity (0-31). We have evaluated the reliability and validity of the translated French version of the FSDC in patients with an established diagnosis of FM in a tertiary care setting.

Methods: After translation of the FSDC into French, the questionnaire was administered on two occasions within a 1 week period to persons with FM, and the FSDC was correlated with the following measures to test construct validity: the Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire (HAQ), McGill Pain Questionnaire (MPQ), and a visual analogue scale (VAS) for global severity and pain. Test-retest reliability was assessed with Pearson's correlation coefficients and internal consistency was evaluated using Cronbach's alpha coefficient. Construct validity was evaluated using the Spearman correlation coefficient.

Results: The study sample consisted of 73 patients, mean age 52 ± 9 years, 67(92%) female, and mean disease duration 12 ± 12 years. Test-retest reliability was between .600 and .888 for the 31 single items of the FSDC, and .912 for the total FSDC, with all correlations significant ($p < 0.0001$). Cronbach's alpha was .846 for FSDC assessment 1, and .867 for FSDC assessment 2 indicating good internal consistency. 0.001). Construct validity showed significant correlations between the FSDC and the FIQ 0.670, HAQ 0.413, MPQ 0.562, global VAS 0.591 and pain VAS 0.663 (p

Conclusion: The French FSDC is a valid instrument for measuring symptom severity in French FM patients FM and showed reliability and construct validity with other measures of symptom status in FM. This new scoring questionnaire, which is easily completed by patients and simple to score, has the potential to become the standard for measurement of symptom severity in FM.

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Development of the "Which Health Approaches and Treatments are you Using?" (WHAT) Questionnaires: A Multidimensional Assessment of Complementary and Alternative Medicine Use in Children with Juvenile Arthritis

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Objective: The objective of this study was to develop child self- and parent proxy-report questionnaires to provide a multidimensional assessment of complementary and alternative medicine (CAM) use in pediatric rheumatology.

Methods: A two-day, interdisciplinary consensus conference, using nominal group technique, was held to develop consensus among key stakeholders on the domains and items that should be included in the questionnaires. Panel members were presented with information on the content of existing pediatric CAM questionnaires gathered from a systematic review as well as domains and items found to be relevant according to a Delphi survey of experts in the field of CAM and pediatric rheumatology.

Results: During the consensus conference, discussions among fourteen stakeholders were used to resolve disagreements concerning the content of the questionnaires. Four CAM domains were found to be relevant: child's CAM use, factors associated with CAM use, perceived impact of CAM use and communication about CAM use with medical providers. A total of fourteen items were agreed upon at the conference, including the types of CAM used by the child, health conditions treated by CAM, modes of payment for CAM, reasons of use, source of information about CAM, difficulty to access CAM as well as benefits and harms of CAM. The research team agreed upon additional items that were suggested by conference attendees and developed the child and parent report questionnaires.

Conclusion: The "WHAT" questionnaires are currently undergoing rigorous validity and reliability testing across two clinical pediatric rheumatology settings in Ontario. Reliable, valid and feasible CAM question-

naires will ultimately improve the quality of CAM research as well as knowledge translation about the use, benefits and harms of CAM in clinical practice.

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Questionnaires Assessing Complementary and Alternative Medicine in Pediatrics: Are they Valid?

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Objective: The objective of this systematic review was to critically appraise and summarize the research evidence on the measurement properties of existing questionnaires of complementary and alternative medicine (CAM) use in general pediatrics and in pediatric rheumatology.

Methods: A systematic search strategy was implemented in major electronic databases in the last week of March 2011. Conference websites, scientific journals and experts in the field of CAM were consulted. Questionnaires were included if they sought to assess the prevalence of a comprehensive range of CAM use in pediatric patients. Methodological quality of the studies reporting the use of a CAM questionnaire was assessed using the COSMIN checklist. Measurement properties of the questionnaires were rated using the Terwee and the Cohen criteria.

Results: A total of 96 CAM questionnaires were found in 104 publications. Studies were conducted in general pediatrics (n=24), in specific pediatric conditions (n=63), such as cancer (n=19), neurological (n=16), respiratory (n=11) and rheumatologic conditions (n=4), as well as in other populations. According to the COSMIN checklist, none of the included studies reported adequate methodological quality concerning validity, reliability or responsiveness testing. The Terwee criteria showed that all included CAM questionnaires had indeterminate measurement properties. According to the Cohen score, none were considered to be a well-established assessment and most of them (n=87) were not described or tested enough to reach the score's minimum standards.

Conclusion: None of the identified CAM questionnaires in children and pediatric rheumatology have been thoroughly validated. This systematic review highlights the need for proper validation of CAM questionnaires in pediatrics, which may in turn lead to improved research and knowledge translation about the use, benefits and harms of CAM in clinical practice.

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Early Radiographic Changes in Patients with Psoriatic Arthritis

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Objective: Psoriatic arthritis is a seronegative arthropathy characterized by axial involvement, peripheral arthritis, and enthesitis. The aim of this study was to describe the radiographic changes in early PsA (EPsA), defined as < 2 years since symptom onset.

Methods: EPsA patients were assessed at a rheumatology clinic specializing in PsA. Standard clinical and laboratory assessments were conducted at baseline. Radiographic changes in peripheral and sacroiliac joints were classified as normal, abnormal-not clinically relevant-, and abnormal-clinically relevant-, and their association with patient baseline characteristics was analyzed.

Results: Eighty four EPsA patients (mean (SD) disease duration = 1.0 (0.8) years) were included in this analysis with a mean (SD) age of 48 (10.6) years and 44 (52.5%) being female. At baseline, mean (SD) PASQ

and PASI scores were 11.3 (4.8) and 3.5 (5.9), respectively. Mean (SD) CRP was 6.7 (6.4) and mean (SD) ESR was 16.0 (18.4). The most common joint involvement was polyarticular (59.5% of patients) presentation and Distal Interphalangeal Predominant (DIP) involvement (57.1% of patients). Among the 79 patients with available baseline radiological assessment until now, radiological damage was identified in 25 (31.6%), of whom 10 (40%) had changes in 2 joints and 3 (12%) in ≥ 3 joints. The vast majority of these patients (n=19, 76%) experienced joint damage within the 1st year of symptoms. The observed radiographic changes included new bone formation, slight-to-moderate narrowing of the joint space, and marginal and central bone erosions, with the majority of abnormalities appearing in the hands, feet and sacroiliac joints. Among the 66 patients evaluated, 15 (23%) had abnormal hand images (9 (60%) in both hands). Furthermore, 10% of the evaluated patients (5/50) had radiographic abnormalities in feet (3 (60%) in both legs) and 10.4% (7/67) in sacroiliac joints (2 (30%) in both sides). Mean (SD) CRP was higher in patients with radiological damage compared to the rest of the cohort (8.8 (7.7) vs. 5.8 (5.5); $P=0.053$). Mean (SD) SJC was also higher (4.4 (6.2) vs. 3.0 (3.7)), without reaching statistical significance. All other parameters were comparable between-groups.

Conclusion: Radiological damage was detected in 32% of EPsA patients, which was associated with increased CRP. Among these, 76% acquired the damage within the 1st year of symptom onset. Asymmetric oligoarthritis was not a dominant pattern in our cohort as was previously reported. The increased incidence of axial and DIP joint involvement are in agreement with previous studies showing that they represent the most common sites in PsA.

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Comparative Analysis of the Cohorts with Early and Established Psoriatic Arthritis (PsA)

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Objective: Early PsA diagnosis/management could prevent disease progression, associated with destructive joint damage, disability, and increased cardiovascular risk. The aim of this study was to analyze the differences in clinical presentation and patient quality of life (QoL) in early (EPsA) vs. established PsA, defined as < 2 and ≥ 2 years from diagnosis, respectively.

Methods: PsA patients (CASPAR criteria) were recruited from a rheumatology clinic specializing in PsA and were followed prospectively. Clinical assessment included TJC, SJC, standard joint radiography or MRI, blood tests, number of involved entheses, PASI, PASQ, HAQ, and DAS28. QoL was assessed with the SF-36 and EQ-5D (EQ-VAS) questionnaires.

Results: A total of 196 patients were included, among whom 84 (42.9%) and 112 (57.1%) belonged to the early and established cohort, respectively. Gender distribution (52.4% vs. 48.2% females) and age (48.0 vs. 49.7 years) were comparable between-cohorts (Early vs. Established). However, EPsA patients were older at Psoriasis (38.7 vs. 34.1; $P=0.030$) and PsA (47.9 vs. 44.3; $P=0.037$) onset. Patients with EPsA had a significantly higher incidence of DIP involvement (OR=1.78, 95%CI 1.00-3.15; $P=0.049$). Mean TJC and SJC did not differ significantly between-groups. However, the Established PsA cohort had a significantly higher number of abnormal, clinically relevant changes in almost all joints (hands, wrists, feet and SI) compared to EPsA. EPsA patients had significantly higher PASQ score (11.3 vs. 6.2; $P<0.001$), DAS28-3 (CRP) (3.8 vs. 3.3; $P=0.011$), and Pain VAS (33.2 vs. 23.8; $P=0.017$). At baseline, NSAID use was non-significantly higher in EPsA patients (81.0% vs. 71.4%), while patients with Established PsA were more frequently treated with MTX (46.4% vs. 31.0%; $P=0.039$), sulfasalazine (21.4% vs. 10.7%; $P=0.055$), adalimumab (13.4% vs. 4.8%; $P=0.052$), etanercept (8.9% vs. 2.4%; $P=0.073$), and infliximab (7.1% vs. 2.4%; $P=0.193$). Finally, significant between-group differ-

ences were observed in QoL with EPsA patients reporting improved physical (PCS 57.2 vs. 42.6; $P=0.003$) and mental functioning (MCS 62.1 vs. 46.2; $P<0.001$), as well as General Health Status (EQ-VAS 65.7 vs. 50.2; $P<0.001$).

Conclusion: Early PsA is a condition with a consistent risk of clinical progression. The results of our study suggest that early diagnosis and management of PsA can effectively help in reducing the burden of disease, preventing the permanent joint damage and improving the patients' QoL.

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Comparing Touch Screen Apple iPad-based © Health Assessment Questionnaire (HAQ) to the Paper Version in Patients with Inflammatory Arthritis

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Objective: We have created an iPad application for the Health Assessment Questionnaire (HAQ) to be compared to the paper copy of the same tool. The original version of both tools was employed in this research. There are few electronic outcome measurement tools available in the apps world. None of those have been validated by the general population. We investigated the validity, accuracy, feasibility and reproducibility of the electronic version of the HAQ. 1. To compare the validity, accuracy and reproducibility of an iPad-based© version of the HAQ to the paper version. 2. To assess patients' acceptability, convenience, preference and ease of administration for the electronic version of the HAQ and their correlation with the patients' demographics and computer literacy.

Methods: We created an iPad application for the Health Assessment Questionnaire (HAQ) to be compared to the paper copy of the HAQ. There are few electronic outcome measurement tools available in the apps world. None of those have been validated by the general population. We investigated the validity, accuracy, feasibility and reproducibility of the electronic version. Patients with RA, PsA and AS were randomly selected from a rheumatology clinic. The subjects completed both touch screen and paper versions of the HAQ. The order of completing the tools was reversed for every second patient in order to reduce the bias. All patients were asked to complete a questionnaire documenting their demographics, time to complete the tool, preferences and computer expertise. Validity and accuracy by comparing differences in the HAQ scores and in the time taken to complete the tools were evaluated by t-test.

Results: Thirty two patients were included in the analysis; from them 62.5% were females. The age distribution was: 34.4% aged 30 to 49 years; 59.4% aged 50 to 69 years and 6.2% aged 70 years and older. There was not a significant difference in the HAQ Scores between the tools (95%CI -0.159-0.345; $p=0.459$). There was not a significant difference in the time taken for patients to complete both versions of the HAQ (95%CI -0.397-1.882; $p=0.193$). 75% of patients found that the electronic version of HAQ was easier to perform and 72% found that the electronic questionnaire took less time to perform. 63% of patients preferred iPad to the paper version. 91% of participants concluded that the electronic version of HAQ was more beneficial for them. The evaluation of the acceptability, convenience and preference of both tools was not statistically significant between genders.

Conclusion: The study results showed that the iPad© version of the HAQ is valid as a measure of health assessment for arthritis patients as scores are near identical to the paper version of the tool. There is no significant difference in the time to complete the two versions of the HAQ. Patients of all ages and computer literacy levels preferred the electronic version of the test and found it more beneficial for them.

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Concomitant Medication Frequency and Profiles in a Real-Life Canadian Cohort of RA Patients Treated with Infliximab

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Objective: The use of concomitant medications, related to rheumatoid arthritis (RA) or to other chronic conditions, is frequent in RA patients. The purpose of this analysis is to determine the frequency and profiles of concomitant medications used in a routine clinical practice setting and to assess the impact of infliximab (IFX) treatment.

Methods: The data for this analysis were obtained from BioTRAC, an observational prospective registry of adult RA patients initiated on treatment with Infliximab since 2002 and managed as per routine care. Patients enrolled were biologic-naïve or had initiated treatment with a biologic for a period of <6 months prior to enrolment. Analyses for RA-related medications was performed on the overall cohort ($N=775$). Since, non-RA related medications started being collected since 2007, a subgroup analysis was also performed in the 272 patients enrolled since then.

Results: In the overall cohort, mean (SD) age was 55.9 (13.5) years, mean (SD) disease duration 10.3 (10.0) years. At baseline, the prevalence of RA-related concomitant medications was 90.1%, 56.0%, 39.6% and 19.9% for DMARDs, NSAIDs, corticosteroids and narcotic analgesics, respectively. Patients with higher disease duration and disease activity (CDAI) at baseline were being treated with an increased number of RA medications ($P<0.001$) and DMARDs ($P<0.001$) at baseline. Treatment with IFX for 12 months reduced the mean number of RA medications between baseline and 12 months ($P<0.001$). In the sub-group analysis, the baseline characteristics did not differ between patients with or without comorbidity-associated medications. The prevalence of medications associated with comorbidities was 31%. The most common comorbidity-associated medication was for anxiety/depression (17.6%), hypertension (7.0%), gastric disorders (6.3%), dyslipidemia (5.5%), and bone disorders (5.5%). The presence of comorbidities had no impact on the DAS-28 response following IFX treatment or the utilization of RA medication. However, patients with comorbidities experienced a higher number of non-serious adverse events (NSAEs) compared to patients without comorbidities (320.7 vs. 146.3 NSAEs/100 patient years (PY), respectively). The incidence of serious AEs (SAEs) was comparable between the two groups (6.4 vs. 6.4 SAEs/100 PY in patients with vs. without comorbidities).

Conclusion: The results of this real-life observational study demonstrate that disease activity and duration seem to be associated with increased use of RA medications. Treatment with IFX slightly decreases the number of RA medications over time. NSAEs were reported by a greater number of patients with comorbidities compared to patients without comorbidities, however, the incidence of SAEs was comparable between the groups.

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