The Successful Switch of Rheumatoid Arthritis Patients who Develop Drug-Induced Lupus on one Anti-TNFα Agent to Another Anti-TNFα Agent

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Case Report:
Background: Anti-TNFα agents occasionally induce autoantibodies, which can be associated with lupus-like symptoms. In drug-induced lupus (DIL), the offending drug is typically withdrawn and avoided in the future; however in some patients, anti-TNFα therapy is essential for disease remission. The question therefore remains whether or not a trial on a different anti-TNFα agent will induce the same reaction.
Objectives: (1) To describe two patients with rheumatoid arthritis (RA) who developed DIL while on one anti-TNFα agent and required a switch to a different anti-TNFα agent; (2) perform a literature review of anti-TNFα-induced lupus and its management. Methods: A chart review of two patients was performed. A PubMed search was completed using key words: “anti-TNFα inhibitor”, “etanercept”, “adalimumab”, “infliximab”, “drug-induced lupus”, “autoantibodies”. Results: Case 1: A 43yo RF+, CCP+, ANA+, SSA+, ds-DNA- female with RA for 15 years was treated with adalimumab. After 4 years of remission on adalimumab, she developed acute onset of pleuritis, arthralgias and new ds-DNA+. Adalimumab was discontinued and she was maintained on leflunomide for 3 years until she required the initiation of etanercept 25mg twice a week. Since starting etanercept, she has remained in remission without recurrence of ds-DNA+ or lupus-like symptoms. Case 2: A 58yo RF+, CCP+, ANA+, ds-DNA- female with RA for 20 years was treated with infliximab. After 2 months of infliximab, she developed oral ulcers, increased arthralgias and ds-DNA+. Infliximab was discontinued and she was maintained on leflunomide for 3 years until she required the initiation of etanercept 25mg twice a week. Since starting etanercept, she has remained in remission without recurrence of ds-DNA+ or lupus-like symptoms. Conclusions: Consistent with the current literature, these cases show that DIL can occur on different anti-TNFα agents. The finding that patients can be successfully transitioned from one anti-TNFα agent to another without recurrence of DIL has only been described in one other case report. The cumulative experience of our 2 patients and the one from the other case report, admittedly limited, suggests that the DIL reaction of anti-TNFα inhibitors is not so class-specific, allowing the safe switch to a different anti-TNFα agent.
Strategies to Improve Recruitment into Rheumatology: Results of the Workforce in Rheumatology Issues STudy (WRIST)

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Objective:
It is projected that by 2026 there will be a 64% shortfall in the number of required rheumatologists in Canada. The combination of an aging population and a stable, low rate of new rheumatology trainees in spite of overall increases in the number of internal medicine subspecialists will only exacerbate the shortage. A doubling of current rheumatology trainees is likely needed to match future needs; however, there are currently no evidence-based recommendations for how this can be achieved. The Workforce in Rheumatology Issues STudy (WRIST) was designed to determine factors influencing the choice of rheumatology as a career in order to make group comparisons and determine the most effective recruitment strategies.

Methods:
An online survey was created and invitations to participate were sent to University of Western Ontario (UWO) medical students, UWO internal medicine (IM) residents, Canadian rheumatology fellows and Canadian rheumatologists. Surveys sent to each group of respondents were identical except for questions related to demographics and past levels of training. Participants rated 24 (medical students) or 25 (IM residents, rheumatology fellows, rheumatologists) factors that influence their choice of residency (from “not at all important” to “extremely important”). Participants also scored 28 factors related to the attractiveness of rheumatology (“very unattractive” to “very attractive”) and 11 recruitment strategies (“very ineffective” to “very effective”). Statistical significance was determined using chi-squared analysis. Questions were examined using factor analysis.

Results:
1,014 individuals were contacted and 491 surveys were completed (response rate 48.4%): 239 medical students (response rate 42.2%), 34 residents (response rate 43.0%), 9 fellows (response rate 22.0%) and 209 rheumatologists (response rate 63.7%). Responses indicated the importance of exposure through rotations and role models/mentors in considering rheumatology. Significant (p < 0.002) differences between groups were evident with respect to what makes rheumatology attractive and effective recruitment strategies, most interestingly with rheumatologists and trainees expressing opposite views on the latter. Female and male medical students and IM residents similarly ranked the importance of factors that influence the choice of residence; however, females were significantly more likely to consider items related to the rheumatology patient population as attractive (p < 0.002).

Conclusion:
Based on these results, six specific recommendations are made in two broad categories: greater exposure and greater information. As medical students and IM residents progress through their training their interest in rheumatology lessens, thus it is important to initiate recruitment initiatives as early as possible in the training process.
Objective:
To determine whether health-care cost differs for SLE patients with & without Nephritis (LN & LNN, based on renal biopsy or ACR criteria).

Methods:
LN and LNN patients enrolled in the Lupus Nephritis New Emerging Team study in Canada, were classified into those with active (ALN & ALNN) and inactive disease (ILN & ILNN) based on SLE disease activity index (SLEDAI). Scores>6 were considered active disease. Patients reported on health care resource utilization including: visits to health care professionals, use of: diagnostic tests, assistive devices, alternative treatments; hospital emergency visits, surgical procedures and hospitalization in the 4 weeks preceding enrolment. Annual cost, not including the medications was calculated.

Results:
141 patients (121 female, 20 male), 79 with LN (ALN: 53, ILN: 26) and 62 with LNN (ALNN: 38, ILNN: 24) were enrolled. LN patients were significantly younger compared to LNN [36.5(13.6) vs. 43.8(15.1) years; P=0.003] and had a higher SLEDAI score [9.5(7.0) vs. 5.1(3.8); P=0.0001]. Compared to LNN, patients with LN were more likely to visit health professionals (88.6% vs. 74.2%; P=0.026) and had a higher number of visits to rheumatologists [0.8(0.1) vs. 0.6(0.1); P=0.09]; family physicians [0.9(0.2) vs. 0.5(0.1), P=0.041] and nephrologists [0.3(0.1) vs. 0.0(0.0); P=0.001]. The cost of visits to medical doctors was higher for LN compared to LNN [$112(96) vs. $86(86); P=0.094]. LN patients were also more likely to undergo diagnostic tests [81% vs. 62.9%; P=0.016], most commonly including blood [1.7(2.0) vs. 1.1(0.2); P=0.036] and urine tests [1.2(0.2) vs. 0.5(0.1); P=0.001]. The use of assistive devices, alternative treatments, hospital emergency visits and hospitalization periods were similar between the two groups. The annual health care cost averaged at $7,361(9,096) for LN and $7,688(13,864) for LNN (P=0.88). Compared to patients with ILN, those with ALN, used more diagnostic tests [4.3(3.8) vs. 1.8(2.0); P=0.003], associated with a higher monthly cost for these tests [$176(294) vs. $53(83); P=0.006] and performed more surgical procedures [9.6% of patients vs. 0.0%], with a difference in monthly cost of $77(239) (P=0.024). The annual health care cost was higher for ALN [$8,525(9,314)] than ILN [$4,888(8,262); P=0.09]. In LNN, there was no difference in annual cost between ALNN [$9,590(16,937)] and ILNN [$ 4,915(6,865); P=0.15]. The use of complementary therapies, assistive devices, emergency hospital visits and hospitalization were similar between all groups.

Conclusion:
Health care resource utilization is much greater in LN and the cost is much higher in ALN than ILN.
Objective:
To describe the characteristics of a real-world registry of patients consecutively referred to the infliximab (IFX) clinic at the Mary Pack Arthritis Centre, over 9 years since clinic inception.

Methods:
The IFX clinic and patient registry were established 2000 at the time when IFX was the first tumour necrosis factor (TNF) widely available to patients with rheumatoid arthritis (RA) through a special access program. We conducted a systematic chart review of all patients in the registry from 2000 to 2008. Charts were reviewed by a rheumatologist and detailed data were abstracted including demographic information (age, gender), disease characteristics (disease duration, tender joint count, swollen joint count), co-morbid medical conditions, quality of life (measured by the Health Assessment Questionnaire [HAQ]), and prior medication use. Analyses were limited to patients with RA. Descriptive statistics for baseline demographic and RA disease characteristics were stratified according to three time periods (T1: 2000-2002, T2: 2003-2005, and T3: 2006-2008) to describe patients initiating IFX in this real-world setting.

Results:
Since 2000, 376 patients were referred to the Mary Pack IFX clinic. Of these, 195 were eligible and received a total of 4,318 IFX infusions. 131 (68%) patients had RA, 22 (11%) ankylosing spondylitis, 22 (11%) psoriatic arthritis, 6 (3%) oculair inflammatory disease, and 14 (7%) other inflammatory arthritis. Females comprised 78% of RA patients and mean age at baseline was 54.7 years. There was a statistically significant difference in age for RA patients at the different registry entry periods. Specifically, mean age at T1, T2, and T3, were 52.4, 57.0, and 62.0 years, respectively (p-value = 0.02). Mean RA disease duration at registry entry was 17 years. RA patients initiating IFX in the three time periods did not differ across RA disease characteristics including erythrocyte sedimentation rate (ESR), duration of morning stiffness, ACR tender joint count, ACR swollen joint, patient global assessment, and patient pain scale. There were also no differences in history of co-morbid medical conditions, and prior DMARD and biologic use.

Conclusion:
These clinical data from a real-world IFX registry show that baseline disease characteristics of RA patients who initiated IFX treatment were fairly consistent over a 9 year period. With the exception of age, there were no statistically significant differences in baseline characteristics of patients in the three time periods when we anticipated differences. This finding requires further analysis.
Real-Life Effectiveness of Infliximab in the Treatment of Ankylosing Spondylitis: The Canadian Experience

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Objective:
Ankylosing Spondylitis (AS) is a chronic inflammatory disorder affecting as much as 1% of the population. In controlled clinical trials infliximab has been proven efficacious in managing patients with AS. Information concerning the effectiveness of drug therapy cannot be obtained only from randomized controlled clinical trials, due to limitations such as a short time frame and narrow inclusion and exclusion criteria. Therefore, 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 outcome in patients with AS treated with Infliximab.

Methods:
A total of 187 AS patients starting treatment with infliximab or on infliximab for < 6 months were enrolled between 2006 and 2008 in the nationwide RemiTRAC registry (Remicade® Treatment Registry Across Canada). This registry was initiated in 2002 and is an ongoing, multi-centre, prospective, observational study of patients treated with infliximab for RA (Rheumatoid Arthritis), AS or PsA (Psoriatic Arthritis). Patients are naïve to Anti-TNFα treatment or were treated with biologics for a period < 6 months (since December 2006). Patients enter the cohort at the time of initiation of treatment and are followed prospectively. Descriptive statistics and when appropriate statistical tests were conducted, Fisher’s exact test for categorical variables or t-test/ANOVA for continuous variables.

Results:
A total of 187 AS patients were enrolled between 2006 and 2008. At enrolment, mean age of the cohort was 45 years, mean disease duration since diagnosis was 10.7 years. At the time of enrolment in the registry, 47% were treated with NSAIDS and 23% with DMARDS including 16% with Methotrexate. Laboratory and clinical parameters of the cohort during the first 24 months of treatment were evaluated. The results show that significant and sustained changes (P < 0.05) were observed for all parameters (CRP, ESR, morning stiffness, HAQ, patient global assessment, BASDAI and BASFI) after 6, 12 and 24 months of enrolment and that 66%, 45% and 29% of patients achieved an ASAS 20, 50 and 70 therapeutic response by 6 months. This therapeutic response was maintained for the 24 months of follow-up.

Conclusion:
The results of this observational study have shown that infliximab is effective in treating ankylosing spondylitis in a Canadian longitudinal observational study.
**Fibromyalgia: Addressing Challenges in Diagnosis and Management in Canadian Medicine**

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**Objective:**
Fibromyalgia (FM), a legitimate condition with objective neurophysiologic abnormality identified in the research setting, remains a challenge in the clinical domain. Our objective was to identify attitudes and practice patterns of Canadian health care providers treating FM patients, and to suggest areas where improvement will enhance clinical care.

**Methods:**
A Canadian task force comprised 8 regional 4-hour meetings of 139 Canadian health care professionals, representing various disciplines, led by 8 chairs. Following 2 formal presentations addressing pathogenesis, diagnosis and treatment options, discussion was focussed towards challenges and recommendations regarding FM clinical care from the Canadian perspective. All discussions were recorded and a global summary was compiled.

**Results:**
Knowledge translation of pathophysiological mechanisms of FM remains poor, resulting in continued clinical uncertainty. Both diagnosis and management of FM patients is problematic. Identified challenges include the insecurity of health care professionals in managing patients with chronic pain in general, and FM in particular, absence of an objective test for diagnosis and clinical outcome, the need to balance efficacy, side effects and adherence to treatments, lack of a gold standard of treatment, confusion regarding international guidelines, and clinical constraints of physician time and resources. The recent “on label” acceptance of pharmaceuticals for treatment of FM is welcome. Recommendations were focussed predominantly towards the need for education, beginning at the undergraduate level and extending across all health care providers and patients, improvement in access to pharmacological and non-pharmacological therapies, and timely access to pain specialists if needed. Recognition of the validity of FM is still lacking by authorities such as governing bodies and insurance providers.

**Conclusion:**
Although ideal care for FM patients is in a multidisciplinary model, still mostly lacking in the Canadian health care system, most FM patients can be well managed in the primary care setting, provided health care workers are adequately educated. Recognition of FM by the medical community and the general public is improving, but with slower acceptance by governing bodies and insurers.
Cross-Cultural Adaptation and Validation of an Early Inflammatory Arthritis Detection Tool in the Canadian Francophone Population

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Objective:
Objective: To cross-culturally adapt and validate the English Early Inflammatory Arthritis (EIA) Detection Tool for the Canadian Francophone population.

Methods:
Methods: Phase 1 & 2: Forward translations of the English EIA Detection Tool into French were conducted independently by two French-mother-tongue translators and then circulated to 7 French-speaking laypersons for feedback. Each final forward translation was independently back-translated into English using English-mother-tongue translators and English-speaking laypersons. The two sets of forward and back translations were reviewed by a 7-person committee comprised of a translator/linguist, laypersons, rheumatologist, primary care practitioners and methodologist. The committee selected the most appropriate adaptation. Phase 3 & 4: The discriminant validity, comprehensibility, and test-retest reliability will be determined on a sample of 402 EIA, established IA, and non-IA patients under rheumatologic care. The validation will be implemented in the three provinces with the highest Francophone population density (% Francophone per 2001 census; number of study rheumatologists): Quebec (81.2; 7); New Brunswick (34.6; 1); and Ontario (5.4%; 2). Each study rheumatologist will recruit 39-42 consecutive adult, French-mother-tongue participants: 13-14 EIA; 13-14 established-IA; and 13-14 non-IA. A 3-site, 90-participant pilot study will be conducted to further pretest comprehensibility and verify site and participant enrolment estimates.

Results:
Results: A translated and cross-culturally adapted to Canadian French version of the 11-question EIA Detection Tool, with 100% committee agreement has been produced. Early data in Phase 3 shows 40 individuals have completed the EIA Detection Tool at Time 1 (T1), (EIA=13; established IA=14; MSK Non-IA=13). Overall, 97.3 percent report strong or very strong understanding of the questions. At Time 2 (T2), 35 patients reported feeling the same as they did when they first completed the EIA Detection Tool. Within this group there was 100% internal consistency of responses. Scoring (number of “Yes” answers), by group for discriminant validity: (EIA, n=13, T1=6.0/T2=7.0; Established IA, n=14, T1=4.8/T2=4.7; MSK Non-IA, n=13, T1=3.2/T2=3.0)

Conclusion:
Conclusions: A cross-culturally adapted and validated EIA Detection Tool for Canadian Francophones may improve appropriate care for this population. Complete validation data will be available by January, 2010.
Validation of a Self-Administered Inflammatory Arthritis Detection Tool for Rheumatology Triage

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Objective:
Objective. The objective of the current study was to validate the tool for the detection of inflammatory arthritis (IA) in the rheumatology wait list population.

Methods:
Methods. The tool was self-administered by 143 patients on the waiting lists of two Canadian, academic rheumatologists. At rheumatology presentation, the blinded rheumatologists assigned a clinical diagnosis and categorized each patient as IA or not. Multivariable logistic regression was conducted using IA as an outcome and age, sex, and the twelve tool items as independent variables. Multivariable-adjusted estimates of independent variable effect sizes were used as weights for the tool. Bootstrap AGGREGATING (BAGGING) of 200 multivariable models was used to refine estimates of independent variable weights and the tool’s performance properties. Receiver operating characteristic (ROC) curves for the models were derived. The predictive performance for the tool was determined from the area under the ROC curve (AUC), and sensitivity and specificity of the optimal model probability cutoff score. The optimal model probability cutoff score was determined from the maximum sum of sensitivity and specificity along the ROC curve. All analyses were performed using SAS/STAT® v. 9.2.

Results:
Results. The sample was comprised of a variety of rheumatologic conditions including 30 IA (ankylosing spondylitis, psoriatic arthritis, reactive arthritis, rheumatoid arthritis, and undifferentiated inflammatory arthritis) and 113 non-IA cases (osteoarthritis, pain syndromes, systemic lupus erythematus, and other miscellaneous rheumatologic disorders. The multivariable logistic regression ROC AUC was 0.92. Using a model probability of 0.33, a sensitivity of 0.80 and specificity of 0.90 was determined. The model goodness of fit was supported by a non-significant Hosmer-Lemeshow test (p=0.64). Upon BAGGING the model, the ROC AUC was 0.95 ± 0.02 with a sensitivity of 0.92 (0.87-0.96) and specificity of 0.92 (0.86-0.96) using a model probability cutoff of 0.29 (0.19-0.42).

Conclusion:
Conclusion. A twelve-item, self-assessment tool has been validated for the detection of inflammatory arthritis in the rheumatology wait list population. Together with its favourable performance properties, this self-assessment tool offers a potential advance in the rheumatology triage of inflammatory arthritis.
Predictors of Radiographic Progression in RA Patients Treated with Anti-TNF Therapy

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Objective:
Determine predictors of x-ray progression in a cohort of anti-TNF treated RA patients.

Methods:
RA patients receiving anti-TNF therapy are monitored in a mandatory pharmacovigilance program, with x-rays performed every 2 years. Digital radiographs of the hands, wrists and feet were read in chronological order by three rheumatologists and scored using the Sharp van der Heijde score (SHS). We used the Smallest Detectable Change (SDC), calculated from the annualized progression rate, to stratify by progression status. Potential predictors of radiographic progression were used as independent variables in a backward stepwise regression analysis. Stratification of progression status using the SDC score was compared to the qualitative opinion provided in the radiologist’s report.

Results:
Twenty-five patients had serial assessments of hands, wrists and feet, mean age 57 years, disease duration 9 years and 76% were female. Anti-TNF exposure included infliximab (56%), etanercept (48%) and adalimumab (44%), and 75% were on concurrent DMARD therapy. Mean baseline scores were: DAS28 6.08 (SD 1.10); HAQ 1.36 (SD 0.69); SHS 93.0 (SD 86.3). At follow-up (mean 2.14 years), 52% achieved a good EULAR response with 44% in remission (DAS28 < 2.6). The annualized mean change in SHS score was 6.57 (SD 7.49), and classification of progression status using the SDC yielded 16 non-progressors and 9 progressors. Both groups had comparable baseline scores and significant improvement in DAS28 scores over the evaluation period, but non-progressors trended to a lower DAS28 score at follow-up (mean difference -1.14, 95%CI -2.37, 0.10, p=0.06). More progressors flared and required a change in therapy during the observation period but this was not statistically significant. No significant predictors of radiographic progression were identified through logistic regression analysis. Two progressors were classified as being in remission by EULAR classification. Seven patients had a second evaluation period and 3 patients had a third, with evidence of slowing of radiographic progression over time (mean change in SHS score per year at 2nd study 4.87 (SD 4.22) and at 3rd study 1.20 (SD 2.08)). There was high concordance between classification using the SDC and the radiologists’ qualitative reports for non-progressors only.

Conclusion:
The majority of patients who respond to anti-TNF therapy exhibit no significant x-ray progression over time. Patients with progression tend to have higher disease activity throughout the evaluation period. Radiology reports are not adequate for assessing progression in observational cohorts.
The Association of anti-CCP antibodies with Polymyalgia Rheumatica

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Objective:
To determine the prevalence of anti-cyclic citrullinated peptide antibody (CCP Ab) in patients diagnosed with Polymyalgia Rheumatica (PMR) in a University based rheumatology cohort.

Methods:
We identified and confirmed by a chart review all patients at the University of Alberta Rheumatic Disease Unit who had been previously diagnosed with PMR. Eligible PMR patients for this study fulfilled criteria pertinent to both the Bird/Wood Criteria (for diagnosis of PMR) and the ACR classification criteria. All classification criteria were met, and were collected from a chart review. The University of Alberta Rheumatology Laboratory stores serum on all samples they are sent, and when possible links with the associated clinical diagnosis. Anti-CCP Ab status was determined on those patients with previously submitted serum. Anti-CCP Ab was measured by the corresponding enzyme-linked immunosorbent assay. Results were reviewed and analyzed.

Results:
Of the 42 patients with initial possible diagnosis, 24 patients (57%) had a final diagnosis of only PMR while the remaining 18 patients (43%) had PMR and concurrent diagnoses or were diagnosed with a different final condition (excluded). 21 of the 24 “PMR only” patients (87%) met the Bird/Wood Criteria based on information collected from the chart review. None of the 24 patients had a positive anti-CCP result. Of the total 42 patients included in this study, 2 patients (5%) were found to have serum autoantibodies to CCP. As information became available about these 2 patients, including a lack of response to steroids, they were eventually diagnosed by a rheumatologist as having either polymyalgic onset of rheumatoid arthritis or palindromic rheumatoid arthritis. As a result, positive serum CCP autoantibodies could be explained by a diagnosis other than PMR.

Conclusion:
This study illustrates that autoantibodies to CCP are not present in a population of North American patients with PMR. A positive anti-CCP antibody result in a patient with suspected PMR would provide support to investigate for an alternate diagnosis.
Preliminary Analyses of Spatial Clustering of the Prevalence of Systemic Autoimmune Rheumatic Diseases in Montreal, Quebec

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Objective:
Systemic autoimmune rheumatic diseases (SARDs) include systemic lupus, scleroderma, Sjogren’s syndrome, inflammatory myopathies, and undifferentiated connective tissue disease. Spatial analyses of SARDs are few. Our objective was to investigate the extent of global and local spatial clustering of SARD prevalence in Montreal, Quebec.

Methods:
Estimates of the prevalence of SARDs by forward sortation area (FSA, defined by the first three characters of the postal code) were generated from provincial hospitalization and physician billing data for 1989-2003. Global and local clustering of the prevalence of SARDs on the Island of Montreal was measured using Moran’s I test and the Local Indicators of Spatial Association test (LISA) respectively. Three of the 95 FSAs on the Island of Montreal were excluded from the analysis because they were not residential in nature. Analyses were adjusted for the differences in age and sex distribution across FSAs.

Results:
Moran’s I test revealed global clustering for the prevalence of SARDs over-all, and for all demographic groups. When local clustering was examined, a large region centred on the boroughs of Villeray and Rosemont was found to be a low-prevalence cluster for all demographic groups except males. The over-all prevalence in this cluster ranged from 298-494 cases per 100,000 people with a median of 395. A smaller high-prevalence region was found centred on the downtown area for the same demographic groups. The over-all prevalence in this cluster ranged from 533-918 cases per 100,000 people with a median prevalence of 740.5. Additional non-overlapping high-prevalence clusters were found for each demographic group. For example, a high-prevalence cluster for people less than 45 years old was centred on Dollard-Des-Ormeaux while a cluster for people aged 45 years and older and a high-prevalence cluster for females was centred further east in Notre-Dame-de-Grace.

Conclusion:
This preliminary work suggests clustering of SARD prevalence on the Island of Montreal among different demographic groups. The distinct locations of high-prevalence clusters for specific demographic groups suggest that environmental triggers for SARDs may affect specific age and sex groups differently. However, potential limitations of our work must be emphasized; first, that we studied prevalence and not incidence, and second, that we did not account for differential sensitivity and specificity of case ascertainment, across age, sex, or regions. Furthermore, the analyses are cross-sectional and do not account for past residential exposures. Ongoing efforts are in progress to study these issues further.
A Retrospective Review of Rheumatology Referral Wait Times

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Objective:
To assess wait times between primary care referral and rheumatology assessment for new-onset inflammatory arthropathies.

Methods:
We performed chart reviews related to new rheumatology consultations (N=202) seen by three rheumatologists practicing within the McGill University Health Centre between September and November 2008. At this centre, no formal triaging of rheumatology referrals exists. Time from referral to rheumatology was determined from clinic notes where possible, along with the provisional diagnosis of the referring physician, where available, and the diagnosis of the rheumatologist.

Results:
Of the 202 charts reviewed, wait times could be calculated in 164 cases. Only consultations for new-onset conditions were analyzed (N=161). Two-thirds of the cases analyzed (106/161, 65.8%) presented with conditions ultimately diagnosed as non-urgent entities, such as soft-tissue rheumatism and osteoarthritis. Roughly one-fifth of the cases (35/161, 21.7%) were diagnosed with potentially urgent conditions, such as inflammatory arthritis or connective tissue diseases. Compared to non-urgent conditions, there was a trend towards shorter wait times for patients who were ultimately diagnosed with either inflammatory arthritis or other potentially urgent conditions. Family physicians had indicated a suspicion of new-onset inflammatory arthritis on their referral for 15 patients, of which 7 were later diagnosed as having inflammatory arthritis. The mean wait time for these cases averaged 35.4 (median 30) days. In addition, there were 17 other patients diagnosed with inflammatory arthritis by rheumatologists, although there was no suspicion of this noted in the referral. The mean wait time for these cases was 30.0 (median 21) days.

Conclusion:
On average, individuals with inflammatory arthritis were seen about a week sooner than non-urgent cases. This trend may not be entirely attributable to possible prioritization of inflammatory arthropathies, as patients with more urgent conditions may call for appointments earlier. In fact, referral wait times for individuals with inflammatory arthritis did not appear to be expedited when a provisional diagnosis of this was clearly stated by the referring physician. The results suggest that there is room to further improve referral wait times for persons with inflammatory arthritis. The implementation of a rapid access program or triage system may contribute to the optimization of care for urgent rheumatologic conditions such as rheumatoid arthritis.
Serious Fungal Infections in Seniors with Rheumatoid Arthritis (RA): A Population-based Study from the Ontario Biologics Research Initiative

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Objective:
The OBRI is an innovative undertaking to promote real-world rheumatic drug surveillance. Our objective was to assess risk of serious fungal infections in seniors with RA.

Methods:
An RA cohort was assembled from Ontario billing and hospitalization data, 1992-2008. Analyses were limited to subjects aged >65 who filled >1 prescription for an oral glucocorticoid, disease-modifying agent (DMARD) or biologic. We studied cases of fungal infection (Aspergillosis, Coccidioidomycosis, Histoplasmosis, Blastomycosis, Paracoccidioidomycosis, systemic Candidiasis) identified from the most responsible diagnoses for hospitalization and/or ER visits. Controls, age and sex matched, were selected by risk-set sampling. Univariate and multivariate regression analyses assessed the effects of demographics, co-morbidity, markers of RA severity (number of rheumatology visits, extra-articular RA features, joint replacement), and medications.

Results:
In 81,497 seniors with RA; 53 serious fungal infections occurred. Cases were more likely than controls (n=265) to be rural and to have more co-morbidity (especially lung and renal disease). Cases also tended to have more extra-articular RA features and more rheumatology visits. Only 17/53 cases were currently exposed to a DMARD at the time of the fungal infection, and no cases were currently exposed to a biologic agent. In both cases and controls, the most common current DMARD exposures were methotrexate(11%) and hydroxychloroquine(9%). In contrast, prednisone exposure >10mg/d occurred in 18.8% of cases, versus 7.2% of controls(11.6% difference, 95% CI 2.6, 24.5). Multivariate models demonstrated that risk of fungal infection was higher among rural-versus-urban residents(OR 6.8, 95% CI 2.6, 17.5) and in subjects with higher co-morbidity (as assessed by number of drugs used in the year prior to index date, OR 1.1, 95% CI 1.0, 1.2). There was a notable trend for greater fungal infection risk with prednisone doses >20mg/d (adjusted OR 4.0, 95% CI 0.9, 17.4).

Conclusion:
Rural-versus-urban and higher co-morbidity were associated with occurrence of serious fungal infections in seniors with RA. Steroids were suggested as an independent risk factor, but neither DMARDs or biologics were clearly implicated in this population-based sample. Important potential limitations of our study include relatively low drug exposure rates, the possibility of incomplete ascertainment of biologic exposures (for individuals receiving drugs through private insurance plans) and ‘channelling’ bias (where persons at highest risk for serious infections may not be prescribed biologics).
Rheumatoid Arthritis (RA) and Risk of Serious Infections: A Nested Case-Control Study from the Ontario Biologics Research Initiative

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Objective:
The Ontario Biologics Research Initiative represents a novel approach to real-world rheumatology surveillance. Our purpose was to evaluate risk for serious infections in Rheumatoid Arthritis (RA).

Methods:
We studied a population-based RA cohort using Ontario physician billing and hospitalization data (1992-2008); we limited analyses to those aged >65. An RA diagnosis was based on >2 billing code diagnoses (>2 months apart but within 5 years). Cohort members were further required to have >1 prescription for an oral glucocorticoid, disease-modifying (DMARD) or biologic agent in the 90 days preceding, or any time following, cohort entry. Cohort entry was defined by the first RA billing code; subjects were followed until the first of: event of interest, death, outmigration, or March 31, 2008. Co-morbidity and history of joint-replacement were determined using hospitalization, billing and procedure code data. Our primary outcome, assessed over 1998-2008, was an infection requiring hospitalization or emergency room visit. Cases were age, sex, and time-matched to controls. Multivariate logistic regression analyses assessed independent exposure effects, adjusting for demographics (rural-versus-urban residence, income quintile), co-morbidity, markers of RA severity (number of rheumatology visits, extra-articular RA features, history of joint replacement), and concomitant/past medications.

Results:
81,497 seniors with RA were followed. During this time 14,214 infections occurred; the most common infection was pneumonia (7,026 events). Comparing these individuals with infection to age and sex matched controls (n=71,058), multivariate models demonstrated that infection was highest among subjects of low income status, high co-morbidity, and greater disease severity. Steroids were an important risk factor for infection, with a four-fold increased risk even for prednisone doses < 5mg/d, compared to no prednisone (adjusted odds ratio, OR 4.0, 95% CI 3.7, 4.3). Compared to no prednisone, prednisone doses >10mg/d increased infection risk by six-fold (adjusted OR 6.1, 95% CI 5.5, 6.7). The OR for infection related to current drug exposures (adjusted for all covariates including concomitant drugs) was 2.3(1.8, 3.0) for azathioprine; 2.2(1.5-3.2) for anti-TNF drugs; 1.9(1.8, 2.1) for methotrexate; and 1.5(1.2, 1.9) for leflunomide.

Conclusion:
Low income status, high co-morbidity and disease severity are associated with infection risk in RA. Our results emphasize corticosteroids as an important independent risk factor for serious infection in RA, but other agents, both biologic and traditional DMARDs, appear to confer risk as well.
Comparison of Clinical Risk Factors for Osteoporosis Between Subjects who Sustained a Traumatic or a Fragility Fracture

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Objective:
The objective of this analysis was to determine whether clinical risk factors can discriminate between individuals who have suffered a fragility fracture (FF) or a traumatic fracture (TF).

Methods:
Recognizing Osteoporosis and its Consequences in Québec is an ongoing prospective cohort study of women over 50y of age who have sustained a FF or a TF. Women were enrolled at their visit to the cast or outpatient clinic 0 to 16 weeks after fracture or by mail using a list of women who sustained a fracture, generated every 3 months by the Quebec Ministry of Health. All subjects were contacted 6-8 months following fracture to complete a questionnaire on demographic features, clinical characteristics, and risk factors for osteoporosis (OP). FF were defined as fractures occurring spontaneously or following a minor trauma, such as a fall from standing height, a fall from the sitting position, a fall from lying on a bed or a reclining deck chair from less than a meter high, a fall after having missed 1 to 3 steps in a staircase, after a movement outside of the typical plane of motion, or coughing. Only women with no diagnosis or treatment for OP at the time of fracture were included in this analysis.

Results:
Of the 2551 women who completed the questionnaire, 1729 (1390 FF and 497 TF) had no diagnosis or treatment for OP at fracture. The mean ages for experiencing a FF or a TF were 62.5y and 59.8y, respectively. The most frequent fracture sites were wrist, ankle, humerus, and the hip region, with all sites having similar proportions of FF (80-90%). In multivariate analysis models, the strongest predictors of a FF (odds ratio, 95% CI) were a personal history of a FF after 40y (12.0, 9.2-15.7), Charlson score < 120kcal/wk) increased the probability of FF (1.68, 1.23-2.30). Those underweight (BMI< 18.5kg/m2) were less likely to experience a FF compared to obese (BMI>30kg/m2) women (0.36, 0.13-0.94).

Conclusion:
Well-known clinical risk factors can discriminate between FF and TF as defined by the mechanism of falling with no reference to bone mineral density. This analysis reinforces that a personal history of fracture is the strongest predictor of a FF.
Von Willebrand Factor Antigen – A Novel Biomarker of Disease Activity in Childhood CNS Vasculitis

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Objective:
To characterize presenting clinical, laboratory and imaging features of children with distinct subtypes of central nervous system (CNS) vasculitis, to determine disease activity trajectories and associated inflammatory markers, and to explore the role of the novel biomarker von Willebrand Factor antigen (vWF) levels as a marker of disease activity.

Methods:
A single centre cohort study of consecutive children diagnosed with primary angiitis of the CNS (cPACNS) or secondary CNS vasculitis between June 1989 and October 2008 was performed. All patients were less than 18 years of age and had to have vWF levels measured. Demographic, clinical, laboratory, imaging and histological data were collected. Primary outcome was disease activity measured by physician global assessment using a visual analogue scale at regular standardized visits. Analysis included descriptive statistics and linear mixed effects models to account for repeated measures.

Results:
The study inception cohort consisted of 31 children: 16 (52%) were female, median age at diagnosis was 9 years (3.3, 17.8 yrs), 18 (58%) had small vessel cPACNS, 10 (32%) had large vessel cPACNS (5 progressive, 5 non-progressive) and 3 (10%) had secondary CNS vasculitis. At diagnosis: elevated CRP 20%, increased ESR in 55%, leukocytosis in 52%, high opening pressure on lumbar puncture in 62%, elevated cerebrospinal fluid (CSF) protein in 54%, CSF leukocytosis in 72%, abnormal MRI in 94%, abnormal CNS angiogram in 42%, and vasculitis on brain biopsy in 71% patients. Disease activity as measured by physician global assessment decreased significantly over time (p<0.0001) and differed significantly between cPACNS subtypes (p=0.0331) with angiography negative cPACNS having higher disease activity. vWF levels decreased significantly over time (p=0.0084) and were significantly associated with disease activity using mixed effects models (p=0.0014.) PSOM scores decreased significantly over time (p<0.0001) and vWF levels were associated with PSOM scores overall (p=0.0083.) ESR and CRP did not correlate with vWF levels or disease activity.

Conclusion:
von Willebrand Factor antigen is a sensitive marker of disease activity in cPACNS. Subtypes of childhood CNS vasculitis are distinguished by their presenting features and follow distinct disease activity trajectories. Disease activity improved significantly in all subtypes during the 24 month follow-up period; however, patients with angiography negative cPACNS had consistently higher disease activity over time. vWF levels mirror disease activity and therefore may be a promising novel biomarker of disease activity in childhood.
Baseline Characteristics & Preliminary Efficacy Results of Patients Receiving Biologic and Traditional Disease Modifying Anti-Rheumatic Drugs (DMARDs) in Ontario: Results from the OBRI

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Objective:
To describe the baseline characteristics & ‘real-world’ efficacy based on OBRI’s clinical registry.

Methods:
Patients were enrolled from 18 rheumatology clinics across Ontario and prospectively followed to assess drug changes, disease activity, and adverse events. Subjects were grouped into 3 cohorts: 1st DMARD, DMARD Change, and Biologic. Baseline data collected by rheumatologists were available for 426 (97%) of enrolled subjects. Patient reported data, collected through telephone interviews, includes patient global assessment, the Rheumatoid Arthritis Disease Active Index (RADAI) and the Health Assessment Questionnaire (HAQ-DI). t-tests of the means were used to evaluate primary efficacy.

Results:
The DMARD change group made up 55% of the enrolled patients. 26% of patients were prescribed a new biologic and 19% their 1st DMARD at the time of enrolment. The 1st DMARD cohort had the eldest population with a mean age of 60.8 (SD of 14.8) yrs., and the largest subgroup of patients over 65 yrs of age (41%). Mean age for the biologic and the DMARD change group were respectively, 54.4 (13.2), and 56.5 (13.4) yrs. The biologic cohort had the longest mean RA duration compared to the DMARD change and 1st DMARD groups [12.5 (10.9) vs 8.9 (9.2) vs 1.2 (3.8)]. The 1st DMARD patients were mostly prescribed methotrexate, 98% vs 86% in the DMARD change patients. Also, 72% of the biologic patients were taking concomitant methotrexate. Compared to the DMARD change cohort, the biologic patients had the highest scores on the physician global assessment (SD)[6.0 (2.1) vs 4.9 (2.1)], patient global assessment (SD) [7.3 (2.4) vs 5.9 (2.8)], 28 swollen joint count (SD) [8.9 (6.1) vs 6.0 (5.2)], 28 tender joint count (SD) [9.8 (7.5) vs 6.9 (6.3)], and CDAI (SD) [31.3 (15.1) vs 23.0 (12.9)]. At the time of their 6 month follow up, biologic and DMARD change patients showed statistically significant improvements (p < 0.001) in physician and patient global assessments, 28 swollen joint count, 28 tender joint count, DAS28, CDAI, RADAI and HAQ-DI.

Conclusion:
While all RA patients showed significant improvements in both physician and patient reported outcomes, regardless of the treatment they received, the largest changes were found in the biologic cohort.
Validation of Rheumatoid Arthritis Disease Activity Index (RADAI) in a North American Cohort of Patients with Early Rheumatoid Arthritis (RA)

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Objective:
The RADAI is a patient self-administered index measure of RA disease activity, easy to complete in a practice setting. We used the Study of new-onset Rheumatoid Arthritis (SONORA) to validate it as a measure of change over time against the Disease Activity Score with C-reactive protein (DAS28-CRP) and Health Assessment Questionnaire-Disability Index (HAQ-DI)

Methods:
The SONORA study recruited patients with new onset RA (symptoms ≥3 but ≤12 months) from 53 US states and 5 Canadian provinces. Correlations between RADAI, DAS28-CRP and HAQ-DI, were calculated cross-sectionally and for changes over one year. Changes in RADAI, DAS28-CRP and HAQ were compared in patients that achieved ACR20 and ACR50. Using standard definitions, we classified patients as mild, moderate or severe on the RADAI and the DAS28-CRP scales and calculated agreement between these two scales.

Results:
A total of 936 patients were analyzed at baseline and year 1. Patients were female (73%), with mean age of 53 years (19 to 85 years) and mean duration of RA signs and symptoms of 170 days at baseline evaluation. The correlations between RADAI and DAS28-CRP were 0.44 and 0.45 at baseline and 1 year respectively (both p< 0.0001). Correlations between RADAI and HAQ-DI were 0.64 and 0.65, at baseline and 1 year, respectively (both p< 0.0001). Classification of patients into mild, moderate, and severe showed a 52% agreement between RADAI and DAS28-CRP at baseline, and 51% at year 1. At baseline, 31% of patients were classified as more active on the RADAI than on the DAS28-CRP and 17% were classified as less active. Mean Change in RADAI, DAS28-CRP, and HAQ-DI scores from baseline to year 1 follow up were 1.2 (SD, 2.2), 1.03(1.4), and 0.17(0.6) correspondingly for all patients. Where as, mean change for patients who achieved ACR20 and ACR50 were 2.5(1.7) and 3.0(1.5). Which shows the same trend as DAS28-CRP (2.21(1.1), 2.59(1.1)), and HAQ-DI (0.6(0.5), 0.75(0.5)) change over time.

Conclusion:
The RADAI is a valid measure of change over time when compared to the DAS28-CRP and the HAQ-DI in groups of patients. There is less agreement between these measures in individual patients. We conclude that the RADAI is a useful and practical measure to monitor trends in patients’ disease in practice settings.
A Risk Model for the Prediction of Radiographic Progression: Results from SONORA Study

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Objective:
Data from SONORA (Study Of New-Onset Rheumatoid Arthritis) was analyzed to explore a prediction model for the high risk of radiographic progression in early RA patients

Methods:
A total of 994 patients diagnosed with early RA (symptoms ≥3 and ≤12 months) by a board-certified rheumatologist across North America were recruited in this study. Hand radiographs were obtained at baseline, year 1, year 2 and scored according to the original Sharp method (range 0 to 280) in random order per patient. Radiographic progression was defined by a change of at least 3.52, in total Sharp Score. The continuous risk factors were included in the model as categorical variables, which includes DAS28 (≤3.2 0 or >3.2), swollen joint count (<10, 10-17, or <17), Rheumatoid factor (≤20 or >20), anti-CCP (≤20 or >20) and Baseline Sharp Score (0, 0-5, 5-10 or >10). Significant predictors of radiographic progression in univariate models were included in a General Estimation Equation (GEE) model.

Results:
Patients had a mean age of 53 years (SD, 14.81), 72% female and 90% Caucasian with mean disease duration of 170 (180) days. The Sharp Score was 5.49 (7.85), 6.38 (8.90) and 6.17 (8.65) at baseline (N=746), year 1 (n=756) and year 2 (n=567) respectively. Among these patients, radiographic progression was observed in 10.4% of the patients at year 1 and 11.7% at year 2. The multivariate GEE model with repeated binary outcomes at year 1 and 2 revealed that a subpopulation of early RA patients with DAS28>3.2, Baseline Sharp Score >10, anti-CCP>20 were those at highest risk of radiographic progression at year 1 and 2. The odds ratio of radiographic progression comparing DAS28≤3.2 to DAS28>3.2 was 0.52 (p=0.003). The odds ratio comparing Baseline Sharp Score >10 to 0, and >10 to ≤5 were also significant (0.35 (p=0.006) and 0.42(p=0.004) respectively) while the odds ratio comparing Baseline Sharp Scope for those > 10 versus 5–10 was not significant (0.54, p=0.085). The odds ratio comparing Anti-CCP >20 to ≤20 was 0.35 (p<0.0001).

Conclusion:
Radiographic progression of RA remains the best method for assessing structural damage associated with the disease. Our model predicts the risks of radiographic progression using easy and accessible clinical and laboratory variables. These identified subgroups can help guide rheumatologists in making treatment decisions for early RA patients.
Demographic and Clinical Characteristics of a North American Early RA Cohort: SONORA

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Objective:
SONORA (Study of New-Onset Rheumatoid Arthritis) was a prospective, 5-year, multicenter cohort study of 994 patients diagnosed with new-onset rheumatoid arthritis (RA) in North America. Initiated in 2000, SONORA was designed to examine clinical, humanistic, treatment patterns, epidemiology and health-related quality of life in these patients.

Methods:
Patients diagnosed as having new onset RA (symptoms ≥3 but ≤12 months) by a board-certified rheumatologist were recruited from 98 rheumatology practices. Clinical and laboratory data were collected by the enrolling rheumatologist at baseline, 1 and 2 years. Patients completed validated questionnaires (e.g., SF-36, HAQ, etc) every 4 months.

Results:
Mean age of patients was 53 years (SD, 14.8), with 72% female and 90% Caucasian. Mean RA symptom duration was 170 days (SD, 180), 61% were seropositive for rheumatoid factor and 43% anti-CCP positive (>20 unit/ml) at baseline. Ninety-four percent of patients completed 2 years of study, 83% completed 3 years. Seventy-four percent of patients had received DMARDs at baseline compared to 90% at year 1 and 87% at year 2. Two percent of subjects were on Biologics at baseline, in comparison to 15% at year 1 and 23% at year 2. During first two years of the study, disease activity score (DAS28) decreased slightly from 4.4 (1.3) at baseline to 3.4(1.4) year 1 and 3.2(1.3) year 2. Similar change was observed in Rheumatoid Arthritis Disease Activity Index (RADAI) from 4.3 (1.9) at baseline to 3.1(2.2) year 1 and 2.8(2.2) year 2. Improvement was greatest in the tender joint counts from 10.1(8.0) at baseline to 5.5(6.7) year 1 and 4.7(6.6) year 2. Swollen joint count improved also from 9.4(7.1) to 5.5(6.4) and 4.6(6.0). Sharp score based on hand radiographs progressed slightly from 5.5(8.0) at baseline to 6.4(8.9) year 1 and 6.2(8.7) year 2. HAQ improvement was modest from 5.5(7.9) baseline to 6.4(8.9) year 1 and 6.2(8.7) year 2.

Conclusion:
Demographics of this cohort were representative of the general early RA population. Overall improvement in disease activity and patient disability scores were moderate compared to the data reported in the controlled clinical trials. This real world patient-reported data represents an important benchmark to measure treatment effectiveness, model of the disease patterns, monitor the productivity and health related quality of life as newer agents were introduced into the community practice. Ongoing data analysis of SONORA will contribute to our understanding of early RA, identify prognostic factors of disease outcomes and optimal treatment regimens.
Documentation of Significant Non-Serological Differences between Primary Sjogren’s Syndrome (PSS) and SICCA.

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Objective:
Purpose: To document significant non-serological differences between Primary Sjogren’s Syndrome (PSS) and SICCA.

Methods:
Method: From September 1993 until May 2008, 498 patients were assessed by protocol at a multidisciplinary Sjogren’s Syndrome clinic. Data was recorded from a first time comprehensive evaluation. 265 patients with PSS by American-European Consensus Criteria were compared with 70 patients with SICCA, defined as dry eye on Schirmer’s-1(S-1) of < 5mm/5 minutes or dry mouth with unstimulated salivary flow (USSF) of < 1.5 ml/15 minutes or stimulated salivary flow (SSF) of < 0.6mm/minute without meeting consensus criteria for Sjogren’s Syndrome.

Results:
Results: The groups were identical for age, weight, and disease duration. Symptom severity for dry eye and dry mouth were each measured on a Visual Analog score. There was no difference between the groups for dry eye. Dry mouth was perceived more severely in PSS. DMF score was equal. Rose Bengal van Bijsterveld score (5.5+2.1 vs 4.6+2.5, p<0.0001), S-1 mm/5min (4.3+4.6 vs 6.2+6.7, p=0.01), Focus score (4.3+3.3 vs 0.4+0.23, p<0.0001), SSF (0.6+0.6 vs 0.8+0.8, p<0.0001) and USSF (0.7+1.3 vs 1.4+1.4, p=0.03) were significantly more severe in patients with PSS. On laboratory assessment, significant differences were seen in white blood cell count (4.8+1.7 vs 5.7+1.8, p=0.0003), lymphocyte count (1.4+0.7 vs 1.6+0.6, p=0.01), ESR (29.5+22.2 vs 13.2+12.1, p<0.0001), IgG (19.9+8.3 vs 12.2+4.0, p<0.0001), IgA (3.1+1.4 vs 2.3+1.1, p=0.0002) and C4 (0.2+0.09 vs 0.3+0.1, p<0.0001). There was no significant difference for IgM or C3.

Conclusion:
Conclusions: 1. Although there was no significant difference in perceived severity of dry eye (VAS), the measured surface damage was more severe in PSS. Ocular damage may be accompanied by lost corneal sensation. 2. Although PSS patients perceive greater distress than Sicca, they experience no difference in DMF score (dental damage). The degree of distress may correlate better with SSF than USSF, indicating that PSS patients may not produce extra saliva when needed. 3. These comparisons demonstrate that dry eye syndrome is just as distressful in the absence of autoimmune disease. 4. IgA, IgG and AMA, but not IgM or SMA are importantly elevated in PSS. C4 but not C3 is depressed in PSS
Utility and feasibility of musculoskeletal ultrasonography (MSK US) in rheumatology practice in Canada: Needs assessment

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Objective:
1) To evaluate current use of MSK US in Canadian rheumatology practice 2) To investigate factors that may encourage or limit the use of rheumatologist-performed MSK US and 3) to determine anatomical areas that are of most interest to Canadian rheumatologists.

Methods:
A 13-question needs assessment survey was modeled after the questionnaire developed and validated by Brown AK, et al1. All Canadian rheumatologists were invited via email by the Canadian Rheumatology Association (CRA) to participate in the survey.

Results:
Out of 156 physicians that took part in the survey, 118 (76.6%) were rheumatologists with adult practices, 13 (8.4%) were rheumatologists with pediatric practices, 9 (5.8%) were researchers, and 14 (9.1%) were trainees. Two responders did not indicate their area of practice. 50 out of 150 participants (33.3%) had over 20 years of practice experience. According to the survey results, 50.6% of participants used ultrasonography in their clinical practice although a lack of training appeared to be the main obstacle to its current use. 83% of participants believed that MSK US should be performed by rheumatologists and expressed a willingness to learn the technique. MSK US was considered to be as important in establishing a diagnosis as in therapeutic decision-making. Skills offering greatest clinical utility were postulated to be assessment of inflammatory arthritis in small joints, shoulders, and ankles. Limited available time, equipment costs, and difficulties with billing were indicated as the main obstacles to MSK US utilization in the clinical setting. Participants indicated a course at the provincial level as the preferred means to learn MSK US. In regard to rheumatologists’ interests and perceived barriers, these data are in accordance with those reported by Leeds researchers1.

Conclusion:
There is a great level of interest in learning and applying MSK US in Canadian rheumatology practice. However, the trade-off between added clinical values versus lack of remuneration, equipment associated costs and time to complete training appears to be the major limiting factor influencing rheumatologists’ willingness to take on MSK US in clinical practice. Training programs need to be highly relevant to rheumatologists needs before MSK US will be adopted in to routine clinical practice by Canadian rheumatologists. Reference: 1.Brown AK, Roberts TE, Wakefield RJ, Karim Z, Hensor E, O’Connor PJ and Emery P. The challenges of integrating ultrasonography into routine rheumatology practice: addressing the needs of clinical rheumatologists. Rheumatology 2007;46:821–829
Assessment in Rheumatology Program Survey: A Snapshot of Rheumatology Care in Canada

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Objective:
The aim of this study is to investigate the practice patterns of rheumatologists and to evaluate the disease management of rheumatoid arthritis (RA) in Canada.

Methods:
All Canadian practicing rheumatologists were invited to participate in a cross-sectional survey via mass e-mails through the Canadian Rheumatology Association web portal. Participating rheumatologists filled out an 8-page survey detailing their practice patterns and a 7-page survey on the first 30 consecutive RA patients visiting their clinic over a 4-week period. The patient survey consisted of questions regarding the patient’s disease activity status, current and past treatment regimens and future plans for treatment. Correlations between rheumatologist assessment of disease activity and composite indices as well as care gaps were assessed.

Results:
Of 279 rheumatologists contacted, 33 rheumatologists whose practice focused on RA contributed a total of 631 patient visits (26.5±7.6 patients contributed by each physician). From the available data, 13.5% (n=84), 8.4% (n=52), and 17.4% (n=108) of patients had measured the required parameters to calculate the DAS28, SDAI, and CDAI composite indices of disease activity (DA), respectively. There was a correlation between physician-rated DA and composite indices; the strongest correlation occurred between physician-rated DA and the DAS28 (Kendall’s tau=0.696, p< 0.001). The physician-assessed DA was more weakly correlated with the CDAI (Kendall’s tau=0.628, p< 0.001) and SDAI (Kendall’s tau=0.559, p< 0.001). The proportion of patients currently treated with steroids was 25.5% (n=154), DMARDs was 89.5% (n=564), and biologics was 23.4% (n=147). A treatment change was being considered for 32.2% (n=200) of patients. Although 88.4% (n=38) of high DA patients were considered for therapy change, only 66.7% (n=82) and 21.5% (n=59) of moderate and low DA patients were considered for a change of regimen.

Conclusion:
In routine practice Canadian rheumatologists make treatment decisions based on individual clinical measures and are not likely aiming for a specific target of remission or even low disease activity. There was only a moderate correlation between rheumatologist assessment of disease activity and composite index-assessed disease activity. Such indices may be required in rheumatology practice to facilitate tight control of disease activity in patients with RA.
Soluble Biomarkers Predict Response to Anti-Tumour Necrosis Factor (TNF) Therapy in Psoriatic Arthritis (PsA)

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Objective:
To identify biomarkers associated with response to therapy with anti-TNF agents in patients with PsA.

Methods:
The study was conducted at a large observational PsA clinic where patients are assessed according to a standard protocol every 6 months and serum samples are collected and stored once a year at the time of clinical assessment. 40 patients with active PsA who had serum samples collected prior to treatment with anti-TNF agent and after at least 3 months of therapy were identified. Patients were classified as anti-TNF responders if actively inflamed joint count (AJC) was < 3, swollen joint count (SJC) was 0 and PASI score was < 4 at the time when the second sample was collected. Those not achieving this state were classified as partial responders. The following biomarkers were tested using commercially available ELISA kits: TNF Super Family member 14 (TNFSF), Matrix Metalloproteinase-3 (MMP-3), Receptor Activator for Nuclear Factor κB Ligand (RANKL), Osteoprotegrin (OPG), Cartilage oligomeric protein (COMP), C-propeptide of type II collagen (CPII), collagen fragment neoepitopes Col2-3/4(long mono) (C2C) and Col2-3/4(short) (C1-2C), Aggrecan 846 epitope (CS-846) and highly sensitive C-reactive protein (hsCRP). Paired t-test and logistic regression was used to detect changes in biomarker levels with treatment and association with anti-TNF responder status.

Results:
The 40 patients (28 males, age 44 years, psoriasis duration 17 years, PsA duration 12 years) had mean actively inflamed Joint Count of 12, swollen Joint Count of 6, and PASI score of 6.4 pre-treatment. After a mean treatment duration of 11 months (Etanercept 28, Adalimumab 6, Golimumab 4, Infliximab 2), 29 were classified as anti-TNF responders. There was a significant decline in the serum levels of hsCRP (p<0.001), MMP-3 (p<0.001) and the ratio CPII/C2C (p=0.039), whereas there was an increase in RANKL (p=0.002) and C2C (p=0.021). Only reduction in MMP-3 correlated with reduction in hsCRP (correlation coefficient 0.43, p=0.005). Multivariate logistic regression showed that baseline level of MMP-3 was associated with attaining responder status [Odds ratio (OR) 1.067 for each one unit increase, p=0.045]. A reduction in MMP-3 levels increased the odds of achieving response (OR 1.213 for each one unit increase, p=0.030), whereas a reduction in COMP decreased it (OR 0.587, for each 100 units increase, p=0.039).

Conclusion:
Baseline as well as reduction in serum MMP-3 levels is associated with response to anti-TNF therapy in PsA.
900+ and 10-minutes Infusions of Abatacept in a community rheumatology practice

Vincent Choi (self employed, Calgary)

Objective:
to report safety and efficacy of 900+ office based Abatacept infusions in routine clinical practice over a three years period and to assess for safety with increased infusion rate

Methods:
over a period of three years the author had personally administered over 900 Abatacept monthly infusions for 51 patients (38F13M) for RA (DMARDs failures, anti-TNF failures), Rupus and Seronegative Arthritis with features of CTD. Clinical and laboroatory parameters of these patients and their conditions were reviewed.

Results:
Monthly serial measurements showed trend of improvement of DAS (-2) and HAQ (-1) and reducdion of Prednisone use (-7.8mg/day). 11/51 patients (20%) reach DAS remission at the end of three years. 11 patients discontinued treatments (4 primary failures, 2 infection, 1 pulmonary fibrosis, 3 insurance loss, 1 weight loss) with 80 percent retention. 4 serious infections occurred (two urinary tract infection, one diverticulitis and one possible epidural infection). One developed cervical myelopathy felt to be unrelated to treatment. No cancer or death occurred. For the 40 patients on active treatments, 10 patients stayed on Prednisone at 5mg per day or less. One patient who has just recently started taking Orencia is on higher dose of Prednisone. With strict supervision by the author, infusion time was gradualll reduced. In the most recent 180 consecutive infusions, the infusions were on average given in less than 10 minutes without any signs of cardiovascular effect or infusion reaction.

Conclusion:
Abatacept infusion is an integral part of arthritis management in this author's community based rheumatology practice. It is associated with favorable safety and efficacy profiles. Retention of patients was high. Acceleration of infusion rate to 10 minutes or less per infusion is a safe alternative to the previously recommended 30 minutes infusion.
Real – Life Effectiveness of Infliximab in the Treatment of Rheumatoid Arthritis: The Canadian Experience

Denis Choquette (Hopital Notre-Dame, Montreal); William Bensen (McMaster University, Hamilton); Hayssam Khalil (Schering-Plough Canada inc., Montreal); John Sampalis (McGill University and University of Montreal, Westmount)

Objective:
In recent years, the efficacy of anti-TNF in the management of Rheumatoid Arthritis (RA) has been demonstrated in numerous controlled clinical trials. Information concerning the effectiveness of drug therapy cannot be obtained only from randomized controlled clinical trials, due to limitations such as a short time frame and narrow inclusion and exclusion criteria. Therefore, longitudinal observational studies assessing real – world 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 outcome in patients with RA treated with Infliximab.

Methods:
A total of 670 RA patients starting treatment with infliximab were enrolled by December 31, 2008 in the nationwide RemiTRAC registry (Remicade® Treatment Registry Across Canada). Of these 138 had completed 36 months of treatment and were included in the analyzes. This registry was initiated in 2002 and is an ongoing, multi-centre, prospective, observational study of patients treated with infliximab for RA, AS (Ankylosing Spondylitis) or PsA (Psoriatic Arthritis). Patients are naïve to Anti-TNFα treatment or were treated with biologics for a period < 6 months (since December 2006). Patients enter the cohort at the time of initiation of treatment and are followed prospectively. Baseline disease activity and treatment response over time were determined in patients who have completed 36 months of treatment. Descriptive statistics and when appropriate statistical tests were conducted, Fisher’s exact test for categorical variables or t-test/ANOVA for continuous variables.

Results:
Mean age of the 138 patients was 57 years and mean duration since diagnosis was 11.6 years. At initiation of treatment, 93% were treated with DMARDS including 73% with Methotrexate. Laboratory and clinical parameters of the cohort during the first 36 months of treatment were evaluated. The results show that by 6 months of treatment, significant and sustained improvements (P < 0.05) were observed on all parameters analyzed (CRP, ESR, morning stiffness, patient and physician global assessment, HAQ, SJC, TJC, ACR 20, 50 and 70) and this improvement was maintained over the 36 months of treatment. Nearly half the patients had achieved an ACR50 response by 6 months.

Conclusion:
The results of this observational study have shown that infliximab is effective in treating rheumatoid arthritis over a three year period in a Canadian longitudinal observational study.
Giant Cell Arteritis and MRI Evaluation of the cranial arteries

Marie Clements- baker (McMaster University, Hamilton); Samir Patel (McMaster University, Hamilton); Ryan Rebello (McMaster University, Hamilton); Nader Khalidi (Mc Master University, Hamilton)

Objective:
To evaluate whether high field Magnetic Resonance Imaging (MRI) can demonstrate mural edema and inflammation within the superficial temporal artery and other intra- and extracranial arteries and how it compares to temporal artery biopsy results in patients who meet American College of Rheumatology (ACR) criteria for giant cell arteritis (GCA).

Methods:
45 patients meeting ACR criteria for GCA were examined by 3T MRI using a head coil. The MRI protocol matured over the course of the study but, in general, high-resolution fluid-sensitive and Gadolinium enhanced images of the clinically-affected STA were obtained, in addition to larger field of view sequences to visualize the other scalp arteries. The images were graded according to protocols reported in recently published studies. All patients except 1 underwent temporal artery biopsy. Images and biopsy were obtained as soon as possible after initiating corticosteroid therapy.

Results:
Overall 15/45 patients had positive scalp artery MRI findings and 6/45 patients had positive biopsy findings. Of these positive biopsies, MRI was reported as positive in 5 with evidence of STA inflammation present in 4 and the fifth patient demonstrating only cavernous carotid artery inflammation. One false negative occurred but an inadvertent protocol deviation had occurred with suboptimal image resolution obtained for that patient. The average biopsy length was 2.79 cm. The average number of days from corticosteroid to MRI was 3.9 days and the average number of days to biopsy was 8.98 days. Other important MRI findings in patients who had negative artery inflammation included 1 case ipsilateral pachymeningitis, 1 cortical infarct, 1 bone lesion questionable for metastatic disease, 1 ipsilateral pansinusitis and 1 case of multiple meningiomas requiring neurosurgical referral.

Conclusion:
In patients meeting ACR criteria for GCA, MRI demonstrates evidence of STA inflammation in 30% of patients. This appears superior to our biopsy positive rate of 7.5%. These results support previous studies and suggest that MRI could replace or complement biopsy as an effective and non-invasive way to diagnose GCA. The MRI protocol and image resolution are crucial components in MRI evaluation of scalp artery inflammation. MRI is clearly useful in diagnosing other pathologies that may clinically mimic giant cell arteritis.
Recurrence of Neonatal Lupus Erythematosus in Siblings

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Objective:
Neonatal lupus erythematosus (NLE) is a model of passively acquired autoimmunity due to in utero exposure to maternal anti-SSA/Ro and/or anti-SSB/La antibodies. Manifestations of NLE include congenital heart block (CHB), rash, hepatic or haematologic abnormalities, and macrocephaly. Much of the research to date has focused on the cardiac manifestations of NLE with a risk of recurrence of CHB related to NLE in 15% of subsequent pregnancies. However, none have examined the risk of recurrence of any manifestation of NLE in subsequent siblings following an index case with NLE which is the focus of this study.

Methods:
A retrospective cohort study consisted of 42 consecutive children born to 36 anti-Ro and/or anti-La positive women followed at a tertiary paediatric hospital March 1984 to April 2009. Detailed patient and maternal medical information was extracted from a rheumatology database and validated by chart review. The women were identified following the delivery of a first-born child with confirmed NLE and all subsequent pregnancies were followed prospectively for the presence of any manifestations of NLE. Patients were excluded if the NLE diagnosis was made retrospectively or the index NLE case was seen at another institution.

Results:
Recurrence of NLE in a subsequent sibling after an index case of confirmed NLE occurred in 72.2% of families (26 recurrences out of 36 families) and 64.3% of subsequent siblings (27 out of 42 siblings). The rate of occurrence of CHB was 8.3% in families and 7.1% of all subsequent siblings after an index case of NLE, but 15.4% if the index case had CHB and 5.9% if the index case had neonatal lupus rash.

Conclusion:
NLE recurred in at least one subsequent sibling in over two-thirds of families and the majority of subsequent siblings following an index case of NLE - however, it mainly presented as transient non-cardiac features. Interestingly, when an index case had CHB, the risk of CHB in any subsequent sibling was higher (15.4%) compared to families where an index case presented with non-cardiac manifestations of NLE. Further studies are needed to identify predictors of NLE recurrence of congenital heart block to guide prospective monitoring of future siblings.
Objective:
Recently, a genome-wide association analysis revealed SNPs in the gene regions near HCP5 to be associated with viral load and SNPs in the RNF39 gene region to be associated with HIV-1 disease course. As concomitant HIV infection can dramatically impact the course of psoriatic arthritis, we examined these SNPs associated with HIV in our PsA population.

Methods:
Psoriatic arthritis was defined using the CASPAR criteria. In total 342 Caucasian PsA patients of North European ancestry and 362 health controls from the same ethnic and geographic backgrounds were assessed. We examined the association of 5 SNPs in chromosome 6p near either RNF39 or HCP5 genes using the Sequenom technology.

Results:
The only significant association was with rs2395029. This SNP is located in Exon 2 of HLA-complex P5 or HCP5. This gene is located within MHC-class I and showed significant association with PsA (p < 3.01 X 10^{-6}; OR = 3.126 (1.895-5.157)). Due to its location in the MHC region, it is crucial to find the allelic correlation of this association (dependence/independence) with other HLA genes. In our genotyping cohort rs9264942 is 32.54kb apart from HLA-C and this SNP shows weak LD(r^2 = 0.11) with rs2395029. We have used tagger algorithm with r^2 > 0.80 to capture tagSNPs from the region 31226380 to 31640198 in chromosome 6 which includes HLA-C, HLA-B, MICA, HCP5 and MICB genes. The captured tag SNP showed strong LD between rs2395029 of HCP5 with MICB gene but no strong LD observed with HLA-C, HLA-B, MICA. This provides strong evidence the independent association of HCP5 gene with PsA.

Conclusion:
We report that a SNP within HCP5 to be associated with PsA. This association within the MHC region appears to be independent of HLA-Cw6.
Time to Development of Nephritis in Patients with SLE

Debra Dye-torrington (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

Objective:
We investigate the first occurrence of nephritis in patients with SLE at inception and over the course of the disease, in an inception cohort of patients followed in a single centre and examined predictive factors for late occurrence of nephritis.

Methods:
Inception patients seen in clinic within one year of diagnosis of SLE, were selected from a single centre cohort and followed in an observational cohort study. Lupus nephritis was defined as sterile hematuria and/or pyuria, granular casts, proteinuria (>500mg/24hr), or elevated serum creatinine (defined as greater than 120µmols/l) on two or more consecutive visits. Or dialysis, transplant or WHO renal biopsy ≥ class 2. Incidence of lupus nephritis was determined for each year following entry into the clinic. In patients with no lupus nephritis at entry into the clinic, a Cox survival regression analysis was run, using the values at 1st clinic visit to predict development of future renal nephritis. Included in the model were sex, disease duration, SLEDAI-2K, SLICC/ACR damage index (SDI), steroids, antimalarial, immunosuppressant, race, complement and dsDNA. Selection of variables retained in the model was done through the stepwise approach. Kaplan-Meier curves were done for significant predictors.

Results:
In a cohort of 633 patients with SLE, 382 (57%) did not have lupus nephritis at inception. These were 87% female, mean age at SLE diagnosis 36yrs. 77% Caucasian, 8% Black, 5% Chinese, 10% other. Their disease duration at first clinic visit was 0.24 yrs; SLEDAI-2K was 8.63 and SDI 0.07. 46% were taking glucocorticoids, 35% antimalarials and 8% immunosuppressants. The mean serum creatinine was 73, 46% had low complement and 48% elevated anti-DNA antibodies. Of the 382 patients, 107 (28%) eventually developed lupus nephritis 77% of them within the first 5 years. Cox regression analysis revealed that only anti-DNA antibody was a statistically significant predictor with HR = 1.59 (95% CI 1.01, 2.48, p=0.04). Kaplan-Meier curve comparing the development of nephritis between patients with normal v/s elevated anti-DNA antibody at 1st clinic visit showed a statistically significant difference (Wilcoxon p=0.04)

Conclusion:
28% of patients with SLE without nephritis at inception develop lupus nephritis later in their course. The majority occur within the first 5 years, but some patients develop nephritis later. The only predictor for future development of lupus nephritis is the presence of anti-DNA antibody at inception.
Response to TNF-α Blockers in Psoriatic Arthritis – An Observational Cohort Study

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Objective:
To determine predictors and probability of response of actively inflamed joints and psoriatic skin lesions to treatment with TNF-α blockers in patients with psoriatic arthritis (PsA).

Methods:
We performed a cohort analysis of patients who were followed prospectively in a large, single centre PsA clinic. All patients who were treated with TNF-α blockers for at least 12 months for active peripheral arthritis were included in the study. We excluded patients who initiated the medication prior to attending the clinic. The collected data included demographic, clinical and laboratory variables at baseline and at 3, 6 and 12 months of treatment. Response to treatment was defined as an improvement of at least 40% in active (tender and/or swollen) and swollen joint count and 50% improvement in the psoriasis area and severity index (PASI) score.

Results:
169 PsA patients with a record of TNF-α blockers treatment were identified. 95 patients (40 males) were included in the final analysis. Their mean age was 45.7 years, mean duration of PsA and psoriasis was 11.8 and 18.9 years, respectively. At baseline, the mean number of actively inflamed joints was 15.4 (6.8 swollen). 8.8 joints were clinically damaged. The mean PASI score was 6.5. 72.6% and 77.9% of the patients demonstrated 40% improvement in active joint counts at 3 and 12 months, respectively. 80.5% and 87.4% of the patients showed 40% improvement in swollen joint count at 3 and 12 months, respectively. PASI 50 was achieved by 54%, 60.4% after 3 and 12 month of treatment, respectively. 11 out of 17 patients (64.7%) who did not achieve 40% improvement in total swollen joint count at 3 month, responded at 12 month. 13 patients received a second TNF-α blocker, 53.8% and 83.3% of them showed improvement in active joint count at 3 and 12 month, respectively. On multivariate analysis the number of swollen joints at baseline predicted response of total active joints at 12 month (OR 1.34, p=0.016), while past use of TNF-α blocker decreased odds of response (OR 0.048, p=0.003). No major life-threatening side effects were documented in the patients.

Conclusion:
TNF-α blockers are effective in most PsA patients and response is seen in most patients within 3 months of treatment. A Significant proportion of the early non-responders will have a delayed response to treatment. Higher swollen joint count at baseline and no prior use of TNF-α blockers predict response.
Environmental Risk Factors for Psoriatic Arthritis Among Patients with Psoriasis - A Case Control Study

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Case Report:
Aim: To investigate the association between potential environmental exposures and the onset of psoriatic arthritis in patients with psoriasis. Methods: In this case-control study, the cases were patients with recent onset psoriatic arthritis (PsA) of less than 7 years since the diagnosis. The control group was composed of psoriasis patients in whom arthritis was excluded after an evaluation by a rheumatologist. Patients and controls were matched by disease duration of psoriasis. The occurrence of the following environmental exposures was evaluated by a self administered questionnaire: infections, injuries and fractures, physically demanding occupational tasks, stressful life-events and vaccinations. The patients were asked to report any such event that occurred in the past 10 years and a positive exposure was defined as the occurrence of an event prior to the year of diagnosis. Participants in the control group were assigned a reference year that corresponding to the year of PsA diagnosis in the matched case. The association between exposure to environmental events and disease status were assessed through logistic regression. Results: There were 119 subjects in each group. There were no differences in age, sex, ethnicity and severity of psoriasis as measured by PASI score between the 2 groups. The mean duration of PsA was 3 ± 2.2 years. The following environmental exposures were significantly associated with PsA: lifting cumulative loads of at least 100 pounds/hr (OR 3.2 p=0.0006), severe infections that required hospitalization (OR 5.7 p=0.03), injury that required medical care (OR 2.7 p=0.007). Pushing cumulative loads of at least 200 pounds/hr showed a trend towards an association with PsA (OR 1.9 p=0.06). No association was found between PsA and smoking, alcohol consumption, vaccination, stressful life events and fractures. Conclusion: Injuries, lifting heavy loads and severe infection were associated with the occurrence of arthritis among patients with psoriasis. Further studies are necessary to determine whether these and other environmental factors are moderated by predisposing genetic factors.
Effectiveness and Safety of Etanercept in Patients with Psoriatic Arthritis in a Canadian Clinical Practice Setting

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Objective:
To describe the long-term effectiveness of etanercept in improving functionality and quality of life in patients with psoriatic arthritis (PsA).

Methods:
In this 24-month, open-label, observational trial conducted at 22 Canadian sites, adults with PsA received etanercept 50 mg/week. Exclusion criteria included active infection, recent malignancy (previous 5 years), and previous treatment with biologics. The primary endpoint was a $\geq 0.50$ unit improvement from baseline on the Health Assessment Questionnaire Disability Index (HAQ-DI) at month 24. Secondary endpoints included adverse events, a change from baseline in Health and Labour Questionnaire score, physician and patient global assessments of disease activity and Fatigue Severity Scale (FSS) score, the proportion of patients achieving an improvement in Psoriasis Area and Severity Index of $\geq 75\%$ (PASI-75) and a Psoriatic Arthritis Response Criteria (PsARC) response. Efficacy analyses were based on a modified intent to treat population (patients with at least one dose of study drug and one post-Baseline HAQ-DI measurement) using last observation carried forward imputation. The safety analysis included all patients receiving at least one dose of study medication.

Results:
A total of 110 adults (mean±SD age: 48.4±10.9 years) with active PsA (duration: 8.9±8.4 years) and current or past evidence of psoriasis (duration: 16.2±12.7 years) were enrolled in this study. At baseline, mean HAQ-DI score was 1.50±0.56. Seventy-one (64.5\%) patients completed two years of treatment. The most common reasons for discontinuation were adverse events (13.6\%) or lack of efficacy (10.9\%). At 24-months, mean HAQ-DI score declined to 0.90±0.68 and in 56\% of patients HAQ-DI score improved by $\geq 0.50$ points. Eighty-six (78.9\%) patients were PsARC responders, and the PASI score improved (baseline: 4.8±7.8; month 24: 1.8±2.9), with 41.8\% of patients achieving a PASI-75. Patients also reported fewer days absent from work due to PsA (mean baseline: 0.8±2.5 days within past 2 weeks; month 24: 0.2±1.5 days) and reduced FSS scores (baseline: 6.4±2.2; month 24: 4.8±2.8). The most common adverse events were nasopharyngitis, upper respiratory tract infection and injection site reaction. There were 20 serious adverse events in 14 patients and two non-drug related deaths which occurred after study discontinuation.

Conclusion:
Results from this study suggest that etanercept (50mg/week) offers PsA patients long-term clinically important improvements in disability, joints and skin in a real world setting.
Identification of Biomarkers for Enhanced Benefit to Rituximab in Rheumatoid Arthritis: Role of Autoantibodies and Inflammatory Markers

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Objective:
To examine serologic markers in randomized clinical trials (RCT) and identify biomarkers that best distinguish rheumatoid arthritis (RA) patient (pt) subsets with high hurdle clinical responses (ACR 50 at 24 weeks) to rituximab (RTX) therapy.

Methods:
With baseline samples from the REFLEX trial of 517 RA pts with previous inadequate response to TNF inhibitors, a threshold sensitivity method was used to identify candidate biomarkers that enriched for placebo-corrected ACR50 response at 24 weeks, and which represented at least 20% of subjects. We examined 19 serological markers and 9 clinical features, and identified the best four biomarkers: levels of IgA isotype of rheumatoid factor (RF), sCD25, and IgG anti-CCP3 antibodies, as determined by ELISA, and of C-reactive protein (CRP), as determined by nephelometry. These biomarkers and five of their two-biomarker combinations as well as levels of IgM and IgG isotypes of RF were then further investigated following a pre-specified diagnostic plan using data from the SERENE RCT of 501 RA pts with an inadequate response to methotrexate. We then calculated odds ratios for achieving an ACR50 response at 24 weeks compared to placebo, as well as additional summary statistics for biomarker positive/negative subgroups.

Results:
In discovery studies we found that, compared to seronegative patients, seropositivity for any isotypes of RF or IgG anti-CCP antibodies was associated with a higher rate of placebo controlled ACR50 responses at 24 weeks. Pts with elevated levels of CRP also demonstrated more frequent clinical benefit. These findings were independently reiterated in the SERENE pt populations. The greatest enhancement was seen in pts with both elevated baseline CRP (>2.9 mg/dL) and positivity for RF of any isotypes or IgG anti-CCP. These pts had better clinical responses across a spectrum of clinical outcome measures (ACR responses, delta DAS, and EULAR response).

Conclusion:
In the REFLEX and SERENE RCT, the presence of autoantibodies and elevated CRP identified a subgroup of RA pts with an enhanced benefit to RTX. However, these findings need to be verified in large independent data sets.
Certolizumab Pegol Added to Methotrexate (MTX) Provides Rapid and Sustained Improvements in Disease Activity in RA Subjects Over Three Years

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Objective:
To determine long-term outcomes in Canadian subjects from a single center treated with certolizumab pegol (CZP) plus MTX for 3 years.

Methods:
Patients who completed 1 year of double-blind treatment with CZP 200 mg or 400 mg plus MTX every 2 weeks (Q2W) in the RAPID 1 study were allowed to enter open-label treatment with CZP 400 mg plus MTX Q2W. Patients were subsequently switched to CZP 200 mg Q2W and followed for a total of 3 years.

Results:
Four patients who received CZP plus MTX were followed for a total of 3 years for a total patient exposure of 12 patient-years. Baseline demographics were mean age 54.8 years (SD 10.2), disease duration 5.5 years (SD 4.6), female 75%, mean MTX dose 18.8 mg/week, with an average of 1 prior DMARD. All 4 patients had severe disease at baseline with DAS28 scores of 6.2, 6.1, 6.4, and 6.9. Disease activity was rapidly reduced by Week 12; DAS28 scores in the 4 patients at Week 12 were 4.8, 3.6, 2.3, and 4.5. These improvements were sustained over 3 years. DAS28 scores at Year 3 were 3.7, 2.0, 2.3, and 1.8, respectively, indicating that 3 of the 4 patients were in DAS remission (DAS28 scores ≤2.6). No serious adverse events and no adverse events leading to withdrawal were observed over the 3-year treatment period.

Conclusion:
In our small group of subjects with severe RA from a single center in Canada, CZP plus MTX Q2W rapidly reduced disease activity. These improvements were sustained over 3 years. Treatment with CZP plus MTX was well tolerated with no serious adverse events.
Perceived Stress in Female Patients with Systemic Lupus Erythematosus (SLE)

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Objective:
To determine in women with Systemic Lupus Erythematosus (SLE) whether there is an association between patients’ perceived stress level and: a) disease activity; b) quality of life; and c) self-reported comorbid conditions.

Methods:
Patients meeting four or more American College of Rheumatology classification criteria for SLE were enrolled in the Lupus Nephritis New Emerging Team (LuNNET) study in Canada. Disease activity was assessed using the SLE-Disease Activity Index (SLEDAI), with SLEDAI ≥7 considered active disease. The 10-point Perceived Stress Scale (PSS) was used to assess stress levels, where PSS >20 (population mean + 1 standard deviation) was considered high. Quality of life was assessed using the mental (MCS) and physical (PCS) component scores of the Medical Outcomes Short Form (SF-36). Comorbid conditions were reported on the Self-Administered Comorbidity Questionnaire and a standardized medical history form.

Results:
156 females with SLE, aged [mean (SD)] 39.4 (14.7) years with SLE duration of 11.2 (9.6) years were included in the analysis. The majority of patients were Caucasian (44.9%), followed by Asian (24.4%) and African American (19.2%), and 44.9% had active disease at enrolment. Mean PSS for the group was 17.3 (6.8), which was higher than the female population norm of 13.7 (6.6); 29.4% of patients had PSS >20. Total PSS was higher for those with active disease compared to those with inactive disease [18.7(6.7) vs 16.2(6.6), p=0.023]. There was also a significant inverse correlation between PSS and: disease duration (r = -0.17, p=0.03), MCS (r = –0.50, p< 0.0001) and PCS (r = –0.67, p< 0.0001). There was no association between PSS and: age, renal status, education level, marital status or having supplementary insurance coverage. Among many comorbidities reported, those with depression [19.7 (8.0) vs 16.7 (6.3), p=0.045] and diabetes mellitus [21.3 (4.5) vs 17.0 (6.8), p=0.031] had significantly higher PSS than those without these conditions. There was also a trend towards higher PSS in those with heart disease [19.9 (6.8) vs 17.0 (6.7), p=0.16] and arthritis [18.3 (6.8) vs 16.6 (6.7), p=0.13] compared to those without.

Conclusion:
Female patients with active SLE have higher perceived stress regardless of age, education, private insurance coverage, marital status or renal status. Presence of comorbid illnesses contributes to the higher PSS in these patients. Management of active SLE and other comorbid conditions may decrease stress level in this patient population.
Categorizing Intensity of DMARD Treatments in Longitudinal Cohorts

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Objective:
To develop a scale to report into discrete categories the intensity of treatment based on the type, duration, dose and combinations of DMARDs used during the first years of follow up of early inflammatory polyarthritis (EPA) patients. This scale would allow comparison of intensity of treatment between cohorts.

Methods:
We set up a longitudinal cohort of consecutive patients with recent-onset polyarthritis (EPA). The types and dosage of DMARDs and corticosteroids (reported as prednisone-equivalent (PRED)) administered were collected at each visit. Dosage was reported as the mean dose of each DMARD/prednisone received between the onset of symptoms and the inclusion visit, and between two scheduled visits. Three levels of treatments were defined: UNTREATED, LOW and HIGH. The UNTREATED category included patients who received no DMARDs, only received steroids at \( \leq 7.5 \) mg of PRED/d, or less than a MINIMAL dose of DMARDs for a preset duration. At inclusion, patients having received total doses corresponding to less than 6 weeks of MINIMAL dose of a single DMARD were considered untreated. At the 18 and 30 months visits, respectively, patients with doses corresponding to less than 4 months and less than 6 months of the MINIMAL dose of a single DMARD were considered untreated. Examples of MINIMAL doses are: 15 mg/w for methotrexate (MTX), 200 mg/d for hydroxychloroquine, 1000 mg/d for sulfasalazine, and 10 mg/d for leflunomide. The low intensity (LOW) category included patients who, over the period, received DMARDs at doses insufficient for being classified as HIGH intensity, but more than the definition for UNTREATED, or who were treated only with PRED at a dose \( \geq 7.5 \) mg/d. The high intensity (HIGH) category included patients who received MTX monotherapy at \( \geq 15 \) mg/w or who received any DMARD combination (at any dose superior to the MINIMAL) or who received biological agents.

Results:
We report on the first 253 patients to complete 30 months of follow-up. At baseline, 225 (88.93%) patients were untreated, while 18 (7.11%) were in the LOW and 10 (3.95%) in the HIGH intensity categories. At the 30 months evaluation, 24 (9.49%) were considered untreated, while 70 (27.67%) and 159 (62.85%) fulfilled criteria for the LOW and the HIGH intensity groups, respectively.

Conclusion:
Using ad hoc criteria, DMARD treatments were categorized into 3 levels of intensity. These scores may be used to compare treatment intensity across cohorts and can also be incorporated into predictive models of outcomes in patients with EPA.
Discordance of ESR Performed On-Site at a Clinic Versus Hospital Laboratory

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Objective:
The erythrocyte sedimentation rate (ESR) is a valuable simple, inexpensive laboratory test that is frequently performed to assess disease activity and response to therapy in inflammatory arthritis. The test measures the distance that erythrocytes have fallen after one hour in a vertical column of anticoagulated blood under the influence of gravity. There are many external factors that can impact the value of the ESR and thus affect the clinical decision making. We assessed the concordance of the ESR performed on site (testing within one hour) as compared to a hospital laboratory (variable times for testing).

Methods:
The ESR was performed using a standard Westergren kit at both sites. The blood was collected in similar EDTA blood tubes (4.0 ml) and all tests were done during routine office hours. The ESR readings performed on-site (rheumatology clinic) were set up within one hour of the venipuncture. For the hospital laboratory, the blood samples were sent to the laboratory immediately after the venipuncture but the ESR test was set up at variable times. An ESR greater than 20mm was considered abnormal.

Results:
We assessed 94 patients (50 females) with inflammatory arthritis that had their ESR performed on-site and performed in the laboratory. In total 71/94 (75%) of the samples were concordant (both ESR readings were normal in 54 patients and elevated in 17 patients). In the 23 patients that were discordant, the on-site ESR was abnormal in all cases compared to the laboratory ESR. For the patients that were discordant, the mean on-site ESR of 33.2mm (sd 9.3) as compared to 11.6mm (5.4); p < 3X10-14). For 17 patients that were concordant for abnormal ESR, the mean on-site ESR was 54.4mm (29.6) as compared to 38.3mm (27.9) for the lab ESR (paired t test - p= 0.00014). Thus the elevated ESR done onsite at clinic was on average 40% higher than the laboratory ESR.

Conclusion:
The reported ESR at the rheumatology clinic is often higher than the ESR determined at the hospital laboratory. Thus careful attention to technical factors is important in determining the true value of the ESR.
Trends In Physician Resources And Trainees In Canadian Academic Rheumatology Centers Over 11 Years

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Objective:
To prospectively evaluate the number and demographic features of physicians, time spent on clinical and academic activities and productivity of training programs in Canadian academic rheumatology centers.

Methods:
The Canadian Council of Academic Rheumatologists (CCAR) performed standardized annual data collection from 1998-2009 on the status of their academic units. The variables included physician and trainee demographics, recruitment, allocation of time to clinical care, teaching and research, and the major career choices of rheumatology trainees. Information was collected at the start of each academic year, centralized, validated and entered into a designated database.

Results:
Over 11 years the number of rheumatologists in academic centers increased from 170 (97 fulltime; 73 part-time) to 221(142 fulltime; 79 part-time). The mean age increased from 47.9 (31–76) to 49.8 (30-83) years and the male:female ratio fell from 2.70 to 1.30. The proportion of time allocated to Clinical care (55%), Teaching (17%), Research (20%) and Administration (7%) was stable over time. The number of unfilled adult and pediatric rheumatology faculty positions increased from 27 (12/16 centers) to 34 (13/16 centers), a trend particularly strong in the last 4 years. The most frequently cited barrier to recruitment was the lack of suitable applicants. Rheumatology trainees (adult and pediatric) fell from 38 to 25 in 2001 but rose to 54 by 2009. The male:female ratio in each year was always lower than in the faculty and fell from 1.11 to 0.35. The proportion of training positions funded by Provincial governments reached a nadir (29%) in 2002 but subsequently became the dominant financial supporter (76%) followed by external funding (22%) and The Arthritis Society (2%). Upon completion of clinical rheumatology training the next career step varied between the pursuit of additional expertise in clinical skills (32-22%), clinical research (63-52%) and basic science (21-0%). Those trainees who remained in Canada selected careers in clinical practice (50-33%) and academic centers (50-67%).

Conclusion:
Over the past decade there have been substantial changes in the demographic features of both rheumatology faculty and trainees, both of which have increased in number. Provincial governments now provide the majority of funding for training positions. The high number of unfilled faculty positions indicates an unmet need either due to insufficient or unsuitable applicants or lack of appeal of these positions for current trainees. These trends indicate challenges to the maintenance of vibrant rheumatology programs in each of the academic centers.
Disease Remission is Achieved Within Two Years In Over Half of Methotrexate Naïve Patients with Early Erosive Rheumatoid Arthritis (RA) Treated with Abatacept Plus MTX: Results from The AGREE Trial

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Objective: To assess the clinical and safety outcomes in methotrexate (MTX)-naïve patients with early erosive RA treated with a combination of abatacept (ABA) + MTX through 24 months

Methods: The AGREE trial was a 24-month study with a 12-month, double-blind period (DB) and a 12-month, open-label period (OL). During the DB, patients were randomized to ABA (~10 mg/kg dose based on weight range) + MTX (dosed up to 20 mg) or placebo + MTX. All patients completing the DB and entering the OL received ABA + MTX. Safety was assessed in all patients receiving ≥ 1 dose of ABA in the OL. Clinical outcomes evaluated included DAS28 remission (DAS28 < 2.6), low disease activity state (LDAS, DAS28 ≤ 3.2), and ACR responses.

Results: All 459 patients completing the DB entered the OL; 94.3% completed the OL. Remission, LDAS, and ACR responses were sustained or increased from 12 to 24 months in original ABA + MTX arm, with more than half (55.2%) in remission and over 70% in LDAS at 24 months. The proportion achieving these outcomes in the original MTX alone arm increased after initiating ABA in the OL, with 44.5% in remission and 60% in LDAS at 24 months. Rates (per 100 patient years) of serious adverse events were similar in the OL and the DB (6.42 vs. 8.35), as were serious infections (1.73 vs. 2.04, respectively). Autoimmune events occurred at a similar rate in the OL as in the DB (1.30 vs. 2.47, respectively). Two deaths occurred. No malignancies or tuberculosis were reported.

Conclusion: Sustained disease remission is an achievable goal for many patients with early RA when treatment with a combination of ABA + MTX is initiated early. Consistent with the long-term safety experience in patients with longer standing disease, no new or unexpected safety signals occurred in this population. These data support the use of ABA + MTX in an early RA population
ERAP1 and ERAP2 Variants Affect the MHC-I Free Heavy Chain Expression on Peripheral Blood Mononuclear Cells of Patients with Ankylosing Spondylitis

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Objective:
Polymorphisms in the Endoplasmic Reticulum Aminopeptidase 1 (ERAP1) and ERAP2 gene were recently reported to be associated with ankylosing spondylitis (AS). ERAP1 and ERAP2 trim peptides for MHC class I presentation. We studied the variation in surface MHC expression, as a surrogate of peptide presentation, on PBMC of AS patients with different polymorphisms in ERAP1 and ERAP2.

Methods:
Caucasian HLA B27 positive AS patients (modified New York criteria) not taking biological therapy were included. Clinical and laboratory data were recorded. DNA was isolated from peripheral blood and genotyped for the SNPS rs30187, rs27044 (ERAP1) and rs2549782 (ERAP2). PBMC were isolated by Ficoll layering and stained with ME1 (HLA B27), HC10 (free class I heavy chains), anti-CD14 APC (monocytes) and anti-C19 PE (B cells) antibodies. PBMCs (N=10,000) were acquired by FACSCalibur and the mean fluorescence intensities (MFI) of ME1 and HC10 on whole PBMC, monocytes and B cells were analyzed using FlowJo. The MFI were compared between the genotypes.

Results:
Fifty-four patients (13 females) with a median (IQR) age of 41 (31, 50) years and disease duration of 15.3 (9.5, 24) years, were included in the study. The median (IQR) values for BASDAI, BASFI and BASMI were 3.5 (2.8, 6), 2.3 (1.3, 4.5) and 1.5 (1, 4) respectively. There was no difference in the age, disease duration, BASDAI, BASFI, BASMI, ESR or CRP between the genotypic groups. The MFI for HC10 staining on monocytes was significantly different across the genotypic groups of rs27044 (H=6.28, df=2; p=0.04). Patients with Q730 variant of ERAP1 had significantly higher FHC expression on the surface of monocytes (p=0.003). Patients with the 392N variant of ERAP2 had significantly higher FHC on PBMC especially B cells (p=0.01). There was no significant difference in the ME1 staining in any population or the HC10 staining in the whole PBMC or B cells in both models.

Conclusion:
This is the first study to demonstrate a link between HLA B27 surface FHC expression and ERAP1 polymorphisms in AS patients. This is the first time a functional relevance for the K392N variants of ERAP2 has been demonstrated. The Q730 variant of ERAP1 resulted in significantly more FHC expression on the surface of monocytes. The 392N variant of ERAP2 resulted in significantly more FHC expression on the surface of B cells. How this novel finding affects the pathogenesis of AS is an area for further study.
Methods to Improve the Triage Accuracy of Referrals for Possible Inflammatory Polyarthritis

Glen Hazlewood (University of Calgary, Calgary); Theresa Lupton (University of Calgary, Calgary); Liam Martin (University of Calgary, Calgary); Susan Barr (University of Calgary, Calgary)

Objective:
To determine the triage accuracy of referrals for possible inflammatory polyarthritis and investigate methods to improve this.

Methods:
We analyzed all referrals from Jan 2007- Dec 2008 for possible inflammatory polyarthritis made to our centralized referral center. We compared the working diagnosis, formulated by a central triage nurse, to the final diagnosis after consultation with a rheumatologist. A convenience sample of 200 sequential referrals was reviewed for completeness of several key data elements: joint distribution, symptom duration, morning stiffness (AMS), joint swelling, past medical history and medications, CBC, RF and either an ESR or CRP. The impact of a rheumatology specific referral form on completeness of information was assessed. The utility of joint swelling, AMS>30min, ESR>20, CRP>8 and RF>20 for identifying inflammatory polyarthritis was determined by calculating likelihood ratios for positive (LR+) and negative (LR-) results. Low cut-points were chosen to maximize sensitivity and minimize misclassification of patients as non-inflammatory.

Results:
A working diagnosis was available for 8284/9182 (90%) of referrals. Polyarthritis was questioned in 3715 (45%), and a final diagnosis was available for 1841/3715 (50%). Of those with a working diagnosis of fibromyalgia (FM), 172/182 (95%) had a final diagnosis of a non-inflammatory disorder. Referrals triaged as osteoarthritis (OA) were non-inflammatory in 328/377 (87%). Referrals triaged as indeterminate were diagnosed with inflammatory arthritis (IA)/possible-IA in 157/433 (36%). Patients triaged as IA were confirmed to have IA in 525/849 (62%). Reported joint swelling, AMS >30 min. and RF were not able to distinguish inflammatory vs. non-inflammatory disorders. An ESR>20 (LR+1.5[95% CI: 1.1-2.1], LR- 0.7[0.5-0.9]), or CRP>8 (LR+1.7[1.0-2.8], LR- 0.8(0.7-0.96]) had minimal utility in isolation. However, a normal ESR, CRP and RF in combination had a moderate LR- of 0.4 [0.3-0.8]. For OA, this would lower the probability of IA/possible-IA from 13% to 6%. The referral form improved the completeness of referral information from 49% to 69% (p< 0.001). Of the 200 referrals reviewed, 62 (31%) were inadequate and additional data was requested to enable triage. Of these, 19 (31%) had abnormal labs or x-rays, and 8 (13%) were ultimately diagnosed with IA.

Conclusion:
Inflammatory arthritis can be reliably excluded for referrals with a working diagnosis of FM. A normal ESR, CRP and RF in combination are helpful in lowering the probability of IA, while joint swelling and AMS are not. A referral form improves reporting of key triage information, but the collection of missing information is still required.
The Impact of a Centralized Referral System in Rheumatology

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Objective:
To evaluate the success of a centralized rheumatology referral system in our city on access to rheumatologic care.

Methods:
A centralized referral system for rheumatology was implemented in 2006 and all rheumatologists in academic and community practice in our city were invited to participate. All referrals are sent to a common referral center, triaged by a specialist nurse, and distributed amongst the participating rheumatologists. Physicians may, however, still refer to a specific rheumatologist if they desire. Data on the triage category, wait times and feedback from the rheumatologists on referral quality are collected prospectively in a database. We used the database to evaluate the success of the project and where appropriate we compared our results to a pre-implementation practice audit.

Results:
Overall, 13/14 rheumatologists (93%) participated in the centralized referral process. During the 2-year study period (Jan 1, 2007-Dec 31, 2008) 9182 referrals were received (383 per month). 80% were booked with the next available rheumatologist, 9% were booked directly with a rheumatologist, 2% were redirected and the remaining 9% were not booked or were waitlisted. Consults were triaged as routine (74%), moderate (19%), or urgent (7%). Feedback was received from the rheumatologist for 3779 referrals (41%). Rheumatologists rated referral quality as moderate or high in 91% of referrals, and the completeness of information as moderate or high in 87% of referrals. The triage category was felt to be appropriate for 90% of referrals. Of the consults triaged inappropriately, 99 (2.6% of all referrals) were “under-triaged” as routine or moderate when they should have been urgent. The most common reasons for misclassification of these urgent referrals were “inadequate referral information” in 34% and “change in health status in 16%.

Conclusion:
A centralized referral system to rheumatology eliminates duplicate consults and improves wait times and wait time variability between rheumatologists. The urgency of referral can be categorized correctly in a high percentage of cases.
Differences in Inflammatory Arthritis Activity Across Mexican Mestizos, Canadian Native American Indians and Canadian Caucasians: HLA Associations

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Objective:
Canadian Native American Indians (NAI) and Mexican Mestizos (MM) have higher disease severity, are more likely to have have anti-citrullinated peptide antibodies (ACPAs) and are less likely to achieve remission at one year than Canadian Caucasians (CC). This may be due to genetic or environmental factors.

Methods:
Patients with early inflammatory arthritis (EIA) followed in outpatient clinics in Canada and Mexico were treated at the discretion of their rheumatologist. Remission (DAS28-3ESR< 2.6) was determined at one year. ACPAs were measured by ELISA; Rheumatoid factor (RF) by nephelometry. HLA-DRB1 typing was determined by DNA sequencing (SE alleles: 0101, 0102, 0401, 0404, 0405, 0408, 0410, 1001, 1402; “protective epitope” alleles (PA): 0103, 0402, 1103, 1301, 1302).

Results:
At their baseline visit, MM (n=52; RA 92%) and NAI (n=51; RA 53%) with EIA were younger than CC (n=202; RA 42%) (39(12) and 40(14) vs 48(14) years p< 0.001), had higher DAS28-3ESR scores (5.6(1.1) and 4.3(1.4) vs 3.8(1.5) p< 0.001), and were more likely to be ACPA +ve (89%, 69%, 42% p< 0.001) or RF+ve (71%, 70%, 54% (p< 0.01). At one year, MM (1/19), NAI (6/33) and CC (79/134) achieved remission (p< 0.001). HLA sequencing was available for 176 patients (MM n=72, 22 EIA, 49 Late rheumatoid arthritis (symptoms >12 months at baseline); NAI n=34 all EIA; CC n=127 all EIA). More NAI had at least one SE copy (FN 27/34(79%) vs MM (37/72(51%) (11/33 MM with EIA) and CC 79/127(62%) p< 0.05). The proportion of NAI, CC and MM with two SE copies was 7/34(15%), 4/72(22%), and 19/127(6%) p< 0.06). NAI were less likely than MM or CC to have at least one PA (1/34(3%) vs 9/72(13%) (2/22 MM with EIA) vs and 24/125(19%) p< 0.01). Early UA were more likely than early RA to have at least one PA (26% vs 8% p< 0.001). In addition EIA subjects with at least one PA (14 REM/18 +ve PA (78%) were more likely to achieve remission than those without PA (29 REM/79 -ve PA (36%) p< 0.01). EULAR treatment response was not associated with SE or PA. Consistent with previous studies, SE was associated with ACPA (OR 4 (2-8) p< 0.001).

Conclusion:
The increased severity of EIA seen in Mexican Mestizos and Canadian Native American Indians compared to Caucasians is only partially explained by increased shared epitope, reduced protective alleles and ACPA. Further study on environmental factors is required.
How Do General Internal Medicine Residents learn Musculoskeletal Skills? Results of the Canadian Internal Medicine Musculoskeletal Education Survey

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Objective:
To determine self-confidence of internal medicine (IM) residents regarding musculoskeletal (MSK) clinical skills, and factors that may affect their confidence.

Methods:
Permission was sought to email a web-based survey to IM residents at all 16 Canadian internal medicine programs. Residents were asked to rank self-confidence in MSK, cardiology, respirology and gastroenterology skills. Further questions included site and year of training, career interests, MSK experiences, learning opportunities, and assessment frequency. These factors were analyzed by univariate and multivariate analyses.

Results:
216 residents (21.8%) from 13/16 sites responded to the survey. Resident self-confidence in MSK diagnosis was 5.24/10, lower than all 3 comparator subspecialties. Increasing teaching exposure had a more significant impact on confidence in rheumatology than on comparator subspecialties. Increasing year of training had no association with higher self-confidence for rheumatology, in contrast to the increase in confidence seen with increased year of training for each comparator subspecialty. Further analysis demonstrated the completion of a rheumatology rotation, increasing learning opportunities, annual assessment and career interest were associated with greater resident self-confidence.

Conclusion:
Resident self-confidence in MSK skills is cautious at best, and is lower than other common subspecialties. Self confidence improves with targeted MSK clinical experience and teaching but does not improve solely with higher year of IM training. Further, the impact of MSK teaching is greater than that of other common IM subspecialties. This information is critical to the planning and implementation of effective MSK curricula within internal medicine residency programs.
Quality of Life of Patients with Systemic Lupus Erythematosus (SLE) and Their Family Members

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Objective:
SLE patients (SLE-P) have a number of co-morbidities affecting their quality of life (QOL) that may also affect the QOL of their family-members. This study assessed the QOL of patients and their family-members and effects of multiple factors on QOL scores.

Methods:
250 SLE-P meeting at least 4 of the ACR classification criteria, and their first degree relatives (parents and siblings) were enrolled from 12 centers across Canada. 272 healthy controls (HC) were also enrolled. QOL was assessed using the Medical Outcome Study Short Form 36 (SF-36) and the Physical (PCS) and Mental Component Scores (MCS) were calculated. Age-gender standardized MCS and PCS were compared between SLE-P, their family-members and HC.

Results:
SLE-P were younger than HC [34.4(9.2) vs. 39.9(12.4)], but were similar to HC with respect to gender distribution (89% female), education level, ethnicity (>80% white) and having a health insurance plan (>70%), but only 50% of SLE-P were married compared to 61% of HC (P=0.008). Compared to HC [50.9(8.3)], PCS was significantly lower in: SLE-P [40.5(11.6); P< 0.0001], mothers [47.0(12.3); P< 0.0001] and sisters [48.6(10.3), P=0.0052]. PCS was below the expected age-gender standardized values in 77% of SLE-P, 51% of mothers, 35% of fathers, 33% of sisters and 32% of brothers compared to 32% in HC. In SLE-P and their family-members, marital status had no effect on PCS, however, SLE-P with no post-secondary education had significantly lower PCS [35.5(10.9)] compared to SLE-P with some post-secondary education [41.5(11.5); P< 0.0001]. Education level had no effect on PCS for any of the family-members. There was a significant correlation between PCS for SLE-P and PCS for the mothers (r=0.284; P< 0.0001) and the fathers (r=0.181; P=0.004). The MCS was significantly lower only in SLE-P [47.3(11.8)] compared to HC [49.9(9.3), P=0.0073]. MCS was below the expected age-gender standardized values in 48% of SLE-P, 38% of mothers, 41% of fathers, 40% of sisters and 42% of brothers compared to 39% in HC. Marital status and post-secondary education had no effect on MCS for both SLE-P and their family-members. In SLE-P, number of co-morbidities was significantly associated with a lower PCS (r=-0.393, P< 0.0001) and a lower MCS (r=-0.257, P< 0.0001).

Conclusion:
Both MCS and PCS are impaired in SLE-P compared to the norm. Poor PCS in SLE-P was associated with a poor PCS in both parents. Health care personnel should consider screening SLE-P for QOL and, more support should be provided to the care givers for SLE-P.
Open Label Study for Treatment of Pediatric Wegener's Granulomatosis with Rituximab

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Objective:
To report an open label treatment study of refractory pediatric Wegener’s Granulomatosis (WG) with the monoclonal anti-CD20 antibody Rituximab.

Methods:
A single centre study of 3 consecutive children age < 18 years, diagnosed with WG fulfilling ≥ 3/6 EULAR/Pres criteria was conducted. All patients had a severe disease flare shortly after receiving standard therapy and were treated with Rituximab for active disease. Active disease was characterized by an increase in symptoms attributed to WG, with changes in serum inflammatory markers and diagnostic imaging despite previous treatment including corticosteroids and at least 6 months of therapy with cyclophosphamide. Clinical information including demographics, organ system involvement, and immunosuppressive therapy were recorded. Baseline T and B cell markers, serum inflammatory markers (ESR, CRP, C3, C4), ANCA serology, and relevant diagnostic imaging were reviewed. Patients received 375 mg/m2 of intravenous Rituximab weekly for 4 weeks. Response to Rituximab was measured at 6 months following treatment including clinical symptoms of active disease, current immunosuppressive therapy, and change in serum inflammatory markers and diagnostic imaging.

Results:
The 3 patients met diagnostic criteria for pedatric WG, and during their disease course displayed symptoms of WG including sinusitis (2), nasal ulcers (1), subglottic stenosis (2), bronchial stenosis (1), pulmonary nodules (3), proteinuria and hematuria (2) and PR-3 specific C-ANCA (3). All 3 patients experienced disease flare characterized by increasing pulmonary symptoms, elevated inflammatory markers and new or increasing pulmonary nodules prompting treatment with Rituximab. Levels of CD20 were within normal range prior to treatment with Rituximab. Inflammatory markers were elevated at baseline, and all patients were receiving immunsuppressive treatment including Prednisone (3), Mycophenolate mofetil (2) or intravenous Cyclophosphamide (1). Six months after treatment with Rituximab, clinical symptoms of active WG were not present. One patient continued on Prednisone 2.5 mg daily, while 2 patients were receiving no immunosuppression. One patient had a decrease in inflammatory markers to normal range, while 2 had persistently elevated inflammatory markers. All patients achieved CD20 count of 0 following treatment with Rituximab, though at 6 months one patient has returned to normal a CD20 level.

Conclusion:
Rituximab is an effective treatment for patients with pediatric WG who fail conventional therapy. All 3 patients in this study had an excellent clinical response to Rituximab, with subsequent decrease and discontinuation of immunosuppression.
Predictors of Hip Disease in the Systemic Arthritis Subtype of Juvenile Idiopathic Arthritis

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Objective:
Hip involvement occurs in 20-40% of all JIA cases. Patients with S-JIA are affected most frequently. The aim of this study is to investigate the predictors of clinical hip disease and radiographic hip damage in S-JIA.

Methods:
The medical records of all children (n = 101) with S-JIA – seen at The Hospital for Sick Children – from 1997 to 2007 were reviewed. Patients who met the following inclusion criteria were further examined: (1) satisfied the ILAR classification criteria for S-JIA; (2) were first seen within 3 months of symptom onset; and (3) were followed for at least 6 months. Potential clinical and laboratory predictors were examined at presentation, and at 3 and 6 months. Clinical data included: fever, S-JIA rash, hepatosplenomegaly, serositis, lymphadenopathy, and arthritis. Laboratory data comprised: hemoglobin, leukocyte count, platelet count, ESR, serum albumin concentration, and quantitative immunoglobulin concentrations. To account for censored observations, we used survival analysis.

Results:
During the study period, 59 children (32 girls) met our inclusion criteria. The mean age at diagnosis was 7.8 years and the mean duration of follow up was 4.3 years. Thirty patients (51%) developed clinical hip disease; with 12 (20%) developing radiographic evidence of hip damage. The mean time to develop clinical hip disease was 19 months and 40 months for hip damage. At presentation, patients in whom clinical hip disease later developed had polyarthritis (HR=2.51, p=0.01), elevated IgG (HR=1.12, p=0.01) and IgM (HR=2.71, p=0.02) levels and higher CHAQ scores (HR=1.65, p=0.02). At 3 months after disease onset, patients in whom radiographic hip damage later developed had fever (HR=4.78, p=0.02), polyarthritis (HR=4.63, p=0.02) and higher CHAQ scores (HR=3.20, p=0.005).

Conclusion:
Half of S-JIA patients will develop clinical hip disease within 19 months of diagnosis. Early presentation with polyarthritis, higher inflammatory markers and more marked disability predict an earlier development of clinical hip disease. Ongoing fever at 3 months as well as polyarthritis and more marked disability predicted the development of radiographic hip damage. The early identification of an increased risk of hip disease in patients with S-JIA might suggest earlier, more aggressive interventions to prevent joint destruction.
Ultrasonographic Assessment of Cartilage in MCP Joints in Early Rheumatoid Arthritis

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Objective:
To determine whether ultrasonography (US) is a useful tool in examining cartilage thickness and quality in the metacarpophalyngeal (MCP) joints in patients with early rheumatoid arthritis (RA). To assess cartilage thickness in RA in relation to disease activity scores and ultrasonographic measures of activity.

Methods:
Synovial tissue and cartilage was imaged in the 2nd -5th MCPJs of 17 patients with early RA and 5 normal volunteers using the Esaote MyLab70XVG at a frequency of 18MHz. Correlations were made between cartilage thickness and disease activity scores, synovial thickness and synovial vascularity in individual joints.

Results:
Disease duration was an average (range) of 13.2 (1-30) months. Mean DAS28 (CRP) was 3.33 (range 1.74 - 5.14). Cartilage could be measured and assessed in all MCP joints analysed. Differences in the echogenicity of cartilage were evident - with some cartilage structures being well demarcated, and others less clearly defined. The right 2nd MCP showed the most variation in cartilage thickness measurements (Mean 0.36mm; range 0.07 – 0.58mm). There were no significant correlations between cartilage thickness in individual joints, synovial thickness or vascularity or DAS28(CRP).

Conclusion:
High resolution US is capable of assessing cartilage thickness and quality in the MCPJs. Whilst cartilage thickness may not reflect disease activity in patients with early disease, the quality of the cartilage may be compromised in early active disease. This is confirmation that US is a useful tool in imaging cartilage in the MCPJ. In association with synovial thickness, synovial vascularity and erosions, assessment of cartilage by US allows for assessment of many of the pathological features of inflammatory arthritis. A study to determine cartilage thickness and quality in a cross-section of patients with RA in comparison to plain radiographs is underway.
Prevalence and Clinical Correlates of Pruritus in Patients with Systemic Sclerosis

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Objective:
There are no studies of pruritus prevalence or clinical correlates in systemic sclerosis (SSc). The objectives of this study were to document the proportion of SSc patients with pruritus on most days, to determine when in the course of the disease pruritus is most prevalent, and to identify clinical correlates

Methods:
Cross-sectional, multi-center study of 400 SSc patients from the Canadian Scleroderma Research Group Registry ≥1 year after Registry enrollment. Patients indicated whether they experienced pruritus during the past month on most days and underwent clinical histories and medical examinations. A multiple logistic regression was used to assess the association between sociodemographic and clinical variables and pruritus

Results:
179 patients (45%) reported pruritus on most days, including 69% (11 of 16) among patients 1-1.9 years since onset of non-Raynaud’s symptoms, 41% (38 of 93) for 2.0-4.9 years, 47% (44 of 94) for 5.0-9.9 years, 43% (60 of 140) for 10.0-19.9 years, and 46% (26 of 57) for ≥20 years. In post-hoc analysis, patients 1-1.9 years from disease onset were significantly more likely to report pruritus (P=0.049). Patients with pruritus had significantly more skin involvement (P=0.029), more gastrointestinal symptoms (P<0.001), worse breathing problems (P=0.001), worse Raynaud’s symptoms (P=0.002), and more severe finger ulcers (P=0.009). Only number of gastrointestinal symptoms predicted pruritus in multiple logistic regression analysis (odds ratio=1.25, 95% confidence interval 1.13–1.37, P<0.001)

Conclusion:
Pruritus is common in SSc and is independently associated with gastrointestinal symptoms. Focused research on sources of pruritus and its management in SSc is needed.
Clinical Correlates of Sexual Impairment in Women with Systemic Sclerosis

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Objective:
Objective: The objective of this study was to assess the correlates of sexual impairment in a sample of women with systemic sclerosis (SSc).

Methods:
Methods: Female SSc patients completed measures of sexual function (Sexual Relationships subscale of the Psychosocial Adjustment to Illness Scale – Self-Report; PAIS-SR), body image (Satisfaction With Appearance Scale; SWAP), and pain (Visual Analog Scale; VAS). Sociodemographic and disease specific variables were recorded. Pearson correlations and multiple regression analyses were run to assess the associations between body image, pain, and sociodemographic and disease variables, with sexual function.

Results:
Results: 117 female SSc patients were sampled (33 [28.2%] diffuse; mean age 51.4±11.9 years; mean time since diagnosis 9.1±8.5 years). Unadjusted analyses revealed a moderate positive correlation between sexual function and pain (r = 0.439, p < 0.001), satisfaction with appearance (r = 0.350, p < 0.001), and a moderate negative correlation with being married (r = -0.338, p = 0.000). Adjusted analyses revealed that being married (β = -0.228, p = 0.006), disease duration (β = 0.171, p = 0.046), and pain (β = 0.290, p = 0.001) are independent predictors of sexual function. Satisfaction with appearance was not independently associated with sexual function (β = 0.158, p < 0.067).

Conclusion:
Conclusion: This is the first empirical study to investigate the clinical correlates of sexual impairment in women with SSc, and the first to document the association between sexual impairment and pain in women with SSc. Pain, longer disease duration, and not being married are associated with increased sexual impairment in women with SSc.
The Course of Depressive Symptoms Over Time in Systemic Sclerosis

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Objective:
Studies find depression to be consistently elevated in chronic disease samples. A recent systematic review found 36-65% percent of scleroderma patients to have significant depressive symptoms. However, little is known about the course of depression over time among patients with chronic disease. The majority of studies in rheumatoid arthritis find depression to be stable over time. These studies, however, fail to account for patient drop-out and how change in depressive symptoms may reflect change in disease symptoms. When multiple imputation was used to account for missing data, we found that disability increased over time in the CSRG registry, and that much of this change in disability was explained by change in the symptoms of systemic sclerosis. The objective of this study was to determine the course of depressive symptoms in our sample, and to see what symptoms of disease might be related to depressive symptoms over time.

Methods:
The sample consisted of all patients in the CSRG registry who were assessed annually between 2004 and 2008. At the annual assessments, patients completed a standardized evaluation including a medical history, physical evaluation, of various measures of disease status, and the CES-D. Multiple imputation was used to account for missing data. Mixed-effects models were conducted to model the CES-D trend over time, taking into account symptoms of scleroderma.

Results:
741 patients presented a baseline, with a sample mean on the CES-D of 14.37 (10.4), 59% having limited disease, 41% having diffuse disease. Of the demographic variables, marital status (unmarried) (β=2.16, 95% CI = 0.18, 4.13) and greater than high school education (β=-1.39, 95% CI = -2.78, -0.00) were predictive of CES-D scores. Of the time varying disease covariates, breathlessness (β=0.83, 95% CI = 0.60, 1.06) and gastrointestinal symptoms (β=0.56, 95% CI = 0.37, 0.75) were the strongest predictors of CES-D scores. Visit number was not predictive of depressive symptoms.

Conclusion:
Despite the increase in disability over time, depressive symptoms were stable. This finding suggests that a person with scleroderma may have already taken into account the uncertain future of living with a chronic disease, resulting in significant but stable depressive symptoms in the face of further reductions in physical health.
Do Lower Extremity Outcome Questionnaires used to Assess Ankle Replacements and Fusions really Capture what Patients Want us to Hear?

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Objective:
The objective of this study was to compare items from patient-reported questionnaires measuring musculoskeletal outcomes with items generated by pre- and post-operative ankle arthrodesis and arthroplasty patients using the patient-selected portion of the Patient-Specific Index (PASI-P). The International Classification of Functioning, Disability and Health (ICF) was used as an organizing framework.

Methods:
A literature review identified 6 questionnaires that assess lower extremity outcomes (AAOS, patient-reported portion of AOFAS, FFI, LEFS, SMFA, WOMAC). Surgical patients (n=142) from an orthopaedic surgeon’s practice completed the patient-selected items from PASI-P. Items from the standardized questionnaires and PASI-P were coded by 3 reviewers according to the ICF framework to allow comparisons. Comparisons were made to see if PASI-P items were covered in standardized questionnaires.

Results:
A total of 690 concepts were identified in the patients’ responses from PASI-P, which corresponded to 45 ICF categories. Most PASI-P concepts fell into Activities and Participation (60.3%) and Body Functions and Body Structures (35.2%), including the second level categories ‘walking’ (21.6%), ‘pain’ (18.7%), and ‘recreation and leisure’ (17.4%). A total of 237 concepts were identified in the 6 questionnaires and linked to 39 second level ICF categories. Overall, SMFA addressed the most second level categories and had the closest proportion of Activities and Participation (68.9%) and Body Functions (23.0%) concepts as compared to the patient-generated responses. The patient-reported portion of AOFAS addressed the fewest categories. LEFS only contained items from Activities and Participation. AAOS was the only questionnaire to address the issue of ‘swelling’, though it represented 5.6% of all patient-generated responses.

Conclusion:
Questionnaires differ largely in their content and no single questionnaire captured all the concerns identified by patients. Clinicians should recognize patients' concerns relevant to the ankle currently not included in available questionnaires. This analysis will guide the development of a new and more comprehensive instrument for evaluating ankle outcomes following ankle arthrodesis or arthroplasty.
Incremental Benefit of Open-Label Certolizumab Pegol + MTX in Rheumatoid Arthritis (RA) Patients Following Double-Blind Placebo + MTX Treatment Out to 2 Years

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Objective:
Certolizumab pegol (CZP) 200 or 400 mg Q2W + MTX significantly reduced the signs and symptoms of RA when compared with placebo (PBO) + MTX in RAPID1. Subjects completing 1 year on either PBO + MTX or CZP + MTX were allowed to enter open-label (OL) treatment with CZP 400 mg Q2W + MTX. Efficacy outcomes data is presented for subjects who completed 2 years’ treatment (1 year of PBO + MTX followed by 1 year of OL CZP + MTX).

Methods:
Analyses over 2 years included, ACR20/50/70 response rates (nonresponder imputation), changes from BL in DAS28(ESR) and HAQ-DI scores (LOCF), and assessment of the inhibition of joint damage progression (assessed in hands, wrists, and feet using change in the modified total Sharp score [mTSS; linear extrapolation] from RAPID 1 BL).

Results:
95.3% of PBO + MTX completers in RAPID 1 reconsented and received OL CZP + MTX. Of these, 92.7% completed 100 wks of observation (52 wks PBO + MTX /48 wks OL + MTX). Reductions in RA signs and symptoms at Wk 52 (ACR20/50/70 responder rates were 63.4%; 39.0%; and 17.1%) were sustained through to at least Wk 100. Change in mTSS for subjects treated with PBO + MTX was 2.5 U at Wk 52 compared with 2.8 U for subjects completing Wk 100, which indicated marked inhibition of radiographic progression (Wk 52 to Wk 100 change of only 0.3). This difference is demonstrated by the differences in the cumulative probability curves of change in mTSS during double-blind (Wks 0-52) and OL (Wks 52-100) treatment. DAS28 and HAQ-DI scores also markedly improved upon switching from PBO + MTX to CZP + MTX and were sustained throughout Year 2; changes from BL at Wk 100 were -3.3 and -0.73 for DAS28 and HAQ-DI, respectively.

Conclusion:
There was a slowing of radiographic disease progression upon initiation of OL CZP + MTX in subjects who completed 52 wks of double-blind treatment with PBO + MTX. Upon switching to OL CZP treatment, these subjects also experienced sustained improvements in the signs and symptoms of RA, including marked improvements in DAS28 and HAQ-DI throughout 2 years.
A Faster Clinical Response to Certolizumab Pegol Treatment is Associated With Better Improvements in Household Productivity in Patients With Rheumatoid Arthritis

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Objective:
When added to methotrexate (MTX), certolizumab pegol (CZP), a PEGylated Fab' anti-TNF, was shown to provide rapid improvements in disease activity, RA signs and symptoms and productivity at work and home. The objective of our analysis was to determine if a faster clinical response to CZP treatment was associated with better long-term increases in household productivity in patients with active RA.

Methods:
Data from patients treated with CZP 200 or 400 mg + MTX in RAPID1 were pooled for analysis. Two subgroups were created for patients who achieved response at Week (Wk) 12. Subgroups were based on response at Wk 6: Wk 6 responders and Wk 12 responders (i.e., those who were non-responders at Wk 6). Responder definitions were based on DAS28 decrease ≥1.2 points from baseline (BL) or ACR20 response. Using a repeated measures negative binomial regression adjusted for BL score and demographic variables, the number of household days lost due to RA, days with productivity reduced by ≥50%, the rate of RA interference with household productivity, and days lost of social activities in the last 4 weeks were compared between responder subgroups. Due to an imbalance in patient numbers between the Wk 6 and Wk 12 responder groups, an analysis of work productivity was not possible.

Results:
BL demographics were similar between the 2 responder subgroups. Wk 6 DAS28 and ACR20 responders lost significantly fewer days of household work (4.4 and 4.2 respectively) than Wk 12 DAS28 and ACR20 responders (6.8 and 6.0, respectively) in the first 4 wks (P≤0.05). Similar results were also seen from wks 49-52: Wk 6 DAS28 and ACR20 responders lost 0.7 and 0.6 days of household work, respectively vs Wk 12 responders who lost 1.5 days (P≤0.001). Wk 6 responders also had fewer days with reduced household productivity and a lower rate of RA interference with household productivity.

Conclusion:
A faster response to treatment with CZP + MTX is correlated with increased household productivity in patients with active RA over 52 wks. Rapid (Wk 6) responders lost fewer days of household work and had fewer days with reduced productivity than the later (Wk 12) responders. These observations are consistent with other studies underscoring the importance of a rapid response to RA treatment.
Improvements in Radiographic, Clinical, and Functional Outcomes for Patients With Rheumatoid Arthritis Treated With Adalimumab Plus Methotrexate Through 8 Years

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Objective:
We describe the long-term (8-year) impact of adalimumab (ADA) plus methotrexate (MTX) on radiographic, clinical, and functional parameters in patients with rheumatoid arthritis (RA).

Methods:
In DE019, patients with RA were randomized to double-blind MTX (N=200), ADA 40 mg every other week (eow) plus MTX (N=207), or ADA 20 mg weekly plus MTX (N=212) for 1 year. Patients completing double-blind therapy received open-label ADA 40 mg eow plus MTX for an additional 7 years. Observed data analyses were performed for all patients who received ≥1 dose of study drug and had data at each visit. Clinical response was assessed using American College of Rheumatology (ACR) criteria and swollen and tender joint counts (SJC66 and TJC68). Remission-like response was defined as 28-joint Disease Activity Score (DAS28) < 2.6, SJC66=0, TJC68=0, or DAS28 < 2.6 and radiographic nonprogression. Physical function was assessed using the Health Assessment Questionnaire (HAQ). Two experts blinded to sequence and order read radiographic films from baseline and Years 5, 6, and 8. Radiographic changes were determined using the modified total Sharp score (mTSS); nonprogression was defined as a change in mTSS < 0.5.

Results:
After 8 years, 81%, 62%, 47%, and 20% of ADA+MTX patients (N=185) achieved ACR20, 50, 70, and 90, respectively. Mean TJC decreased from 26 to 4, and mean SJC decreased from 20 to 4. DAS28 < 2.6, SJC=0, and TJC=0 were achieved by 60%, 42%, and 40% of patients, respectively. Mean HAQ decreased from 1.33 to 0.65 (N=186). Radiographic nonprogression occurred in 56% of patients. Patients treated with MTX in Year 1 experienced a relative increase of 29% in the percentage of patients with radiographic progression.

Conclusion:
After 8 years of therapy, ADA+MTX provided sustained improvements in clinical remission for 60% of patients and prevented radiographic progression for 56%. Early initiation of ADA 40 mg eow+MTX prevented radiographic progression and led to better outcomes over 8 years than when combination treatment was delayed for 1 year. Reference: 1. Keystone EC, et al. Arthritis Rheum. 2004;50:1400-11.
Patients With Early Rheumatoid Arthritis Reported Better Physical Functioning With Adalimumab Plus Methotrexate Than With Methotrexate Alone

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Objective:
Global physical functioning in rheumatoid arthritis (RA) is commonly measured by the overall score on the patient-reported Health Assessment Questionnaire (HAQ). We evaluated patient-relevant aspects of physical functioning during treatment with a combination of adalimumab (ADA) and methotrexate (MTX) vs. MTX alone.

Methods:
Data were derived from PREMIER, a 2-year, randomized, double-blind, Phase III trial in MTX-naïve patients with early RA (< 3 years). On the HAQ, patients rated their ability to perform a variety of tasks on this scale: 0=without any difficulty, 1=with some difficulty, 2=with much difficulty, and 3=unable to do. Ordered logistic regression techniques were adopted to estimate the effects of treatment on individual HAQ item responses in a proportional-odds model at baseline, Week 52, and Week 104. A similar model was used to estimate the effect of radiographic damage (using modified total Sharp scores [mTSS]) on individual HAQ item responses.

Results:
Baseline distributions of HAQ item responses were similar between treatment groups. At Weeks 52 and 104, the ADA+MTX group (N=269) reported better physical functioning than the MTX monotherapy group (N=257) for 15 of 20 HAQ items (odds ratios: 1.77 to 2.78 at Week 52; 1.62 to 2.77 at Week 104; p< 0.05 for each comparison). ADA+MTX-treated patients were approximately 3 times more likely than MTX-treated patients to find it easier to open car doors and to cut their meat and approximately 2 times more likely to have better ability to do most of the remaining activities assessed by the HAQ. The effect of mTSS on HAQ was significant for 4 items at Week 52 and for 6 items at Week 104 (all comparisons p< 0.05). Two items (walking outdoors on flat ground; bathing) were affected by mTSS at both time points (both p< 0.05).

Conclusion:
Patients with early RA treated with ADA+MTX reported better outcomes than patients treated with MTX alone for most aspects of physical functioning measured by the HAQ. Activities involving the hands had the greatest improvements. Several aspects of physical functioning were affected by radiographic damage, with greater impact over time.
**Golimumab and Radiographic Progression in Rheumatoid Arthritis: Results of GO-BEFORE and GO-FORWARD Studies**

*Edward Keystone (MacDonald Ctr for Arthritis and Autoimmune Disease, Toronto)*

**Objective:**
To evaluate the effect of golimumab (GLM) on radiographic progression in pts with rheumatoid arthritis (RA).

**Methods:**
In both GO-BEFORE (MTX-naïve pts; n=637) and GO-FORWARD (MTX-inadequately responding (IR) pts; n=444) pts were randomized to PBO+MTX, GLM 100mg+PBO, GLM 50mg+MTX, or GLM 100mg+MTX. Subcutaneous injections were administered q4wks. The GO-BEFORE had a control period of 52 wks with early escape [EE] at wk28 and GO-FORWARD had a control period of 24 wks with EE at wk16. Pts in control grps meeting EE criteria start receiving GLM 50mg+MTX. Radiographs of hands and feet at baseline, wk24 (wk16 for EE pts) and wk52 in GO-FORWARD, and baseline, wk28, and wk52 in GO-BEFORE were scored by 2 independent readers and an adjudicator using the van der Heijde-Sharp score (vdHS). Different readers were used for the two trials. Linear extrapolation was used for radiographs taken at EE visits.

**Results:**
In GO-BEFORE, mean baseline vdHS ± SD for the PBO+MTX, GLM 100mg+PBO, GLM 50mg+MTX and GLM 100mg+MTX groups were 19.71±35.44, 20.42±30.90, 18.69±32.39, and 18.22±35.47, respectively. In this MTX-naïve population, mean vdHS changes from baseline to wk52 (co-primary endpoint) in both the 50mg and 100mg GLM+MTX grps were significantly lower compared with those in the PBO+MTX grp (0.74±5.23 [p=0.015] and 0.07±1.83 [p=0.025], respectively, versus 1.37±4.56). In GO-FORWARD, mean baseline vdHS ± SD for the PBO+MTX, GLM 100mg+PBO, GLM 50mg+MTX, and GLM 100mg+MTX groups were 36.70±52.06, 37.42±52.45, 29.67±39.29, and 39.57±56.09, respectively. In this MTX-IR population, vdHS changes from baseline to wk24 (primary analysis) were minimal in all grps (0.6±2.74 for GLM 50mg+MTX [p=0.953], 0.23±1.34 for GLM 100mg+MTX [p=0.293], 0.55±2.35 for PBO+MTX), preventing any significant effect of GLM to be detected. The proportion of pts with change in vdHS above the smallest detectable change (SDC=2.58 for the study) was 4% in the PBO+MTX grp. The lack of progression in the PBO grp may have been due to the short placebo-control period (in PBO+MTX grp 32% EE at wk16 and remaining pts crossed over at wk24 to receive GLM) and relatively less active pt population (median CRP of 0.9, lower joint counts, lower baseline vdHS scores) than in previously reported trials in similar populations.

**Conclusion:**
Both GLM 50mg+MTX and GLM100mg+MTX demonstrated statistically significant and comparable inhibition of radiographic progression in MTX-naïve population compared with MTX alone. In the MTX-IR population the minimal radiographic progression in the MTX alone grp prevented any effect of GLM to be detected.
Multiple Courses of Rituximab (RTX) Produce Sustained Efficacy in Patients (pts) with Rheumatoid Arthritis (RA) with An Inadequate Response (IR) to One or More TNF Inhibitors

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Objective:
To assess the effect of repeat courses of RTX in pts with a prior inadequate response to TNF inhibitors (TNF-IR).

Methods:
RA pts recruited into Phase II or III studies with RTX and who had previously had an IR to a TNF inhibitor were permitted to receive further courses of RTX in open-label extensions. Eligibility for retreatment included a response to the initial course (at least 20% reduction in swollen and tender joint counts [SJC/TJC]), with courses no more frequently than every 4 months. Criteria for retreatment included active disease defined as either ≥8 SJC and TJC or DAS28≥2.6 (depending on the study). Each course (C) consisted of 2 x 1000 mg given as IV infusions 2 weeks apart. Efficacy was determined 24 weeks following each course of RTX with outcomes assessed relative to the patient’s pre-RTX treatment baseline. Analyses were performed using observed data on all pts, and on all pts with efficacy data at 24 wks following each of their first 4 courses of RTX, the within pt, within visit (WW) population.

Results:
500 RA TNF-IR pts had been exposed to at least 1 course of RTX and had efficacy data at Wk 24, with 146 evaluable at 24 wks following each course (WW population). Observed efficacy in all pts show higher responses for C2 onwards compared with C1. However, retreatment criteria cause this analysis to become enriched for RTX responders as pts were required to achieve a response to C1. The same maintained or improved responses were seen in the WW population. From C1 to C4, the proportion of pts in the WW population achieving DAS28 low disease activity (LDA) or remission doubled (C1: 12.9% and 7.9%, respectively; C4: 25.2% and 16.5%, respectively). Safety over repeat courses did not show any unexpected findings with rates of infection, including serious infection unchanged.

Conclusion:
Repeated courses of RTX were associated with sustained levels of efficacy in TNF-IR pts with an initial response to RTX.
Benefit of Continuing Treatment Beyond 12 Weeks in Patients With Rheumatoid Arthritis Who Were Treated with Tocilizumab or Methotrexate Monotherapy

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Objective:
To determine the proportions of patients (pts) with active rheumatoid arthritis (RA) who achieved ACR responses, LDAS, and DAS28 remission at wk 24, if they were non-responders (NR) at wk 12, having continued tocilizumab (TCZ) or methotrexate (MTX) monotherapy.

Methods:
Post hoc analysis was performed using data from pts who participated in the phase 3 clinical trial, AMBITION. Pts included in the trial had not been treated with MTX within 6 months before randomization and had not discontinued MTX treatment because of lack of clinical response or occurrence of clinically important adverse events. Pts were treated for 24 weeks with TCZ 8 mg/kg every 4 weeks or with an initial dose of MTX 7.5 mg/week, titrated up to 20 mg/week within 8 weeks, for 24 weeks. The proportions of pts who were ACR20 NRs at wk 12, achieved ACR20 at wk 24. Thus, of pts who achieved ACR20 at wk 24, 23% achieved it between wks 12 and 24. Higher-level responses became more apparent after 24 weeks of TCZ treatment for patients who were wk 12 NRs. For example, of pts treated with TCZ who achieved ACR70 at wk 24, 49% achieved it between wks 12 and 24. Numerically higher proportions of wk 24 Rs treated with MTX than of those treated with TCZ were late responders and achieved clinical responses between wks 12 and 24.

Conclusion:
Study results demonstrated that continuing TCZ treatment beyond 12 weeks is important because substantial proportions of pts who do not achieve clinical responses by week 12 of treatment will achieve them by week 24.
Patients in the RAPID1 (Rheumatoid Arthritis Prevention of structural Damage) Clinical Trial of Certolizumab Pegol (CZP) Have Similar High/Moderate vs Low... Moderate and Poor Responses

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Objective:
To examine the proportion of patients with high/moderate vs low activity/remission at baseline and endpoint according to DAS28, CDAI and RAPID3, and for good, moderate or poor EULAR-DAS and proposed RAPID3 responses in patients who took certolizumab pegol (CZP) + methotrexate (MTX) vs placebo (PBO) + MTX in the RAPID1 clinical trial.

Methods:
Data from RAPID1 200 mg and 400 mg CZP and PBO patients were pooled and classified as high, moderate, low activity or remission at baseline and endpoint according to DAS28 [≥5.1, 3.21-5.1, 2.61-3.2, < 2.6 (total=10)], CDAI [≥26, 10.1-26, 3.1-10 or < 3 (total=76)], and RAPID3 [≥12, 6.01-12, 3.01-6, < 3 (total=30)]. Results were calculated for low activity/remission vs high/moderate activity, and indicate a need to strongly consider changing therapy. Results also were calculated for EULAR-DAS28 response categories: good=decrease >1.2 units AND final < 3.2; moderate=decrease < 1.2 AND final >3.2 OR decrease of 0.6-1.2 AND final < 5.1; poor=decrease < 0.6 OR final >5.1, and proposed RAPID3 response categories: good=decrease >3.6 units AND final < 6; moderate=decrease >3.6 AND final >6 OR decrease of 1.8-3.6 AND final < 12; poor=decrease < 1.8 OR final >12. Comparisons involved cross-tabulations, kappa and weighted kappa statistics.

Results:
At baseline, almost all patients exhibited high activity for all 3 indices. At final visit, 32%, 45% and 27% of patients treated with CZP demonstrated low activity/remission for DAS28, CDAI and RAPID3, respectively vs 2%, 7% and 6% of PBO patients. For DAS28, good, moderate, and poor responses were seen in 32%, 50%, and 18%, of CZP patients respectively, and 23%, 42%, 35%, respectively for RAPID3. Good, moderate and poor responses in DAS28 for PBO patients were 2%, 25%, 73%, respectively and 5%, 20%, 75% for RAPID3. Kappa/weighted kappa values in these comparisons ranged from 0.26 to 0.59, indicating fair-to-good agreement.

Conclusion:
CZP is distinguished from PBO in the RAPID1 clinical trial through RAPID3, DAS28 and CDAI scores. While the 3 indices are similar, DAS28 is more specific for clinical trials. In addition, RAPID3 may be useful for clinical trials and usual care as it requires < 10% of the time needed for DAS28 or CDAI.
A Novel Pre-Filled Syringe for Self-Administration in Patients with Rheumatoid Arthritis May Offer Advantages Over the RAPID2 Syringe

Objective:
For patients (pts) with rheumatoid arthritis (RA), self-administering injectable RA therapy may be difficult due to limited dexterity, hand pain and weakness. Using input from RA pts, a new syringe was designed and developed to improve the ability to self-administer therapy. This was completed using a 3-phase scientific approach: design consideration, optimization and evaluation. The Syringe Usability Study (SUS), which quantitatively evaluates the usability of a syringe, was conducted during design evaluation to determine if syringe design improves pts’ ability to self-administer therapy. This study assessed the new vs RAPID2 pre-filled syringes in RA pts.

Methods:
Pts with mild, moderate or severe RA participated in the SUS (n=23: 10 women, 13 men). In random order, pts were given the new and RAPID2 syringes, asked to inject into fake skin, and then evaluate the usability of the syringes using a questionnaire. The questionnaire used a 7-point Likert-like scale (1=negative, 7=positive) ranking 19 attributes on performance and preference. Mean scores and means of differences between the new and RAPID2 syringes were calculated. Also measured were maximum isometric injection force with plunger fixed at mid-length or plunger fully depressed, and dynamic force during injection. Paired t-tests were used to compare differences between the new and RAPID2 syringes in both attributes and forces.

Results:
In 15 of the 19 attributes on the SUS, the new syringe rated significantly higher than the RAPID2 syringe. On 6 performance measures, including difficulty removing cap and comfort, the mean difference was statistically significant (SEM: new syringe vs RAPID2 syringe = 1.54). Durability scored higher on the new syringe vs RAPID2 syringe (mean score 6.26 vs 3.74, respectively) and it was preferred by pts vs the RAPID2 syringe (mean score 6.00 vs 3.59, respectively). The new syringe enables pts to exert maximum forces of 77.1 N with plunger at mid-length (isometric), 66.5 N with plunger fully depressed (isometric), and 45.4 N during injection (dynamic), compared with 52.0 N, 45.3 N, and 33.1 N, respectively, with the RAPID2 syringe (P≤0.001). This is up to 48% more isometric force.

Conclusion:
The new syringe, developed using input from RA pts, is easier to use and preferred over the RAPID2 syringe. Biomechanical advantages of the new syringe may improve the ability to self-administer injectable therapy in RA pts.
Prevalence of Co-Morbidities in Early and Established Psoriatic Arthritis Cohorts

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Objective:
Psoriatic arthritis (PsA) affects 10-35% of patients with psoriasis (PSO) and is associated with progressive joint damage and significant morbidity. Co-morbidities associated with PsA are still not fully defined specifically in early stages of the disease compared to the general population. We set to define the co-morbidities present in early and established PsA patients.

Methods:
Data was collected from a rheumatology clinic specializing in patients with PSO and PsA diagnosed greater than 2 years (Established PsA) compared to cohort of PsA patients diagnosed less than 2 years (Early PsA) in Newfoundland. Data for controls with no history of PSO or PsA were collected from the Newfoundland and Labrador Center for Health Information (NLCHI). Controls were matched 3:1 to the established cohort. Co-morbidities associated with PsA will be compared to the general population using age adjusted standardization rates by gender.

Results:
148 patients with PsA were identified, of which 38 were in the Early PsA group and 60,521 controls were identified from the NLCHI. Mean (SD) age of the established group was 53 (11.0) and 48 (11.3) for the Early group. There were more females in the Early PsA group compared to the Established (60.5% vs. 42.6%) respectively. The age adjusted standardization rates revealed that prevalence of co-morbidities such as hypertension, obesity, diabetes and depression are more prevalent in the PsA population in comparison to the general population. These high rates were present in the females and males of the early group (Disease duration 12.6 months) as well as the established group (duration 8 years). For example, the observed/expected rate of obesity in females with early PsA was 18.2 in the early female patients vs 14.1 in the established group. Observed hypertension rates in same population were 16.9 and 17.8 times more than expected respectively.

Conclusion:
Patients with PsA have a high prevalence of cardiovascular disease and metabolic syndrome abnormalities. Interestingly, patients in the Early PsA cohort had a slightly higher rate compared to the Established cohort. Surveillance, detection and management of these co-morbidities is important in managing PsA patients.
Aortitis of the Abdominal Aorta associated with Iritis and HLA B27

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Case Report:
A 52-year-old aboriginal woman from remote northern B.C. presented to the ER in June 2008 with a 3 week history of worsening of severe cramping lower abdominal pain. There was a 2 year history of similar intermittent epigastric and suprapubic cramps of various descriptions, leading to hospitalization in the north and investigations of suspected cholecystitis and renal colic. Cholecystectomy was done in 2007 because of findings of gallstones. For 17 years she had received topical and oral steroids, including prednisone up to 30 mg daily for acute recurrent left anterior iritis and she was known to be positive for HLA B27. Treatment with methotrexate had failed due to intolerance to both oral and parenteral administration. In April 2008 she underwent in Calgary enucleation of her left eye for painful iritis, permanent visual loss, and steroid dependence. At no time did she see a rheumatologist. Postoperatively she was recommended to taper prednisone from 30 mg maintenance. At the time of ER presentation she was on 10 mg prednisone. She denied a history of chronic low back pain, morning stiffness, psoriasis, colitis or urethritis. On examination, she was cushingoid and obese. BP was 135/65. She was afebrile. There was midline lower abdominal tenderness and rebound tenderness without guarding. There were no vascular bruits. The CT abdomen showed thickening and stranding of the infrarenal abdominal aorta to the level of the bifurcation, findings, typical of aortitis. The ESR was 48, CRP 33 Spine xrays showed osteoporosis with compression fractures, no sacroiliitis and no radiographic findings of ankylosing spondylitis. Within 6 hours of prednisone 30 mg bid, abdominal pain disappeared. Subsequent treatment over 1.5 years has included cyclosporine 100 mg bid and reduction in prednisone dose to 5 mg. Repeat abdominal CT in July 2009 showed marked improvement, and persisting mild periaortic thickening. Cardiovascular manifestations of AS include aortic insufficiency, AV block, and aortitis of the ascending aorta with or without aneurysm. The literature also includes 3 reports of Takayasus arteritis, 3 diagnosed with polyarteritis nodosa, and 10 reports of retroperitoneal fibrosis. There are 2 reports of aortitis of the descending aorta in individuals with AS. Our patient had severe B27 + iritis and no AS. We suspect a relationship between her B27 positive disease and her abdominal aortitis. Future research in this area
Characterization of Patients Referred for Gold Therapy in the Era of Biologics

Jessica Cheung (University of British Columbia, Vancouver); Debra Scarsbrook (Mary Pack Arthritis Program, Vancouver); Alice Klinkhoff (Mary Pack Arthritis Program, Vancouver)

Objective:
To describe the clinical characteristics of patients referred for gold therapy at one centre and determine the reasons for referral.

Methods:
This is a review of prospectively collected data concerning all patients referred for gold monitoring in the Mary Pack Arthritis Program, Vancouver, between July 2007 and July 2009. The following information was extracted from the charts: age, gender, diagnosis, disease duration, RF status, prior and concomitant DMARDs, number of prior courses of gold, and reason for referral.

Results:
The sample included 81 patients, 10 of whom were referred but did not actually start treatment. There were 69 females and 12 males. Diagnosis is RA in 71/81, PA in 5, JIA in 2, Sjogrens Syndrome in 1, undifferentiated polyarthritis in 1 and spondyloarthritis in 1. Age at the time of referral was under 30 in 3, 31-50 in 21, 51-70 in 35 and greater than 70 in 12 patients. RF was positive in 63, negative in 13 and unknown or unmeasured in 5. Twenty of 81 patients had received gold before and were referred during the study time period for a second course in 15, a third course in 4 and a fourth course of gold in 1 patient. Ten of 81 were referred for gold as their first DMARD. Seventy-one had received prior DMARDS: 1 prior DMARD in 22, 2 prior DMARDs in 24, 3 prior DMARDs in 15 and more than 3 prior DMARDs in 6 patients. Four patients had received prior biologic as well as 2-4 prior DMARDs. During the time period of the chart review, 12/71 received gold monotherapy, 56/71 received gold/DMARD combinations and 3 received gold/biologic/DMARD combinations. Reasons for referral to gold clinic fell into the following categories which are not mutually exclusive: failure of other DMARDs in 54, limited DMARD options for reasons of safety in 52, failure of biologics in 3, inappropriate for biologics in 7, previous benefit from gold in 10, benefit of clinic support and monitoring in 10, patient choice in 4, and physician choice in 12. The category ‘limited DMARD options’ included 34 patients with chronic liver disease, 5 with high alcohol consumption, 7 with sulfa allergy and 4 women planning pregnancy.

Conclusion:
The most common reasons for referral to gold clinic in 2007-2009 are failure of other DMARDs and limited DMARD options due to underlying liver disease.
Efficacy of Combination Therapy with a Biologic Agent vs. Methotrexate Monotherapy in Early Rheumatoid Arthritis: A Meta-Analysis of Clinical and Radiographic Remission

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Objective:
The target outcome in early rheumatoid arthritis (ERA) is now remission. This meta-analysis compared the efficacy of initial methotrexate (MTX) monotherapy versus combination therapy (MTX + biologic agent) for clinical remission and radiographic remission among ERA patients with minimal or no prior MTX exposure.

Methods:
A systematic search was performed for randomized controlled trials of ERA using predefined criteria. A random effects model was used to pool the risk ratio (RR) for clinical and radiographic remission at 52-56 weeks of follow-up.

Results:
Seven trials of combination therapy with infliximab, adalimumab, etanercept or abatacept were included. The majority of studies defined clinical remission as a 28-joint Disease Activity Score score \( \leq 2.6 \). Radiographic remission was primarily defined as a modified total Sharp score change of < 0.5 units. All trials demonstrated risk estimates in favour of combination therapy: the pooled RR for achieving clinical remission was 1.74 (95% CI 1.54 to 1.98) and for radiographic remission was 1.30 (95% CI 1.01 to 1.68). Significant heterogeneity among studies for the latter outcome was detected (p < 0.001).

Conclusion:
The efficacy of combination therapy with a biologic agent is superior to MTX monotherapy for remission. Initial combination therapy has a greater effect on clinical remission than radiographic remission and suggests that dissociation between clinical inflammation and structural damage may exist. Uniform definitions of remission are needed and the proportion of subjects who achieve the combined endpoint of clinical and radiographic remission should be considered as a meaningful outcome in future studies of ERA.
Resolution of Osteonecrosis of the Jaw after Teriparatide [Recombinant Human PTH-(1-34)] Therapy

Arthur Lau (McMaster, Hamilton); Jonathan Adachi (McMaster University, Hamilton)

Case Report:
Background: Although exceedingly rare, osteonecrosis of the jaw (ONJ) poses a significant impact on the morbidity for those unfortunate patients who develop it. The current recommended treatments have proven to be suboptimal, as many patients remain unresponsive to such therapies. This report presents the second described case of implementing teriparatide [recombinant human PTH-(1-34)] for the treatment of ONJ which was otherwise unresponsive to conventional therapies. Case Presentation: In this case, we describe a 56-year-old Caucasian female with localized alveolar necrosis of the right lower mandible. She suffered from glucocorticoid-induced osteoporosis, secondary to 18 months of prednisone for fibromyalgia. She was trialed on a variety of medications, including Etidronate, Calcimar, Clodronate, and Pamidronate, but her BMD continued to decline on all these agents and developed multiple vertebral compression fractures. She was ultimately placed on monthly Zoledronate in 2002. About one year prior to presentation, she had multiple maxillary teeth removed in addition to one right mandibular tooth. Subsequent to this she did not heal well, developing chronic draining lesions and recurrent alveolar bone chips persisted. This developed into a local purulence and small areas of fistulation. X-rays showed localized alveolar necrosis that appeared to be limited to those sites, which was consistent with ONJ. After the diagnosis, the zolendronate was discontinued, and she underwent conventional treatment with multiple surgical debridements and various courses of antibiotics. She was started on teriparatide (20μg subcutaneous daily) in November 2005 to help prevent future fractures from occurring. The plan was for her to continue on this anabolic agent for a duration of 18 months. She noticed an improvement in her mandibular pain and ulcer healing about 2 months after starting teriparatide. After finishing her 18 month course, she reported completely healed oral ulcers and negligible pain from the site. Discussion: The exact mechanism leading to development of ONJ is still unknown. The management of ONJ presents a challenge as there are no effective treatments at this time. Teriparatide use was first introduced as a treatment of ONJ unresponsive to conventional therapy in 2007, with noticeable improvement in the oral mucosa noted by 3 months after initiating teriparatide, and a normal appearing oral mucosa by 10 months after initiating therapy. Although both this case, and the one presented here resulted in a successful resolution of the ONJ, it by no means proves the efficacy of this treatment. However, it does provide an interesting possibility for future
Biologic Therapy for Pediatric Rheumatic Diseases - Is Canada Doing Enough?

Claire Leblanc (University of Alberta, Edmonton); Lori Tucker (BC's Children Hospital, Vancouver); Spady Donald (University of Alberta, Edmonton); Garry Spence (University of Alberta, Edmonton); Bianca Lang (Dalhousie, Halifax)

Objective:
To perform a Pan-Canadian survey of provincial biologic agent formulary reimbursement for children with rheumatic diseases.

Methods:
In 2008-2009 a pediatric biologics questionnaire was designed based on a previous ‘biologics report card’ for adult rheumatic diseases. This assessed provincial formulary reimbursement of the following biologic agents: etanercept, adalimumab, anakinra, abatacept, infliximab and rituximab. The questionnaire was sent to a lead pediatric rheumatologist in one rheumatic disease centre per province for completion. Nova Scotia was the site lead for the Maritimes. Data was summarized by province. Northwest territories, Yukon & Nunavut were not represented.

Results:
Whereas every province covers almost all biologics for adults with RA, less than half cover biologic agents other than etanercept for children. Etanercept is primarily reimbursed for polyarticular JIA. Other JIA subtypes (PsA, Oligo, ERA, SOJA) and chronic uveitis are also approved for treatment with etanercept with a mean of 3.3 conditions per province. Sixty three percent of provinces reimburse anakinra primarily for systemic JIA. Infliximab is reimbursed in 50% of provinces for JIA, uveitis and vasculitis. Only 3 provinces reimburse adalimumab and abatacept. Mean number of biologics covered per province is 2.6 for pediatric indication. Saskatchewan reimburses the most biologics and Alberta/Nova Scotia the fewest for children. Rituximab is available primarily for connective tissue diseases and vasculitis on a case -by-case basis.

Conclusion:
Etanercept is the only biologic treatment universally available across Canada for the treatment of polyarticular JIA; few of the other currently available medications are reimbursed. These data demonstrate a serious discrepancy between the provincial biologic agent formulary reimbursement programs for Canadian children with rheumatic diseases. There is an urgent need to create policy to address these deficiencies to reduce ongoing morbidity among affected children.
The Launch of an Innovative Interprofessional Training Program in an Arthritis Setting: The Journey Uncovered

Lorna Bain (Southlake Regional Health Centre, Newmarket); Sandra Mierdel (Southlake Regional Health Centre, Newmarket); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket)

Objective:
The Arthritis Program (TAP) at Southlake Regional Health Centre in Newmarket, Ontario has been a high performance, patient centered, interprofessional team since its inception twenty years ago. Winner of the 2009 Team Interprofessional Award of Excellence awarded through the Faculty of Interprofessional Education at U of T. With frequent requests for consultation to evolving teams from within and external to the province, the team identified the need for a formalized method of disseminating information on the TAP Model. The question was what was the best way to do this and what needed to be included.

Methods:
Through an industry awarded grant, in December 2008, development of the TAP Training Program was launched. Curriculum has been developed referencing Best Practice in Arthritis Care, Self Management Model of Chronic Disease, as well as the results gathered from a National Interprofessional Rheumatology TAP Needs Survey (TAP, 2009). The TAP Training Program is being developed as a structured training model with broad based team applicability.

Results:
This presentation will outline the model, customizable for small group and e-learning applications. Model components include: exploration of the TAP framework- management and communication structures, as well as tools necessary to develop an expanded view of the knowledge, skills, and attitudes present in TAP. This model draws heavily upon the current literature on collaborative competencies in interprofessional teams and situates them within a dynamic working team where they’ve actualized for more than two decades. Current concepts in successful business models are also applied. Program evaluation strategies have been included to address pre/post quantitative surveys and qualitative methods.

Conclusion:
The Arthritis Program -Interprofessional Training Program is completed. It will be marketed as a training program that uses inflammatory arthritis as the dynamic example to illustrate the workings of the TAP model of care. This model has wide applicability in all areas of chronic disease. It uses online learning modules and the use of virtual classrooms which are strategies that are only recently making their way to health care applications.
Profile of Interprofessional Rheumatology Care in Canada: A Needs Assessment Leads Development of an Interprofessional Patient Centred Collaborative (IPC) Training Program

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Objective:
There is growing consensus that IPC practice improves patient care, access to care, patient safety and satisfaction. The purpose of this study was to assess the current models of practice, knowledge and skills, attitudes and readiness for IPC practice, challenges and barriers among rheumatology professionals.

Methods:
A convenience sample of 151 professionals participated. The survey included demographics, current and dream models of care, knowledge and skills, attitudes towards health teams, knowledge/previous exposure to IPC training, readiness for IPC, challenges/barriers to IPC. Analysis: Descriptive summaries for each variable. ANOVA was used to test for differences across Attitudes Towards Health Care Teams (ATHCT) Scale (significance p< 0.05).

Results:
81% were between 30-59 years. 76% were female. Highest professional designation among respondents was: MD (43%), PT/OT (30%), advanced practitioner (PT/OT/RN) (15%) and other (13%, RN/pharmacist/researcher). Practice setting included: ambulatory (15%), community (22%), hospital (32%) and mixed (32%). Most respondents were from Ontario (52%) & British Columbia (27%) with others from Alberta, New Brunswick, Newfoundland and Quebec. 81% reported being a member of a rheumatology health care team. 57% had not received IPC training. Self-rated knowledge and skill level (1=not very much to 7=very much) for using outcome measures, adult education principles and IPC principles was lower (50% rated < 5) and inflammatory arthritis pathology, MSK exam, blood work analysis and triage skills was higher (>70% rated > 5). The mean score on ATHCT Subscales: Quality of Care/Process (QP) was 52/70 (70= highest perception of quality of care delivered by health care teams) and Physician Centrality (PC) was 15/30 (30=highest perception of physician authority/control over team). Differences by profession: MD had lower QP scores than non-MD (p< 0.05); Mean PC scores were higher for MD (18) vs therapist/RN/pharmacist (14) vs advanced practitioner (11) (p< 0.05). Stages of readiness for IPC practice: 23% precontemplation stage, 40% contemplation stage, 5% prepared for action stage and 31% action stage.

Conclusion:
There are many diverse models of rheumatology care in Canada. Teams were at varying stages of readiness for IPC practice. Only 30% felt their team was currently working in an IPC practice model. Respondents identified a greater need for IPC practice training than for clinical skills training related to rheumatology practice. MDs had higher attitudes of their authority in teams and control over information. These findings will help to develop the framework and content for an IPC training program.
Downregulation Of Citrullination In Vitro By DMARDs Used Alone Or In Combinations: Potentiating And Antagonistic Mechanisms.

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Objective:
Cellular citrullinated (cit) proteins are by-products of inflammation but they become cit-antigens (e.g. cit-vimentin or the Sa antigen) only in rheumatoid arthritis (RA). Pharmacologically heterogeneous DMARDs used in combination or added to biologics are more efficient then any drug given alone. Our work explores the in vitro effect of DMARDs on cit-protein and Sa/cit-antigen production as a unifying mode of action.

Methods:
We used the ECV304 cells which have peptidylarginine deiminase (PAD) activity at all times and UMR106 cells with PAD activity only at confluence. They were treated with increasing therapeutic doses of methotrexate (MTX), sulfasalazine (SSZ), azathioprine (AZA), hydroxychloroquine (HCQ) and prednisone (Pred) used alone or in combinations. The qualitative and semi-quantitative effect on cit-proteins and cit-antigens production was estimated by western blot (WB) using a rabbit anti-chemically modified citrulline antiserum and polyvalent RA sera (anti-Sa), respectively. Quantitative PAD activity was also measured colorimetrically using the conversion of citrullinated BAEE, a PAD synthetic substrate to its ureido-derivative.

Results:
MTX treatment of UMR106 showed a dose dependent decrease in PAD activity with significantly less production of both cit-proteins and cit-antigens. That effect could be prevented by folinic acid and was not influenced by adenosine receptors. At the same low dosage, MTX had no effect on ECV304. SSZ and AZA decreased the amount of PAD activity under all conditions except in confluent ECV304 assays. Pred had no effect under any conditions. In contrast, HCQ decreased PAD activity under all conditions tested. The amount of PAD2 protein, the isoenzyme present in both cell lines and in articular tissues like synovium, muscle, cartilage and, bone was influenced quantitatively by SSZ, AZA and HCQ treatments but not by MTX or Pred treatments. Combination treatment with these DMARDs at sub-optimal concentrations showed that addition of HCQ 10µM had the greatest inhibition of citrullination of all the DMARD combinations studied.

Conclusion:
The data presented support the hypothesis that in RA, DMARDs combine in various ways to down regulate the production of cit-proteins/antigens during inflammation. That occurs either via decreasing the quantity of PAD2 or blocking its activity. In those RA patients with anti-Sa antibodies, DMARDs will thus decrease the antigenic input into the disease specific auto-immune synapse. The data support a common but variable explanation for the good therapeutic results obtained empirically with DMARDs.
Juvenile Fibromyalgia: Greatest Areas of Impairment, and Impact of an Aerobic Exercise Program

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Objective:
Patients with juvenile fibromyalgia (FM) have generalized MSK pain, fatigue, and poor sleep, as well as high rates of school absence and functional disability. This study determines which areas of functioning are most impaired in children with FM, as well as the effect of an aerobic exercise program on ability to do specific activities.

Methods:
FM patients aged 8-18 were asked to complete the FM Impact Questionnaire and Functional Status and Symptom Questionnaire while participating in a randomized, 12-week trial of either aerobic exercise or control (qigong) (Ref 1). Data were collected before and after the intervention, and included measures of daily function (e.g. school attendance), physical function (e.g. running, sports), and social function (e.g. visiting friends), as well as FM symptoms. A repeated measures analysis of variance was used to compare the rates of change in ability between the groups after the exercise intervention.

Results:
Thirty patients participated in the study, and 24 patients completed the program (13 in aerobic and 11 in qigong group). At baseline, a minority of patients reported difficulties with daily function (homework 11%, chores 23%) and social function (31%); whereas, on average, 56% reported difficulty with physical function. Specific activities associated with great difficulty or inability included playing sports after school (43%), running long distances (35%), and participating in gym class (25%). The most prominent symptom during physical activities was pain. Subjects also reported difficulty with waking up for school and attending overnight camp (37% and 26% respectively), mostly due to fatigue and sleep difficulties. After the exercise intervention, subjects in both groups showed improvement in function. However, when compared with subjects in the qigong group, those in the aerobic group demonstrated a significantly greater improvement in ability to run long distances (P=0.023), walk in the mall (P=0.064), attend school every day (P=0.036), and complete homework (P=0.003).

Conclusion:
Juvenile FM causes significant difficulties in function, mostly seen in physical activities and activities affected by poor sleep. Daily and social activities tend to be relatively spared. The most prominent symptoms experienced are pain, fatigue, and sleep difficulties. Aerobic exercise was found to have greatest impact in improving physical and daily functions but, in our sample, did not affect social function.

Estimating the Incidence of Uveitis for Patients With Ankylosing Spondylitis: A Population-Based Approach

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Objective:
Noninfectious uveitis is the most common extra-articular manifestation of ankylosing spondylitis (AS), with a reported lifetime prevalence exceeding 30%. Because the current prevalence estimates were based on self-report, examination, or chart review and lacked standardized definitions of uveitis, we aimed to calculate accurate, population-based estimates of the incidence of uveitis due to AS by comparing its incidence in patients with AS vs. the general population.

Methods:
We designed a retrospective cohort study using the Régie de l’Assurance Maladie du Québec (RAMQ) databases, which contain population-based, longitudinal, patient-level, physician-billing data. These data include records of patient sociodemographic data and physician services delivered in outpatient clinics, offices, and hospitals. Entry into the AS cohort was defined at first physician diagnosis (ICD-9 720.0) between 1998 and 2006, with no such diagnosis in the 2 preceding years. A comparison cohort was generated using a 1% random sample of individuals from Québec without AS (no ICD-9 720.0 diagnosis within the period). Incident cases of noninfectious uveitis were identified using ICD-9 codes 363.2, 363.3, or 364.0. Cohort members were censored at RAMQ plan deregistration or at the end of the study period (December 31, 2006). A standardized incidence ratio (SIR) was calculated comparing the 10-year incidence rate of uveitis in persons with AS vs. without AS, adjusted for age and sex.

Results:
The sample included 7,663 patients with AS (Québec 2006 population: 7,631,552); 54.5% were male. The crude 10-year incidence rate of uveitis in the AS population was 374.0/10,000 persons compared with 21.1/10,000 persons in the non-AS population. The SIR for the development of uveitis during the study period was 22.7 for those with AS vs. those without AS.

Conclusion:
Noninfectious uveitis is much more common for patients with AS than for the general population without AS; patients with AS have a >20-fold increased risk of developing uveitis. This robust, population-based approach to estimating the incidence of uveitis could be incorporated into AS models. Because uveitis imposes a cost, failing to incorporate uveitis incidence in AS models may underestimate the true burden of illness.
Frequency and Cost of Hip and/or Knee Replacement Surgery for Canadian Patients With Rheumatoid Arthritis: A Population-Based Approach

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Objective:
Clinic- and hospital-based studies have estimated that 7–27% of patients with rheumatoid arthritis (RA) require total joint replacement surgery. Because variable follow-up periods and/or small sample sizes limit the generalizability of these estimates, we used a population-based database to estimate the frequency, timing, and cost of joint replacements for patients with RA.

Methods:
A retrospective cohort study was conducted using the population-based, longitudinal Régie de l’Assurance Maladie du Québec patient-level, physician-billing, provincial database. The incident RA cohort included continually registered patients with \( \geq 2 \) physician ICD-9 diagnoses of RA (714.0, 714.1, or 714.2) from 1998 to 2007, with first RA diagnosis in 1998. Total joint replacements were classified according to the Canadian Classification of Diagnostic, Therapeutic, and Surgical Procedures codes 93.5 (hip) and 93.41 (knee), and Canadian Classification of Health Interventions codes 1.VA.53 (hip) and 1.VG.53 (knee). Only 1 hip or knee replacement per patient was included in the analysis. Direct hospitalization costs were estimated using Case Mix Group resource use and cost data from the Canadian Institute for Health Information.

Results:
The incident cohort included 3,340 patients; 70.9% were women and median age at entry was 52 years. Nine percent of patients had \( \geq 1 \) total joint replacement, 5.4% had total knee replacement, 4.3% had total hip replacement, and 0.7% had both total hip and total knee replacements. The mean and median times from first diagnosis of RA/cohort entry to surgery were: 3.7 and 3.2 years (interquartile range [IQR], 1.3–5.8), respectively, for total hip replacement and 4.1 and 4.2 years (IQR, 1.7–6.0), respectively, for total knee replacement. Hip and knee replacement surgeries were estimated to cost approximately \$3.18 million in 2009 Canadian dollars, averaging \$9,370 per knee replacement and \$10,367 per hip replacement.

Conclusion:
Total hip and/or knee replacements contribute substantially to the burden of RA. In this large, longitudinal, population-based study, almost 1 in 10 patients with RA required joint replacement surgery, with 25% of these surgeries occurring within the first 2 years after diagnosis.
New Onset of Two Distinct Skin Lesions in a Patient with Rheumatoid Arthritis being treated with an Anti-TNF therapy

Ranjani Somayaji (University of Calgary, Calgary); Regine Mydlarski (University of Calgary, Calgary); Liam Martin (University of Calgary, Calgary)

Case Report:
Objective: Our objective is to report on the case of a woman who develops psoriasis and cutaneous lupus erythematosus concurrently while on adalimumab therapy for rheumatoid arthritis. Methods: A detailed chart review was done to obtain clinical information to include patient demographics, past medical history and previous therapies. Results obtained: A 77 year old woman with a 40 year history of sero-positive rheumatoid arthritis who was being treated with adalimumab presented with a 4 week history of a skin rash involving her chest, back and her extremities. She had no previous of skin rashes. On examination she had 2 different rashes: on her back and upper extremities she had erythematous well-demarcated scaly plaques consistent with psoriasis; on her lower extremities she had erythematous annular edematous non-scaly plaques. Both rashes had increased in severity since they started. She was assessed by a Dermatologist. She had a biopsy of the rash on her legs which revealed changes consistent with cutaneous lupus. The adalimumab was discontinued and she was treated with prednisone, 60 mg daily initially. Both skin rashes improved with the prednisone therapy and were resolved after 6 months. Conclusions: Tumor necrosis factor-alpha (TNF) inhibitors such as adalimumab are increasingly used in treatment of rheumatoid arthritis. There are many reports of the occurrence of skin rashes in patients treated with these agents. These include case reports of induction of psoriatic and systemic lupus erythematosus associated rashes in patients with no history of either disease. However, to the best of our knowledge, this is the first report of the concurrent development of both types of skin rashes in a patient being treated with adalimumab therapy. One postulated mechanism suggested for the development of psoriasis is that anti-TNF therapies cause Th1 cell migration away from joints towards the skin. There is also an increased expression of interferon-alpha when TNF levels are reduced. These changes can result in the development of psoriatic lesion on susceptible individuals. The underlying mechanism causing cutaneous lupus erythematosus is unclear.
Long-Term Safety and Tolerability of Tocilizumab in Patients with a Mean Treatment Duration of 2.4 Years

Ronald Van vollenhoven (Karolinska Institute, Stockholm); Tim Mccarthy (Manitoba Clinic, Winnipeg); Daniel Siri (CAICI Institute, Rosario)

Objective:
To assess the longer-term safety of tocilizumab (TCZ) as monotherapy or with DMARDs in patients (pts) with rheumatoid arthritis (RA).

Methods:
The study included all pts who received ≥1 dose of TCZ in 24-wk, phase 3 clinical trials (OPTION, AMBITION, RADIATE, TOWARD), in a phase 3 clinical trial (LITHE), in a phase 1 study, or in ongoing, open-label extension studies (GROWTH95, GROWTH96). Safety data were pooled and analyzed from the time of initial TCZ exposure to cutoff.

Results:
TCZ was administered to 4009 pts, with mean treatment duration 2.4 years, and total treatment exposure 9414 pt-years (PY). Rate of withdrawals due to adverse events (AEs) was 5.8/100 PY and was driven by elevated liver enzyme levels, infections, and benign and malignant neoplasms. Overall rate/100 PY of serious AEs was 14.91, of serious infections was 4.7, of deaths was 0.53, and of deaths from infection was 0.13. Rates/100 PY for stomach/duodenum, small intestine, appendix, and large intestine were 0.01, 0.03, 0.02, and 0.19, respectively. Malignancies occurred at an overall rate of 1.16/100 PY, without excess of any one type. Overall rates/100 PY for MI and stroke were 0.25 and 0.19, respectively, and did not increase with TCZ exposure. Total cholesterol, low-density lipoprotein, high-density lipoprotein, and triglyceride levels increased at wk 6 and remained relatively stable over time; 313 (7.8%) pts initiating lipid-lowering therapy while on TCZ generally responded to treatment without complications. Incidences of ALT and AST elevations >3× upper limit of normal were 3.6% and 1.4%, respectively, during the first 24 weeks of treatment, with rates not increasing over time. Transaminase elevations were not associated with clinically apparent hepatitis or hepatic dysfunction.

Conclusion:
The study results show that no new safety signals have emerged with longer-term exposure to TCZ. Transaminase elevations in this analysis were not associated with clinically important events. During longer-term treatment with TCZ (median duration > 2.5 years), risks for AEs and serious AEs were stable over time, and laboratory changes could be effectively managed. These results support a favorable benefit-risk ratio for TCZ in pts with moderate to severe RA.
Quality Assurance Study of the Use of Preventative Therapies in Glucocorticoid Induced Osteoporosis (GIOP) in Early Inflammatory Arthritis: Results from the CATCH Cohort

Emily Mckeown (University of Toronto, London); Janet Pope (University of Western Ontario, London); Faye De leon (McMaster University, London); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket); Carol Hitchon (University of Manitoba, Winnipeg); Gilles Boire (Sherbrooke University, Sherbrooke); Vivian Bykerk (Mount Sinai Hospital, Toronto)

Objective:
This study characterizes steroid use and compliance with glucocorticoid induced osteoporosis (GIOP) guidelines within a large early inflammatory arthritis (IA) cohort.

Methods:
Using the Canadian Arthritis Cohort Database (CATCH), patients with IA on glucocorticoids [oral or intramuscular (IM)] were identified. Chronic steroid exposure was defined as using glucocorticoids for two consecutive clinic visits (at least 90 days apart). The primary outcome was the proportion of patients receiving calcium, vitamin D or a bisphosphonate among chronic users of oral glucocorticoids. Secondary analysis was done to determine which factors were associated with use of preventative therapies.

Results:
655 patients were in the CATCH database, where 338 (51%) were identified as glucocorticoid users (of whom 51% were users of oral prednisone while 40% were using IM, and 9% on both). Chronic users (CU) data compared to non-users (NU) had similar age (56 years, SD=15 vs. 52 years, SD=15, p=0.64); similar proportion of females (67% vs. 68%) and rheumatoid factor positivity (86%, RF mean 75 IU/mL in CU vs. 85%, RF mean 132 IU/mL in NU, p =0.04); DAS (CRP) was 4.56, SD=2.0 in CU vs. 4.16, SD=2.19 in NU, p=0.13). Mean oral daily dose of prednisone was 6 mg (SD =7.5) among those on chronic oral steroids (N=72). Approximately half (52%) on chronic oral steroids were treated with calcium, 47% with vitamin D, 43% with both and 17% were taking a bisphosphonate. Treatment rates were similar among patients on steroids for one year compared to those treated for at least 90 days, so longer duration of steroids did not increase prophylaxis. There were no significant differences in use of calcium, vitamin D or bisphosphonate among females compared to males (OR1.07, CI 0.34 – 3.39), or among post-menopausal females (OR 1.26, CI 0.39 – 4.07). Women with a history of hormone treatment and smokers had no significant increase in being treated (OR 1.39, 95% CI 0.40-4.89 and OR 1.69, 95% CI 0.46-6.13).

Conclusion:
Glucocorticoid therapy is frequently used in early IA. The use of calcium, vitamin D or a bisphosphonate was low among chronic glucocorticoid users and illustrates the need for due diligence to prevent GIOP. Even with longer duration of steroids, prophylaxis rates did not increase nor in high
The Proportion of Patients with Work Disability (WD) in Early Inflammatory Arthritis: Results from the Canadian Early Arthritis Cohort (CATCH) Cohort

Lauren Mussen (University of Western Ontario, London); Vivian Bykerk (Mount Sinai Hospital, Toronto); Faye De leon (McMaster University, London); Janet Pope (University of Western Ontario, London)

Objective:
To determine the prevalence of WD in early RA (ERA) and early inflammatory arthritis (EIA) in the CATCH study.

Methods:
Data from 655 patients were collected from the CATCH study, a multi-centre observational prospective cohort of patients with EIA; 69% have RA (CRA criteria). At baseline patients were asked about employment status with possible answers including employed, retired, unemployed, on sick leave (SL), work disabled, on maternity leave, in school or a homemaker. The Dictionary of Occupational Titles (DOT) was used to determine the physical demands of each type of employment.

Results:
54% were employed, 22% retired, and 6% reported WD or SL, with the remaining 18% homemakers, students or on maternity leave. Patients who were neither employed nor WD/SL were excluded leaving N=391 (351 employed, 40 WD). Of the 351 employed, mean age (SE) was 47 (0.6); 74% female; 57% positive RF; 68% met ACR criteria; and DAS-CRP, TJC (0-28) and SJC (0-28) were 4.7 (0.1), 8.3 (0.4) and 7.3 (0.4). In the WD group (N=40) mean age (SE) was 47 (2.3); 68% female; 58% positive RF; 80% met ACR criteria; and DAS-CRP, TJC (0-28) and SJC (0-28) were 5.4 (0.2), 11.9 (1.1) and 8.2 (1.0). 86% of the employed had jobs with sedentary or light physical demands. Patients were further classified according to ACR criteria for ERA and those who did not meet them (designated as EIA). WD/SL was not different in EIA vs. ERA (3.9% vs. 7.1%, p=0.1). Factors associated with WD/SL in the overall group of 391 included TJC, DAS28 and SF-12, whereas SJC, RF and anti-CCP did not differ significantly between the WD/SL and employed. Factors associated with WD in subgroup analysis were similar to the group overall except DAS-28, which differed significantly between employed and ERA.

Conclusion:
WD is low at entry into an ERA cohort and there is a chance to intervene effectively early to prevent WD from occurring. As in established RA, WD was related to patient factors, HAQ, damage and disease activity. In patients classified as both ERA and EIA, WD is related to TJC, DAS-28 and SF-12, and elevation in these parameters may indicate a point at which intervention may prevent WD. Although p=NS, there appears to be more baseline WD in those who met ERA criteria and as the cohort grows, this may become significant.
Early Optimal Doses of Parenteral Methotrexate Increases Sustained Remission Vs. Other Therapeutic Strategies in Patients From a Nationwide Early Rheumatoid Arthritis (ERA) Cohort

Vivian Bykerk (Mount Sinai Hospital, Toronto); David Rowe (Saba University School of Medicine, Stouffville); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket); Faye Deleon (McMaster University, London); Janet Pope (University of Western Ontario, London); CATCH Scientific advisory committee (Canadian Arthritis Cohort, Toronto)

Objective:
Previous studies established the value of early diagnosis and intervention in patients presenting with Early Rheumatoid Arthritis (ERA). There appears to be growing support for parenteral administration of MTX (pMTX) at optimal doses (> = 20 mg sc weekly), however there is still no clear recommendation for standard route and dosage. The objective of this study was to compare effectiveness of pMTX (> = 20mg) with other treatment strategies in achieving the following outcomes: any visit with 1) DAS-defined remission or 2) LDAS (DAS < 3.2); and 3) "sustained remission" as defined by 2 consecutive visits with DAS-defined remission.

Methods:
Patients were recruited to the Canadian early Arthritis Cohort (CATCH) (a multi-centre observational prospective "real world" cohort of patients with EIA). Patients selected for analysis (n=358/600) had baseline DAS28 scores > 2.6 and > = 1 DAS28 score at 3,6,9 and 12 months. For nonparametric analysis, patients were stratified into those receiving pMTX (> = 20 mg (n=85) within 100 days (the first protocol required visit) of baseline -vs. those receiving all other treatment regimens, including other doses and routes of MTX, other DMARDs, biologics, oral and parenteral steroids (n = 273). Each group was assessed for achievement of the 3 discussed outcomes within the 1st 12 months. Binary logistic regression models for each outcome evaluated multiple treatment and patient variables.

Results:
At baseline patients on pMTX were more likely to be seropositive(p < 0.01), have higher DAS scores(p < 0.001) and exhibit erosions on x-ray(p = 0.01). DMARD use increased by 12 months in the non-pMTX group(p < 0.05). Logistic regression models found early doses of pMTX (> = 20 mg (n=85) within 100 days (the first protocol required visit) of baseline -vs. those receiving all other treatment regimens, including other doses and routes of MTX, other DMARDs, biologics, oral and parenteral steroids (n = 273). Each group was assessed for achievement of the 3 discussed outcomes within the 1st 12 months. Binary logistic regression models for each outcome evaluated multiple treatment and patient variables.

Conclusion:
The cohort given early pMTX (> = 20 mg had more clinical predictors of persistence and x-ray progression at baseline. Despite this, they were still able to achieve higher rates of remission and LDAS, although not at the p< 0.05 level. To address possible confounders found with a multifaceted, more aggressive treatment strategy in patients presenting with more active disease, binary logistic regression analysis confirmed nonparametric results, specifically for pMTX (> = 20 mg predicting sustained remission. The data are compelling that pMTX (> = 20 mg should be considered as 1st line therapy in ERA.
Inflammatory Arthritis Education Program Outcomes: Comparing Sustainability of Clinical Outcomes Following Transition from a Three week Program to a Two Week Program

David Rowe (Saba University School of Medicine, Stouffville); Lorna Bain (Southlake Regional Health Centre, Newmarket); Carolyn Bornstein (Southlake Regional Health Centre, Newmarket); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket)

Objective:
The Arthritis Program (TAP) at Southlake Regional Health Centre in Newmarket, Ontario offers an interprofessional, patient-centred, patient education program for Inflammatory Arthritis. Originally designed as twelve 3.5-hour classes over a 3 week period, the program has recently been reorganized into ten 4-hour classes over 2 weeks in an effort to make this valuable program more accessible to participants. The objective of this study was to evaluate clinical outcomes between the two class designs in order to evaluate if there is sustainable clinical benefit with respect to functional outcomes and acquired knowledge.

Methods:
Data was collected from 3-week classes run September to December, 2008 (n=50) and January to June, 2009 (n=112). Clinical outcome measures between 2-wk and 3-wk class participants were evaluated at baseline (class day 1), immediately post-class (2 vs. 3 weeks) and 6 months after baseline. Participants completed Inflammatory Arthritis Knowledge Questionnaires and were clinically examined at each stage. Changes in Knowledge, HAQ, Active Joint Count, and CDAI were analyzed at 6 months vs. baseline. Knowledge scores were scored out of 100. HAQ changes of -0.2 and -0.4 were assessed. Active Joint Count < 5 at 6 months (from >5 at baseline) was recorded. Differences in CDAI score changes at 6 months between the 2-wk and 3-wk class are being actively evaluated – a score reduction of >/=6.5 will be considered clinically significant. Student t test and Chi square analysis were used.

Results:
Mean knowledge scores for 2- and 3-wk class participants were 65 (n=97) vs. 68.5 (n=42), respectively, at baseline, and 80.5 (n=9) vs. 80.2 (n=16) at 6 months (p=0.96). At 6 months 35.3% of 2-wk class participants achieved a HAQ reduction of >0.2 vs. 38.5% of 3-wk class participants (p = 0.86). A HAQ reduction of >0.4 was seen in 30.7% of 3-wk class participants (n=13) vs. 47.1% of 2-wk class participants (n=17), (p=0.37). Only 7 two-wk and 10 three-wk class participants were eligible for analysis of Active Joint Count at 6 months, however data is still being collected. Likewise, CDAI scores at baseline and 6 months, along with MCID tallies between 2- and 3-wk class participants, will be reported.

Conclusion:
Currently there appear to be no differences in clinical outcomes at 6 months between 2- vs. 3-week class participants. Preliminary results will be strengthened with higher n values, reportable at time of conference. Still, early results suggest equal sustainable clinical benefit from the new 2-week Inflammatory Arthritis education program compared to the previous 3-week model.
Heterozygous mutation in LRP5 gene is associated with osteoporosis, metaphyseal dysplasia and maxillary hypoplasia in two sisters

Laëtitia Michou (Laval University and CHUQ-CHUL Research Centre, Québec); Francis Glorieux (McGill University and Hôpital Shriners pour Enfant, Montréal); Jacques Brown (Laval University and CHUQ-CHUL Research Centre, Québec)

Case Report:
Background: Pediatric primary osteoporosis is usually due to osteogenesis imperfecta or juvenile idiopathic osteoporosis. The association between a rare autosomal dominant disorder in two sisters and the occurrence of osteoporosis with fractures during childhood without any visual impairment, but with metaphyseal dysplasia, is presented. Patients and methods: One sister experienced a right shoulder fracture at 10 years of age and at 16 years of age had low bone mineral density (BMD) with cortical thinning and depression of osteoblastic activity as evidenced by transiliac bone biopsy. Up to 20 years of age she possessed delayed secondary dentition with dystrophic yellowish teeth. The other sister experienced a left tibia fracture at five years of age, a second one at 12 years of age, as well as a finger and toe fracture. At 14 years of age she had a low BMD and transiliac bone biopsy that revealed a similar pathology to her sister. Her teeth were small-for-age with hypoplastic enamel and she had a dental malocclusion secondary to maxillary hypoplasia. X-rays in both sisters showed parietal osteolytic lesions, maxillary hypoplasia, bilateral metaphyseal flare of the distal femur and proximal humerus, platyspondyly and an enlarged pelvis. Similar phenotypes were observed in their mother, at least one of her sisters, one of her brothers and her father. Some of the affected family also possessed shortness of metacarpal 5 and/or the middle phalanx of fingers 2 and 5. Genomic DNA was extracted from blood samples and the coding and flanking sequences of all the exons of the COL1A1 and COL1A2 genes and the exon 3 of the LRP5 gene were PCR amplified before sequencing.

Results: No DNA mutations were detected in the COL1A1 and COL1A2 genes. Both sisters carried a heterozygous missense mutation of the LRP5 gene, a 518 C->T substitution which leads to a T173M mutation.

Conclusions: This investigation uncovered an autosomal dominant disorder characterized by osteoporosis with fractures during childhood, metaphyseal dysplasia and maxillary hypoplasia associated with a T173M heterozygous mutation in the LRP5 gene. This mutation was previously reported in a British woman with abnormal retinal vasculature and retinal folds with an unknown skeletal phenotype, as well as in a 15-year-old Finnish boy who experienced three low-energy fractures despite normal bone mineral density. Interestingly, mice with a targeted disruption of LRP5 develop a low bone mass phenotype with a delay in osteogenesis leading to a similar phenotype as reported here.
Pregnancy and Rheumatoid Arthritis in First Nations

Gabriela Montes aldana (University of Manitoba, Winnipeg); Irene Smolik (University of Manitoba, RR149-800 Sherbrook St.); Hani El-gabalawy (University of Manitoba, Winnipeg)

Objective:
This secondary data analysis explores the potential association between pregnancy history and joint symptoms in First Nations RA patients (RA-pro) and their first-degree relatives (FDR) as part of a longitudinal study entitled “Early Identification of Rheumatoid Arthritis in First Nations.”

Methods:
First Nations RA-pro and FDR were recruited at the Arthritis Centre, University of Manitoba, and at rheumatology clinics held in two northern FN communities. All participants were asked to complete a study questionnaire that captured socio-demographic data, pregnancy outcomes, and RA-like joint symptoms for FDR. The current study analyzed baseline data collected between September 2005 and May 2009. SPSS version 16.0 was used to examine the association between previous pregnancy and the presence of joint symptoms in the FDR using parametric and non-parametric comparisons.

Results:
Study population: RA-pro n=98; FDR n=167. Of the 1,011 reported pregnancies, 75% ended in live births and 14% ended in miscarriages. Eighty-eight percent of females reported having been pregnant at least once, with 52% of all female participants having been pregnant at least 4 times. Forty-seven percent of the participants reported having their first pregnancy at 18 years of age or younger (range 12-40 years). Joint symptoms were common in FDR and 51% experienced pain, 35% experienced subjective swelling and 40% experienced morning stiffness in their hands. Univariate analysis indicated that women who had been pregnant had a higher likelihood of having pain, swelling and stiffness in hands, although the confounding effects of age could not be ruled out.

Conclusion:
High pregnancy rates were reported in both RA-pro and FDR. The data suggest a high prevalence of RA-like joint pain and stiffness in FDR, indicating that a proportion of this population may be experiencing the early stages of inflammatory arthritis. Prior pregnancy may increase the risk of joint symptoms in FDR, but the confounding effect of age cannot be ruled out in the current analysis.
The Business Case for Managing Arthritis in Canada

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Objective:
ACAP, a coalition of over 30 arthritis stakeholder organizations in Canada, is working to establish the ‘business case’ to support the need for enhanced governmental attention to arthritis. The business case will model the current and future burden of rheumatoid arthritis (RA) and osteoarthritis (OA) in Canada and the impact of specific interventions in reducing this burden.

Methods:
A Life at Risk® simulation platform was used to model the estimates of RA/OA incidence, prevalence, mortality rates, and economics (direct and indirect costs) associated with ‘current care’ versus specific targeted interventions over a 30-year period (2010-2040). Arthritis interventions were identified through a review of the published literature and a consensus process with arthritis subject matter experts (SMEs) and stakeholders. Four intervention scenarios were identified and evaluated: 1) Reduction in Obesity (BMI>30); 2) Total Joint Replacement Surgery for OA; 3) Effective Pain Management for OA; 4) RA DMARD and Biologic Response Modifier (BRMs) Treatment. All relevant data components, including those from Canadian population-based studies, cohort and administrative billing databases, and published literature, were contributed or recommended by the SMEs.

Results:
Simulations show that an estimated 10.4 million people will be living with OA and more than half a million with RA by 2040. The main driving force is the aging Canadian population and the future obesity trends. The models project that over the next 30 years, approximately 43% of Canadians will be over the ages of 50 and the number of obese Canadians will almost double. If the current model of care is continued, the total cumulative economic burden associated with OA and RA is estimated to be $667.2 billion and $127.2 billion (2010 present value dollars) by 2040, respectively. All four interventions, including a 50% reduction (over 30 years) in the number of obese Canadians without OA, provision of hip and knee TJR and effective pain management strategies to OA patients, and early treatment and access to DMARDs and BRMs for RA patients, demonstrate significant direct and indirect cost savings both in the short (10-year) and long-term (30-year).

Conclusion:
Arthritis places a significant health and economic burden on Canadians. Enhanced funding is needed to ensure that people living with arthritis receive cost saving, timely and effective interventions to reduce the incidence and associated disability of arthritis. Cost estimates and sensitivity analyses around these estimates will be presented using a range around our key assumptions.
Case Series: Atypical Fractures of the Femoral Diaphysis in Patients on Long Term Bisphosphonate Therapy.

Manisha Mulgund (McMaster University, Ancaster); Mark Matsos (Mcmaster University, Hamilton); Ameen Patel (Mcmaster University, Hamilton); Jonathan Adachi (McMaster University, Hamilton)

Case Report:
Objective: We discuss a case series of five patients on long term bisphosphonate therapy who presented to our clinic within the last 2 years with low energy femoral fractures. Methods: All patients seen in our clinic since April 2007 on long term bisphosphonate therapy with evidence of low energy femoral fracture were included. Data Extraction included: demographics, duration of bisphosphonate therapy, type of fracture, mechanism of fracture, pain prior to fracture, evidence of bilateral stress reaction on x-ray/MRI/bone scan, medical history, fracture history, family history, medication list and laboratory investigations. X-rays of femur were analyzed for the following: bone diameter at lesser trochanter (LTD in mm), Medial and lateral cortical thickness at distance of 2 LTD’s below the lesser trochanter; Bone diameter at 2 LTD’s level; Ratio of maximum cortical thickness to total bone diameter at 2 LTD’s below the lesser trochanter. Results: All patients were female with average age of 67 years. Four of the five patients were on alendronate for an average of 9.5 years. One patient was intermittently on bisphosphonate therapy (alendronate/etidronate) for four years prior to fracture. Two patients had prior personal fracture history and two patients had a positive family history of osteoporotic fracture. Three patients were exposed to corticosteroids (inhaler/PO) in the previous 3 months prior to fracture, two patients were on PPI's, three patients had prior estrogens treatment and two patients had a positive smoking history. Two of five patients had bilateral femoral fracture. Two of five patients had spontaneous fracture, while three of five patients had an associated fall from standing height. Two patients had antecedent thigh pain leading up to the fracture. Cortical thickness was increased uniformly in all patients with an average LTD of 36.83mm and the ratio of largest cortical thickness/diameter at 2 LTD =0.319. These figures are higher than those seen in a patient population with low energy femoral fractures reported from our institution in another case series, in whom the LTD was 35.59+/−3.54 and the ratio was 0.267+/−0.042. Conclusions: Long term bisphosphonate therapy for osteoporosis may be associated with risk of low energy femoral fractures. There is a higher likelihood of unusual cortical thickening and bilateral stress reaction in these patients. Subtle changes on X-ray and bone scan exist that may help identify those at risk for fracture.
Silk Route Syndrome in Arizona

Vivek Nagaraja (University of Arizona /University Physicians Healt, tucson); Naktal Hamoud (University of Arizona/ University Physicians Healt, Tucson); Anita Narayanan (University Medical Centre, Tucson); Jeffrey Lisse (University Medical Center, Tucson, Tucson); Merilyn Goldschmid (University of Arizona/ University Physicians Healt, Tucson)

Case Report:
We present two cases of Neuro-Behcet's disease (NBD). Both patients were young females (aged 30 and 35 years) and Caucasians. The first patient was diagnosed with Behcets disease (BD) at the age of 26 years and had multi-systemic manifestations. She developed aseptic meningoencephalitis with seizures, cranial nerve abnormalities, personality changes and was diagnosed with NBD. She was on several treatment regimens, both immunosuppresive and biologic agents without much benefit. Eventually she had improvement in her symptoms with a combination of Rituximab and Azathioprine. The second patient was diagnosed with BD at the age of 25 years and had several manifestations. She developed headaches, partial complex seizures with olfactory hallucinations, personality changes and was diagnosed with NBD. She endured many exacerbations especially when immunosuppressive medicines were weaned. At presentation, she was on Methotrexate, Azathioprine, Lamotrigine and Prednisone. She was previously tried on Infliximab with minimal relief. Behcet's disease (BD) was first described by Hippocrates. However, it was brought to the attention of the modern medical community by a Turkish dermatologist, Hulusi Behcet. BD is more common along the ancient silk route (especially Mediterranean countries). It is very rare in Northern American (1:100000) and Northern European countries. Neurological involvement can be seen in only 5-10% of patients and is one of the serious causes of long-term morbidity and mortality. NBD has been reported 2.8 times more commonly in men than women. The mean duration between the onset of BD and development of NBD has been reported to be 3-6 years. There are two categories of NBD namely parenchymal form and non-parenchymal form (usually vascular complications commonly involving veins and sometimes arteries). Sub-acute meningoencephalitis accounts for 75% of cases in parenchymal NBD. Epilepsy has been reported as a manifestation of NBD in 2-2.5% of patients in large case series. Generalized seizures are the pre-dominant type. NBD is a clinical diagnosis and a diagnosis of exclusion. MRI and MRA are sensitive imaging tests. The symptoms of NBD exacerbate and remit and gradually cause irreversible disability. In the terminal stage, dementia becomes evident in about 30 percent of affected patients. A combination of mild immunosuppressive agents and TNF antagonists have been reported to relieve disease flare-ups. Neuro-Behcet disease manifesting as meningoencephalitis and partial complex seizures in Caucasian females is extremely rare. There have been no case reports about the use of rituximab in treatment of NBD.
Retreatment with Rituximab (RTX) Based On a Treatment to Target (TT) Approach Provides Better Disease Control than Treatment as Needed (PRN) in Patients with Rheumatoid Arthritis (RA)

Paul Emery (Leeds General Infirmary, Leeds); Wojciech Olszynski (N/A, Saskatoon); Philip Mease (Seattle Rheumatology Associates, Seattle)

Objective:
To assess differences in efficacy and safety profiles of two treatment (tx) strategies employed in clinical trials of RTX in RA, to help determine an optimal tx regimen.

Methods:
RA pts with an inadequate response to methotrexate (MTX) recruited into Phase II or III studies with RTX received further courses of open-label RTX based on 2 approaches: a) TT whereby pts were assessed at 24 weeks (wks) following each course. Those with DAS28≥2.6 were retreated, while those with DAS28< 2.6 were retreated if and when DAS28 increased to ≥2.6; b) PRN whereby pts were retreated at the physician's discretion after a minimum period of 16 wks if both swollen and tender joint counts were 8. Study visits were at least every 8 wks, with unscheduled visits at any time if required. RTX (2 x 1000 mg) was given as IV infusions 2 wks apart in combination with MTX. Observed data were pooled and analyzed according to tx strategy. Clinical outcomes including ACRn, DAS28-ESR and HAQ-DI responses were determined over time. Safety data were compared.

Results:
Over multiple courses of RTX, responses were maintained or improved irrespective of tx strategy. However, compared with PRN, TT provided tighter control of disease activity (greater improvements in DAS28-ESR, lower HAQ-DI and higher ACRn). PRN resulted in the recurrence of disease symptoms between courses: DAS28-ESR scores returned close to pre-RTX treatment levels, with higher rates of withdrawals due to RA flare. TT also resulted in more pts achieving major clinical response (ACR70 ≥ 6 months) compared with PRN (12.3% vs. 5.9%). TT resulted in more frequent retreatment (median time between courses approx. 25 wks vs. approx. 62 weeks for PRN). Despite this, regimen safety profiles were comparable. Importantly, TT was associated with a reduced incidence of RA flare (19 vs 42%) with no increase in the rate of serious infection, serious adverse events or proportion of pts with Ig below normal compared with PRN.

Conclusion:
Repeat treatment to a target of DAS28 remission with RTX led to tighter control of disease activity compared with PRN treatment.
Effectiveness of Adalimumab in a Multicenter, Clinic-Based Cohort in Canada

Wojciech Olszynski (University of Saskatchewan, Saskatoon); Hyman Tannenbaum (Montreal Rheumatology Centre, Montreal); Michael Starr (McGill University, Montreal); Michel Gagné (Polyclinique Saint-Eustache, Saint Eustache)

Objective:
To assess patient self-reported effectiveness of adalimumab for the treatment of rheumatoid arthritis (RA) using multiple clinical, demographic, and functional covariates.

Methods:
Through PROGRESS, an adalimumab patient support program in Canada, patients with RA receiving adalimumab (N=250) completed a questionnaire on demographics, RA disease characteristics and status, current and past RA management, medication adherence, and patient–physician interaction.

Results:
A total of 167 women and 83 men provided data. Mean age was 56.2 years, duration of RA was 13.2 years, duration of adalimumab therapy was 2.1 years, average Health Assessment Questionnaire (HAQ) score was 0.75, visual analog scale (VAS) pain score was 33.7 (past week), and VAS fatigue score was 41.6 (past week). For approximately 70% of patients, their physician had outlined the risks and benefits of various treatment options and provided a recommendation for therapy but allowed the patient to make the final decision. Approximately 77% of patients rated their relationship with their rheumatologists as excellent. Patients reported the occurrence of joint pain or tenderness as follows: never, 2%; rarely, 14%; sometimes, 42%; very often, 26%; or always, 16%. Approximately 81% reported a general well-being of average or better. When estimating the tenderness and swelling in their joints prior to adalimumab therapy, 36% felt better and 56% felt much better after adalimumab; this positive effect was correlated with lesser HAQ, VAS pain, VAS fatigue, pain frequency, and stiffness duration (r=0.32 to 0.47, p< 0.01). Disease control was a very important characteristic of RA medications for 83% of patients, and 80% claimed that it was either quite important or very important that the medications not cause adverse events. Stronger beliefs that RA medications have a positive effect were associated with lesser HAQ, VAS fatigue, and VAS pain scores (r=–0.18 to 0.23, p< 0.01). Patients who were better able to take adalimumab themselves had lesser HAQ scores (r=–0.28, p< 0.01).

Conclusion:
In a real-world setting in Canada, 92% of patients reported an improvement in their joint swelling and tenderness after initiation of treatment with adalimumab.
Takayasu’s Arteritis Progression on Anti-TNF Biologics: A Case Series

Mohammed Osman (University of Alberta, Edmonton); Stephen Aaron (University of Alberta, Edmonton); Michelle Noga (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Case Report:
Takayasu's Arteritis (TA) is a rare granulomatous vasculitic disease that affects the aorta and/or its major branches. Recent studies have suggested that anti-TNF biological therapies are highly effective in treating TA refractory to conventional immunosuppressive therapy. Objectives: We describe two female patients with TA: one who failed anti-TNF therapy despite management with two different anti-TNF agents: infliximab and adalimumab. The other patient developed TA while treated with infliximab for the management of pre-existing Crohn's Disease. Results: The first patient was 39 yo when diagnosed with type I TA initially presenting with symptoms of exertional dyspnea, fatigue, bilateral lower limb claudication, and right upper extremity weakness. Laboratory investigations were essentially unremarkable, (ESR mildly elevated 24mm/h (normal 0-20)). Her symptoms were initially controlled by high dose corticosteroids. Subsequent immunosuppressive disease modifying agents including methotrexate, azathioprine, and the biological agents infliximab and adalimumab were of little efficacy, and she had progression of disease. The second patient was a 17 yo with an 18 mo history of Crohn's Disease treated with infliximab for nine months. She presented to the emergency room with headache, photophobia, oral ulcers, anterior chest pain, abdominal pain, vomiting and a 1 week history of lower limb claudication. Laboratory investigations showed a microcytic anemia (Hg 94 g/L, MCV 70) and significantly elevated inflammatory markers - ESR over 140 mm/h (normal 0-20) and C-reactive protein 143 mg/L (normal 0-8). Subsequent CT scan of her abdomen revealed moderate concentric aortic wall thickening, and concentric bilateral common femoral artery thickening. Her TA was diagnosed while on treatment with infliximab. Conclusions: We describe two cases of TA with either progression or development of disease while on an anti-TNF agents. As the use of anti-TNF agents is increasing in “orphan diseases”, we would recommend caution while using anti-TNF agents in patients with TA. From our observations, we believe that a multicentered randomized study should be initiated in order to determine the extent of progression when anti-TNF agents are used.
Osteoporosis Management in Patients with Medical Co-Morbidities: An Evidence Based Approach
Tripti Papneja (McMaster University, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Objective:
Therapeutic osteoporosis trials and treatment guidelines have focused mainly on postmenopausal women; however patient populations presenting with low bone mineral density (BMD) in clinical practice is varied, with cases encompassing the spectrum of complexity. The purpose of this evidence-based approach is to address some of the major considerations and challenges that plague physicians when treating osteoporosis for patients with medical co-morbidities using derived clinical scenarios.

Methods:
We identified several key practice challenges in the management of osteoporosis, including particular cases of premenopausal osteoporosis (patients with primary biliary cirrhosis(PBC), post-organ transplant, or chronic glucocorticoid therapy) and tailoring of osteoporosis treatment based on patient comorbidities (chronic kidney disease, or Barrett’s esophagus). We reviewed the literature for all publications in Pubmed and developed a flow chart for how best to manage patients with these medical comorbidities.

Results:
In an evidence-based review of the literature, we have determined an approach for management of these patients. Complete assessment of risk factors for low BMD and fractures and measurement of serum calcium, phosphorus, parathyroid hormone, creatinine, alkaline phosphatase, 25-hydroxyvitamin D, and possibly thyroid and gonadal function depending on the medical history is warranted. Stopping excessive alcohol intake and smoking, maximizing physical activity including weight-bearing exercises, minimizing falls, and calcium and vitamin D supplementation has been recommended for all patients at increased risk for osteoporosis. Replacement of gonadal steroids in men if deficient is advisable. Current evidence supports the use of oral bisphosphonates for prevention or treatment of osteoporosis in patients with PBC, post-organ transplant, chronic glucocorticoid therapy, and stages 1-3 chronic kidney disease (CKD). Efficacy of IV bisphosphonate has also been demonstrated in patients with chronic glucocorticoid therapy, post-organ transplant and stages 1-3 CKD. Teriparatide has been shown to improve BMD in patients on chronic glucocorticoid therapy or stages 1-3 CKD. IV bisphosphonates, raloxifene, teriparatide, and calcitonin are recommended to treat osteoporosis in patients with Barrett’s esophagus based on expert opinion. In stages 4 through 5D CKD, treatment of osteoporosis is opinion based and bisphosphonates or teriparatide can be considered for selective patients with osteoporosis who are fracturing without other co-existent CKD mineral and bone disorders.

Conclusion:
Patients with PBC, post-organ transplant, chronic glucocorticoid therapy, CKD, and Barrett’s esophagus present a special therapeutic challenge as few data exist to guide osteoporosis clinical care for them. This evidence based approach would be a useful tool for busy clinicians in managing these complex patients with low BMD.
Comparison of anti-TNF treatment initiation in RA databases demonstrates wide country variability in patient parameters at initiation of anti-TNF therapy

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Objective:
Clinical and demographic characteristics of Canadian rheumatoid arthritis (RA) patients were compared to those of RA patients from 12 other countries.

Methods:
Canadian data were obtained from the Optimization of HUMIRA trial (OH), the Ontario Biologics Research Initiative (OBRI), the Real-Life Evaluation of Rheumatoid Arthritis in Canadians Receiving HUMIRA (REACH) and compared to published data from American, Australian, British, Czech, Danish, Dutch, Finnish, German, Italian, Norwegian, Spanish and Swedish RA databases. Patient characteristics at initiation of anti-tumor necrosis factor α (anti-TNF) therapy were compared between countries and temporal trends for disease activity analyzed.

Results:
Disease activity (DAS28) scores varied from 5.3 (OBRI, REACH, Dutch databases) to 6.6 (Czech and British databases). Both OBRI and REACH showed significantly lower DAS28 than OH (2 tailed t-tests, \( p< 0.001 \)). Lower disease severity was noted in databases from countries with more generous anti-TNF coverage: Dutch (based on previous DMARD use, DAS28, SC, TJC, HAQ-DI), Danish (previous DMARD use, DAS28), Norwegian (DAS28, SJC, TJC, VAS of global health) and two Swedish (DAS28, SJC, TJC, HAQ-DI for both) RA databases showed lower disease severity than did OH (\( p< 0.05 \) in all cases). The two US databases also showed lower severity (CORRONA database: previous DMARD use, SJC, TJC; NDB database: HAQ-DI, \( p< 0.001 \)). Registries from the UK and Czech Republic, which had among the most restrictive coverage, had higher mean baseline DAS28 scores than OH (\( p< 0.001 \)). Remaining databases showed few or no differences from OH. There was a lowering of mean baseline DAS28 in the registries with published data over time (British, Norwegian, Danish and Swedish) but significantly less so for the British registry (\( p< 0.001 \) in each case).

Conclusion:
These results confirm that regional variation exists in the initiation of treatment with anti-TNF agents among RA patients. Although in some countries the mean baseline disease activity declined over time, regional reimbursement policies are likely to strongly affect initiation of anti-TNF therapy in RA.
Clinical Characteristics and Quality of Life of Patients with Primary and Secondary Antiphospholipid Syndrome

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Objective:
To describe and compare the clinical characteristics, general health and quality of life (QOL) of patients with previous thrombovascular events (TE) followed at a systemic lupus erythematosus (SLE) and antiphospholipid (APS) clinics.

Methods:
Demographic and clinical data (including type and numbers of TE) from the prospective University of Toronto SLE and APS clinic databases were studied. Four patient groups were defined as patients with: 1) primary APS (PAPS) (n=52), 2) APS secondary to SLE (SAPS) (n=65), 3) SLE with TE but who do not meet the criteria for APS (SLE+TE) (n=112), and 4) SLE but without antiphospholipid antibodies (aPL) or previous TE (SLE-TE) (n=1094). Group 4 was only used as control for the QOL. TE were divided into arterial (ATE) and venous (VTE). QOL was determined using the Medical Outcomes Study Short Form 36 (SF-36) at the most recent visit. Canadian age and gender standardized SF-36 Physical (PCS) and Mental component scores (MCS) were calculated. Data was analyzed and compared using descriptive statistics, Chi-square and analysis of variance (ANOVA).

Results:
The majority of the subjects in all groups were female: PAPS: 63.5%, SAPS: 87.7%, SLE+ TE: 60.4% and SLE-TE: 87.8%, mean (SD) age at the time of analysis was 48.3(15.7), 53.2(13.1), 50.5(17.4), 43.3(15.7) years, respectively. Total number of TE by 100 person-year for ATE/VTE was 8/15, 10/5 and 16/16 for PAPS, SAPS and SLE+TE, respectively. Analysis of the first TE showed that ATE was less prevalent in patients with PAPS (40.4%) compared to those with SAPS (67.7%, P=0.0031) and SLE+TE (52.7%, P=0.14). The most common ATE location was: 1) cerebral for PAPS (n=17); coronary and cerebral for SAPS (n=17), coronary for SLE+TE (n=31). The most common VTE location was deep vein thrombosis in all 3 groups. Adjusted PCS in PAPS [mean (SD): 42.5(11.0)] was below the general population norm but was significantly higher than those with SAPS [46.8(11.0)] and SLE+TE [36.8(11.0), P=0.0076], but not different from SLE-TE [39.2(11.7)]. MCS was similar in all groups: PAPS: 47.4(11.4), SAPS: 44.2(11.6), SLE+TE: 46.1(11.2) and SLE-TE: 47.5(11.8).

Conclusion:
ATE is less prevalent in PAPS compared to the other groups. The physical health reported by patients with TE was better in patients with PAPS than those with SLE with and without APS.
Characterization of Patients Enrolled in an Etanercept Patient Support Program

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Objective:
There is limited information about patients enrolled in Patient Support Programs (PSP) for biologic agents. We conducted a retrospective review of data from a PSP for etanercept (Enliven® Services Support Program), a program that provides services such as structured clinical telephone follow-up, a toll-free support line, self-injection training, insurance assistance for drug reimbursement and educational materials. The goal was to describe Enliven® enrollee characteristics.

Methods:
Demographic information was collected for all individuals enrolled in the Canadian Enliven® PSP between July 2000 and December 2007. Patients with active Ankylosing Spondylitis (AS), moderate to severe Rheumatoid Arthritis (RA), moderate to severe Psoriasis (PsO) or Psoriatic Arthritis (PsA) were included in this study. Descriptive statistics were used to characterize the information collected. Data were stratified by indication, province and year.

Results:
16440 individuals were enrolled in the Enliven® program between July 2000 and December 2007. The average age at time of enrollment was 55.8 years (SD 13.8; range 6 to 98). Two thirds of the patients were female (65.5%). Regionally, 42.4% of patients were from Ontario, 21.3% from Quebec and 11.5% from British Columbia. Most enrollees were English speaking (80.7%). Approximately, 73.4% of individuals enrolled in the PSP were being treated for RA, 13.2% for PsA, 6.5% for AS and 6.8% for PsO. Almost all enrollees reported being etanercept-naïve (94.5%). More than half of enrollees were receiving etanercept twice weekly (58.4%). Specifically, 52.7% were receiving 25mg twice a week, followed by 40.0% receiving 50mg once a week. Almost a third (31.8%) of enrollees received training for drug administration at home, while 27.6% received training at their physician’s office (66% Rheumatologist, 33% other). About a quarter (25.1%) of enrollees had treatment delayed because they were awaiting government coverage.

Conclusion:
These data present a snapshot of patients administered etanercept therapy over a 6 year timeframe in the Enliven® PSP. PSP are a valuable source of utilization data for biologic therapies in addition to offering support to those patients prescribed biological therapy.
A Randomized Double Blinded Placebo Controlled Study of Probiotics in Active Rheumatoid Arthritis (RA)

Maria Pineda (University of Western Ontario, London); Sarah Thompson (University of Western Ontario, London); Gregor Reid (University of Western Ontario, London); Faye De leon (McMaster University, London); Janet Pope (University of Western Ontario, London)

Objective:
To examine the efficacy of probiotics as adjunctive therapy for the treatment of rheumatoid arthritis (RA).

Methods:
We performed a double-blind, placebo-controlled study using an orally administered probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteri RC-14 capsule as the active agent. Each capsule contains 2 billion colony-forming unit (CFU) viable bacterial cells. Twenty-nine patients with active RA were randomized to treatment with two probiotic or two placebo capsules daily for 90 days. Patients had at least 4 swollen and tender joints, were on stable DMARDs, steroids and/or NSAIDs for at least one month prior to randomization and could not receive steroids within one month before enrolment or during the study. ACR20 responses, serum cytokine levels (indicating changes in inflammation) and safety parameters were assessed.

Results:
Fifteen patients were assigned to the probiotic group and 14 to the placebo group. In the placebo group, 2 were lost to follow-up and 1 was withdrawn due to increased disease activity. At baseline, the mean swollen joint count (SJC)/tender joint count (TJC) for the placebo and probiotic groups were 8.5/8.9 and 9.5/13.6. At the last visit, the mean SJC /TJC were 7.3/6.7 (placebo group) and 9.1/13.7 (treatment group). Three patients in the probiotic (20%) and one in the placebo group (7%) achieved an ACR20 response (p=0.4). There were no statistically significant differences between individual components of the ACR20 criteria or cytokine markers measured within each group. At baseline the probiotic group had (on a 0 to 10 scale): patient global rating of disease (2.7) and fatigue rating (3.4), which was not different from placebo (4.1, 4.0). At final visit, there was a statistically significant between group difference in mean patient globals of disease activity and fatigue (p =0.031 and p= 0.010). TNF-alpha levels were significantly lower in the probiotic group than in placebo at study completion (P=0.049), but the within group difference was not significant.

Conclusion:
The patients selected were stable with chronic synovitis, and it may have been difficult for an adjunctive therapy to demonstrate improvement with probiotics within three months. Ethically, they could not be taken off DMARDs and put on placebo or probiotics as monotherapy. Thus, although using ACR20 criteria, probiotics did not clinically improve RA. It was interesting that patient global, fatigue and TNF-alpha levels were lower for patients in the probiotic group versus placebo at last visit.
Objective:
Psoriatic disease refers to joint, eye, and gut manifestations that are associated with psoriasis (Ps). Previous studies have implicated alleles of the major histocompatibility complex chain-related A (MICA) locus in increasing susceptibility to psoriatic arthritis (PsA). The present study aims to delineate the genetic contribution of MICA alleles to the development of PsA compared to Ps using high-resolution allelic typing.

Methods:
Unrelated Caucasian PsA patients, Ps subjects, and healthy controls (200 each) were genotyped for MICA using a PCR-SSP method and for HLA-A, B, and C by PCR-SSO reverse line blot. All PsA patients satisfied CASPAR criteria and Ps subjects were diagnosed by a dermatologist and examined by a rheumatologist to exclude PsA. MICA and HLA allele carriage frequencies were compared across groups by chi-squared analysis with Fisher’s exact test where necessary (p< 0.05). Data analysis included conditioning on the presence of HLA-B*27.

Results:
PsA patients (84 females:116 males) had a mean age of 40 years, Ps duration of 13 years, and mean PsA duration of 6 years. Ps patients (76 females:124 males) averaged 46 years of age and a disease duration of 17 years, and controls (115 females:85 males) averaged 52 years of age. MICA*00201/020 (p=0.007, OR=1.85) and MICA*00701/026 (p=0.007, OR=1.23) were significantly associated with PsA when compared to controls, whereas MICA*016 (p=0.0009, OR=5.21) and MICA*017 (p=0.003, OR=2.18) were significantly associated with Ps when compared to controls. Furthermore, MICA*00701/026 and MICA*00801 were found to be significantly associated with PsA compared to Ps. HLA-B*27 was associated with PsA compared to controls (p=0.00006, OR=3.59) and compared to Ps (0.000005, OR=4.83). Excluding HLA-B*27 positive subjects from the analysis, all associations remained significant with the exception of MICA*00701/026 with PsA.

Conclusion:
MICA alleles are associated with Ps and PsA and may differentiate PsA from Ps alone. Our data support previous findings of associations between MICA*017 with Ps and MICA*00201/020 with PsA; however, the previously reported association of PsA with MICA*00701/026 seems to be due to linkage disequilibrium with HLA-B*27.
Results of A Pilot Randomized Placebo Controlled Trial in Raynaud’s Phenomenon (RP) with St. John’s Wort (SJW)

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Objective:
Most of the treatments for Raynaud’s Phenomenon (RP) cause hypotension which can limit the tolerability of drugs in RP. St. John’s Wort (SJW) is a plant extract which works on serotonin receptors as well as other properties. It is proven to be effective in mild to moderate depression. Thus we thought it could possibly affect serotonin receptors of blood vessels and help RP, and one RCT demonstrated that prescription selective serotonin receptor inhibitors (SSRIs) can improve RP.

Methods:
We performed a double blind RCT with a two week run where patients had to have at least 14 attacks over two weeks. They were then randomized to SJW or identical placebo for 6 weeks, stratifying by primary and secondary RP (and within secondary by SSc or other CTD). Testing was done to ensure quality of SJW. Serum was collected at each visit and patients kept a diary recording all RP attacks (#/day, duration of each and severity). Tests of vascular mediators including sE-Selectin, sVCAM-1, sICAM-1, MMP-9, tPAI-1, cytokines, and VEGF were done and between groups comparisons were made with ITT analyses. Data were analyzed blinded to allocation (group A and B).

Results:
Twenty-seven patients were screened (some withdrew consent or failed due to insufficient number of attacks) and 18 were randomized (2 primary RP, 16 secondary RP of whom 8 had SSc) with 8 on active SJW and 10 on placebo. The between groups differences in # of RP attacks over 1 day (decrease in the mean # of attacks per day) were 0.75 in active and 1.01 in placebo, p=0.06 (favoring placebo). Duration and severity of attacks was not different between the two groups. There were within group differences between baseline and completion of the study where frequency, severity and duration of attacks improved, some of which were statistically significant, but active SJW did not alter RP more than placebo. The serum analyses demonstrated that there were no between groups differences on all parameters studied. There was one SAE (a patient with diffuse SSc and atrial fibrillation hospitalized for congestive heart failure on active treatment.)

Conclusion:
This study demonstrates that there is no benefit, both clinically and from a basic science perspective, with SJW in RP.
Best Practices in Scleroderma: An Analysis of Guidelines for Management in SSc from a Large Database (CSRG: Canadian Scleroderma Research Group)

Sarah Harding (University of Western Ontario, London); Sarit Khimdas (University of Western Ontario, London); Ash Bonner (McMaster University, London); Murray Baron (McGill University, Montreal); Janet Pope (University of Western Ontario, London)

Objective:
There is currently no consensus on best practice in SSc and as a result, treatment and investigation practices are highly variable. To determine how thoroughly guidelines are achieved and in order to eventually achieve consensus, the investigation and treatment practices currently employed by physicians within the Canadian Scleroderma Research Group (CSRG) were documented. Additionally, practice variability among treatment centres was assessed and CSRG practices were compared to those recommended by the European League Against Rheumatism (EULAR) and the EULAR Scleroderma Trials and Research (EUSTAR) group.

Methods:
Prospective clinical and demographic data from adult SSc patients are collected annually from 15 CSRG treatment centres. Laboratory parameters, self-reported socio-demographic questionnaires, current and past medications and disease outcome measures are recorded. Descriptive statistics were performed for specific investigation and treatment options for organ involvement characteristic of SSc. For centres more than fifty patients enrolled, treatment practices were analyzed to determine if a site effect existed and determine practice variability. Treatment guidelines from EULAR and EUSTAR were then compared to those within the CSRG.

Results:
Data from 938 patients within the CSRG database were analyzed. 85.03% were female, the mean ± SEM age was 55.4 ± 0.4, 50.0% had limited SSc and 43.9% had diffuse SSc (6.1% uncharacterized). Several of these investigation and treatment practices were found to be inconsistently applied among the 6 centres with more than 50 patients. There was a significant difference in the number of patients with receiving PDE5 inhibitors for Raynaud’s phenomenon (p=0.036) and for the treatment of skin (p=0.004). Use of esophageal dilatation (p=0.000) and use of bosentan (p=0.015) differed significantly among centres for dysphagia and PAH respectively. Cyclophosphamide use varied in the treatment of ILD (Shortness of breath and DLCO < 70% or corrected DLCO < 70% and TLC < 70% and FVC < 70%) for all patients (p=0.002). CT (p=0.000) scan, CXR (p=0.000) and ECG (p=0.000) use varied significantly among centres with n>50 of all SSc patients. CSRG practices were generally comparable to recently published guidelines, however, use of iloprost for digital ulcers and use of antibiotics for small bowel overgrowth differed.

Conclusion:
Site variation in SSc management among CSRG centres suggests a need for a standardized approach to the investigation and treatment of SSc. The documentation of current practices and comparison of those practices to the EULAR and EUSTAR group guidelines represent a point from which to begin building consensus for best practice in SSc.
A Randomized Controlled Trial of Treating to Target in Active RA: Results from the Optimization of Humira Trial.

Janet Pope (University of Western Ontario, London); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket); Boulos Haraoui (University of Montreal, Montreal); John Sampalis (McGill University and University of Montreal, Westmount)

Objective:
In early RA, treating to clinical target is more effective in producing a therapeutic response when compared to routine care. This has not been documented for established RA. This randomized trial was conducted on patients with established RA who were to receive adalimumab as part of their care.

Methods:
The Optimization of Humira trial is an 18-month real-life Canadian RCT in patients with established active RA. Physicians were randomized to the following groups: routine care (RC) (N=87 patients), or treating to clinical target of low DAS28 (DAS) (N=109 patients) or 0/28 SJC (SJ) (N=113 patients). The primary outcome measure was the change in DAS28 at 12 months.

Results:
of the 309 enrolled patients, 209 (68%) (46 in RC, 77 DAS and 86 SJ groups) completed a 12 month follow-up and were included in this analysis. Mean age was 55 years, 80% were female, mean baseline DAS28 was 5.9 and the mean number of previous DMARDs used was 2.7. There were no between groups differences in baseline characteristics except for current number of DMARDs used (RC = 1.5, DAS = 1.8, SJ = 1.9, P = 0.009). There was a similar and significant (P < 0.001) decrease in DAS28 at 12 months for all groups (RC=3.2, DAS=3.1, SJ=3.5) and there were no between group differences observed for the following secondary outcomes: change in TJC, SJC, patient global assessment of disease activity, MD global assessment, HAQ, ESR, CRP and patient satisfaction and in the proportion achieving DAS28 targets. The majority of patients (55%) had a DAS28 < 3.2 at month 12 and 4 to 7% had a DAS28 < 2.6. 91% of patients were satisfied with treatment at 12 months. 78% had at least one RA medication change throughout the trial. The rate and reasons for discontinuation were not different between the groups.

Conclusion:
Treating to target with the same anti-TNF therapy in established RA may not alter the outcomes vs. routine care. This may be due to high effectiveness of anti-TNF (adalimumab) and/or efficient treatment by physicians. The results observed in this trial would suggest that in routine care, therapeutic response with adalimumab is higher than that observed in RCTs for patients with established RA.
Associations with Digital Ulcers (DU) in a Large Cohort of Systemic Sclerosis (SSc)

Sarit Khimdas (University of Western Ontario, London); Sarah Harding (University of Western Ontario, London); Ash Bonner (McMaster University, London); Brittany Zummer (University of Western Ontario, London); Murray Baron (McGill University, Montreal); Janet Pope (University of Western Ontario, London)

Objective:
To investigate whether digital ulcers (DU) are associated with other organ complications and SSc subsets in a large SSc cohort.

Methods:
Data from the CSRG (Canadian Scleroderma Research Group) are collected annually on an incident and prevalent SSc cohort. Presence, location and number of digital ulcers are collected annually as well as complications and other internal organ involvement, skin score and labs results. Correlation coefficients, Chi squared and logistic regression modeling were done to determine the associations of DUs (and subset of complicated DU) with other factors such as internal organ complications.

Results:
938 patients were included. 86% were women, mean age was 56 and disease duration was 14 years. 53% had limited SSc. 15% had a DU currently, 46% had a DU ever and 53% had digital pits. DUs were not associated with PAH (P=0.35). Complicated DUs including gangrenous (P=0.72) and amputated (P=0.93) digits were not associated with PAH. In patients with a disease duration longer than three years, DUs were associated with higher skin scores (P=0.00). Gender (P=0.95) and smoking (0.91) were not associated with DUs. Organ involvement including renal crisis (P= 0.66) and interstitial lung disease (P=0.20) were not associated with DUs. DUs were associated with: a decreased DLCO in diffuse SSc (P=0.01) and both earlier age of Raynaud’s (P=0.00) and first non-Raynaud’s symptom (P=0.00). DUs were further associated with GERD in diffuse SSc (P=0.00) and esophageal hypomotility as measured by esophageal dilatation (P=0.00). DUs were associated with the presence of topoisoomerase 1 (Scl-70) antibodies (P=0.00). Patients with diffuse SSc were almost twice as likely to have had a DU than patients with limited SSc. However, neither patients with gangrenous (P=0.61) nor amputated digits (P=0.46) were associated with a subtype of SSc.

Conclusion:
It appears that DUs are not associated with PAH. DUs increase with diffuse SSc, early onset of disease, low DLCO, esophageal involvement and presence of topoisoomerase 1 (Scl-70) antibodies. Complicated DUs are not associated with an SSc subtype or specific organ involvement. Some of the associations are confounded as diffuse SSc onsets earlier than limited and thus earlier age of onset increases DU risk. Understanding the associations with digital ulcers in scleroderma may help to risk stratify patients and better treat or prevent this
Clinical Audit: NSAID Related Gastrointestinal Adverse Events

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Objective:
Published data have shown that patients at high risk of complications from NSAID therapy are often not prescribed appropriate gastroprotective therapy. We compared against defined audit standards the preadmission pharmacologic treatment in patients admitted to hospital with upper GI bleeds or intestinal perforations. The audit was performed as a retrospective clinical chart review. We also examined pharmacologic regimens of patients with cardiovascular risk factors.

Methods:
All patients admitted to Kingston General Hospital during the 24 months between December 31, 2006 and December 31, 2008 with melena/upper GI bleed or a GI perforation were identified using the hospitals data collection system. Patients taking an NSAID were identified and stratified as low or high-risk for GI and cardiovascular events based on defined risk factors; additional consideration was given to patients taking anticoagulants, low dose ASA, and clopidogrel. Patient charts were relied upon for determining patients’ medication lists at the time of admission.

Results:
161 patients fulfilled the inclusion criteria. Fifty-three patients were taking one or more NSAIDs at the time of admission; 51 (74%) of these patients were identified as being at high risk for GI bleed/perforation but received no GI prophylaxis (PPI, H2-RA, or coxib). Twenty patients were taking both low dose ASA and NSAID; 15 (75%) of whom did not receive GI prophylaxis. Seven Patients were on anti-coagulation and NSAID; 3 (43%) of which did not receive GI prophylaxis. With respect to combinations of medicines for cardiac prophylaxis, 9 patients were taking both ASA and ibuprofen and 2 patients were taking both a PPI and clopidogrel despite evidence suggesting these combinations should not be taken concomitantly.

Conclusion:
The findings of this audit indicate that high-risk patients continue to be given NSAIDs without GI prophylaxis. Some of these admissions may have been avoidable. This study also shows that patients are taking medications that may conflict with the effectiveness of low dose ASA and clopidogrel for cardiac prophylaxis.
Ultrasound Findings on Patients with JIA in Clinical Remission – A Pilot Study

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Objective:
Recent studies in adult rheumatology have suggested that a significant percentage of patients in clinical remission will show signs of active arthritis defined as positive power doppler signal on ultrasound examination. Structural abnormalities found on grey scale ultrasound such as joint effusions or synovial thickening might be residual findings and not necessarily represent ongoing active disease. The aim of this pilot study was to assess whether patients with juvenile idiopathic arthritis (JIA) in clinical remission would show abnormalities on either grey scale or power Doppler ultrasound.

Methods:
JIA patients who were in clinical remission for a minimum of 3 months were eligible for the study. Ultrasonography of the wrist, knee, the tibiotalar as well as the talonavicular joint was carried out on previously affected joints. A General Electric Logiq e ultrasound device equipped with a multifrequency linear probe at a maximum frequency of 13 Mhz for grey scale sonography and 6.7 Mhz for power Doppler sonography was used. The images were read by 2 independent readers. Findings were compared with published normative data as well as own controls and were categorized as structural abnormalities if there was synovial thickening or increased joint fluid and Doppler positive if there was an increased power Doppler signal on top of the

Results:
In 23 patients with varying previous joint involvement 3/8 had normal wrist ultrasound, whereas 5/8 had grey scale and 1/8 Doppler abnormalities. In 17/17 patients knee joints were normal, one had a small baker cyst as an incidental finding but no Doppler signals were detected. 6/14 patients with previous ankle involvement had normal ultrasound of the tibiotalar joint, 8/14 grey scale and 2/14 Doppler abnormalities. Finally 9/14 had normal talonavicular joints, 5/14 grey scale and 1/14 Doppler abnormalities.

Conclusion:
While some joints like the knee joint might not benefit much from additional ultrasound assessments others like the wrist and ankle show signs of structural abnormalities in a significant number of patients. The number of joints with positive power Doppler signals was nevertheless low. This might be due to technical limitations of the device used in this trial or indicate that the structural abnormalities do not necessarily translate into the presence of active inflammation that can be detected by Doppler. This study will inform the design of larger scale trials to determine a potential role of diagnostic ultrasound in JIA.
Arthritis Care Toolkit: Development of an Evidence-Based Toolkit to Improve Access to Care for People Living with Arthritis

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Objective:
With the aging of the population, the health and economic burden associated with people living with arthritis is expected to increase. As part of a project which aims to develop an arthritis toolkit to facilitate timely and appropriate arthritis management, a literature review was conducted to identify existing tools that facilitate transition of patients through the continuum of care.

Methods:
A literature review of published and grey literature was conducted using a comprehensive search strategy developed in collaboration with a medical information specialist and arthritis experts. Inclusion criteria were: articles which addressed the development, implementation or validation of a tool at the clinical, system or institutional level that could be used to improve the ability of arthritis stakeholders to transition patients across the continuum of care. Experienced reviewers independently applied the inclusion criteria to each article. Consensus was used to solve discrepancies in evaluation; where consensus was not reached, a third reviewer was consulted. Articles were reviewed and results of the accepted articles synthesized according to the types of tools which emerged, through informed scientific and clinical consensus.

Results:
The literature search strategy identified 15,207 articles from published literature. Based on an initial review of the title and abstracts, 597 articles remained for review of the full-text. Application of inclusion criteria to full-text articles using a standardized screening questionnaire identified 48 relevant articles in the peer-reviewed literature and 9 articles in the grey literature. The tools found in the articles most commonly addressed rheumatoid arthritis (n=18) or osteoarthritis (n=10). Tools were classified based on the type of tool. The majority of tools were classified as: 1) algorithms (clinical pathways or algorithms for management and treatment which included guidance on the type of health care provider and referrals recommended with different disease presentations and symptoms) or 2) referral tools (primarily early referral tools which included diagrams outlining steps for early detection and referral for people with rheumatoid arthritis). While scientific evidence and expert opinion were used in the development of some of the identified tools, the majority of tools were not formally evaluated (e.g. testing of measurement properties).

Conclusion:
There is a need for evidence-based tools that can help facilitate transition of patients across the continuum of care to ensure that people living with arthritis have timely access to therapies that can prevent and manage disease disability and progression.
The Effect of Diary Use on Healthy Subjects: Symptom Amplification

Robert Ferrari (University of Alberta, Edmonton); Anthony Russell (University of Alberta, Edmonton)

Objective:
The objective is to examine the effect of keeping a symptom diary on symptom frequency and intensity in healthy female subjects. Diaries are commonly used in chronic pain patients as a method of tracking their illness and/or for monitoring treatment effects. There may be a problem, however, with diary use because diaries may create symptom amplification (noticing and experiencing ordinary symptoms in a more severe fashion because of increased attention to symptoms). This may be etiologic in a number of controversial syndromes such as fibromyalgia, chronic whiplash and chronic fatigue syndrome as clinical experience suggests these patients frequently maintain diaries of their symptoms.

Methods:
A convenience sample of female university students were randomly assigned to one of two groups: the Diary group and Control group. Both groups were asked to complete an initial symptom checklist comprised of headache, neck pain, back pain, fatigue, abdominal pain, elbow pain, jaw pain, and numbness/tingling in arms or legs. They were asked to indicate their symptom frequency (number of days in the last 14 they recalled having a given symptom) and their perceived average symptom severity (on a numerical scale 1 – 10) in the last 14 days. The Diary group was asked then to examine the symptom checklist daily for 14 days while the control group was not. After 2 weeks, both groups then repeated the symptom checklist assessing their recall of symptoms and symptom severity.

Results:
A total 35 of 40 initially-recruited subjects completed all the questionnaires, 18 in the Diary group and 17 in the Control group. The groups were similar in mean age, smoking and alcohol use. At the outset, both groups had similar frequencies and intensities of symptoms. After 2 weeks of symptom diary use, however, Diary group subjects had an increased frequency (doubled) of recalled symptoms, and the average intensity of symptoms was significantly increased in the Diary group compared with the Control group, which had not changed its reported mean frequency or intensity of symptoms.

Conclusion:
The use of a symptom diary for 2 weeks, even in generally healthy subjects, results in increased recall of daily symptoms and increased perception of symptom severity. The use of symptom and pain diaries in clinical populations may be contributing to the symptom burden and clinical picture.
Assocition of Symptom Expectation and Coping Style for Whiplash Injury

Robert Ferrari (University of Alberta, Edmonton); Anthony Russell (University of Alberta, Edmonton)

Objective:
The objective of the present study is to compare the expectations following and the coping style for whiplash injury in injury-naive Canadian subjects. Coping styles for illness have been described as combinations of active and passive coping mechanisms. Passive coping is generally found to be associated with increased severity of depression, higher levels of activity limitation and helplessness. In pain conditions, active coping has been found to be associated with less severe depression, increased activity level and less functional impairment, but to be unrelated to pain severity. Previous studies have suggested that Canadians have a high expectation for chronic pain following whiplash injury. Expectation for recovery has been shown to predict recovery in whiplash victims.

Methods:
The Vanderbilt Pain Management Inventory (an assessment of coping strategies) was administered to University students and staff. Subjects who had not yet experienced whiplash injury were given a vignette concerning a neck sprain (whiplash injury) in a motor vehicle collision, and were asked to indicate how likely they were to have the thoughts or behaviors indicated in the questionnaire. Subjects also completed expectation questionnaires regarding whiplash injury. Coping Style scores were categorized in reference to the median scores of both PASSIVE and ACTIVE responses. Those with scores below the median on both scales, for example were classified as LOW ACTIVE/LOW PASSIVE; those below the median on the active and above the median on the passive scale were classified as LOW ACTIVE/HIGH PASSIVE. Others thus could be HIGH ACTIVE/LOW PASSIVE or HIGH ACTIVE/HIGH PASSIVE in coping style.

Results:
One hundred subjects completed the questionnaires. The mean age of subjects was 25.7 ± 6.0 years, 57% of subjects being male. Four coping style responses were noted for whiplash injury: 21% had HIGH ACTIVE/HIGH PASSIVE styles, 33% had HIGH ACTIVE/LOW PASSIVE styles, 27% were LOW ACTIVE/HIGH PASSIVE, and 19% had LOW ACTIVE/LOW PASSIVE styles. When coping style responses were compared to expectations for chronic pain after whiplash injury, those with high passive coping styles had a higher mean expectation score (i.e. passive coping style was associated with a higher expectation of chronic pain after whiplash injury).

Conclusion:
Both expectations and coping styles may interact or be co-modifiers in the outcomes of whiplash injury in Canadian whiplash victims. Further studies of coping style as an etiologic factor in the chronic whiplash syndrome are needed.
Significance of Familial Relations in Occurrence of Manifestations of Behcet's Disease

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Objective:
To investigate the occurrence of similar manifestations in pairs of family members. We compare the frequent and important characteristics of BD in familial pairs with randomly selected sporadic control pairs (Age and sex matched)

Methods:
In a retrospective review of 6167 BD patients, registered at Rheumatology Research Centre in Tehran, since 1975, the patients with positive familial history of BD were selected for this study. These included 38 pairs of siblings, 19 pairs of parent/child and 10 pairs of second relatives. An age-sex matched non-familial control pair of BD cases was then randomly selected for each familial pair. A list of 15 more frequent and more important clinical manifestations was prepared. Occurrence of a manifestation in a single pair was treated as similar if that manifestation was present or absent in both members of a pair. We compared the percentage of similar occurrences of each manifestation in the familial pairs with their counter pairs. McNemar test was carried out to compare matched pairs (familial vs. non-familial pairs) and the p-values, p1, p2 and p3 were calculated for each manifestation for the 1st, 2nd and 3rd group respectively.

Results:
Oral Aphthosis (OA) as First Manifestation (FM): (p1=0.26, p2=0.37, p3=0.25), Uveitis (FM): (p1=0.54, p2=0.12, p3), Mucous Membrane: (p1=0.25, p2=1, p3=0.48), OA (p1=0.37, p2=1 p3=0.48) Genital Aphthosis (p1=0.17, p2=1 p3=0.38), Skin Manifestations (p1=0.31, p2=0.51, p3=0.45), Pseudofolliculitis (p1=1, p2=0.75, p3=0.69), Erythema Nodosum: (p1=0.61, p2=1, p3=0.25), Ocular Manifestations: (p1=0.48, p2=1, p3=1), Uveitis (ant): (p1=1, p2=0.69, p3=1), Retinal Vasculitis: (p1=0.09, p2=0.51, p3=0.38), Joint Manifestations (p1=0.61, p2=0.34, p3=1), Positive Pathergy test: (p1=0.06, p2=0.51, p3=1) and diagnosis for complete form: (p1=0.45, p2=1, p3=1) and for incomplete form: (p1=0.48, p2=1, p3=1). Neurologic, Pulmonary, Cardiac and Large Vessel Involvements showed no difference. Pathergy test was performed for all the patients. Positive Pathergy was higher and Retinal Vasculitis was lower, in sibling pairs, but not significant.

Conclusion:
The study showed that familial relations do not play a significant role in occurrence of a particular manifestation in Behcet's disease
MRI Findings in Scurvy; Still a clinical diagnosis

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Case Report:
HPI- A previously well 54-year-old female was admitted to hospital for investigation of bilateral leg pain preventing ambulation. She had a three-week history of pain which started in the knees and progressed to involve her leg muscles diffusely. This pain was associated with mild swelling and bruising. She also noted red dots on her lower legs. Review of systems was positive for a progressive history of fatigue and a fifty-pound weight loss over two years. She was referred to rheumatology for possible vasculitis. Physical Exam- Diffuse ecchymosis and non-palpable purpura of the lower limbs were the predominant findings on physical exam. Small bilateral knee effusions and mild pitting edema were the only other findings in an essentially normal physical exam. Investigations- Mild normocytic anemia with normal coagulation profile and liver enzymes on lab work. Negative urinalysis, infectious workup and serology including ANA and ANCA. MRI of the lower extremities showed mild peripheral increase in T2 muscle signal in the distal vastus medialis and lateralis with more prominent bilateral subcutaneous edema and deep fascial edema. Similar findings were seen in the gastrocnemius muscles bilaterally and also in the calves with prominent subcutaneous and deep fascial edema. The medial gastrocnemius muscles also demonstrated fatty infiltration but no atrophy. More focal enhancing marrow lesions in the right femur were felt to represent islands of red marrow. Enhanced images did not demonstrate areas of muscle necrosis or fluid collections to suggest abscess. The findings are non-specific and reported to be in keeping with an inflammatory process. Intervention- Scurvy was suspected and she was started on oral vitamin C. The patient improved rapidly and vitamin C levels confirmed the diagnosis. Discussion- Scurvy is relatively rare in industrialized countries and there are few reports of MRI findings associated with it. Nonspecific bone marrow edema and signal changes have been reported in previous cases. Our study is the first to report edema in muscle, subcutaneous tissue and fascia. This case highlights the MRI findings in scurvy as well as the importance of considering this diagnosis in the differential diagnosis of vasculitis.
Objective:
Behcet’s disease (BD) is well known to be associated with HLA-B51 antigen. Associations of other HLA-B antigens with BD was not evaluated in Korean. The recurrent oral aphthous (ROA) frequently occur as a first clinical manifestation of BD, but it may be indistinguishable from those of recurrent aphthous stomatitis. The aim of this study was to determine which HLA-B antigens as genetic factors influencing susceptibility of BD in Korea. And we evaluated to clarify the association of HLA-B antigens in Korean patients with BD and with ROA. We also evaluated the strength of this associations with onset of age of oral ulcer.

Methods:
We genotyped HLA-B alleles in 128 BD patients and 133 ROA patients. The diagnosis of BD was determined according to revised international study group criteria. Early onset BD was defined that the age at the time of oral ulcer presentation is under 19 years old. We used data from the HLA-B allele frequencies in Korean as a control. The genotyping was performed using 66 sets of sequence specific DNA probe (PCR-SSP).

Results:
HLA-B51 allele frequency in BD was more frequent than in controls (p=0.048 OR 1.530 CI 1.002-2.335). No significant differences of other allele frequencies were found between BD and controls. HLA-B51 allele in early onset BD was more frequent than in controls (p=0.031 OR 2.171 CI 1.059-4.454). But, HLA-B51 allele frequency in late onset BD did not differ in controls. No significant difference in any of HLA-B allele frequencies was found between BD and ROA and between ROA and controls.

Conclusion:
Only HLA-B51 allele is associated with BD. Especially, HLA-B51 allele is associated with early onset disease group. As the onset of disease is earlier, genetic factor might have more effect on development BD than environmental factors.
The Role of Advanced Glycation End Products (AGEs) in Diabetes-Osteoarthritis Animal Model

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Objective:
Osteoarthritis (OA) is one of the most prevalent and disabling chronic conditions affecting the elderly. Its etiology is largely unknown, but the age is the most prominent risk factor. One of the intriguing changes in articular cartilage by ageing is the accumulation of advanced glycation end products (AGEs). This study was designed to test whether accumulation of advanced glycation end products, which are known to adversely affect cartilage turnover and mechanical properties, provides a molecular mechanism by which diabetes contributes to the development of OA.

Methods:
The hypothesis that elevated AGE levels predispose to the development of OA was tested in the rat anterior cruciate ligament transection (ACLT) model of experimental OA. Cartilage AGE level were enhanced by inducing diabetes with streptozotocin. The 28 experimental animals were divided into 4 subgroups, which were DM/OA group (n=15), control/OA group (n=5), DM/control group (n=5), and control/control group (n=3). The severity of OA was assessed 60 days after ACLT surgery in normal versus diabetic rat model. Assessment was done with chemical, histological and behavioral analysis. A novel AGE crosslink breaker (ALT-711, Alagebrium) was also challenged to reverse or diminish the severity of OA.

Results:
Diabetic animals show increased AGE level in articular cartilage. Collagen damage was also increased mostly in the diabetic group. In histologic analysis, the severity of OA was in concordance with AGE level and collagen damage. There were no statistical differences between diabetic and non-diabetic OA group by view of the behavioral assessment. In the treatment group (with AGE crosslink breaker), It was found that the AGE levels were remarkably reduced after treatment, but the severity of OA was not significantly different with non-treatment group.

Conclusion:
These findings demonstrate increased severity of OA at higher cartilage AGE levels and provide the first in vivo experimental evidence for a molecular mechanism by which diabetes may predispose to the development of OA. And the novel AGE crosslink breaker Alagebrium could reduce the AGE content in the cartilage, but 15-week treatment of Alagebrium could not significantly change the histologic severity of OA.
Associations Between the TNF-α -308 and -238 G/A Polymorphisms and Shared Epitope Status and Responsiveness to TNF-α Blockers in Rheumatoid Arthritis: A Meta-Analysis Update

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Objective:
To investigate whether or not TNF-α promoter-308 A/G and -238 A/G polymorphisms and shared epitope (SE) status are associated with responsiveness to anti-TNF therapy in RA patients.

Methods:
A comparative meta-analyses was conducted on A allele carriers (genotypes A/A + A/G) of the TNF-α promoter-308 and -238 A/G polymorphisms and SE status in responders and non-responders to anti-TNF therapy.

Results:
A total of 13 studies were included in the meta-analysis. Meta-analysis showed that the TNF-α -308 A/G polymorphism is not associated with responsiveness to TNF-blockers in RA patients. Studies with a small subject number (< 100) showed that the OR for the A allele carrier state was significantly lower among responders (OR = 0.344, 95% confidence interval = 0.152 - 0.779, p = 0.01). However, studies with a large subject number (≥100) found no association between the TNF-α -308 A/G polymorphism and responsiveness of TNF-blockers. Overall meta-analysis showed that the TNF-α -238 A/G polymorphism is not associated with the responsiveness of RA patients to TNF-blockers, and stratification by TNF-blocker revealed that the TNF-α -238 A/G polymorphism is associated with response of infliximab (OR = 0.441, 95% CI = 0.203 - 0.609, p = 0.039). Furthermore, SE status was not found to be associated with response to TNF-blockers.

Conclusion:
This meta-analysis of available data revealed an association between treatment response to infliximab and the TNF-α-238 A/G polymorphism, but no associations between treatment response and the TNF-α-308 A/G polymorphism or SE status.
Prolonged Serologically Active Clinically Quiescent (SACQ) Systemic Lupus Erythematosus (SLE): Predictors of Flare

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:
Some patients with SLE are clinically quiescent despite persistent serologic activity, thus presenting a clinical dilemma. While some patients remain SACQ indefinitely or become serologically quiescent (SQCQ), others’ SACQ periods are terminated by flare, for which reliable predictors have not been identified. Some suggest fluctuations in anti-dsDNA antibody and complement levels may be instructive. We analyze the two SACQ visits prior to flare for potential predictors thereof.

Methods:
Patients followed in the Lupus Clinic between 1970 and 2008 with visits ≤ 18 months apart were identified. SACQ was defined as a ≥ two year sustained period without clinical activity and with persistent serologic activity (increased anti-dsDNA antibody by Farr assay and/or hypocomplementemia at each visit), during which patients could be taking antimalarials, but not steroids or immunosuppressives. Anti-dsDNA antibody and complement levels at the two visits immediately preceding flare (FLARE group), were compared to those drawn at the third- and second-last visits in patients who remained SACQ or became SQCQ at their last visit (NON-FLARE group). Difference in anti-dsDNA antibody levels was analyzed categorically (normal (≤ 7), low (8-20), moderate (21-50), or high (>50)) and continuously, and if complement changed to or from normal between visits in the FLARE and NON-FLARE groups. Descriptive statistics were used. Comparisons were made using t-tests and chi-squared tests.

Results:
56/924 (6.1%) patients were SACQ. Median time between visits, and between last SACQ visit and outcome (e.g. flare) was 0.5 years. 33/56 (58.9%) patients comprised the FLARE group, and 23 (41.1%) the NON-FLARE group. Serologic profile over the visits analyzed did not differ between groups (p=0.83). Of the 25 patients with elevated anti-dsDNA antibody in the FLARE group, nine (36%) had significant categorical change in level: increased in five patients, decreased in four. Of the 18 NON-FLARE patients with elevated anti-dsDNA, two (11.1%) had significant change in levels; both increased. When analyzed as a continuous variable, anti-dsDNA antibody level did not differ between FLARE and NON-FLARE groups. Among FLARE patients with hypocomplementemia, 2/27 (7.4%) changed between normal and abnormal levels in the two visits preceding flare versus 4/21 (19%) in the NON-FLARE group.

Conclusion:
Changes in complement and anti-dsDNA levels do not predict flare in SACQ patients. Decision to treat these patients must be based on clinical acumen from close observation; alternate predictive biomarkers must be studied. Anti-dsDNA antibodies in SACQ require further characterization.
Evaluating Cardiac Risk in Systemic Lupus Erythematosus versus Other Inflammatory Arthritis Patients

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Objective:
Objective: Systemic Lupus Erythematosus (SLE) and other inflammatory arthritides (OIA) are independent risk factors for cardiovascular disease (CVD). Cardiovascular risk stratification scoring systems are a starting point in evaluating CVD risk. The main study objective was to determine how effective rheumatologists are at CVD risk stratification in SLE patients and compare this to OIA patients.

Methods:
Methods: A retrospective chart review of 504 patients attending the practices of nine rheumatologists at the University of Alberta Hospital was performed with pre-specified case report forms reviewing disease indices and medications, cardiac risk factors and Framingham 2008 and Reynolds risk scores.

Results:
Results: In this group of 504 patients, 64 (12.7%) had SLE (M:F =4:60), 440 (87.3%) had an OIA (M:F =117:323). Of the SLE patients, 33 (51.6%) met four or more ACR criteria, 31 (48.4%) had less than four ACR criteria. Of the OIA patients, 156 (35.5%) were CCP positive and 257 (58.4%) were RF positive. Complete Framingham risk scores were calculable for 1 (1.6%) SLE patient and 3 (0.68%) OIA patients. The Reynold’s risk score was not calculable for any patients. The number (%) of SLE vs. OIA patients where common cardiac risk variables were not recorded included: (1) positive family history of MI 62 (96.9%) SLE vs. 440 (100%) OIA patients, (2) diabetes 62 (96.9%) SLE vs. 421 (95.7%) OIA patients, (3) lipids status 48 (75%) SLE vs. 322 (73.2%) OIA patients and (4) smoking status 35 (54.7%) SLE vs. 275 (62.5%) OIA patients. The number (%) of SLE vs. OIA patients where cardiovascular medications (whether positive or negative) were recorded included: ASA 62 (96.9%) SLE vs. 311 (70.7%) OIA patients, anti-hypertensives 62 (96.9%) SLE vs. 317 (72.0%) OIA patients, and lipid lowering medications 61 (95.3%) SLE vs. 310 (70.5%) OIA patients. Systolic blood pressure was documented in 60 (93.8%) SLE and 247 (56.1%) OIA patients.

Conclusion:
Conclusions: Cardiovascular risk assessment in both SLE and OIA is sub-optimally performed by rheumatologists. Cardiovascular medication history and blood pressure documentation in SLE patients, however, is better than that of the OIA’s. The multi-system nature of SLE including renal disease potentially leads to closer monitoring of CVD risk factors such as diabetes and hypertension. Increased documentation of CVD risk factors and possible use of existing risk scores is the first step in establishing effective CVD risk reduction in these higher risk rheumatic disease groups.
Objective: We conducted a systematic review and meta-analysis to assess the effectiveness and safety of Mycophenolic Acid (MPA, Myfortic) and Mycophenolate Mofetil (MMF, Cellcept) in the induction treatment of Lupus Nephritis (LN).

Methods: We searched MEDLINE, EMBASE, and the Cochrane Library for relevant articles without language restriction up to October 20, 2009. We also searched the bibliographies of selected articles. The primary outcome was renal remission (complete, partial and overall); secondary outcomes were adverse events (infections, leucopenia, gastrointestinal symptoms, herpes zoster, amenorrhea and alopecia) at end of original study, death and end stage renal disease (ESRD) using reported extended follow-up data. For binary outcome variables (renal remission and adverse events), we calculated the relative risks (RRs), as well as respective 95% confidence intervals (CIs). The Mantel-Haenszel random-effects model was used to deal with heterogeneity among studies and to determine the pooled RR along with its 95% CI for renal remission and adverse events for MMF versus Cyclophosphamide (CYC). We assessed statistical heterogeneity among RCTs using Cochran Q test and by calculating I^2 values. The Cochrane collaboration’s software program, RevMan 5 was used to prepare and complete this review.

Results: The literature search resulted in 1614 citations. Abstracts of potentially relevant citations were reviewed. 76 citations were retrieved for detailed evaluation. We included RCTs comparing MMF/MPA versus CYC for induction therapy in patients with biopsy-proven LN with no restriction to age. We identified 4 RCTs with 618 patients for inclusions in the meta-analysis comparing MMF versus CYC. In 4 RCTs MMF was compared to intravenous CYC. In all 4 RCTs patients were treated simultaneously with prednisone at 1mg/kg and tapered thereafter. We observed no significant difference for renal remission (partial, complete, and overall) comparing MMF with CYC. There was a lower frequency of alopecia, leucopenia and amenorrhea when MMF was compared with CYC. The analysis of the extended follow up data showed a significantly lower number of subjects with ESRD in the patients treated with MMF as compared to CYC. There was no difference in the death. There were no significant differences for infections, gastrointestinal symptoms and herpes zoster.

Conclusion: There was no significant difference for the induction treatment of LN when comparing MMF to CYC. Patients treated with MMF showed reduced risk for alopecia, amenorrhea, leucopenia and lower number of subjects with ESRD. MMF is an alternative to CYC for the treatment of lupus nephritis.
Do we Need a New Questionnaire to Assess Quality of Life in Lupus Patients?

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Objective:
The LupusQOL questionnaire has been developed in the United Kingdom as a disease-specific health-related quality of life instrument for adults with systemic lupus erythematosus (SLE). We aimed to assess whether the LupusQoL contributed additional information not obtained using the SF-36 (Short Form-36) in a cohort of lupus patients.

Methods:
Forty one patients seen at a single centre, were followed at monthly intervals for 12 months. The LupusQoL and SF-36 questionnaires were co-administered to the patient on each visit when a complete history, physical exam and laboratory tests were performed. For both questionnaires, 0 reflects worst and 100 best. We determined the correlation of the 4 similar domains of the LupusQoL and SF-36; Physical Health and Physical Functioning, Emotional Health and Mental Health, Pain and Bodily Pain, and Fatigue and Vitality. We determined the correlation between each domain of the LupusQoL with both the physical component score (PCS) and the mental component score (MCS) of the SF-36. We analyzed the mean score for all comparable and non-comparable domains in LupusQoL and SF-36 in 351 patient-visits and 41 patients’ average scores.

Results:
Among the 41 patients 37 were female and 4 were male. Three hundred fifty one patients-visits were recorded for both questionnaires. We found that related domains of the LupusQoL correlated with the SF-36 domain; Physical Health and Physical Functioning r=0.74, Emotional Health and Mental Health r=0.83, Pain and Bodily Pain r=0.75, and Fatigue and Vitality r=0.75 (all with p< 0.0001). For the 4 non-comparable domains of the LupusQoL, there was a correlation between Body Image and MCS SF-36 r=0.61, Planning and MCS SF-36 r=0.68, Intimate Relationships and PCS SF-36 r=0.73, and Burden to Others and MCS SF-36 r=0.70 (all p< 0.0001). The mean score for comparable domains in LupusQoL and SF-36 in 351 patient-visits was always higher in LupusQoL; (Mean score in 351 patients-visits: Physical Health and Physical Functioning 70.7±22.8/63.6±27.5, Emotional Health and Mental Health 76.8±22.9/67.9±22.3, Pain and Bodily Pain 73.8±23.9/64.5±27.2, Fatigue and Vitality 63.8±26.6/50.0±26.2). The same was seen with mean of patient’s averages.

Conclusion:
LupusQoL correlated with the comparable domains of the SF-36. Non-comparable domains of LupusQoL offer no additional information to SF-36. There is no superiority of LupusQoL over SF-36 in assessing lupus patient’s quality of life. The utility of LupusQoL change over time and with disease activity needs to be evaluated in future studies.
Adult Presentation of Stickler Syndrome Type III

Kayi Li (University of Toronto, Markham); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket)

Case Report:
OBJECTIVE Few clinical cases have been published on Stickler syndrome type III. We describe an adult presentation of the syndrome in a 67-year-old woman and provide a comprehensive report on the clinical and radiographic features supporting diagnosis. METHOD(S) USED A chart review and updated investigations were performed to elucidate the presenting history and disease progression in the patient. A direct interview was also conducted to clarify any uncertain case details and elicit potential missed findings. RESULT(S) OBTAINED Clinical: The patient was 42 years old when she presented with a 22-year history of bilateral knee pain and atypical osteoarthritis (OA) of an inflammatory but non-erosive character. There were no associated symptoms or history. At age 29 years she underwent a right medial meniscectomy and symptoms were relieved. New onset of ‘osteoarthritis’ in the first metatarsophalangeal (MTP) joint bilaterally was reported again at aged 38 years. The patient also reported increasing hearing loss for high-pitched frequencies. Radiography: X-rays to investigate bilateral knee pain experienced by the patient at age 42 years showed severe, non-erosive tri-compartmental OA changes. Genetics: The son of the patient developed left knee pain and bilateral knee swelling since the age of 9 years, was diagnosed with early-onset OA and also underwent bilateral knee arthroplasties in his third decade, similar to his mother. Remarkably, the grandson also presented at age 4, with recurrent, acute episodes of pain and swelling in his ankles and knees and was diagnosed with pediatric OA. These findings prompted a more directed genetic analysis, specific for hereditary OA disorders in the family, namely an otospondylomegaepiphyseal dysplasia (OSMED) in the patient, her son and her grandson. Remarkably, the grandson also presented at age 4, with recurrent, acute episodes of pain and swelling in his ankles and knees and was diagnosed with pediatric OA. These findings prompted a more directed genetic analysis, specific for hereditary OA disorders in the family, namely an otospondylomegaepiphyseal dysplasia (OSMED) in the patient, her son and her grandson. A mutation of the COL11A2 gene was confirmed in the patient at aged 63 years. BRIEF CONCLUSION(S) This is the first clinical case report on the adult presentation of Stickler syndrome type III. In particular, early-onset OA or an unrecognized skeletal dysplasia can be considered as rationale for genetic testing, screening and surveillance of both past and present family members of an affected patient. Further studies are needed to illuminate the variants of Stickler syndrome type III in adults.
Nailfold Capillaroscopy in Juvenile Dermatomyositis: Correlation with Flow Mediated Vasodilatation

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Objective:
Pathogenesis of inflammatory diseases often includes the impairment of the vascular endothelium. Our objective was to evaluate the correlation of nailfold capillaroscopy with brachial reactivity as measured by flow mediated dilatation (FMD) in children with juvenile dermatomyositis (JDM).

Methods:
Subjects with JDM who were enrolled into a prospective longitudinal study were considered for this nested cohort study. Nailfold capillaroscopy and FMD were assessed. Drug therapy and disease activity - physician global assessment (PGA) were recorded. Descriptive statistics and correlations were performed using parametric methods. Multiple imputation of missing nailfold capillaroscopy data was performed.

Results:
Of the 27 children tested (mean age 13.9 ±2.3, 50% female), nailfold capillary abnormalities were seen in 71% of patients (mean: 6.1 ±1.4) and most had little disease activity (mean PGA: 1.0 ±1.3) at the time of measurement. Children had been followed for a mean of 5.5 ±3.6 years. Nailfold capillary density was found to correlate with FMD (r= 0.5, p=0.020), disease activity (PGA) (r= -0.5, p=0.038), and CRP (r= -0.4, p=0.071).

Conclusion:
Our findings suggest that nailfold capillaroscopy may be used as a non-invasive technique not only to evaluate microvascular involvement but also vascular endothelium function in children with JDM. In future studies, we will determine if changes in nailfold capillaroscopy correlate with changes in FMD and clinical features of JDM.
A Direct Comparison of the Reliability and Validity of 5 Measures of Lower Extremity Pain, Function and Disability in Ankle Arthroplasty and Arthrodesis

Taucha Inrig (St. Michael's Hospital, Toronto); Kelly Warmington (St Michael's Hospital, Toronto); Ellie Pinsker (St. Michael's Hospital, Toronto); Timothy Daniels (St. Michael's Hospital, Toronto); Dorcas Beaton (St. Michael's Hospital, Toronto)

Objective:
Assessment of hindfoot surgical interventions via validated and specific functional outcome scores has evolved over the past decade. A number of outcome measures have been used, but they vary substantially in content, have not been directly compared, and some have not been psychometrically validated in this patient population. The purpose of this study is to directly compare the measurement properties of 5 self-report lower extremity measures and to evaluate their reliability and validity in light of patient preferences.

Methods:
A cross-sectional survey, convenience sample of 42 pre-operative and 100 post-operative (18 arthrodesis, 82 arthroplasty) ankle patients were recruited from an orthopaedic practice in an urban teaching hospital. Patients completed the following lower extremity instruments on 2 occasions: the Foot Function Index (FFI), patient-reported section of the American Orthopedic Foot and Ankle Society Questionnaire (AOFAS), Lower Extremity Functional Scale (LEFS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Short Musculoskeletal Function Assessment Form (SMFA). The SF-12, EQ-5D, measures of instrument preference, satisfaction and current status were also included in the survey.

Results:
Scores were in the mid-range of the scales. Internal consistency was high for all the scales and subscales (α 0.83-0.96; ICC (2,1) 0.81-0.96). Correlations between scales ranged from 0.50 (WOMAC Stiffness subscale and FFI Activity Limitations subscale) to 0.96 (FFI Disability and FFI Overall). Higher correlations occurred between subscales from the same instrument and similar subscales from different instruments. Construct validity showed moderate-high correlations to NRSs of pain, stiffness and daily activity. The highest correlations (≥0.75) occurred in the pain NRS and WOMAC Pain/FFI/AOFAS; stiffness NRS and WOMAC Stiffness/WOMAC Physical Function; daily activity NRS and all of the instruments except the WOMAC Stiffness/FFI Pain/SMFA Emotional Status. Instruments were ranked by patients for preference. FFI, WOMAC, LEFS and SMFA were favourably ranked by patients in terms of length. FFI, WOMAC, LEFS, and AOFAS ranked high for understandability. The FFI was rated the most likely to capture the surgical experience by post-op patients, and the SMFA was rated the best overall questionnaire.

Conclusion:
Direct comparison of measures revealed similarity between scales in terms of construct validity and internal consistency. Patient preferences supported the use of these scales. Foot specific instruments offered no clear advantage over lower extremity instruments.
A User-centered Design Process to the Design of a Tool for Rheumatologists - Clickable Homunculus

Andrew Chow (Credit Valley Rheumatology, Mississauga); Tom Robinson (University of Waterloo, Kitchener); Deon Jajalla (University of Waterloo, Toronto); Catherine Burns (University of Waterloo, Waterloo)

Objective:
Computerized support tools, when designed with a user-centered design process, have the potential to improve the efficiency and quality of physician-patient interactions. A user-centered design aims to make the user’s work more efficient and is based on the principle of accommodating the design to the person, not the person to the design. In this example we examine the development of a functional computer application, integrating the Stanford Health Assessment Questionnaire (HAQ), Clickable Homunculus and sliding Pain Scales in order to provide the ability to more accurately calculate disease activity in patients. In addition, output screens offer the physician the ability to maintain more accurate record keeping, and the opportunity to effectively track disease activity over time in order to treat disease to a predefined target.

Methods:
The tool was developed in close collaboration with a rheumatologist who wanted to improve the efficiency of his clinic. The process began with an in-depth interview to understand his needs and the clinical context of the application. Following this interview we developed prototypes using PowerPoint. Various iterations were developed in order to have the software better meet the clinical requirements for this physician and provide an aesthetically pleasing interface.

Results:
The program was implemented in Java to permit deployment across a variety of computing environments. The program allows the rheumatologist to click on each joint to indicate whether the joint is tender or swollen. Rheumatologists can also indicate if the joint is damaged, fused, replaced, or attach their own notes to each joint. Joint counts of tender and swollen joints are provided. As well, the program calculates DAS28-ESR, DAS28-CRP, CDAI and SDAI. Three slider scales are provided for the Patient Global Assessment, Patient Assessment of Pain, and Patient Global Assessment of Disease Activity. A notes field is provided where a rheumatologist can add his or her additional notes to the assessment. On the summary screen, the homunculus for tender and swollen joints is shown with lab results and assessment calculations. The assessment is converted into plain language summaries that could be used for more accurate record keeping in addition to improving information transfer to the referring physician.

Conclusion:
This project has demonstrated the potential of user-centered design to allow the rheumatologist to develop technology innovations that work within their clinical context.
Screening for Sexual Concerns and Sexual Dysfunction in Rheumatic Disease Patients - A Survey of Canadian and British Rheumatologists

Fiona Aiston (Queen's University, Kingston); Henry Averns (Queen's University, Kingston)

Objective:
To survey Canadian and British rheumatologists with respect to: • Sexual concern and sexual dysfunction screening practices. • Beliefs on barriers to discussing sexual dysfunction. • Views on importance of improving the sexual functioning of rheumatic disease patients. • Desire of rheumatologists for a sexual dysfunction screening tool designed for rheumatic disease patients

Methods:
Twenty-three item on-line surveys sent to members of the Canadian Rheumatology Association (CRA) and the British Society for Rheumatology (BSR) (n = 84). The survey included both closed-ended and open-ended questions.

Results:
Approximately one third of rheumatologists surveyed screen for sexual concerns of their patients and among those who screen, the vast majority (90.0%) only screen a minority of their regular patients. Sexual concern and dysfunction screening was conducted most frequently by female rheumatologists and also by rheumatologists who were comfortable taking a sexual history. The majority of rheumatologists believe that family physicians should be addressing the sexual concerns and sexual dysfunction of rheumatic disease patients. In addition, while over 80% of rheumatologists think that improving the sexual well-being of rheumatic disease patients is important or very important, only 52% of rheumatologists would use a sexual dysfunction questionnaire if specifically designed for rheumatic disease patients in their practice.

Conclusion:
The results of this study suggest that important areas of intervention include improving education for both rheumatologists and family physicians on the sexual impact of rheumatologic disease, as well as highlighting the resources that are available to help address the sexual concerns and sexual dysfunction of rheumatic disease patients. Interventions by rheumatologists, family physicians and other health professionals may improve sexual function and overall quality of life of rheumatic disease patients. A direction of further study involves creating and evaluating a tool to be used by rheumatologists and family physicians that can help screen for sexual concerns or sexual dysfunction among rheumatic disease patients.
Deep Infrapatellar Bursitis in Children with Juvenile Idiopathic Arthritis

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Objective:
Anterior knee pain is a common pediatric complaint. Children with juvenile idiopathic arthritis (JIA) can rarely present with localized anterior knee pain or swelling in addition to generalized knee pain induced by JIA. Five cases of deep infrapatellar bursitis in children with JIA are reported, to emphasize the differential diagnosis, evaluation and management of anterior knee pain or swelling in the context of juvenile idiopathic arthritis.

Methods:
The clinical features, radiological findings, management and outcome of five children with JIA seen at BC Children’s Hospital Rheumatology Clinic, who developed anterior knee pain and / or swelling secondary to deep infrapatellar bursitis are discussed.

Results:
Three boys and two girls with a mean age of 9.4 years (range 6 to 13 years) were reviewed. Four children had persistent oligoarticular JIA and one child had extended oligoarticular JIA. The presentation of deep infrapatellar bursitis in those five patients with JIA was variable. In two patients the bursal swelling was the presenting problem while in three patients the swelling developed follow treatment for known JIA. In only one patient was the bursal swelling painful. Knee MRI was performed in three patients and demonstrated coexistent knee joint synovitis in one. In one patient with clinically suspected arthritis, gadolinium enhanced MRI showed no knee joint synovitis. Treatment included targeted corticosteroid injections into the deep infrapatellar bursa in two cases with complete resolution. One case was treated with corticosteroid injection by an outside health care provider with poor clinical response. Two cases are being treated with non-steroidal anti-inflammatories (NSAIDs) and Methotrexate.

Conclusion:
Deep infrapatellar bursitis can occur as an isolated finding or concurrently with knee joint synovitis in patients with JIA. Therefore, palpation of the deep infrapatellar bursa should be routinely performed during a knee examination in these patients. Awareness of this entity is important because direct injection of the bursa may be needed for treatment as the bursa does not communicate with the knee joint. Furthermore, when bursitis is suspected in JIA, MRI can be helpful to confirm the diagnosis, detect concurrent knee joint synovitis and exclude other causes of anterior knee pain.
Changing Profile of Patients with Rheumatoid Arthritis treated with Infliximab in Canada between 2002 and 2008 – RemiTRAC Rheumatology

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Objective:
The efficacy of Infliximab (IFX) in Rheumatoid Arthritis (RA) is well established. Patient profiles and use of biologics have reportedly changed since their introduction. The aim of this analysis is to describe the Canadian patient profiles at the time of initiation of IFX and treatment outcomes in the years 2002 until 2008.

Methods:
RemiTRAC is an ongoing Canadian prospective observational study of patients treated with IFX that was initiated in 2002. Patients who were biologic naïve or had initiated treatment with a biologic within six months are enrolled in the cohort and are followed prospectively as per routine care. Patients were analyzed by the year of their entry.

Results:
A total of 679 patients have been enrolled between 2002 and December 31st, 2008. Patient characteristics at baseline changed between 2002 and 2008 towards less severe disease. A trend test showed a significant reduction over the years in mean baseline DAS28 and for all DAS components (SJC, TJC, patient global assessment and CRP or ESR) analyzed separately, except for ESR. Additionally, a significant decrease was observed in the mean baseline duration of morning stiffness, HAQ, pain and physician global assessment. Mean disease duration also decreased, but only numerically, while age and baseline IFX dose remained relatively unchanged. The mean number of previous DMARDs used before initiation of IFX treatment also decreased significantly over the years. Despite the trend to less severe disease no significant between-year difference in EULAR response rates or proportion of patients achieving remission or low or moderate disease activity after 12 months was observed. However, regression analysis showed a similar improvement over time for DAS28 and HAQ, independent of year of IFX initiation.

Conclusion:
Patient characteristics at initiation of IFX in Canada changed between 2002 and 2008 towards lower disease activity. Also patient management changed, with a trend to treat patients with less DMARDs before initiation of IFX. IFX was effective in significantly reducing disease activity independently of the treatment initiation year.
The Arthritis Program (TAP) Inflammatory Education Program: The Importance of Hope within a Chronic Disease Educational Framework

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Objective:
The Inflammatory Education Program offered through TAP is a self-management education program. The group program takes place over a two week period, totaling 40 hours. Sessions are facilitated by an interprofessional team including a physiotherapist, occupational therapist, rheumatologist, pharmacist, kinesiologist and social worker. The program is offered on a monthly basis with the intended outcome of empowerment and self-efficacy. The aim of this investigation was to explore the desired educational needs of this population.

Methods:
Day one of the class, the social worker asked the group two specific questions: 1. “What do you hope to learn in this program?” 2. “At the end of this program how are you going to know you got what you came for?” These questions were posed again to the group on the last day of class. These questions set in motion lively group discussion facilitated by the social worker. Responses were gathered, recorded and shared without delay among the inter-professional team to tailor the individualized educational needs of the participants in that particular session. Responses were also used to evaluate the program and adjust both content and tone for future participants. A qualitative approach to coding participant feedback, gathered from January – October 2009, was applied to capture key concepts, categories and emerging themes. Approximately 120 class participants were consulted.

Results:
The two questions, with their subtle difference in focus tapped into content issues (“what do you hope to learn”) and issues of self perception/how I will be different after the class (“how are you going to know you got what you came for?”). Key themes clustered around: tone (hope), empowerment (becoming an informed consumer) and decreased feelings of isolation (feeling supported). The prominent recurring theme of hope was an unexpected finding. Participants not only stated their need to hear hopeful information (e.g. new research) but also emphasized the importance of presenters adopting a hopeful approach to presenting that information (e.g. how to go on living despite having arthritis).

Conclusion:
The feedback emphasizes the importance of presenting information about Inflammatory Arthritis within a hopeful framework. This is vital according to the majority of class participants. These findings will be used to enhance clinical care and provide evidence-based patient education. Whether a correlation exists between hope and self-efficacy is an interesting relationship to explore in future investigations.
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Primed Primary Care Practitioners to Treat Osteoporosis in their Patients with a Fragility Fracture

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Objective:
To compare current care with 2 strategies to increase osteoporosis (OP) treatment by Primary Care Practitioners (PCPs) in patients with fragility fractures.

Methods:
Outpatients ≥50 years seen by orthopedists at the Centre hospitalier universitaire de Sherbrooke were screened for incident fragility fracture. Consenting patients with fragility fracture were randomized to Standard Care (SC; no intervention) or to either Minimal (MI) or Intensive Interventions (II). Current use of OP treatments was collected at inclusion and at each phone follow up and confirmed with patients' pharmacists at 1 and 2 years. Appropriate OP treatment was defined as Calcium and Vitamin D supplements plus effective OP treatments (usually an aminobisphosphonate). Patients untreated at 12 months were offered a rescue. In SC, OP treatments were obtained at 6 and 12 months; if untreated at 12 months, an II was offered. In MI, a research assistant informed the patient verbally and in writing about OP, sent a standardized letter notifying the PCP of the patient's fragility fracture, the rationale and importance to treat OP rapidly after such a fracture, and outlining the appropriate investigation and treatments. In untreated patients, at 6 months, the PCP was again urged to treat; at 12 months, an II was offered. Intensive Intervention (II) included all initial components of a MI plus immediate labs to identify conditions possibly affecting treatment of OP. The PCP also received in writing the results of the investigation and personalized counsels to treat the patient. When patients were untreated at 4, 8 or 12 months, PCPs were again urged to treat their patient's OP. Rates of appropriate treatment at 12 months were compared between groups.

Results:
From January 15 2007 to September 1 2009, 614 patients from 244 PCPs were recruited: 200 in SC, 216 in MI, and 198 in II. Follow up at 12 months was obtained from 88.3% of the patients having reached one year. Appropriate OP treatment at inclusion and at 12 months was present in 15% and 38% (+23%) in SC, 17% and 55% (+38%) in MI, and 15% and 60% (+45%) in II, respectively.

Conclusion:
Both OPTIMUS interventions improve management of OP at one year in patients with fragility fractures. PCPs remain responsible for the treatment of their patients, minimizing costs and burden on specialized human resources. Dedicated personnel appears required to identify fragility fractures, notify the PCP, reinforce adherence of the patient, and possibly modify long term behaviours of PCPs towards OP treatment.
Strength of Evidence in Guidelines regarding the pharmacological management of RA

Pooneh Akhavan (University of Toronto, Toronto); Orit Schieir (University of Toronto, Toronto); Glen Hazlewood (University of Calgary, Calgary); Vivian Bykerk (Mount Sinai Hospital, Toronto); Claire Bombardier (CLINICAL DECISION MAKING AND HEALTHCARE, TORONTO)

Objective:
To determine what percentage of clinical practice guidelines (CPG) and consensus statements (CS) on the pharmacological treatment of rheumatoid arthritis (RA) have been developed based on systematic review of literature (SRL).

Methods:
A systematic review of all CPG and CS regarding treatment of adults with RA, published between January 2000 and July 2009, was performed in Medline, EMBASE and CINAHL databases and was supplemented by a comprehensive grey literature search. Quality of guidelines was assessed by 2 independent raters, using the Appraisal of Guidelines Research & Evaluation (AGREE) Instrument. An overall assessment was reported as “Recommend (R)”, “Recommend with Provisos (RWP)” and “Would Not Recommend (WNR)” using AGREE criteria. An assessment was also done to see if a systematic review of literature was performed in the process of guideline development and the level of evidence for each recommendation was provided.

Results:
Results: 57 (33 CPG, 24 CS) relevant guidelines were identified from 17 different countries. SRL was performed in 23/57 (40%, 16 CPG and 7 CS) guidelines. Level of evidence and the grading system used to assign levels of evidence was provided in 17/23 (74%, 14 CPG and 3 CS) of these guidelines. Out of 16, 9 CPG were rated as R and the rest were rated as RWP. There was a significant heterogeneity in the grading systems (12 different systems) used. All CS were rated as RWP. Out of 16 CPG, 4 were focused on biologic agents, 2 on DMARDs, 1 on steroids and 9 covered general RA management including different therapeutic agents. Among 23 out of 57 (40%, 9 CPG and 14 CS) guidelines for which a SRL was not performed, 3 CPG were based on other existing guidelines and in 2 CPG evidence provided by manufacturer were critically appraised. Out of 9 CPG, 2 were rated as R, 4 as RWP, 3 as WNR. 8 of above 9 CPG were focused on biologics. For the rest of the guidelines it was unclear whether a SRL was performed.

Conclusion:
Among all RA management guidelines developed between 2000 and 2009, regardless of the therapeutic agents, less than half are based on a SRL. For most of CPG focused on newer agents a SRL has not been performed in the process of guideline development.
Finding Guidelines to AGREE on: A Quality Appraisal of International Guidelines on the Pharmacological Treatment of Rheumatoid Arthritis

Glen Hazlewood (University of Calgary, Calgary); Orit Schieir (University of Toronto, Toronto); Pooneh Akhavan (University of Toronto, Toronto); Vivian Bykerk (Mount Sinai Hospital, Toronto); Claire Bombardier (CLINICAL DECISION MAKING AND HEALTHCARE, TORONTO)

Objective:
To assess the quality of international clinical practice guidelines (CPG) and consensus statements (CS) on the pharmacological treatment of rheumatoid arthritis (RA).

Methods:
We performed a systematic search of Medline, EMBASE and CINAHL databases and the grey literature for CPG and CS addressing pharmacological treatment of adult patients with RA published between January 2000 and July 2009. Guideline quality was assessed by two independent raters (GA & PA) using the Appraisal of Guidelines Research & Evaluation (AGREE) Instrument, which consists of 23 questions across 6 domains: scope and purpose, stakeholder involvement, rigour of development, clarity and presentation, application and editorial independence. We calculated scores for each question and domain, and made an overall assessment of the CPG as “Recommend (R)”, “Recommend with Provisos (RWP)” and “Would Not Recommend (WNR)” using criteria published by AGREE. Quality of CS was also evaluated using AGREE as no comparable quality assessment tool for CS is currently available.

Differences in quality between CPG and CS were examined and a descriptive analysis of publication status and year by study type was performed.

Results:
57 (33 CPG, 24 CS) relevant guidelines were identified from 17 different countries. Inter-rater agreement was excellent for all 6 AGREE domain scores (intraclass correlation coefficients (ICC) ranging from 0.74 to 0.93) and for the single item overall assessment [R/RWP/WNR] (Kappa = 1). CPG rated higher than CS: R (CPG: 12/33 [36%] vs. CS: 0/24 [0%]), RWP (CPG: 17/33 [52%] vs. CS: 17/24 [71%]) and WNR (CPG: 4/33 [12%] vs. CS: 7/24 [29%]). CPG also rated higher than CS across all 6 domains [data not shown]. Both CPG and CS scored highest for “scope and purpose” and “clarity and presentation” and lowest for “applicability” and “editorial independence.” Descriptive analyses of publication status and year by study type showed that only 16/33 (48.5%) CPG vs. 23/24 (96%) CS were published in a journal and that while the overall assessment of quality for CPGs improved over time, the quality of CS remained stable.

Conclusion:
The methodological quality of published guidelines on the pharmacologic treatment of RA is variable, with few guidelines rating as high quality. CS rated as lower quality than CPG, however this may reflect differences in measurement properties of the AGREE instrument for CS. Less than half of CPG are published in journals suggesting that broader search strategies for identifying CPG are warranted.
Access to Anti-TNF Agents for the Treatment of Rheumatoid Arthritis in Canada Differs from Published International Guidelines

Glen Hazlewood (University of Calgary, Calgary); Pooneh Akhavan (University of Toronto, Toronto); Orit Schieir (University of Toronto, Toronto); Jessica Widdifield (UHN-Toronto General Hospital, Toronto); Claire Bombardier (CLINICAL DECISION MAKING AND HEALTHCARE, TORONTO); Vivian Bykerk (Mount Sinai Hospital, Toronto)

Objective:
To compare whether Canadian provincial formulary requirements for accessing anti-TNF agents in adult patients with rheumatoid arthritis (RA) are consistent with international guidelines.

Methods:
A broad systematic search of all clinical practice guidelines (CPGs) and consensus statements (CS) on the pharmacologic treatment of adults with RA from January 2000 to July 2009 was performed, and a subset of guidelines with recommendations regarding access requirements for anti-TNF therapy was selected for the present study. Recommendations for defining DMARD failure prior to anti-TNF therapy were abstracted and compared to Canadian formulary requirements across all 10 provinces.

Results:
Twenty out of 57 (35%) treatment guidelines in RA (11 CPG and 9 CS) addressed criteria for defining DMARD failure prior to initiation of anti-TNF therapy. Six CPGs were excluded from further analysis (3 for having recommendations derived from other CPGs and 3 were deemed to be of very poor quality and limited relevance). The mean number of DMARDs required to have failed was higher according to Canadian formularies (mean 2.4, SD: 0.52) than international guidelines (mean 1.4, SD: 0.21) (mean difference: 1.0, 95% CI: 0.43-1.6). DMARD failure requirements in Canada were: methotrexate (MTX): 9/10 provinces; sc. MTX: 2/10; leflunomide (LEF): 7/10 and combination therapy: 8/10. Failure of MTX was mandated in 9/14 (65%) of CPG/CS, and combination therapy in just 1/14 (7%). No CPG/CS required patients to fail sc. MTX or LEF. The minimum time required to start anti-TNF therapy in DMARD naïve patients was similar between the provincial formularies and guidelines: provinces; mean 4.9 months (SD: 0.56), guidelines; mean 5.0 months (SD: 1.1) (p=0.93). Minimizing time to anti-TNF initiation in DMARD naïve patients, however, requires starting with combination therapy in 9/10 provinces vs. 1/14 CPG/CS.

Conclusion:
Canadian formulary requirement for accessing Anti-TNF agents for the treatment of rheumatoid arthritis are more stringent than published international guidelines. Canadian formularies require patients to have failed more DMARDs, and often require the failure of leflunomide and combination therapy, which is not recommended by most international RA treatment guidelines. The minimum time to initiation of anti-TNF therapy in DMARD naïve patients is similar between Canadian formularies and published guidelines, but to achieve this, most Canadian formularies require starting with combination therapy.
Adapting ADAPTE: A Novel Methodology for the Development of National Clinical Practice Guidelines

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Objective:
To develop a novel methodology based on the ADAPTE framework to produce a Canadian clinical practice guideline for the pharmacological management of RA.

Methods:
A modified procedure based on methodology developed by the ADAPTE collaboration was used to systematically identify, appraise, synthesize and adapt existing guidelines in RA. We assembled a representative working group of regional and local RA stakeholders on behalf the Canadian Rheumatology Association, including rheumatologists, methodologists, patient representatives and a general practitioner. Key questions for the guideline were developed a priori in an iterative fashion and a final set of questions was selected by consensus. A systematic review of all clinical practice guidelines (CPG) and consensus statements (CS) regarding treatment with traditional and biologic DMARDs for adults with RA, published between January 2000 and July 2009, was performed in Medline, EMBASE and CINAHL databases and was supplemented by a comprehensive grey literature search. Guideline quality was independently assessed by 2 rheumatology fellows using the Appraisal of Guidelines Research & Evaluation (AGREE) Instrument and recommendations relevant to the key questions were abstracted along with levels of evidence. We presented an overview of the new methodology and evidence tables for the key questions selected to the full committee at an initial face to face meeting. All committee members voted on whether this guideline adaptation procedure was feasible for developing Canadian recommendations on a scale ranging from 1 (fully disagree) to 10 (fully agree). A new decision algorithm for developing recommendations through adaptation was developed resulting in 1 of 3 decision outcomes for each key question: 1) develop recommendation by adaption; 2) develop new consensus recommendation; or 3) cannot develop recommendation without consulting original literature. This procedure was used to develop recommendations for the Canadian guideline at a second face to face meeting.

Results:
28 key questions were selected; 33 international CPG and 24 CS were identified as relevant and abstracted. Results of the first meeting showed that the committee was strongly in favor of the new methodology (2/9 [22%] voted 8; 3/9 [33%] voted 9 and 4/9 [44%] voted 10). Results of the second meeting showed that 21 (75%) recommendations could be developed by adaptation, 5 (18%) could be developed by consensus, and only 2 (7%) could not be developed without consulting original literature.

Conclusion:
This is a novel and systematic framework for creating tailored clinical practice guidelines that is cost saving and allows for more rapid guideline dissemination.
The Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program: Impact on Community Practice (A Pilot Study)

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Objective:
1) To compare practice between advanced practice practitioners (APPs) and non-APP trained therapists working in the community as documented in client charts (retrospective chart review) 2) to provide a descriptive analysis of the therapists’ investigations, assessments, therapeutic interventions and outcomes in preparation for designing a randomized controlled trial.

Methods:
Client charts of APP trained physiotherapists (PTs) or occupational therapists (OTs) and from non-APP therapists were selected from a random selection of charts matched on therapist discipline, urban/rural location, and time of referral. The sample (n=60) was limited to the charts of adult clients with suspected or confirmed Inflammatory Arthritis (IA). Three trained multidisciplinary reviewers used standardized forms to independently extract data from charts. The research team reviewed a 10% sample of charts to establish inter-rater reliability of the reviewers.

Results:
Fifty-eight charts were reviewed. Client demographics were similar for APPs and non-APPs and had the following characteristics: 79% female, mean age 59 years (min:max; 19:87), 76% English speaking, 55% married/common law, 29% living alone and 78% not working for pay. Client goals were similar in both groups as well. More APP clients lived in rural communities (p=0.041) and were more likely to be referred for assessment rather than management (P=.007). Disability level was significantly different (P=0.011) with non-APPs seeing more clients with mild and severe disease and APPs seeing more clients with moderate disease. APPs were more likely to assess and record comorbidities (p=0.028), treat those without a confirmed diagnosis (P=0.002), and assess and record morning stiffness (P=0.026) and grip strength (P=0.053). Length of treatment in days was longer for clients seen by APPs (P=0.008) and marginally more interventions took place over the phone (P=0.058). APPs were more likely to advocate with the client’s family, physician or specialist (P=0.014) and recommend or provide exercise or physical activity (P=0.035). Non-APPs provided significantly more education about community resources (P=0.021) and provided or recommended more assistive devices (P=0.046).

Conclusion:
Based on the results of this retrospective chart review, APP therapists served a different population of clients compared to non-APP therapists. Differences were seen in the types of referrals and client disease characteristics which may explain in part the longer treatment times and more advocacy with general practitioners and specialists. It will be important to capture the details of these differences in planning for a future RCT to evaluate the efficacy of APP interventions.
Proximal Muscle Weakness and Statin Use: A Case of Mistaken Identity

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Case Report:
Objectives: 1. To develop a diagnostic approach to muscle weakness. 2. To recognize the cardinal features of myopathy and learn how to differentiate the etiology in patients on statin therapy. 3. To recognize paraneoplastic syndromes associated with myopathy, especially lung cancer in non-smokers. Abstract: A 61-year-old man with a past medical history of hypertension and dyslipidemia presented to ER with a two-month history of painless proximal arm and leg weakness, multiple falls and a 10 pound weight loss. The patient was a non-smoker and was on lisinopril and atorvastatin for the last 4 years. Review of systems was non-contributory. Physical examination was only significant for proximal muscle weakness in the shoulders and hip flexors/extensors. Initial bloodwork revealed a CK of 15198, AST 304, ALT 390, creatinine 43, and 2+ blood/1+ protein in urinalysis. He was referred as a “statin-induced myopathy”. We held his lipitor and started him on intravenous fluids for rhabdomyolysis. Given his history of weight loss, further investigations (including muscle biopsy and nerve conduction studies) were completed resulting in a diagnosis of polymyositis by the rheumatology service. As part of the paraneoplastic workup, chest X-Ray showed a left upper lobe mass, which was biopsied, revealing primary lung adenocarcinoma. Full metastatic workup was negative. The patient was treated with prednisone and successfully underwent left upper lung lobectomy and adjuvant chemotherapy with no long-term complications. His muscle strength continued to improve post-tumour resection, reaching near-baseline approximately one month post-op. This case illustrates that statin-induced myopathy is a diagnosis of exclusion. Also, although classically, dermatomyositis is associated with underlying malignancy, polymyositis might also warrant investigations for underlying malignancy. Lastly, this case reminds us that although most cases of lung cancer are due to smoking, lung cancer among non-smokers is a significant health problem.
Case Report:
Objectives: 1. Describe a unique case of SLE with positive cANCA, pANCA and anti-Scl-70 antibodies in the absence of vasculitis. 2. Describe the cardinal diagnostic features of SLE. 3. Describe the prevalence/clinical significance of cANCA, pANCA and anti-Scl-70 positivity in SLE (literature search).
Case: A 47-year-old man with impaired fasting glucose and GERD presented to the outpatient respirology clinic with worsening dyspnea and pleuritic chest pain. His acute presentation was preceded by 6 months of progressive dyspnea, non-productive cough and episodic chest tightness. Review of systems revealed fatigue, morning stiffness, periodic warm swollen painful joints (hands, wrists, knees, ankles), Raynaud’s phenomenon, worsening GERD, chills, night sweats and a non-intentional 10 pound weight loss. Family history included rheumatoid arthritis and lymphoma. He was a smoker on ibuprofen and ranitidine PRN. Physical exam identified a tachypneic (RR 28) but otherwise hemodynamically stable gentleman. He had scleral icterus and occasional crackles at the lung bases. Investigations revealed a hemolytic anemia (Hgb 94, spherocytosis, LDH 573, total bilirubin 36, Coomb’s positive), mildly impaired GFR (creatinine 90) and hypoxemia (ABG PaO2 55). Serology was positive for ANA (160 titre), c-ANCA (1.8 AI), p-ANCA (1.8 AI) and anti-Scl-70 (2.4 AI). The patient was admitted under respirology with rheumatology consultation. Acute cardiac work-up was negative. CT chest excluded PE, but showed mediastinal adenopathy and extensive ground-glass opacities with reticular interstitial change. The diagnostic dilemma became differentiating between a vasculitis versus connective tissue disease. Eventually, open lung biopsy showed organizing pneumonia, respiratory bronchiolitis without vasculitis. A 24-hour urine specimen confirmed nephropathy (0.54 g/day, negative for casts). Therefore, the final diagnosis was SLE. He was started on prednisone 50 mg po BID and tapered to 25 mg po daily one month post-admission. His anemia/dyspnea gradually improved; he continues to be followed by the combined respirology/rheumatology clinic. In the literature, both ANCA and anti-Scl-70 positivity have been individually described in SLE with a predominance of p-ANCA. There were no reported cases of both p-ANCA and c-ANCA positivity and furthermore no cases of combined p-ANCA, c-ANCA and anti-Scl-70 positivity. In conclusion, lupus is a multi-system disease that can present variably. We describe a case of SLE presenting with organizing pneumonia, hemolysis and a unique antibody pattern. The clinical significance of the above presentation and associated auto-antibodies with respect to prognosis is yet to be determined.
Psychiatric Illness of Systemic Lupus Erythematosus in Childhood

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Objective:
1) To describe characteristic clinical, laboratory and imaging features; 2) To determine distinct entities in the spectrum of psychiatric disease of Juvenile SLE and 3) to report treatment and outcomes.

Methods:
Single centre cohort study of consecutive JSLE patients followed between 08/1985 and 12/2008 was performed. Patients were evaluated following standardized protocol. All patients were assessed by an experienced psychiatrist. Clinical features of psychiatric disease of Lupus were identified and classified according to ACR nomenclature except cognitive dysfunction. Cognitive dysfunction was defined as memory or attention deficits reported by patients/ parents, affecting academic performance. Specific investigations (neuroimaging and lumbar puncture) were extracted. Psychiatric outcomes: 1) response- no psychiatric symptoms, stopped anti-psychotic medications and Prednisone < 50% maximal dose for at least 3 months; 2) remission- no psychiatric symptoms, stopped anti-psychotic medications and Prednisone ≤ 10mg/day for at least 3 months; 3) relapse- recurrence of symptoms (after response) requiring 50% increase in dose of Prednisone, change of 2nd line immunosuppressive not due to adverse

Results:
447 JSLE patients followed during the study period: 12% (53) developed psychiatric disease of JSLE; 87% (46) females, median follow- up from psychiatric diagnosis 2.0 years (0.5-6.8). Half (27/53) had psychiatric disease at diagnosis of JSLE. Median interval from first psychiatric symptom to diagnosis was 60 days (1-1460). Features of psychiatric disease of JSLE: Psychosis-like symptoms in 75% (40), hallucinations predominant- 73% visual, 85% auditory and 20% tactile hallucinations. Insight preserved in 70%. Novel symptom of visual distortions seen in 38% of Psychotic patients. Clinically significant cognitive dysfunction present in 25% (13). No patient had isolated depression or anxiety. Specific investigations: 42 had Magnetic Resonance Imaging (MRI): 45% normal, 29% cerebral atrophy and 17% white matter changes. Lumbar puncture performed in 53% (28/53) at diagnosis: 29% had abnormally elevated total protein, 7% had elevated white cells. Treatment: Prednisone started/ increased following protocol. 60% (24) of patients with Psychosis required antipsychotic therapy. All but 3 were treated with 2nd line agents during their course: 85% (45) Azathioprine, 55% (29) Cyclophosphamide and 28% (14) Mycophenolate. Outcomes: 74%(39) responded by last follow-up, 25 attained remission (but 3 relapsed), 6 relapsed, 8 improved but not

Conclusion:
Psychiatric illness of JSLE was different from neuropsychiatric SLE in adults, with mainly psychosis and cognitive dysfunction. All patients with psychosis had hallucinations but insight was intact. Unique symptom of visual distortion was seen. Most patients (74%) responded to
Lack of Seroconversion of RF and anti-CCP in Patients with Early Inflammatory Arthritis: A Systematic Literature Review

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Objective:
Serological markers are thought to be useful in predicting which patients with Early Inflammatory Arthritis (EIA) will progress to RA. However, it is unknown what percentage of RF and anti-CCP negative UIPA patients will become positive over time. The objective of this study is to determine the percent RF and anti-CCP seroconversion in UIPA patients at 1 to 5 years of follow-up.

Methods:
We conducted a systematic literature review of all English language publications addressing the progression of RF and anti-CCP positivity over time in patients with EIA. We searched Medline, EMBASE and the Cochrane Library, as well as abstracts from ACR and EULAR (2004-2009). Patients greater than 15 years old with at least one swollen joint and having symptoms less than 2 years were included.

Results:
Twelve publications were included: 10 studies included data on RF, while only 5 addressed anti-CCP. EIA populations from these studies included Undifferentiated Inflammatory Peripheral Arthritis (UIPA), Early Rheumatoid Arthritis (ERA), defined as meeting ACR criteria for RA, and mixed populations (patients with UIPA, ERA and/or meeting ACR criteria for rheumatic diseases other than RA). Sample sizes ranged from 15 to 395 and follow-up was 6 months to a median of 48 months. There was marked heterogeneity between studies and therefore results could not be pooled for a meta-analysis. Baseline RF and anti-CCP positivity was also highly variable: 8-55% and 4-45% respectively. Seroconversion rates for ERA averaged 5.8% at 1 to 2 years for RF and 6.8% at 5 years for anti-CCP. In mixed populations, RF seroconversion averaged 3.5% at 1 year follow-up and anti-CCP seroconversion ranged from 1.3% at 1 year to 8.9% at 2.5 year follow-up. There was no seroconversion in the UIPA studies.

Conclusion:
There is minimal change in RF or anti-CCP positivity over time (up to 5 years of follow-up). Prevalence data for RF in established RA is significantly higher than the baseline values reported here. The low rates of seroconversion would suggest a lower prevalence in EIA and the reason for this difference remains unknown. It is unclear whether antibody negative patients are more likely to remit and be lost to follow up in established RA populations.
Validation of Early Inflammatory Arthritis Detection Tool within Primary Care Practices in Canada

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Objective:
Objective: To determine the sensitivity, specificity, positive and negative predictive value of the Early Inflammatory Arthritis [EIA] Detection Tool, within primary care practices.

Methods:
Methods: A prospective cohort of adult patients presenting to primary care with MSK complaints will be recruited within primary care practice settings in Canada using a phased strategy: Alberta and Newfoundland are nearly complete. Focus of recruitment is now on Ontario and Manitoba, to be followed by Nova Scotia and New Brunswick and finally British Columbia and Saskatchewan. Inclusion criteria: ≥18 years of age, read English, self-reported MSK symptoms of 6-52 weeks duration and availability to attend a Rheumatology clinic for assessment. Exclusion criteria include: diminished capacity to provide informed consent, a medical history of an inflammatory arthritis. Patients who meet criteria and provide consent will be assigned an anonymous study number and will complete the 11 question EIA detection tool. Their primary care practitioner (PCP) will record their diagnosis on the tool and fax it to the study centre for data entry, and will refer the patient to rheumatology for assessment and confirmation of diagnosis. The rheumatologist, blinded to results of the EIA detection tool, will report the patient diagnosis to the study team via a fax-back form. Complete data on 1152 subjects will be recruited to capture 288 EIA participants, while the recruitment of 864 non-EIA study participants will result in a precise estimate of the sensitivity and specificity of the tool.

Results:
Results: One hundred and thirty-one patients have been recruited to date, of this number rheumatology diagnosis confirms: 22.8% EIA, 1.8% established IA, 63.1% established non-IA and 12.3% other diagnosis.

Conclusion:
Conclusions: The ability of the EIA Detection Tool to identify EIA in primary care practices appears to be good at this early phase of this validation study. By November 2009 the cohort will be larger and the frequency of finding EIA, established IA, established non-IA and other diseases will be calculated.
Peer to Peer Mentoring: Facilitating Individuals with Early Inflammatory Arthritis to Manage their Arthritis – Exploring Learning and Support Needs

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Objective:
Objective: The purpose of this study is to identify educational preferences as well as informational, emotional and appraisal support needs of individuals with early inflammatory arthritis (EIA) from the perspectives of patients, family and friends, and health care providers (HCPs).

Methods:
Method: Semi-structured, one-on-one interviews with individuals were performed with a purposive sample. Themes were identified through constant comparative analysis.

Results:
Results: Interviews were conducted with patients with EIA (n=15), family and friends (n=6), and HCPs (n=9). Individuals with EIA reported using a variety of information sources (books, Internet, physicians) with informational needs evolving over time. Data from family and friends suggested a network of emotional support was valuable to cope with and learn about EIA. Both individuals with EIA and their family and friends thought that peers would be viable sources of informational, appraisal, and emotional support. Disease stage, personal qualities and one-on-one vs. group format were important considerations. HCPs cautioned that peers acknowledge the limits of their knowledge base when providing support. Yet they too suggested that peers could play an important role in reinforcing information provided by doctors and allied health professionals. Across the three categories of participants, there was a desire for peer support (learning preferences, delivery method) to be context-driven, paying attention to specific disease phases and individual life circumstances.

Conclusion:
Conclusions: Peers may be considered an instrumental part of decision support and stress management and an adjunct to clinical care for persons with EIA. Peer support is particularly relevant to individuals with EIA who report frustrations due to delays in diagnosis, and unpredictability and invisibility of their disease. Peer support was a much-lauded approach to help individuals cope with lifestyle changes and treatment concerns brought by their new diagnosis. Data across interview categories revealed peers as a source of informational support (sharing experiences, providing new perspective on challenges), emotional support (building self-esteem, alleviating anxiety) and appraisal support (providing feedback on decisions). While format preferences were often predicated on individuals’ personalities and life circumstances, all agreed that empathy, and being knowledgeable and understanding were invaluable peer qualities.
The Role of Hormones in Flares of SLE, RA, and Fibromyalgia: Results of a Case Control Study

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Objective:
Based on clinical observation, our hypothesis was that approximately 25-30% of systemic lupus erythematosus (SLE) patients flared immediately before menses and a lesser amount of rheumatoid arthritis (RA) patients. Thus we wanted to determine the self-reported rate of flaring prior to menses in SLE, RA and fibromyalgia (FM) and determine if there were between group differences.

Methods:
Women with SLE, RA or FM from one clinic were mailed a questionnaire that inquired about flares during certain points in their menstrual cycle, changes due to the oral contraceptive pill (OCP), and changes that occurred during menopause. Four hundred and ninety-eight (498) were mailed a survey and 278 (56%) were completed: 81 SLE, 136 RA, and 61 FM. If patients had more than one of these diagnoses they were excluded; thus 25 were excluded.

Results:
We analyzed 68 with SLE, 130 RA, and 55 FM. The ages (standard deviation, SD) were 45 (8.8) SLE, 45 (12.5) RA and 50 (9.9) FM (p=0.009); mean age (SD) at diagnosis was 26.4 (10.0) SLE, 32.9 (11.5) RA and 36.6 (10.6) FM (p= < 0.001). Participants were asked if they had ever taken the OCP while they had their disease: 52.4% of SLE had, 40.5% of RA, and 32.6% of FM (p= 0.114) and the percent currently in menopause was: 43% of SLE, 35% of RA, and 53% of FM (p=0.634). The percent who flared before their menses when not on hormones were 36% SLE, 28% RA, and 54% FM (p=0.0832). There were no significant differences within diseases for flaring before menses vs. flaring before withdrawal bleed while on the OCP. However, more reported they flared before their period when not on hormones: 21/58 on hormones vs. 6/22 off hormones in SLE (p=0.4), 31/109 vs. 9/41 in RA (p=0.2) and in FM 22/41 vs. 4/13 (p=0.1). Menstrual cycle related disease flares stopped in menopause as reported overall by: 20% of SLE, 40% of RA, and 43% of FM (p=0.635).

Conclusion:
There could have been recall bias and participants may have confused premenstrual syndrome (PMS) with flares. However, there seems to be menstrual cycle complaints of flares in SLE, RA and FM. In addition, participants believed that cycle related flares decreased when on OCPs. The relationship between flares and menopause is difficult to conclude as many patients were not yet in menopause.
A Population-Based Ecological Investigation of the Relationship between Road Density and Systemic Autoimmune Rheumatic Disease Prevalence

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Objective:
Air pollutants, including those emitted by on-road vehicles, are believed to induce harmful effects on humans, through local and systemic inflammation. We aimed to investigate the association between road density and systemic autoimmune rheumatic disease (SARD) prevalence (including systemic lupus, scleroderma, Sjogren’s syndrome, inflammatory myopathies, and undifferentiated connective tissue disease) using population-based data in Quebec, hypothesizing that SARD prevalence would be correlated with increased road density.

Methods:
We estimated SARD prevalence by forward sortation area (FSA, the first three characters of the postal code) using administrative databases from hospitalization and physician billing records, for all Quebec residents from 1989-2003. Road length data were obtained from the 2001 CANMAP Street Files and included all major highways and local arteries. Road density was calculated by dividing road length in a FSA by its area according to the 2001 Canadian census. Three FSAs were excluded because they were not residential, bringing the total number of FSAs used in the analysis to 388. Disease prevalence according to four demographic groups (<45 years old, 45 years and older, male and female) and total prevalence were each square root transformed and regressed on log-transformed road density.

Results:
FSA road density ranged from 0-14.16 km/km², and over-all SARD prevalence ranged from 0-960 cases per 100,000 people. Road density was positively related to over-all SARD prevalence (slope=1.98, 95% CI=1.51-2.45). This means that SARD prevalence increases from 343 cases per 100,000, to 388 cases per 100,000, as the road density increases from 0.75 to 1.75 km/km². All demographic groups demonstrated substantial correlations between prevalence and road density. The strongest associations were seen for females (slope=2.74, 95% CI=2.07-3.41; an increase in prevalence from 538 to 616 cases per 100,000 people as road density changes from 0.75 to 1.75 km/km²) and for people 45 years and older (slope=2.94, 95% CI=2.18-3.70; an increase in prevalence from 602 to 690 cases per 100,000 as road density increases from 0.75 to 1.75 km/km²).

Conclusion:
These ecological analyses suggest that SARD prevalence is associated with FSA road density. Whether FSA road density is indicative of higher pollution exposure among SARDs patients requires further investigation. Important potential limitations of our work include that the analyses are cross-sectional and do not account for past residential exposures. Moreover, we studied prevalence, not incidence, which may mean that some of our findings may be due to the migration of chronically ill persons to locations where specialty care is more available.
Family Physician Responses to New-onset Rheumatoid Arthritis

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Objective:
Rheumatoid arthritis (RA) can potentially cause severe joint destruction and functional disability. Optimal outcome depends on the prompt prescription of disease-modifying anti-rheumatic drugs (DMARDs), which can slow down or even reverse disease progression. Current evidence suggests that an individual with RA should be given DMARDs within 3 months of symptoms onset. However, many patients are not seen in such a timely fashion. At least some of the delay appears to occur between first primary care assessment and rheumatology referral. Our objective was to study the response of primary care physicians to a classic presentation of new-onset rheumatoid arthritis.

Methods:
Online surveys were administered to family physicians practicing within the Queen Elizabeth Health Complex and the Herzl Family Practice Centre, Montreal, Quebec. The survey featured a case scenario of an individual with classical RA symptoms of new onset. The physicians were questioned regarding their clinical suspicion of RA, and what approach they would normally take, in terms of investigation and management, for such a case.

Results:
We present the results based on 45 respondents. Just over one-third (35.6%) of the primary care physicians had high clinical suspicion for RA, based on the classic scenario. Almost half (44.4%) of the respondents indicated that they would refer the patient to a rheumatologist only after they had received all test results and reviewed them. In the event that RA was strongly suspected, only 6.7% of the physicians would start a DMARD and 11.1% would prescribe prednisone.

Conclusion:
These results showed that family physicians were cautious in making a provisional diagnosis of RA, and that they were likely to rely on test results rather than RA symptoms. This may in part delay rheumatology referrals. DMARD initiation before any consultation with a rheumatologist appears to be rare. These factors, in part, likely explain some of the delay between the first primary care assessment, rheumatology referral, and prescription of DMARDs.
Systemic Lupus Erythematosus in Nova Scotia, Canada

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Objective:
Chronic disease surveillance is increasingly important to rheumatic disease stakeholders. We provide an in-depth assessment of SLE in the province of Nova Scotia, based on both administrative data and rheumatology records. This included explorations of regional patterns.

Methods:
A list of residents diagnosed with systemic autoimmune rheumatic diseases (International Classification of Diseases, ICD-9 codes 710.0-710.9) was generated from population-based administrative billing and hospitalization databases. This list was restricted to Nova Scotia residents who had seen one or more of the eight rheumatologists serving the Capital Health area. We determined from this list, the number of SLE cases (ICD-9 code 710.0 on billing or hospitalization data) who were confirmed to have SLE on their clinical records. We also explored potential differences in SLE distribution across regions within the province, and the spatial relationship to possible environmental triggers of disease. To do this, the province was divided into five areas, based in part on Statistics Canada’s definitions of a census metropolitan area or a census agglomeration. Information about the location of industrial sources of solvents, such as trichloroethylene, was obtained from the federal database of industrial pollutants. We also mapped all known major industrial sources of respirable silica, using compiled lists of high-exposure industries.

Results:
844 residents had a diagnosis of a systemic autoimmune rheumatic disease within administrative data and had undergone at least one rheumatology encounter. Of these, 392 had been coded as SLE, and 438 had been given another diagnosis. Charts were unavailable for six of the 392, but among the 386 whose charts were available, the diagnosis of SLE was confirmed in 264 (68.4%). The majority of non-SLE diagnoses were other systematic autoimmune rheumatic diseases. Of the 438 subjects with administrative database diagnoses for diseases other than SLE, four actually had SLE according to clinical records. Across the province, no specific regional differences were demonstrated. Exploratory analyses by counties within the five census-based divisions did not demonstrate any patterns that might suggest correlations with potential environmental triggers (i.e., potential environmental sources of industrial solvents or respirable silica). However, these results are likely highly limited by misclassification of exposure among subjects, given the ecological nature of the analyses.

Conclusion:
Our work highlights some of the potential usefulness and limitations of the use of administrative data for chronic disease surveillance. Our attempt to correlate potential environmental triggers to regional patterns is highly limited by the ecological nature of the analyses.
Medication Use in Systemic Lupus Erythematosus

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Objective:
To evaluate factors affecting therapeutic approaches used in clinical practice for the management of SLE, in a multi-centre cohort. A priori, factors of potential interest include patient age, race/ethnicity, disease duration, lupus activity, and accumulated damage.

Methods:
We combined data from 10 clinical adult SLE cohort registries in Canada. We used multivariate generalized estimating equation methods to model dichotomized outcomes, running separate regressions where the outcome was current exposure of the patient to specific medications. Potential predictors of medication use included demographic (age at baseline, sex, residence, race/ethnicity) and clinical factors (disease-duration, time-dependent damage index scores and adjusted mean SLE Disease Activity Index (2K) scores. The models also adjusted for clustering of subjects by centre.

Results:
Higher disease activity and damage scores were each independent predictors of exposure to non-steroid immunosuppressive agents, and for exposure to prednisone. This was not definitely demonstrated for anti-malarial agents. Older age at diagnosis was independently and inversely associated with exposure to any of the agents studied (immunosuppressive agents, prednisone, and anti-malarial agents). An additional independent predictor of prednisone exposure was black race/ethnicity (adjusted rate ratio, RR 1.46, 95% confidence interval, CI 1.18, 1.81). For immunosuppressive exposure, an additional independent predictor was race/ethnicity, with greater exposure among Asians (RR 1.39, 95% CI 1.02, 1.89) and persons identifying themselves as First Nations/Inuit (2.09, 95% CI 1.43, 3.04), compared to whites. All of these findings were reproduced when adjustment for disease activity was limited to renal involvement.

Conclusion:
Ours is the first portrayal of determinants of clinical practice patterns in SLE, and offers interesting real-world insights. Further work, including efforts to elucidate how differing clinical approaches may influence outcome, is ongoing.
Decreased Live Births in Women with SLE

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Objective:
Though well-designed studies are lacking, there is a general notion that live births are not decreased in SLE, compared to healthy women. We calculated live births in women with SLE, and compared this with general population rates.

Methods:
We studied women with SLE from a subset of centers participating in the SLICC Registry for Atherosclerosis inception cohort study. Women diagnosed with SLE before age 50 were included. We determined the number of children borne as of the last follow-up visit, and summed the years from age 15-50, or oldest age attained if the subject was < 49. We applied age- and country-specific general population birth rates, and relevant calendar-period rates to these years to determine the expected number of live births. We then calculated the standardized incidence ratio (SIR) of observed to expected live births. We performed a multivariate analysis with the SIR as the dependent variable to explore potential predictors of live births, including marital status, drugs (immunomodulators, prednisone, aspirin, anticoagulants), antiphospholipid antibodies, disease activity and damage.

Results:
339 women with SLE were studied. Mean age at diagnosis was 35.3 years (standard deviation, SD, 13.3) and mean disease duration at the last visit was 2.7 years (SD 2.0). Most (43%) women were from the US, 27% from Canada, 27% from the UK, and 3% from Sweden. The majority of women (61%) were white, 19% were black, 10% were Asian and 5% were Hispanic. Most (42%) were currently married or living common-law. Overall, the number of live births over the interval (313) was substantially below what would be expected (479) (SIR 0.65; 95%CI 0.58-0.73). In sensitivity analyses, we used race-specific general population birth rates with similar results (SIR 0.65; 95%CI 0.58-0.72). In multivariate analyses, being married or living common-law (SIR 2.07; 95%CI 1.58-2.69) and current use of aspirin (SIR 1.36; 95%CI 1.02-1.80) were associated with increased live births. There were trends for fewer live births in women exposed to cyclophosphamide (SIR 0.82; 95%CI 0.53-1.27) and in those with high disease activity (SLEDAI ≥ 5) (SIR 0.76; 95%CI 0.54-1.07). We did not establish a decrease in live births independently attributable to positive antiphospholipid antibodies (SIR 0.98: 95%CI 0.73-1.32) or disease damage (SLICC score ≥ 2) (SIR 1.02: 95%CI 0.70-1.48).

Conclusion:
Women with SLE have fewer live births compared with the general population. Marital status and current aspirin use were the most important predictors of live births in our sample.
Long-Term Safety of Rituximab: Long-Term Follow-up of the RA Clinical Trials and Retreatment Population

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Objective:
To evaluate the long-term safety of rituximab (RTX) in RA patients (pts) in clinical trials.

Methods:
Pooled analysis of safety data from pts treated with RTX + methotrexate (MTX) in a global clinical trial program. All pts were offered retreatment with RTX based on clinical need. Pts receiving placebo during placebo-controlled study periods were pooled to provide a placebo population.

Results:
As of September 2008, 3095 pts had been treated with RTX providing 7198 pt-years (pt-yrs) of exposure. Over 750 pts had been followed for >3 years with 2365, 1581, 1038 and 497 pts receiving ≥2, ≥3, ≥4 and ≥5 courses, respectively. Other than infusion-related reactions (IRR), the safety profile of RTX was similar to the pooled placebo population. In the RTX group, the most frequent adverse event (AE) was IRR (35%), mostly CTC grade 1 or 2, and occurring after the first infusion of the first course (23%), with < 1% considered serious. The rates of serious AEs (SAEs) and infections remained stable over time and also between RTX courses. The rate of serious infection was 4.25 events/100 pt-yrs and was comparable to that observed in the placebo population (4.33 events/100 pt-yrs). The most frequent serious infections were of the lower respiratory tract, predominantly pneumonia (1%). No cases of TB or reactivation of hepatitis B were reported. Serious opportunistic infections were uncommon, but included one confirmed case of Pneumocystis jiroveci pneumonia in each of the RTX and pooled placebo groups and one case of progressive multifocal leukoencephalopathy (PML) in the RTX group. The causal relationship of PML to RTX in this case was unclear due to recognized risk factors including carcinoma of the oropharynx treated by chemoradiotherapy. Rates of MI and stroke were consistent with the general RA population. The standardized incidence ratio (SIR) for malignancy compared with the SEER 2008 database was 1.06 (95% CI 0.81–1.37). The most frequently reported malignancy (excluding non-melanoma skin cancer) was breast cancer (SIR 0.69; 95% CI 0.35–1.24).

Conclusion:
In prolonged follow-up of RA pts treated with RTX in clinical trials, RTX has remained well tolerated over multiple courses with a stable safety profile similar to the pooled placebo population.
Reliability of Radiographic Scoring Methods in Axial Psoriatic Arthritis (AxPsA)

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Objective:
To determine the reliability of available scoring systems for assessing radiographic spinal damage in AxPsA

Methods:
A scoring module that facilitates scoring individual spine radiographic features and calculates total scores for the available scoring methods for ankylosing spondylitis (AS) [New York radiographic criteria for sacroiliac joints (SI), Bath AS radiology index (BASRI-spine), modified Stoke AS Spine score (mSASSS), radiographic AS spinal score (RASSS)] and AxPsA [PsA spondylitis radiology index (PASRI)] was developed. Spinal radiographs of 40 patients with AxPsA (defined as at least unilateral grade 2 sacroiliitis and/or inflammatory back pain and/or restricted spinal mobility) were obtained. The radiographs were duplicated, patient identifiers removed, and order randomized. Four assessors blinded to patient information were provided with an e-handbook and one hour training session. Radiographs were read by the four observers individually, data entered into the module and scores obtained. Intraclass correlation coefficient (ICC) estimates of the inter- and intra-rater reliability of scoring methods were obtained.

Results:
The 40 patients (24 males, age 54 years, disease duration 18 years) had mean cervical rotation of 61 degree, Occiput to wall distance of 2.3 cm, Schober’s test of 4.7 cm, Domjan lumbar lateral flexion of 15.5 cm, actively inflamed joint count of 5 and damaged joint count of 16 at the time of radiographic assessment. The intra-and inter-rater reliability for the radiographic scoring methods were: SI- 0.81, 0.67; BASRI-spine- 0.77, 0.52; mSASSS- 0.79, 0.67; RASSS- 0.77, 0.71; PASRI- 0.92,0.88, respectively.

Conclusion:
Available radiographic scoring systems have at least moderate inter- and intrarater reliability when applied to AxPsA. The method developed specifically for AxPsA (PASRI) has the highest reliability in AxPsA.
The Impact of Central Nervous System Vasculitis of Childhood on Health-Related Quality of Life

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Objective:
Central nervous system (CNS) vasculitis of childhood is a newly recognized inflammatory brain and spine disease. CNS vasculitis interferes with many aspects of one’s day-to-day life, and may therefore have an impact on health-related quality of life (HRQOL); however this has not previously been examined. The purpose the present study was therefore to examine the impact of CNS vasculitis on the HRQOL of children with the disease through conducting a needs assessment to identify important elements of HRQOL that may not be addressed in existing measures of HRQOL.

Methods:
Children (aged 7-18) diagnosed with CNS vasculitis and their parents participated in interviews focusing on impact of the disease on different areas of their life. The interviews were designed to capture four domains of HRQOL addressed on the PedsQL 4.0, a previously established generic measure of HRQOL. The domains were: physical functioning, emotional functioning, social functioning, and school functioning. An additional area, termed family functioning, was added to the interview protocol to obtain information regarding the impact of the disease on the patient’s family. The interview was designed in a manner such that general questions regarding each of the domains were asked first, followed by more specific follow-up questions if the general questions failed to elicit responses. School-aged children (< 12 years) were interviewed with their parents. Teenage patients were interviewed separately from their parents. In total, two school-aged children and their parent(s) were interviewed, three teenagers were interviewed, and three parent(s) of teenagers were interviewed. Interviews were taped and transcribed. Interview transcripts were reviewed by two independent reviewers to identify themes that arose from the interviews. Common themes by multiple interviewers over multiple interviews were determined.

Results:
Children with CNS vasculitis and/or their parents identified aspects of HRQOL that were unique to CNS vasculitis, such as body image concerns, decreased self-esteem, family stress, financial issues, changes in sibling relationships, and uncertainty about the future. In addition, other aspects of HRQOL that have been previously addressed on generic questionnaires such as physical changes, mood changes, decreased memory/concentration, fatigue, and social relationships were also identified.

Conclusion:
CNS vasculitis uniquely impacts on the life of children and their families. Beyond areas that are assessed with generic tools, novel, unexpected themes were consistently identified. These findings support the need for a disease-specific HRQOL measurement tool in order to capture additional dimensions of the impact of childhood CNS vasculitis on HRQOL.
Preliminary, 12-Month Analysis of REACH: Real Life Evaluation of Rheumatoid Arthritis in Canadians Receiving HUMIRA® (Adalimumab)

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Objective:
To describe clinical response, physical function, and disease activity of Canadian patients with rheumatoid arthritis (RA) receiving adalimumab in REACH, an ongoing, multicenter, open-label, observational study.

Methods:
This interim analysis includes 251 patients who received ≥12 months of adalimumab therapy. REACH is expected to enroll a total of 1,000 patients from approximately 150 sites across Canada. Eligible participants must be ≥18 years old; have moderate to severe, active RA; and be either naïve to adalimumab therapy or have received adalimumab therapy for ≤4 months prior to baseline. Patients were followed by their rheumatologists every 6 months for up to 2 years. Patients with baseline data and ≥1 follow-up visit on treatment were analyzed through 12 months of therapy using last-observation-carried-forward imputation. Because the baseline assessment could occur >1 month after initiation of adalimumab therapy, subgroup analyses for disease measures (28-joint Disease Activity Score [DAS 28], Health Assessment Questionnaire [HAQ], and Rheumatoid Arthritis Disease Activity Index [RADAI]) were performed for patients whose baseline assessment was before the adalimumab start date vs. after.

Results:
Of the 480 patients enrolled to date, 79% were women, 88% were white, mean age was 55.4 years, mean disease duration was 9.0 years, 97% had received ≥2 disease-modifying antirheumatic drugs (mean=3.28), and 55% had high disease activity (DAS28>5.1) at baseline. Mean baseline disease measures were DAS28=5.30, HAQ=1.48, and RADAI=5.52. Mean decrease (improvement) from baseline to 12 months was 1.46 for DAS28 (N=242), 0.43 for HAQ (N=244), and 2.23 for RADAI (N=244) (all p<0.001). The baseline visit was within 1 week (mean=6.8 days) of initiation of adalimumab therapy for 375 patients and was >1 month (mean=69.9 days) after initiation of adalimumab for 105 patients. After 12 months of adalimumab therapy, 61% of patients had achieved a EULAR response of good or moderate, 14% had achieved low disease activity (2.6≤DAS28<3.2), and 28% were in clinical remission (DAS28<2.6). Moreover, 17% maintained clinical remission from their 6-month assessment. For HAQ at Month 12, 41% of patients met the minimum clinically important improvement of ≥0.22.

Conclusion:
Most patients in this preliminary analysis of REACH maintained clinically important improvements in disease activity and physical function after 12 months of adalimumab therapy.
Clinical Prognostic Factors for Radiographic Damage in Early Rheumatoid Arthritis: Results from SONORA Study

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Objective:
Data from SONORA (study of new-onset rheumatoid arthritis) was used to determine clinical prognostic factors of radiographic damage and radiographic progression in early RA.

Methods:
A total of 994 patients diagnosed with early RA (symptoms ≥3 and ≤12 months) by a board-certified rheumatologist across North America were recruited in this study. Hand radiographs were obtained at baseline, year 1 and year 2 and scored according to original Sharp Method (range 0-280) in random time order. Radiographic progression was defined by a change of at least 3.2, 2.9 and 3.4 in the erosion score, narrowing the score and total Sharp score, respectively1. General estimation equation (GEE) models were used to identify the prognostic factors associated with presence or absence for radiographic progression longitudinally.

Results:
Patients had a mean age of 53 years (SD, 14.81), 72% female and 90% Caucasian with mean disease durations 170 (180) days. The Sharp Score was 5.49 (7.85), 6.38 (8.90) and 6.17 (8.65) at baseline (N=746), year 1 (n=756) and year 2 (n=567) respectively. The mean change from baseline was 0.69(4.21) at year 1 and 1.04 (4.48) at year 2. Among these patients, 69% had evidence of erosion (positive Sharp score) at baseline, increasing to 72% at year 1 and 79% at year 2. Radiographic progression was observed in 14.7% of the patients at year 1 and 19.4% at year 2. By univariate analysis, radiographic progression was significantly (P-values< 0.05) associated with the baseline values of Sharp score, IgM rheumatoid factor (RF), anti-CCP positive, C-reactive protein (CRP) level, disease activity scores (DAS28), clinical disease activity index (CDAI) and simplified disease activity index (SDAI) . No significant correlation was observed with the baseline values of age, sex, smoking status, disease duration, duration of morning stiffness, rheumatoid arthritis disease activity index (RADAI), pain scores and swollen or tender joint counts. The multivariate GEE model with repeated binary outcomes at year 1 and 2 revealed that the only significant prognostic factors were baseline Sharp score (P=0.0001), anti-CCP (P=0.0015), CRP (P=0.0027) and disease activity scores, which is either DAS28 (P=0.033), CDAI (P=0.039) or SDAI (P=0.039).

Conclusion:
Radiographic progression of RA remains the best method of assessing structural damage associated with the disease. These identified prognostic factors for radiographic damage in early RA are useful for us to predict which patients are at high risk for radiographic progression over a short period.
Objective:
Data from SONORA (study of new-onset rheumatoid arthritis) was analyzed to examine the longitudinal relationship between short term radiographic damage, radiographic progression and physical function in early rheumatoid arthritis (RA) patients

Methods:
A total of 994 patients diagnosed with early RA (symptoms ≥3 and ≤12 months) by a board-certified rheumatologist across North America were recruited in this study. Hand radiographs were obtained at baseline, year 1 and year 2 and scored according to original Sharp method (range 0 to 280) in random order per patient. Health Assessment Questionnaire (HAQ) scores were used as the measurement for physical function and they were surveyed every 4 months. For the purpose of this study, only data at baseline, year 1 and year 2 were used. General mixed linear models with random intercept were used to examine the longitudinal relationship of radiographic damage or radiographic progression and HAQ controlling for confounders. Baseline HAQ score, age, gender, treatment, disease duration and disease activity score (DAS) were also included.

Results:
Patients had a mean age of 53 years (SD, 14.8), 72% female and 90% Caucasian with mean disease durations of 5.6 (5.9) months. The mean (SD) for HAQ score was 1(0.73), 0.82(0.71) and 0.77(0.72). The sharp score was 5.49 (7.85), 6.38 (8.90) and 6.17 (8.65) at baseline (N=746), year 1 (n=756) and year 2 (n=567) respectively. The mean change from baseline of Sharp score was 0.69(4.21) at year 1 and 1.04(4.48) at year 2. When the radiographic progression was divided into 3 categories2 (no progression, ≤0; minor progression, 0-3.4; greater progression, >3.4), results showed that patients with greater progression had the highest HAQ score at follow up, 0.93 (0.67) and patients with no progression reported the lowest HAQ score, 0.74 (0.70). Linear mixed model showed that after adjusting baseline HAQ, age, gender, treatment, disease duration and DAS, both Sharp Score (P=0.05) and change from baseline in Sharp Score (P=0.03) were significant predictors for HAQ score.

Conclusion:
The progression of radiographic damage over a short period of time is significantly associated with poor physical function; this association is independent of the effects of disease activity in early RA patients.
Objective:
PURPOSE: Evaluate correlation of SSF vs Unstimulated Salivary Flow (USSF) with pathology in MSG biopsies.

Methods:
METHOD: From 1993 to 2008, 468 patients were assessed on protocol at a multi-disciplinary Sjogren’s Syndrome clinic. All MSG biopsies were read blindly by the same individual (DB). Information has been collected from a single first-time comprehensive standardized evaluation. MSG biopsies were examined for focus score per 4mm2, degree of atrophy and degree of fibrosis each graded 0 to 3. All patients were assessed with a Schirmer’s 1 and SSF. Since 2002 USSF was done in 197 subjects. Comparisons were made between 265 patients with PSS by Consensus Criteria and 70 patients with sicca (USSF < 1.5ml/15min, or if absent SSF < 0.6 ml/min, or Schirmer’s 1 < 5mm/5min).

Results:
RESULTS: Groups were comparable in age, weight, gender and duration of symptoms. On a 10 cm VAS for symptom severity, intensity of xerophthalmia was equal in PSS and sicca (6.2±2.7 vs 5.6±3.2, p=0.14), but xerostomia was significantly worse in PSS (6.8±2.4 vs 5.6±3.1, p=0.0086). As expected, the Rose Bengal, Schirmer’s 1, USSF, SSF and focus score were significantly worse in PSS. Comparing MSG biopsies across PSS patients alone there was an association by univariate linear regression between grade of atrophy and focus score (p< 0.0001), as well as DMF (decayed, missing, filled) score (p=0.02). DMF worsened with fibrosis (p=0.005) and focus score (p=0.0003). There was also a correlation of compromised SSF with grade of fibrosis (p=0.02), duration of dry mouth (p=0.0008), focus score (p< 0.0001) and DMF (p< 0.002). None of the correlations with SSF could be seen in sicca. USSF did not change significantly with any of these parameters in PSS or sicca.

Conclusion:
CONCLUSIONS: Although USSF is important for diagnosis, these findings demonstrate the importance of SSF as an indicator of pathological changes of inflammation (focus score) and damage (fibrosis and atrophy) in MSG biopsies in PSS, and may indicate the utility of this measure as a tool for documenting progression of glandular damage. This study also documents for the first time the important correlation of fibrosis and atrophy with DMF (the measure of dental damage in PSS). With demonstrated benefit of B-cell targeted therapy, measures must be developed that will be useful to monitor disease course with respect to progression of glandular damage in PSS.
The Prevalence of CNS Lupus in Canada: Results from the 1000 Faces of Lupus Cohort

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Objective:
Neuropsychiatric systemic lupus erythematosus (NPSLE) can vary widely depending on the definition used and has been found to range from 12 to 80%. We determined the prevalence of NPSLE and associated factors in 1000 Faces of Lupus, a large multi-centre Canadian cohort.

Methods:
Adults who satisfied the ACR classification criteria for SLE were included and had completed SLEDAI, SLAM and/or SLICC damage indices. NPSLE was defined as: (i) NPSLE by ACR diagnostic index which has strict criteria consisting of psychosis and seizure in which a metabolic etiology had been excluded, ACR, SLEDAI, SLAM and SLICC with indices with (ii) and without (iii) minor nonspecific NPSLE manifestations, and (iv) ACR and SLEDAI indices. Factors associated with NPSLE were explored using univariate and multivariate regression.

Results:
Total cohort size was 1417; 86% were female, with mean +/- standard deviation (SD) age at study entry and disease duration of 41.0 +/- 16.3 and 11.7 +/- 10.2 years respectively. Subgroup size and characteristics were dependent on the specific definition of NPSLE. Group (i) contained N=1253 with NPSLE prevalence of 6.4% (n=80). Group (ii) contained 681 and NPSLE prevalence of 38.6% (n=263). Group (iii) had 586 and NPSLE prevalence of 28.7% (n=168). Group (iv) had 1125 and NPSLE prevalence was 10.2% (n=115). In univariate analysis, Aboriginals had increased prevalence of NPSLE at 12.5%, Caucasian 61.1%, African 6.9% and Asian 19.4% (p=0.04) in group (i). Anti-Ro and antiphospholipid (aPL) antibody + were also significant in this group; aPL+ remained significant in groups (ii) and (iii). In group (iv) absence of anti-Sm and presence of anti-Ro were significant. In multivariate analysis, anti-Ro and aPL (i) and anti-Ro+ and lack of anti Sm (iv) were significant. Age at diagnosis, disease duration, anti-DNA, RNP and anti-cardiolipin antibody alone were not found to be significant.

Conclusion:
Prevalence and factors associated with NPSLE varied depending on the definition used. Prevalence of NPSLE was nearly two-fold greater in Aboriginals. NPSLE may be less in this database than other publications as it may be decreasing, or due to selection bias of those who enter an observational cohort. NPSLE was associated with aPL and often anti-Ro and varied by ethnicity.
The Implementation and Evaluation of a Pilot Project in Telerheumatology

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Objective:
To evaluate and implement a pilot project in Telerheumatology.

Methods:
Two studios with two-way audio-visual communication were identified. The remote site was equipped with a magnifying camera which was validated to detect soft tissue swelling around joints. A rheumatologist who visits the site for face to face clinics and a physiotherapist trained in joint assessment were at either end. All investigations on patients were made available online to the rheumatologist. Patients were selected based on urgent referrals (screened) between clinic visits and follow ups (f/u) who required assessment of medication effectiveness or disease flare. All patients were seen in subsequent face to face clinics to determine outcomes. All patients were asked to fill out a satisfaction questionnaire. Wait lists for face to face clinics were monitored.

Results:
Over a period of 4 months with one half day per month, 11 new and 23 f/u were seen. Clinical encounters took approximately the same time as face to face encounters. Of the new patients, 5 were early RA, 3 were new onset CTD, 3 others were osteoporosis with fractures, discoid lupus and autoimmune thyroid disease with joint pain. At subsequent f/u, 4 RA patients were improved (> ACR 20) and 1 in remission. The CTD patients were well controlled, the discoid lupus patient 60% better. The remaining two were not seen in f/u. The f/u patients consisted of 8 RA flares, when seen subsequently 5 improved, 3 in remission. 4 CTD flares, subsequently all improved. 3 people requiring biologic renewals. 8 patients had follow ups scheduled for a previous face to face clinic (RA and CTD) because of anticipated need to monitor response (6 improved and 2 unchanged). 31/34 patients completed the questionnaire and indicated the high level of satisfaction with the process, the communication and the outcome. No new patients remain on the wait list for face to face clinics and only a few follow ups.

Conclusion:
The pilot project was effective. It allowed for timely review of early RA, new onset CTD and RA flares. Patient satisfaction was high. Wait times were reduced.
One-year Drug Retention in Individuals Enrolled in an Etanercept Patient Support Program

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Objective:
Retention is defined as treatment with the same drug over a continuous time period. A review of a Patient Support Program (PSP) for etanercept (Enliven® Services Support Program), a program providing services such as structured clinical telephone follow-up, a toll-free support line, and insurance assistance, was used to determine etanercept retention at 1-year post-treatment initiation.

Methods:
Individuals enrolled in the Enliven® PSP between July 2000 and December 2007 were followed for at least 1 year through structured clinical telephone contact. Data from these points of contact were collected for Canadian patients who were diagnosed with active ankylosing spondylitis (AS), moderate to severe rheumatoid arthritis (RA), moderate to severe plaque psoriasis (PsO) or psoriatic arthritis (PsA). In this study, retention at 1 year was defined as continual treatment with etanercept. Confirmation of continual treatment was obtained during a telephone follow-up at ≥1-year after program enrolment. Descriptive statistics were used to characterize the information collected. Data were stratified by indication.

Results:
There were 16,037 subjects with complete retention data enrolled between July 2000 and December 2007. Eighty-two percent of enrollees reported that they were either still using etanercept or that they were receiving financial assistance for etanercept at 1 year (90% based on follow-up call and 10% on financial assistance data). By indication, PsA enrollees had the highest retention rate (85%, 1806/2121) followed by AS (83%, 891/1069), RA (81%, 9499/11750) and PsO (80%, 877/1096). Individuals reporting financial assistance from government and/or private insurer had an 84% (12355/14691) retention rate, compared to 53% (719/1346) of individuals who did not receive financial assistance. The most common reasons for drug discontinuation (18%) before 1 year were “lack of efficacy” (23%, 693/2963), “MD recommendation” (15%, 442/2963), and “side effects” (13%, 382/2963). For individuals who experienced a delay between the time etanercept was prescribed and when it was first administered at the beginning of treatment, 80% of enrollees were taking etanercept at 1 year (448/561). Most common reasons for delay included waiting for provincial coverage (26%, 143/558), awaiting special authorization (19%, 106/558), waiting for training (10%, 54/558) and personal reasons (10%, 56/558).

Conclusion:
The data presented suggest that there is a high retention rate with etanercept at 1-year post therapy start with individuals enrolled in the Enliven® Services Support program. Longer term retention will be evaluated in future studies.
Golimumab, a New, Human, TNF-α Antibody Administered Subcutaneously Every 4 Weeks, in Ankylosing Spondylitis: 104-Week Efficacy and Safety Results of the Randomized, Placebo-Controlled GO-RAISE Study

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Objective:
To assess golimumab (GLM) efficacy/safety in patients with active ankylosing spondylitis (AS).

Methods:
356 patients were randomized (1.8:1.8:1 ratio) to SC GLM 50 or 100mg or PBO q4wks. Eligible patients had definite AS (modified NY criteria), BASDAI ≥ 4, and a back pain score of ≥4. At wk16, PBO or GLM 50mg patients with < 20% improvement in total back pain and morning stiffness entered early escape to GLM 50 and 100mg q4wks, respectively (double-blind). At wk24, patients still receiving PBO crossed over to blinded GLM 50mg SC injections q4wks; others continued their regimen through wk100, with evaluation 4 wks later. Key data summaries are based on randomized treatment groups with no statistical comparisons; other summaries show observed data only by regimen followed.

Results:
As previously reported, the primary endpoint (proportion of patients with ASAS20 at wk14), was achieved. At wk 104, ASAS20 was achieved by 60.1% and 75.6% of GLM 50mg and GLM 100mg patients, respectively; ASAS40 was achieved by 55.8% and 54.3%, respectively. Patients not responsive to GLM 50mg who increased to 100mg had lower rates of ASAS response and less improvement in other parameters versus other GLM-treated patients. BASMI, BASDAI and BASFI scores improved at wk52 and were maintained through wk104. At wk104, BASDAI scores were 2.65 (0.84, 6.08) and 2.73 (1.08, 5.34) for GLM 50mg and GLM 100mg, respectively; BASFI scores were 2.22 (0.52, 5.80) and 1.77 (0.49, 4.79), respectively. Improvements in SF-36 MCS & PCS scores were also maintained through wk 104. AEs through wk104 were reported for 94% of GLM patients (little variation across GLM doses). Through wk104, 11% of GLM patients had a serious AE; the rate of GLM injection-site reactions was 1.4% (106/7705 injections) through wk104. There were no deaths.

Conclusion:
Clinical improvements in AS patients previously observed at wk24 were maintained through wk104, with no major differences in efficacy/safety between GLM doses. GLM was generally well tolerated through two years of this five-year study.
Impact of Disease Duration on the Outcome of RA Patients Treated with Infliximab in Canada

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Objective:
The efficacy of anti-tumor necrosis factor (TNF)-α agents in the treatment of rheumatoid arthritis (RA) has been demonstrated in controlled clinical trials and in recent years several individual patient characteristics have been evaluated for an association with a response to anti-TNF agents. In this analysis, we will evaluate the hypothesis that patients with shorter disease duration will have increased beneficial effect from early treatment with an anti-TNF.

Methods:
A total of 679 RA patients starting treatment with infliximab were enrolled by December 31, 2008 in the nationwide RemiTRAC registry (Remicade® Treatment Registry Across Canada). 112 patients have completed 36 months of treatment and are included in this report. This registry was initiated in 2002 and is an ongoing, multi-centre, prospective, observational study of patients treated with infliximab for RA, AS (Ankylosing Spondylitis) or PsA (Psoriatic Arthritis). Patients are naïve to Anti-TNFα treatment or were treated with biologics for a period < 6 months (since December 2006). Patients enter the cohort at the time of initiation of treatment and are followed prospectively. Baseline disease activity and treatment response overtime were determined based on the disease duration of patients at the time of initiation of treatment with Infliximab. Descriptive statistics and when appropriate statistical tests were conducted, Fisher’s exact test for categorical variables or t-test/ANOVA for continuous variables.

Results:
Disease duration was ≤ 3 years (as per ERA population, ASPIRE trial) for 26 patients and > 3 years for 86 patients. Mean age of the two groups was 56 and 57 years respectively. Although both groups experienced significant improvement in all clinical parameters over time (CRP, ESR, morning stiffness, patient and physician global assessment, HAQ, SJC, TJC, ACR 20, 50 and 70) patients with ≤ 3 years of disease duration at treatment onset had significantly (P< 0.05) more improvement in the Health Assessment Questionnaire (HAQ), swollen joint count (SJC) and higher proportion with ACR70 endpoint through month 36. A higher proportion of patients with ≤ 3 years disease duration also achieved a therapeutic response defined by the ACR20, ACR50 and ACR70 criteria by month 2 and sustained it through month 36.

Conclusion:
The results of this observational study have shown that infliximab is effective in managing RA, however, earlier initiation of treatment may increase the beneficial effect.
Reduced Incidence of Infusion Reactions to Infliximab in Patients Pre-Medicated with Acetaminophen

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Objective:
Patients treated with infliximab (IFX) sometimes receive pre-medication in order to reduce the risk of infusion reactions (IR). These pre-medications include anti-histamines (AH), intravenous steroids (Ster) or acetaminophen (Acet) either alone or in combination.

Methods:
RemiTRAC Infusion is an observational registry (12 Canadian sites) where patients receiving IFX are followed prospectively to document pre-medication use, adverse events, IR and the management of IR. 850 subjects have been enrolled since 2005 (registry inception). 9459 infusions were recorded with a mean of 11.2 ± 8.3 infusions per patient representing 1171 years of exposure. The majority of patients (n=422 or 50%) had rheumatoid arthritis whereas 16% (n=137) had ankylosing spondylitis and 6% (n=50) had psoriatic arthritis, the remaining patients had gastroenterological or dermatological diseases.

Results:
Among all infusions recorded (n=9459), 197 infusions resulted in an IR (2.1%) and almost all IR were mild to moderate in severity (185/197 or 94%). About 42% of infusions were carried out following pre-medication of patients. AH were used in 2006 infusions (21%) compared Ster and Acet which were used in 1912 (20%) and 2428 (26%) of infusions, respectively. For infusions that were not preceded by any pre-medication, the incidence of IR was 1.9% (102/5444). There was more IR in infusions that were pre-medicated with an AH (67/2006 or 3.3%, p< 0.0001) or Ster (56/1912 or 2.9%, p< 0.01). Surprisingly, infusions following Acet pre-medication had a significantly reduced incidence of IR (35/2428 or 1.4%, p=0.01). The higher incidence of IR under AH or Ster pre-medication may result from a selection bias since patients who experienced an IR were more likely to receive pre-medication and to have a subsequent IR. Indeed, the highest incidence of IR was observed in infusions pre-medicated with AH alone (22/556 or 4.0%, p< 0.01) or in combination with Ster (24/335 or 7.2%, p< 0.001). Nonetheless, there was no increased incidence of IR following any pre-medication strategy that included Acet either alone (9/1001 or 0.9%, p< 0.01) or in combination with AH (6/425 or 1.4%, p< 0.01), Ster (7/325 or 2%), p=1.0) or all 3 drugs combined (10/583 or 1.72%, p=0.7).

Conclusion:
In a “real-life setting” registry, acetaminophene appears to be a pre-medication that significantly reduces the incidence of IR to IFX. The mechanism is unknown but suggests that most IR might be non-immunogenic in nature. The rate of IR to IFX is low and is easily managed by health care professionals.
Evaluating the Colour of Communication: Different Patients: Different Interventions

Paul Davis (University of Alberta, Edmonton)

Objective:
Objective: A 2008 needs assessment identified rheumatologist knowledge gaps regarding biologic use in specific patient subpopulations and ineffective patient communications. A continuing medical education (CME) program was designed to address the gaps. This investigation assesses the initial success of the CME program.

Methods:
Methods: Using needs assessment results, a development committee (DC) created a CME program for rheumatologists (currently accredited by the University of Alberta for up to 3.5 Section 1 credits under Maintenance of Certification Program). Phase 1, with a personalized communications profile, video presentations and discussion, addresses the communications gap using the proprietary Insights communications concept. Phase 2 addresses the knowledge gap and encourages application of Phase 1 knowledge using case studies. Program development phases included: - Kick-off meeting (DC members established the program objectives and structure) - Development (the DC created and assembled the content) - Pilot (five rheumatologists participants provided feedback) - Revision (DC members made changes based on feedback) - Train-the-trainer (TTT) (six rheumatologists were trained to present the program) Evaluation forms including five-level Likert scale and short-answer questions were collected from participants following the pilot and TTT sessions. The sections directly related to program content were analyzed to assess program success.

Results:
Results: Using the Likert scales 100% of participants strongly agreed the program is relevant to their practices and allows for interaction between participants. At the pilot session, 60% strongly agreed and 40% agreed the program met the stated learning objectives and the format makes it possible to efficiently absorb and integrate content. 40% strongly agreed and 60% agreed the program would impact their practice and is well balanced and without bias. 100% strongly agreed time allocated was adequate. At the TTT session, 100% strongly agreed the program met the stated knowledge and communication learning objectives, would impact participants’ clinical practice and is well balanced and without bias. 83% strongly agreed and 17% agreed time allocated was adequate. 67% strongly agreed and 33% agreed the format makes it possible to efficiently absorb and integrate content. Short answer responses from both sessions were generally positive. Participants expressed the program was novel and innovative and they had the intention of integrating their learning in clinical practice.

Conclusion:
Conclusions: Early feedback suggests this CME program addresses rheumatologists’ communications gaps and knowledge gaps regarding the use of biologics in specific patient subpopulations.
Educational Needs Assessment in Inflammatory Arthritis: Perspective from Rheumatologists, Nurses, and Patients

Martin Dupuis (AXDEV Group, Brossard); Paul Davis (University of Alberta, Edmonton)

Objective:
The purpose of this study was to determine clinical care challenges and educational needs of Canadian rheumatologists and nurses specialized in rheumatology who provide care to patients with inflammatory arthritis.

Methods:
An IRB-approved mixed-method approach was employed. In Phase one (exploratory), one discussion group with rheumatologists (n=6), one discussion group with nurses specialized in rheumatology (n=8), and eight telephone interviews with patients diagnosed with inflammatory arthritis were conducted. Patients were included to assess their experience receiving care for inflammatory arthritis and to obtain a broader perspective of the challenges and needs of healthcare professionals. In Phase two (validation), 50 rheumatologists and 21 nurses specialized in rheumatology completed a quantitative survey to validate and triangulate the qualitative findings. A total of 93 individuals participated in the study. In both phase, purposive sampling was used based on demographic criteria, level of specialization, and practice profile.

Results:
Findings revealed suboptimal collaboration and lack of consensus on the roles and responsibilities of rheumatologists, nurses, and primary care physicians caring for patients with inflammatory arthritis. Results also indicated that rheumatologists are challenged to deliver a precise diagnosis in patient with early inflammatory arthritis because of the overlap between diseases’ symptoms and poor access to specialized testing. However, rheumatologists indicated that it is not always critical to differentially diagnose because treatment may be the same. Despite high level of knowledge on treatment options, rheumatologists and nurses still reported a lack of confidence in long-term effect and discontinuation of biologic therapy. Rheumatologists and nurses also acknowledged a lack of comfort in dealing with patients’ beliefs, fears, and unrealistic goals, contributing to inconsistent and incomplete patient education and emotional support.

Conclusion:
Identification of challenges faced by professionals providing care for patients with inflammatory arthritis revealed perceived as well as unperceived educational needs. Those findings are instrumental in informing the design of targeted educational initiatives, especially to enhance healthcare professionals’ knowledge and confidence in diagnosing and assessing early inflammatory arthritis, knowledge and confidence in long-term treatment with biologic therapies, and management of patients’ emotional and educational needs by improving communication skills.
Use of Oral Contraceptive Pills in Patients with SLE - A Survey of Rheumtologists in Canada

Sanjay Dixit (MCMASTER UNIVERSITY, HAMILTON); Susan Waserman (MCMASTER UNIVERSITY, HAMILTON); Nader Khalidi (MCMASTER UNIVERSITY, HAMILTON)

Objective:
1. To assess current trend in prescribing oral contraceptive pills (OCPs) to patients with SLE 2. Effect of SELENA trial on current practice

Methods:
An e-mail based survey consisting of six questions was sent to CRA members. Participation was anonymous and voluntary. Responses were then collected and analyzed from the server.

Results:
114 physicians responded to the survey. Majority had less than 25% of their practice as SLE patients. Only 1.8% suggested that more than 50% of their patients are on OCPs. A quarter admitted of counseling patients on using OCPs less than 25% of the time. However over 73% stated they use OCPs in stable patients. Interestingly almost one in five were not aware of SELENA trial. Rest confirmed that this trial has reinforced their current practice or made them more comfortable in using OCPs for patients with SLE. Over 20% of physicians reported to spend more time to counsel patients about OCPs after the trial.

Conclusion:
Our survey concludes that majority of physicians do use OCPs in their patients with SLE. Although there have been 2 big trials involving safety of OCPs in patients with SLE, many of the physician are still skeptical about their use. Lack of time spent to counsel the patient regarding OCPs and their safety has a role to play. Many of the physicians do not feel comfortable in using OCPs. We recommend the development of practice guidelines regarding the use of OCPs in patients with stable SLE. Also, better tools need to be developed to educate practicing rheumatologist regarding landmark trials and their outcomes.
Expressing Urinary Protein Excretion in Lupus Nephritis

Debra Dye-torrington (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto)

Objective:
To determine the correlation between p/c ratio and 24 hr urine protein among patients with SLE over a range of proteinuria.

Methods:
Patients recruited from the Toronto Western Hospital Lupus Clinic were asked to collect a spot urine within 24hrs after the end of a 24hr urine collection. 24hr protein excretion was categorized into three groups: Low < 0.5g/24h, intermediate 0.5-2g/24h, high >2.0g/24h. Comparison of P/C ratio with levels of proteinuria was done through correlation coefficients.

Results:
76 samples of 24hr urine and spot urines were collected. (86%) of the patients were female, 50% Caucasian, 19% Black, 18% Chinese and 12% Other. Age (std) at SLE diagnosis was 28.8 ± 12.4 years and disease duration at the time of sampling was 11.8 ± 6.9 years. 84% of the samples were positive for protein. 25(33%) were in the low range, 21(28%) were intermediate and 18(24%) were high. The mean Spot P/C (± std) by protein levels was; for no protein, Spot P/c 0 ± 0; for low protein, Spot P/C 0.02± 0.03; for intermediate protein, spot P/C 0.15 ± 0.14; for high protein, spot P/C 0.39 ± 0.21 Overall, the correlation coefficient between all 24 hours protein and spot P/C was 0.79 (p< 0.0001). For each of the protein level, the correlation coefficient with spot P/C was; for low protein, r=0.69 (p=0.0001); for intermediate protein, r=0.44 (p=0.05); for high protein, r = 0.34 (p=0.16).

Conclusion:
There is poor correlation between spot P/C ratios and 24 hour urine protein excretion at levels of proteinuria of 2 grams or more. Protein-to-Creatinine ratios should not be used to monitor protein excretion in patients with lupus nephritis.
Macrophage Migration Inhibition Factor gene polymorphism is associated with relapse in joints that achieved remission after intra-articular steroid injection in psoriatic arthritis.

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Objective:
Macrophage Migration Inhibition Factor (MIF) is a pro-inflammatory cytokine that has emerged as a potential factor that could regulate glucocorticoid sensitivity. The aim of the study was to determine the association between MIF promoter polymorphism and response to IAS injections in patients with psoriatic arthritis (PsA).

Methods:
A cohort analysis of patients followed prospectively from 1978 to 2008 in the University of Toronto PsA clinic was performed. Only injections performed in the clinic for which there was a post-injection follow-up visit within 6 months were included. Remission was defined as no stress pain or effusion in the injected joint at the first post-injection assessment. Relapse was defined as re-occurrence of joint pain or effusion. MIF 173C G genotyping (rs755622) was achieved using the Sequenom platform from DNA isolated from peripheral blood. A logistic regression model that included sex, age, duration of PsA and MIF genotype as covariates was used to assess the association of MIF polymorphism and response to IAS injections.

Results:
191 patients with 264 IAS injections were included in this analysis. 53 (27.7%) patients were carriers of the MIF –173G allele, while 138 patients (72.3%) were homozygous for the MIF –173C allele. The probability of achieving remission at 3 month following the injection was 42.6%, and relapse at 6 or 12 months given remission was 25. A carrier status for MIF –173G allele was not associated with remission at 3 month following IAS injection. However, carrier status for MIF –173G allele was associated with relapse at 6 or 12 month following remission at 3 months (OR 3.2, p=0.03). When the statistical model was broadened to include clinical covariates of disease activity, the association between MIF –173G allele and relapse was no longer present. The other covariates found to be associated with relapse included duration of psoriasis (OR 1.08, p=0.006), duration of PsA (OR 0.81, p=0.0005), involvement of large joints (OR 5.49 p=0.015), and absence of clinical or radiographic damage (OR 0.16 p=0.025) which means that clinical or radiographic damage was associated with relapse. and elevated ESR (OR 44.33, p=0.0007).

Conclusion:
MIF gene polymorphism is associated with relapse of joint inflammation but not with response to IAS injection in actively inflamed joints in PsA patients. However this effect is not present when adjusting for clinical variables that reflect disease activity, suggesting that MIF reflects inflammatory activity.
Sonographic Diagnosis and Treatment of a Spinoglenoid Cyst Associated with a Posterior Labral Tear: Case Report

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Case Report:
Objective: To describe the sonographic features of a spinoglenoid cyst associated with a posterior labral tear and to discuss the role of ultrasound in diagnosis and treatment of supra-scapular nerve entrapment at the spinoglenoid notch. Case: A forty-year-old right-handed man, occasional volley-ball player had been complaining of left shoulder pain for a few months. The shoulder pain was diffuse and worsened by movements. Initial diagnosis was supraspinatus tendinopathy, and the patient received a blinded extra-articular subacromial injection without efficacy. On our initial examination, we observed marked amyotrophy of the left infraspinatus and decreased strength (3+) in left external rotation. These features were suggestive of an infraspinatus lesion which led to our sonographic assessment of the spinoglenoid notch area. Ultrasound (US) exam showed a hyperechoic left infraspinatus muscle compared to the right, a spinoglenoid notch cyst, and a tear in the posterior labrum. MRI findings were consistent with sonographic findings and confirmed the diagnosis. Electromyography was normal. After the patient had a surgical posterior labral repair, we injected the cyst with 60 mg of triamcinolone acetonide under US guidance, which completely relieved the patient’s symptoms. Discussion: Spinoglenoid cyst associated with a posterior labral tear is a rare cause of suprascapular neuropathy, which is more often due to repetitive movements or nerve entrapment at the suprascapular notch. Electromyography and MRI are the gold standard diagnostic tools. However, US is a reliable method to investigate a lesion that could be responsible for nerve compression in case of a hyperechoic and atrophic muscle and can determine the location of this lesion. The cyst is seen as a hypo-anechoic delineated lesion. US also allows to look for an associated posterior labral tear which is otherwise not easily detected. The main differential diagnosis includes varicosities. In this case report, we propose the use of US-guided percutaneous aspiration followed by an intracystic glucocorticoid injection for efficacious pain relief. Nevertheless, pain recurrences are frequent, especially in the case of a labral tear leading to a surgical approach. Conclusion: US is helpful for the diagnosis and the treatment of a suprascapular nerve entrapment caused by a spinoglenoid cyst. However, the existing literature is limited to case reports or small cases series. Thus, larger studies are warranted to define the role of US in diagnosis and treatment of spinoglenoid cysts.
Temporal Artery Biopsy… Does Length Really Matter?

Leilani Famorca (Mc Master University, Maple); Nader Khalidi (Mc Master University, Hamilton)

Objective:
To investigate if the length of a temporal artery biopsy (TAB) influences the sensitivity of the test in diagnosing temporal arteritis or giant cell arteritis.

Methods:
Retrospective review of patients who underwent temporal artery biopsy (TAB) during a 6 year period at Saint Joseph’s Healthcare, Hamilton, McMaster Hospital, Henderson Hospital, and Hamilton General Hospital (2002-2008). A retrospective chart review collecting data regarding patient’s age, sex, length of biopsy specimen following fixation, unilateral or bilateral biopsy, surgeon’s subspecialty, histopathological results revealing giant Cell Arteritis/temporal Arteritis and time from onset of symptoms to temporal artery biopsy. Furthermore, we determined the number of temporal artery biopsies read at the pathology lab of each site. If any discrepancies in results will be revealed between the number of charts reviewed and number of temporal artery biopsies read, chart review from missing data were done.

Results:
Among 261 charts reviewed, 3 excluded due to an age less than 50 years old. Mean age was 72.8 years with a standard deviation of 9.6. There were 203 females (78%) .Mean arterial temporal artery length was 1.9 cm with a standard deviation of 1.8. Biopsy proven for temporal arteritis was 34 (13%). One temporal artery biopsy was nerve tissue by histopathology. A logistic regression analysis was done with TAB length as a factor revealing an odds ratio of 1.31 (95% Confidence Interval of 0.946 to 1.351). A categorized TAB length of 1 cm showed the biggest increase in positive TAB at a 3 cm cut off point. TAB length less than 3 cm had 24/188 (11.3%) and TAB length greater than or equal to 3cm had 10/38 (20.8%) that were positive. However, the difference in percentage is not statistically significant (p value = 0.0958).

Conclusion:
There is an indication though not statistically significant that an increase the TAB length may increase the sensitivity of the test. A 3cm cut off length may provide an increase in yield of this diagnostic test.
Serum Albumin as a Marker for Disease Activity in Patients with Systemic Lupus Erythematosus (SLE)

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Objective:
To determine whether serum albumin reflects disease activity in SLE patients with and without nephritis (LN, LNN).

Methods:
Patients with ≥3 clinic visits within a maximum follow-up period of 10 years were selected from the University of Toronto Lupus Clinic Database (1969-2009). Subjects were divided into: LN proven by renal biopsies (LN-B, n=290), LN by laboratory abnormalities in the absence of biopsy (LN-L, n=239) and non-LN (LNN, n=549). They were further stratified by age to < 50 and ≥50. The association between SLE-Disease-Activity-Index (SLEDAI-2K) and serum albumin was examined using Spearman correlation and mixed model regression analysis.

Results:
1078 patients [89% female, 71.4% Caucasian], mean(SD): age: 33.6(12.6) years, follow-up period: 6.1(3.3) years, SLE duration: 10.3(6.4) years and median SLEDAI of 8 were studied. LN and LNN were similar with respect to age, but LN group had less females [84% vs. 94%; P< 0.0001], longer follow-up period [6.7(3.2) vs. 5.6(3.4) yr; P=0.0001], longer SLE duration [10.6(6.3) vs. 9.4(6.3) yr; P=0.0013] and higher SLEDAI-2K [9 vs. 6; P=0.0001] and anti-dsDNA-antibody levels at baseline [22 vs. 12 U/mL; P=0.0001] when compared to LNN. Baseline serum albumin was lower in LN compared to LNN [36.9(7.6) vs. 41.0(5.9) g/L; P=0.0001]. LN-B and LN-L groups were similar for duration of follow up, SLE duration at last visit, and baseline anti-dsDNA antibody and serum albumin. There were significant (P< 0.0001) associations at each visit between serum albumin and SLEDAI-2K in LN-B (r=–0.28), LN-L (r=–0.24) and less so in LNN (r=–0.08). In LN this association was stronger in those with proteinuria (n=372, r=–0.229) compared to those without proteinuria (n=157, r=–0.11; P< 0.0001). In mixed model analyses and stratifying by age, serum albumin was also significantly associated with SLEDAI-2K in LN-B: (age< 50: β=–0.319, P< 0.0001; age≥50: β=–0.341, P< 0.0001), LN-L: (age< 50: β=–0.301, P< 0.0001; age≥50: β=–0.267, P< 0.0001) and less so in LNN: (age< 50: β=–0.101, P< 0.0001; age≥50: β=–0.111, P< 0.0001). Given that a SLEDAI-2K of ≥6 reflects active disease, a serum albumin level of 30g/L would be expected to be associated with clinically active SLE in LN, but not necessarily so in LNN

Conclusion:
Serum albumin is inversely associated with SLEDAI-2K and this association was stronger in those with LN and proteinuria. Future studies will need to assess the clinical utility of serum albumin as a marker for disease activity and perhaps renal activity in SLE patients.
Low Bone Mass in Female Patients with Systemic Lupus Erythematosus (SLE): A Canadian Study

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Objective:
To determine the prevalence and risk factors for low bone mass in a Canadian population of SLE patients enrolled in a CIHR-funded Health Improvement & Prevention Program (HIPP).

Methods:
253 female patients with SLE and without history of osteoporosis were recruited from three Canadian hospital lupus centers and had bone mineral densitometry (BMD) of the lumbar spine and hip evaluated using DXA scans. Low bone mass was defined as T-score of -1.0 or lower. Clinical data collected included: age, smoking, BMI, menopausal status, physical activity, use of calcium and vitamin D, SLE duration, falls, fractures ever, and use of corticosteroids at the time of enrolment.

Results:
Baseline characteristics were: mean (SD) age: 44.1 (13.0) years, SLE duration: 11.5(10.3) years, BMI (kg/m2): 25.8 (6.0), current smoking: 24.9% (n=63), sedentary lifestyle: 48.2% (n=122), post menopausal: 36.8% (n=93) and; 69.2% (n=175) were taking prednisone at the time of enrolment. Calcium and vitamin D were used by 48.6% (n=123) and 40.3% (n=102) respectively, 27.6% had falls in the preceding year and 25.3% had fractures at some point in their life time. Low BMD occurred in the hip and the spine in 33.2% (n=84) and 32.8% (n=83) of the patients respectively. Surprisingly, 61% of patients with abnormal BMD were using prednisone compared to 73.4% of those with normal BMD (P=0.040) however, the data regarding duration of prednisone was not collected. As well, 57.1% of those with abnormal BMD were using calcium/vitamin D supplements compared to 44.4% of those with normal BMD at the time of enrolment (p=0.056). Including: smoking, sedentary life style, post menopausal status, BMI>25 kg/m2 and the use of prednisone, as common risk factors for low BMD, there were only 10 patients (4%) with no risk factors, 143 (56.4%) had 1-2 and 100 patients (39.6%) had greater than 3 risk factors.

Conclusion:
The prevalence of osteoporosis risk factors was 24-69% in this study and 40% carried multiple risk factors. Despite young age and the exclusion of known osteoporosis, abnormal BMD was detected in >30%. Osteoporosis is under recognized in women with SLE in both current steroid users and non users. Therefore, routine BMD should be considered.
Objective:
To evaluate the effect of golimumab (GLM), a new human monoclonal anti-TNFα antibody, on the progression of structural damage in psoriatic arthritis (PsA) pts.

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 double-blinded manner to GLM 50mg (PBO pts) or GLM 100mg (GLM 50mg pts). All pts randomized to PBO received GLM 50mg from wk24 through wk52. Hand and foot radiographs were obtained at wks0,24&52. Erosions (ERO) and joint space narrowing (JSN) 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. Changes from baseline in modified vdH-S scores were compared at wk24 using ANOVA with pts’ baseline MTX usage as a factor in the model based on the van der Waerden normal score (primary endpoint). Wk24 comparisons were between the GLM and PBO grps, based on the original randomized grp. Missing data were imputed using median change from baseline in total vdH-S scores for pts within the same MTX stratum or by linear extrapolation. No statistical comparisons were performed at Wk52.

Results:
405 pts were enrolled. Mean age was 46-48 yrs, median swollen/tender joint counts were 12-14/22-24, HAQ scores were 1.0-1.1, CRP levels were 0.6 mg/dL, and total vdH-S scores were 9.00-10.50. At wk24, GLM 50mg pts had significantly less radiographic damage than PBO, as measured by mean change from baseline in total vdH-S score (-0.16±1.31 versus 0.27±1.26, p=0.011; -0.02±1.32 for GLM 100 mg, p=0.086 versus PBO). Significantly more GLM-treated pts had no progression as defined by change in total vdH-S score ≤0 (78.8% for GLM 50mg [p=0.007], 76.6% for GLM 100mg [p=0.020]) compared with PBO-treated pts (62.7%). In pts without ERO or JSN at baseline, 87.1%, 89.1%, and 71.6% of GLM 50mg, GLM 100mg, and PBO pts, respectively, maintained erosion-free status; in these respective grps, 97.0%, 96.4%, and 88.2% maintained JSN-free status. GLM-randomized pts had less progression at wk52 (mean change from baseline in total vdH-S score: -0.22±1.64 for GLM 50mg and -0.14±1.53 for GLM 100mg) versus PBO-randomized pts (0.22±1.38 ) who began GLM treatment at wk16/24.

Conclusion:
GLM treatment demonstrated inhibition of structural damage through wk24 with the maintenance of this benefit through wk52.
Golimumab, A New, Human, TNF Alpha Antibody, Administered SC Every 4 Weeks in PsA Patients: 104-Week Efficacy and Safety Results of the Randomized, Placebo-Controlled GO-REVEAL Study

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Objective:
To assess long-term efficacy & safety of golimumab (GLM) in PsA.

Methods:
PsA pts with ≥3 swollen and ≥3 tender joints and psoriasis were randomized to SC PBO or GLM (50 or 100mg) q4wks. At wk 16, pts with less than 10% improvement in swollen and tender joints entered early escape (EE). All pts received GLM from wk24 through wk104. Investigators could dose-escalate pts receiving GLM 50mg to 100mg based on clinical judgement after all pts reached wk 52. Results are provided through wk104. Analyses were based on pts with data. Due to lack of an adequate control arm , no statistical comparisons were made at wk 104.

Results:
405 pts with active PsA were randomized (113 PBO, 146 GLM 50mg, 146 GLM 100 mg). GLM was significantly better than PBO in improving signs and symptoms of PsA at wk24, and efficacy was maintained through wk52. At wk104, the percent of pts with ACR responses among the GLM 50mg and 100mg pts were 91.4%(64/70) and 73.1%(95/130) for ACR20, 65.7%(46/70), and 53.8%(70/130) for ACR50, and 44.3%(31/70) and 36.9%(48/130) for ACR70. In the GLM 50mg and 100mg grps, in pts with psoriasis ≥3% BSA, 68.8%(33/48) and 76.0%(73/96) achieved PASI75; mean improvement in HAQ scores were 0.54(69 pts) and 0.46 (127 pts). At wk104, GLM 50mg pts who switched to 100mg in EE or via dose escalation also achieved clinically meaningful responses for ACR20, ACR50, and ACR70 (56.6%, 35.5%, and 22.4%, respectively), although lower than in pts in the 50 or 100mg grps. PASI75 response for pts switching from 50 to 100mg was 62.5%; mean improvement in HAQ scores was 0.36. Of all GLM-treated pts, 8.6%(34/394) experienced SAEs and 5.8%(23/394) d/c treatment due to AE through wk104. Injection site reactions occurred in 8.9%(35/394) of pts. There was 1 case of histoplasmosis(GLM 100mg) that was successfully treated. Malignancies reported in pts receiving GLM 50mg included basal cell skin cancer(1 pt), colon cancer(1 pt), and small cell lung cancer(1 pt) and in pts receiving GLM 100mg, basal cell skin cancer(3 pts), prostate cancer(1 pt), and small cell lung cancer(1 pt). Two deaths occurred (GLM 50mg grp): 1 due to small cell lung cancer and 1 due to a climbing accident.

Conclusion:
GLM 50 and 100mg SC q4 wks maintained high levels of improvement through wk104. GLM was generally well-tolerated, with a safety profile similar to that observed for other anti-TNF agents.
Measurement of Autoantibodies Using Multiplex Methodology in Patients with Systemic Lupus Erythematosus

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Objective:
Autoantibodies are central to the diagnosis and assessment of systemic lupus erythematosus (SLE). Addressable laser bead immunoassay technology (BioPlex 2200) permits the simultaneous detection of multiple autoantibodies. Advantages include improved efficiency due to the shorter time to perform the assay and low volume of test samples and reagents. We have compared this technique to more traditional measures of autoantibody detection.

Methods:
Clinical and laboratory data and stored serum samples from the enrollment visit into a lupus registry at a single academic medical center were used. Sera were examined for a panel of autoantibodies using the BioPlex ANA screen. The results were compared to the historical data on autoantibody profiles using indirect immunofluorescence (IIF) and ELISA. The association with global and organ specific SLE disease activity (nephritis) was also examined.

Results:
192 patients, predominantly female (87%) and Caucasian (91%), with mean disease duration of 8.8 years were studied. The frequency of ANA and anti-dsDNA by IIF and ELISA was 81.3% and 46.6% respectively and was higher than that found with BioPlex (75.5% and 31.8%). Bioplex detected a higher proportion of patients with autoantibodies to Sm (7.5% vs 16.7%), RNP (21.8% vs 24.0%), Ro (37.4% vs 41.7) and La (13.9% vs 23.4%). Overall agreement between assays was 71.4% - 92.5%. Additional autoantibodies identified by BioPlex were anti-chromatin antibodies (33.9%) anti-ribosomal P (6.8%), anti-Scl-70 (5.2%), anti-centromere B (3.7%) and anti-Jo-1 (0.5%). Several autoantibodies revealed significant associations with SLEDAI scores but in a multivariate analysis the only autoantibodies that approached statistical significance were anti-Sm (p=0.094) by ELISA and anti-dsDNA (p=0.082) by BioPlex. There was no association between autoantibodies, regardless of the method of detection, and cumulative organ damage scores. Fifty-three patients (27.6%) had lupus nephritis of which 17 (32%) had active nephritis at the time of autoantibody determination. There was no significant association between a positive ANA (IIF) or autoantibodies detected by ELISA with either the cumulative occurrence of lupus nephritis or active nephritis. In contrast, univariate analysis indicated an association between BioPlex detected anti-dsDNA with the cumulative occurrence of nephritis (p=0.074) which reached statistical significance with active nephritis at the time of antibody testing (p=0.012). This association was confirmed by multivariate analysis (p=0.047).

Conclusion:
These results suggest reasonable agreement between the detection of lupus autoantibodies by ELISA and Bioplex. The latter demonstrated a better correlation with lupus nephritis.
Reduced Radiographic Progression in Patients with Early Rheumatoid Arthritis (RA) Treated with Abatacept + Methotrexate Compared to Methotrexate Alone: 24 Month Outcomes

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Objective:
To assess the 24-month radiographic outcomes in methotrexate (MTX)-naïve patients with early, erosive RA and poor prognostic factors who are treated early with abatacept (ABA) + MTX compared to MTX alone

Methods:
The AGREE trial was a 24-month study, with a 12-month double-blind period (DB) and a 12-month open-label phase (OL), in adult MTX-naïve patients with early, erosive RA and poor prognostic factors. During the DB, patients were randomized to ABA (~10 mg/kg dose based on weight range) + MTX (dosed up to 20 mg) or placebo + MTX. All patients received ABA + MTX during the OL. Radiographic outcomes were assessed using Genant-modified Sharp scores. Changes in erosions [ES], joint space narrowing [JSN] and total score [TS] are reported. A change in TS \( \leq 0 \) defined nonprogressors

Results:
Of the 459 patients completing the DB and entering the OL, 94.3% completed the study. From baseline through 24 months, patients originally randomized to the ABA + MTX arm experienced less progression of structural damage as measured by change in TS (0.84 vs. 1.75) and a greater proportion of nonprogressors (56.8% vs. 43.8%) compared to those originally randomized to MTX monotherapy. Moreover, among patients originally randomized to the ABA + MTX arm, there was an increasing degree of inhibition of progression seen in year 2 compared to year 1 (TS = 0.18 vs. 0.66, respectively, \( p < 0.0001 \)), with 91.1% of year 1 nonprogressors remaining nonprogressors in year 2.

Conclusion:
Early use of combination therapy with ABA and MTX results in greater long-term sustainable radiographic benefit in MTX-naïve early RA patients than MTX alone and supports the use of ABA earlier in the RA disease process.
Predicting the Risk of Rapid Radiographic Progression for Patients With Early Rheumatoid Arthritis: Data From PREMIER

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Objective:
Identifying patients at risk of radiologic progression is important when determining therapeutic interventions for patients with early rheumatoid arthritis (RA). We investigated predictors of rapid disease progression (RP), as defined by a change in modified total Sharp score (mTSS) >3 units/year, in PREMIER.1

Methods:
Univariate logistic regression analyses using quartile ranges (Qs) were performed to identify baseline variables associated with RP.

Results:
After 2 years of treatment with methotrexate (MTX), adalimumab (ADA), or ADA+MTX, 33%, 23%, and 6% of patients, respectively, exhibited clinically relevant RP. For MTX, increasing Qs for C-reactive protein (CRP), baseline 28-joint Disease Activity Score (DAS28), rheumatoid factor (RF), mTSS, joint erosion (JE), or joint space narrowing (JSN) were strongly associated with increasing risk of RP. Except for JSN, this relationship was not observed for the ADA+MTX group. For patients with normal/near normal CRP (Q1, 0.35–1.12), more patients receiving MTX (27.8%) than ADA+MTX (6.1%) exhibited RP (p=0.012). Except for mTSS and JE Q1, ADA+MTX treatment was associated with significantly less risk of RP than MTX for each Q. Results were similar for increasing Qs for Patient’s Global Assessment of Disease Activity. Increasing Qs for swollen or tender joint counts were not associated with an increased risk of RP, nor were increasing Qs for the Health Assessment Questionnaire, patients’ assessments of pain, or Physicians’ Global Assessments of Disease Activity. For every Q of each variable, ADA+MTX treatment was associated with lesser risk of RP vs. MTX. For all variables, fewer patients in Q4 of the ADA+MTX group had RP than in Q1 of the MTX group. For the MTX group, ≥19% of patients in Q1 for all variables except mTSS and JE had RP.

Conclusion:
After 2 years of treatment, fewer patients treated with ADA+MTX had rapid radiologic progression of their RA compared with MTX monotherapy. Patients treated with MTX who had less severe baseline characteristics (Q1) were at greater risk than patients who had more severe baseline characteristics (Q4) and were treated with ADA+MTX. Reference: 1. Breedveld FC, et al. Arthritis Rheum. 2006;54:26–37.
Systemic Lupus: A Newly Discovered Risk Factor for Restless Legs Syndrome?

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Objective:
Restless Legs Syndrome (RLS), a disorder affecting 10-12% of the population, is characterized by sensory symptoms and motor disturbances of the limbs. RLS is believed to be common in several rheumatic diseases. Yet, data in Systemic Lupus Erythematosus (SLE) are lacking. Our aim was to determine the prevalence of RLS in SLE.

Methods:
Unselected consecutive SLE patients were recruited from a hospital-based lupus clinic. A validated RLS questionnaire was administered during a face-to-face or telephone interview. Smoking history and height/weight data were also collected. RLS prevalence was determined similarly in a comparator group of general rheumatology clinic patients attending the same health centre. The controls were frequency-matched by age group and sex to the SLE subjects; otherwise, they were unselected.

Results:
We studied 37 subjects with SLE (33 females, 4 males), and 38 controls (32 females, 6 males). The control population had a variety of rheumatic diseases (14 rheumatoid arthritis, 8 soft-tissue rheumatism, 4 MCTD, 12 other conditions). Thirteen SLE patients (36.1%, 95% CI 22.5, 52.4) and eight controls (21.1%, 95% CI 11.1, 36.3) scored positively for RLS. Twelve of 33 female SLE subjects (37.5%, CI 22.9, 54.7) and one of four male SLE subjects (25%, CI 4.6, 69.9) had RLS. In the comparator group, four of 32 females (12.5%, CI 5.0, 28.1) and four of 6 males (66.7%, CI 30.0, 90.3) had RLS. Three of the 13 SLE patients with RLS, and two of the eight controls with RLS reported smoking. Obesity (BMI ≥ 30) was present in two of the 13 SLE patients with RLS, and four of the eight controls with RLS.

Conclusion:
RLS prevalence in SLE was higher than most general population estimates. The prevalence of RLS in our control group concords with available general population estimates. Females with SLE appeared to be three times more likely to have RLS than females in the comparator group (though confidence intervals overlapped). In this sample, we did not see consistent correlations between RLS and obesity or smoking. In ongoing work, we will further assess the relationships between various clinical factors and RLS prevalence in SLE.
Patient Self Reported Health Related Quality of Life Improves with Effective Treatment in Early Inflammatory Arthritis (EIA)

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Objective:
Treatment strategies aiming for disease remission improve clinical outcomes in early inflammatory arthritis (EIA). Clinical trials also report improvement in patient health related quality of life (HRQOL). HRQOL data are limited in patients with EIA receiving routine clinical care. The objective of this study is to assess self reported functional status and HRQOL in a "real world" cohort of EIA patients.

Methods:
Subjects enrolled in the Canadian early arthritis cohort (CATCH) a multi-centre observational cohort of adult patients with EIA. (Symptom duration 6-52 weeks, 2 effused joints or 1 swollen MCP or PIP and 2: +RF, + anti-CCP, morning stiffness >45 minutes, response to NSAIDs, or painful MTP squeeze test). Clinical features (tender and swollen 28 joint counts, ESR) were recorded every 3 months. Functional status (mHAQ) and HRQOL (short form 12 health survey (SF12)) were recorded at baseline and one year. SF12 domain scores, physical and mental component summary scores (PCS, MCS) were norm-transformed (US population). DMARD use was at the clinician's discretion. Clinical outcomes assessed at one year were EULAR treatment response, remission ((REM) DAS28< 2.6) and sustained remission ((sREM) REM for 6 consecutive months). Data are mean(SD).

Results:
One year data was available for 116 subjects (69% female; 81% Caucasian; 75% RA) with baseline symptom duration 5.4(3.9) months, DAS28 4.9(1.9), (86% DAS28≥2.6), SJC 9(7), TJC (11(7), ESR 28(24)). 82% were prescribed DMARDs (MTX n=75; HDQ n=77; SSZ n=27; combination n=62). By 1 year DMARDs were intensified in 31 subjects (7 new start, 24 added) and reduced in 33 subjects. At one year 70% had a EULAR treatment response and 54% were in REM. Baseline SF12 scores were below US population norms(PCS 34(13);MCS47(12) p=ns REM vs nonREM at one year). One year PCS(p< 0.001) and MCS (p< 0.01) improved over baseline paired scores (REM and nREM). At one year REM had > PCS (50(10) vs 44(10) p< 0.001) but similar MCS (52(9) vs 50(9) p=ns) compared to nonREM. sREM had > PCS (49(10) vs 42(12) p< 0.01) but similar MCS (51(8) vs 50(10) p=ns) compared to non-sREM. At one year, DAS28 correlated with PCS (r= -0.3 p< 0.01) and mHAQ (r= -0.6 p< 0.01); mHAQ correlated with PCS (r= -0.6 p< 0.01).

Conclusion:
HRQOL improves with effective DMARD treatment in "real world" practice. Disease activity contributes partially to HRQOL responses in EIA patients.
Measuring Body Image Avoidance in Patients with Scleroderma (SSc)

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Objective:
Patients with systemic sclerosis, or scleroderma, experience substantial disfigurement, often in visible and socially relevant areas of the body. Social avoidance related to body image distress is a significant problem for individuals with acquired disfigurement from medical illness or injury. However, body image avoidance has never been systematically studied in patients with scleroderma and existing measures are designed for non-disfigured individuals with body image and/or eating concerns. The objective of this study was to compare the validity and reliability of a general Body Image Avoidance Questionnaire for Acquired Disfigurement (BIAQ-AD; N = 181) with a disease-specific measure for patients with acquired disfigurement from scleroderma (BIAQ-Scleroderma; N = 93).

Methods:
203 female patients completed the BIAQ-AD, the BIAQ-Scleroderma, or both between 1997 and 2002. The BIAQ-AD was adapted from the Body Image Avoidance Questionnaire (Rosen et al., 1991) by removing weight and eating-related items, and the BIAQ-Scleroderma included items reflecting scleroderma-specific concerns (e.g., I wear long sleeves to hide skin changes). Confirmatory factor analysis and exploratory factor analysis were performed with MPLUS to determine the factor structure; internal consistency reliability was assessed using Cronbach’s alpha; and concurrent validity was assessed by comparing BIAQ-AD and BIAQ-Scleroderma with the Adapted Satisfaction with Appearance Scale (ASWAP), Beck Depression Inventory (BDI) and the McGill Pain Questionnaire Short-Form (MPQ-SF).

Results:
A 1-factor model provided the most parsimonious fit for both the BIAQ-AD ($\chi^2(21) = 44.25$, CFI = .98, TLI = .99, RMSEA = .08), and the BIAQ-Scleroderma ($\chi^2(19) = 53.28$, CFI = .92, TLI = .94, RMSEA = .14). The BIAQ-AD (Cronbach’s alpha = 0.87) correlated 0.44 with the ASWAP, 0.72 with the BDI, and 0.25 with the MPQ-SF. The BIAQ-Scleroderma (Cronbach’s alpha = 0.83) correlated 0.68 with the ASWAP, 0.59 with the BDI, and 0.27 with the MPQ-SF.

Conclusion:
The high correlation of the general measure (BIAQ-AD) with the Beck Depression Inventory suggested it overlapped with general distress substantially more than the scleroderma-specific BIAQ-Scleroderma, which better addressed distress related to body image avoidance. Therefore, the BIAQ-Scleroderma is the preferred tool for assessment of body image avoidance in patients with scleroderma. The development and validation of the BIAQ-Scleroderma is a necessary initial step towards better assessment of body image avoidance in patients with scleroderma, however, further research is needed towards the development and testing of interventions to help these patients function better socially.
A Comparison of Systemic Sclerosis in 3 Canadian Ethnic Groups

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Objective:
To identify differences in clinical and serological manifestations of SSc in 3 Canadian ethnic groups, French Canadians, Aboriginals and Whites.

Methods:
Data from the multi-center Canadian Scleroderma Research Group registry was reviewed. Ethnic background was self-reported and patients could indicate as many categories as applicable. French Canadians were defined as those who reported being French Canadian and having 4 grand-parents born in the province of Quebec. Whites excluded French Canadians and Aboriginals. Others were those who did not report being French Canadian, Aboriginal or White. Clinical and serological characteristics of French Canadian and Aboriginal patients were compared to those of White patients. Linear regression was used to determine whether ethnicity was an independent predictor of disease severity and damage (measured using physician global assessments), after adjusting for clustering and demographic, clinical and serological differences between the groups.

Results:
Data from 975 patients, of whom 133 were French Canadian, 46 Aboriginal, 394 Whites and 402 others were available. French Canadian patients were more likely to have diffuse disease (44.4% vs 32.0%, p 0.01), lung fibrosis (35.3% vs 26.1%, p 0.04), finger contractures (41.4% vs 24.6%, p 0.0002) and anti-topoisomerase antibodies (17.3% vs 8.9%, p 0.02) compared to Whites. Aboriginals were more than 6 years younger than Whites (49.3 vs 55.7 years, p 0.001) but their disease duration was only one year shorter than Whites (10.1 vs 11.4 years, p 0.31). Aboriginals were more likely to have diffuse disease (47.8% vs 32.0%, p 0.04), lung fibrosis (41.3% vs 26.1%, p 0.03), gastrointestinal symptoms (mean number 6.1 vs 3.9, p 0.0001), finger contractures (50.0% vs 24.6%, p 0.0003) and tender joints (mean number 3.8 vs 1.1, p 0.004) compared to Whites. They also tended to have a history of inflammatory myositis (15.2% vs 9.6%), fingertip ulcers (28.3% vs 17.0%), anti-topoisomerase (13.0% vs 8.9%) and PM/ScI (19.6% vs 13.7%) antibodies more frequently than Whites, although these numbers did not reach statistical significance. Linear regression revealed that French Canadian, but not Aboriginal, ethnicity was an independent predictor of disease severity (estimate 0.55, p = 0.02) and damage (estimate 0.54, p = 0.02), after adjusting for clustering and other demographic and clinical differences between groups.

Conclusion:
Clinical and serological differences exist between different ethnic groups of SSc patients. Genetic and/or environmental factors likely contribute to disease expression in SSc.
Objective: Disease activity in SLE patients, measured by SLEDAI-2K, is evaluated at each clinic visit and covers a period of 30 days prior to the assessment. Having consecutive monthly clinic visits would capture the entire disease activity for that period of time. Adjusted Mean SLEDAI (AMS) calculates the areas under the curve of SLEDAI-2K over time. AMS evaluated using monthly visits would be the gold standard for disease activity over time. The usual clinical practice is to see patients every 3-6 months. The aim of this study is to compare the AMS obtained over a one year period when visits are done monthly and compare it to AMS obtained using quarterly, semi-annual or annual visits.

Methods: Patients followed monthly for 12 consecutive visits are included. AMS is evaluated using all of the SLEDAI-2K (AMSGOLD using all 12 visits), only quarterly visits (AMS3, using visits 3 months apart), semi-annual visits (AMS6, using 1st, middle and last visits only) and annual visits (AMS12 using only the 1st and last visits). Comparisons between AMS3, ASM6 and AMS12 with AMSGOLD are made using descriptive statistics.

Results: 5.≥78 patients were seen monthly for a year. 72 (92%) were women with mean (std) age at SLE diagnosis of 30.1 (11.4) years and mean age and disease duration at study start of 46.2 (12.0) years and 15.5 (9.7) years respectively. The SLEDAI-2K values seen have a mean (std) of 2.05 (2.07) and range in values from 0 to 15, with 7% of all visits having a SLEDAI-2K. The mean (std) AMSGOLD for the entire year is 2.05 (1.66), for AMS3 = 1.99 (1.65), for AMS6 = 2.12 (1.87) and for AMS12 = 2.08 (1.83). Mean (std) of the absolute differences with AMSGOLD are: for AMS3 = 0.29 (0.33), for AMS6 = 0.45 (0.59) and for AMS12 = 0.61 (0.58). Differences which were < 1 were deemed important. Comparing AMSGOLD to AMS3, 82% of the differences were minimal and 3% were important. When comparing to AMS6, 68% were minimal and 10% were important while when comparing to AMS12, 50% were minimal and 21% were important.≥0.5 were considered minimal while those

Conclusion: Usual clinical visits occurring quarterly offer a good estimation of disease activity over a one year period and are preferred over semi-annual and annual visits.
Objective:
To determine if referral letters to rheumatologists include the key elements recommended by Canadian Rheumatology Association (CRA) guidelines.

Methods:
We examined referral letters received over a one-year period by one full-time rheumatologist practicing at a tertiary-care centre. We assessed whether the letters contained the key elements recommended by the CRA, which include purpose of the consult, symptom duration, joint pattern, systemic symptoms (e.g. morning stiffness), and suspected diagnosis.

Results:
In total, 140 referral letters were screened. Criteria for exclusion from the study were referrals from one rheumatologist to another (N=26), consults with no reference letter (N=7), referrals outside of the one year period (N=5), one patient who did not attend, and one letter with zero legible words; in sum, 100 charts were included for analysis. Approximately 26% of referrals came from general practitioners; the rest were from specialist physicians or the emergency room (ER). The average patient age was 51 years, with a female-to-male ratio of 1.9:1. Approximately 15% of referral letters made mention of some small joint involvement, including either poly-arthritis/synovitis, ≥ 4 or more joints, ‘wrists’ or ‘hands,’ and/or any mention of MCP/MTP joints. The majority (62%) of consults included ‘joint pain’ in the referral letter; however, only 2% mentioned any circadian rhythm of symptoms (such as morning stiffness). In 94% of referral letters, no information was provided as to the functional status of the patient. In contrast to the low clinical suspicion raised by the referral letters themselves, close to one in three consults was found to involve an inflammatory etiology (29%) after assessment by a rheumatologist, and a final diagnosis of inflammatory arthritis was applied to 20% of referrals.

Conclusion:
We provide objective evidence that referral letters sent to rheumatologists are often lacking in key elements of the medical history. The vast majority of referral letters do not conform to CRA guidelines. This lack of information means that appropriate triage of referrals by rheumatologists is very difficult, at least at our centre. As a response to this, we have developed, with family physicians and rheumatologists, a standardized referral template which is being piloted. Further steps may include assessing referrals from other sources, such as referrals from ER doctors and other subspecialists. Our ultimate goal is to improve wait times for patients with urgent conditions such as inflammatory arthritis.
Distance to Lupus Centre and Health Care Barriers in Systemic Lupus Erythematosus

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Objective:
Previous studies have suggested that certain health care barriers (HCBs) may be associated with Systemic Lupus Erythematosus (SLE) disease progression. It is suspected that distance to nearest lupus centre (DNLC) contributes to patient-perceived HCBs and may therefore be associated with SLE activity/damage. This study tested if DNLC was associated with various HCBs, disease activity (as measured by the SLE Disease Activity Index (SLEDAI)), or damage (as measured by the SLICC Damage Index (SDI)).

Methods:
Of 1739 patients initially considered, 543 were excluded due to missing postal codes/SDIs. Descriptive statistics were calculated for provinces with greater than 50 cases (Quebec, QC=103, Ontario, ON=677, Manitoba, MB=211, Nova Scotia, NS=143). DNLC was calculated for each patient using the spherical law of cosines formula (using postal code-derived latitudes/longitudes). Differences in demographic variables and HCBs were assessed using chi-square tests. HCBs were correlated with DNLC (Spearman) and univariate and multivariate logistic regression models using DNLC (predictor) and either SLEDAI or SDI (outcome) were built (using age, SLE duration, high school graduation status, and census-derived household income as covariates).

Results:
Mean (± SD) age and disease duration were 45.1 (±14.4) and 11.7 (±9.8) years, respectively. Median (IQR) for SLEDAI, SDI and DNLC were 4.0 (2.0 - 8.0), 1.0 (0.0 - 2.0) and 17.0 (6.7-70.9) km, respectively. The patient-reported HCB “Traveling to a rheumatologist” showed a moderate, positive correlation with DNLC in QC (r=0.28, p=0.05), ON (r= 0.32, p< 0.001) and MB (r=0.276, p=0.006). No physician-reported HCBs were correlated with DNLC. For SLEDAI, positive associations were observed with age, high school graduation status and (log) DNLC in ON, while negative associations were found with age in NS and SLE duration in ON. For SDI, positive associations were observed with age in ON and SLE duration in ON, MB and NS, while a negative association was found with high school graduation status in ON. Limitations of this study arise from: (1) possible selection bias and (2) the method of distance calculation (used postal codes instead of exact addresses).

Conclusion:
The only HCB significantly correlated with DNLC was “traveling to a rheumatologist.” DNLC was found to be positively and significantly associated with SLEDAI score but not with SDI. This suggests that living further away from a lupus center is associated with higher lupus activity but not necessarily higher disease damage.
Etanercept Levels in the Breast Milk of a Nursing Mother with RA

Stephanie Keeling (University of Alberta, Edmonton); Gert-Jan Wolbink (Jan van Breeman Institute Rheumatology, Amsterdam)

Case Report:
Objective: The use of biologics in the nursing mother with RA is controversial because of the limited available data quantifying how much TNF inhibitor is transferred to the newborn via the milk. The goal of this study was to assay the levels of etanercept in the breast milk of a nursing mother with RA at her request. METHODS: Six samples of breast milk were collected over a 2-month period. The patient had been taking both 25 mg SC twice a week and then switched to 50 mg SC once a week for convenience. Breast milk samples were sent to Sanquin Laboratories in Amsterdam and an ELISA performed quantifying etanercept levels through anti-etanercept antibodies. RESULTS: Levels for etanercept 25 mg SC twice a week were as follows: pre-etanercept 25 mg (no prior etanercept exposure) = <1.5 ng/ml, 24 hrs post-etanercept 25 mg = 4.48 ng/ml. Upon switching to weekly dosing, levels for etanercept 50 mg SC weekly were as follows: immediately pre-50 mg etanercept = 5.25 ng/ml, 24 hrs post-etanercept 50 mg = 4.48 ng/ml and 72 hrs post-etanercept 50 mg = 7.50 ng/ml. Average volume of breast milk per sample was 60 ml. Therefore, the highest concentration of etanercept occurred 72 hrs post-etanercept 50 mg at 7.50 ng/ml (450 ng assuming 60 ml volume). CONCLUSIONS: These samples confirm the negligible amount of etanercept excreted in the breast milk in a nursing mother with RA. This confirms findings by Oostensen et al. (2004 J Rheum) of the minimum amounts of etanercept in breast milk. Ideally, infant serum samples would be collected to confirm that very little etanercept is available in the breast milk for absorption into the newborn’s GI tract. More importantly, it would clarify if the infant’s gastric secretions destroyed any etanercept still transferred to the baby. The mother stopped nursing at 6 months and the child remains healthy at 3 years of age. This report suggests that agents such as etanercept may be a safer option for the nursing RA mother but further confirmatory studies, detailing all the pharmacokinetics and validating the assay specifically in breast milk are needed.
System Level Evaluation of the ACPAC (Advanced Clinician Practitioner in Arthritis Care) Trained Practitioner in Ontario

Laura Passalent (St Michael's Hospital, Toronto); Kelly Warmington (St Michael's Hospital, Toronto); Carol Kennedy (St. Michaels Hospital, Institute for Work and Health, Toronto); Leslie Soever (Mount Sinai Hospital, Toronto); Rachel Shupak (St Michael's Hospital, Toronto); Sydney Lineker (The Arthritis Society, Toronto); Rayfel Schneider (The Hospital for Sick Children, University of Toronto, Toronto); Ryan Thomas (St Michael's Hospital, Toronto); Katie Lundon (St Michael's Hospital, Toronto)

Objective:
The Advanced Clinician Practitioner in Arthritis Care (ACPAC) Program is an innovative, clinical and academic training program focused on the assessment, diagnosis, triage and independent management of selective musculoskeletal and arthritis disorders. The aim of the program is to prepare experienced physical and occupational therapists for expanded scope of practice roles and to develop innovative models of arthritis care across diverse clinical settings in Ontario. It is now critical to evaluate the extent to which the ACPAC program graduates have developed and integrated new models of arthritis care throughout the province of Ontario. This evaluation will provide ACPAC faculty, graduates, healthcare organizations, policy makers and other stakeholders with feedback about internal processes and external outcomes at the patient, organization and system levels. The objective of this presentation is to describe the methodological framework that has been chosen to evaluate the impact of the ACPAC program graduates on the Ontario health care system.

Methods:
The Balanced Scorecard Approach has been chosen as the methodological framework to guide this evaluation. Such a framework allows for performance measurement, as well as management and strategic planning. In the province of Ontario, the Hospital Report: Rehabilitation Series has derived four quadrants from the original Balanced Scorecard Approach. This adapted model will be used to frame the evaluation of the ACPAC program graduates. This will include the following quadrants (and its respective indicators): Client Perspectives (patient, worker and stakeholder); Clinical Utilization and Outcomes (patient volumes, community practice and educational interventions); System Integration and Change (integration with community resources, access to care, interprofessional collaboration and extended scope practice) and Financial Performance and Condition (productivity and cost-savings). Each quadrant will use a variety of primary data collection methods throughout 2 fiscal years (2009/2010 and 2010/2011), including cross-sectional and longitudinal surveys, case studies, key informant interviews and focus groups.

Results:
Results from the above evaluation will be used to guide continuous performance improvement of the ACPAC graduates with respect to their patient, organization and system level impact. It is expected that this process will reveal an effective interprofessional approach to managing patients with arthritis disorders more efficiently, and, contribute to improved access to effective arthritis care.

Conclusion:
Completion of this multidimensional evaluation will determine the impact of the ACPAC program graduates on various levels of the Ontario healthcare system and help to ensure the vitality and sustainability of this new cadre of human health resource for
Predicting Remission at 1 Year in Early Rheumatoid Arthritis: A Subanalysis of PREMIER

Maxime Dougados (University of Paris V, Paris); Edward Keystone (University of Toronto - Mount Sinai Hospital, Toronto); Benoît Guérette (Abbott Laboratories, Rungis); Kaushik Patra (Abbott Laboratories, Abbott Park); Frederic Lavie (Abbott Laboratories, Rungis)

Objective:
In PREMIER, adalimumab (ADA)+methotrexate (MTX) was superior to MTX monotherapy in preventing nearly all radiographic progression in patients with early rheumatoid arthritis (RA), regardless of clinical response to therapy. Although therapy adjustment is recommended at least every 3 months for patients with persistent active disease, the efficacy of currently available therapies increases during the first year. Using the PREMIER database, we aimed to answer: (1) After initiating a therapy because of active disease, how long should we wait before considering this treatment ineffective and deciding to change it? (2) Is the time to reach this decision the same regardless of the treatment used?

Methods:
Clinical outcomes were 28-joint Disease Activity Score (DAS28) at Weeks 4, 8, 12, and 26 and change (∆) from baseline in DAS28. Predicted probability plots of remission at 1 year were obtained, depending on DAS28 or ∆DAS28 at Weeks 4, 8, 12, and 26. At each time point, probability of remission was also evaluated for 4 categories of DAS28 (< 2.6, 2.6–< 3.2, 3.2–< 5.1, and ≥5.1) and 2 categories of ∆DAS28 (improvement of ≤0.6 or >0.6) for ADA+MTX and MTX alone.

Results:
Probability of remission at 1 year was greater for patients treated with ADA+MTX vs. MTX alone for each level of DAS28 or ∆DAS28 at all time points (p< 0.05). A probability of < 15% to reach remission at 1 year was found as early as Week 8 for MTX-treated patients with an improvement of < 0.6 in their DAS28. For ADA+MTX-treated patients with the same level of response, a < 15% probability of remission was not observed before Week 26.

Conclusion:
Depending on the treatment and the patient’s response category, the time to the decision to change treatment in patients with early RA may vary. Some patients treated with MTX and presenting nonsignificant improvement of their DAS28 at Week 8, DAS28 ≥5.1 at Week 12, or DAS28 ≥3.2 at Week 26 could be considered good candidates for treatment adjustment. Clinicians should consider waiting ≥6 months before adjusting therapy for patients treated with ADA+MTX. Reference: 1. Breedveld FC, et al. Arthritis Rheum. 2006;54:26–37.
Objective:
To review the safety profile of CZP demonstrated in RA clinical trials and open-label extensions (OLEs).

Methods:
Data pertaining to adverse events (AE) were pooled from Phase 1, 2 and 3 studies of CZP (Phase 3: RAPID 1, RAPID 2, FAST4WARD and 014) and their OLEs. Analyses were performed using cut-off dates of January 31, 2007 (initial) and August 31, 2007 (update) and are presented by incidence (AEs/100 patient-years [pt-yrs]). Data were censored per pt at first occurrence of the AE or serious AE [SAE]) and by proportion of pts experiencing each AE. Malignancy data are presented as standardized incidence ratios (SIRs) compared to the GLOBOCAN database (excluding non-melanoma skin cancers and cancers within 30 days of first study drug injection).

Results:
2367 RA pts treated with CZP with 4065 pt-yrs of exposure were available for safety analyses as of Aug 2007. Most AEs were mild/moderate, with infections being the most common reported by 55.5% and 61.2% (70.6 vs 65.8/100 pt-yrs) in Jan and Aug 2007, respectively. Respiratory tract infections and tuberculosis (TB) were the most frequently reported serious infections. However, no cases of TB were reported in the US; most occurred in countries with a high prevalence of latent TB. Opportunistic infections included 1 case each of geotrichosis and Pneumocystis and 3 cases of fungal esophagitis. In addition, 1 patient had gastrointestinal perforation. 7.9% and 1.8% of patients in Jan and Aug 2007, respectively, experienced injection site reactions and pain. Malignancy SIRs were 1.06 (95% CI:0.65-1.61) and 1.22 (95% CI:0.82-1.74) in Jan and Aug 2007, respectively; lymphoma SIRs were 4.97 (95% CI:1.03-14.54) and 4.10 (95% CI:0.84-11.97). The standardized mortality ratios were 1.02 (95% CI:0.67-1.49) and 0.96 (95% CI:0.65-1.36), respectively.

Conclusion:
With the addition of 850 pt-yrs of CZP exposure, the incidence rate of AEs and SAEs and the overall safety profile of CZP remained consistent with previous analyses. Data obtained from the analyses maintain there is a positive benefit/risk balance for CZP in RA.
DAS28 (ESR) Response at Week 12 is Predictive of Long-Term Disease Activity in Rheumatoid Arthritis Patients Treated with Certolizumab Pegol

Michael Schiff (University of Colorado School of Medicine, Denver); Edward Keystone (Mount Sinai Hospital, Toronto); Tore Kvien (Diakonhjemmet Hospital, Oslo); Jeffrey Curtis (University of Alabama at Birmingham, Birmingham); Paul Emery (Leeds General Infirmary, Leeds); Kristel Luijtens (UCB, Braine-l’Alleud); Ernest Choy (King’s College Hospital, London)

Objective:
To determine if EULAR DAS28(ESR) response (change ≥1.2 units from baseline) at Week (Wk) 12 is predictive of disease activity (DAS28) at Wk 52 in RA patients treated with CZP.

Methods:
RA disease activity was categorized as high (DAS28 >5.1), moderate (DAS28 >3.2-≤5.1) or low (DAS28 ≤3.2) using data from patients treated with CZP + MTX in RAPID1. At Wk 52 data was assessed among patients who did/did not achieve a DAS28 response at Wk 12. Results were analysed for the completer population (patients who completed 52 wks of treatment) and the ITT (LOCF) population.

Results:
98% of the 982 patients randomized in RAPID1 had high disease activity at baseline and 2% had moderate disease activity. At Wk 52, patients treated with CZP 200 mg had high, moderate and low disease activity of 31%, 40% and 29%, respectively. At Wk 12, 57% of CZP 200 mg + MTX-treated patients achieved a DAS28 response ≥1.2; these patients were more likely to achieve low disease activity (DAS28 ≤3.2) at Wk 52 compared with patients who did not have a change in DAS28 ≥1.2 units at Wk 12 (37% vs 6%). In an analysis of CZP completers, patients treated with CZP 400 mg + MTX achieved similar results.

Conclusion:
Patients treated with CZP who had an improvement in DAS28 of ≥1.2 at Wk 12 had a 6 times higher probability of having low disease activity at Wk 52 than patients with a DAS28 change < 1.2. Conversely, improvement in DAS28 of < 1.2 units over BL at Wk 12 was highly predictive of sustained moderate or high disease activity at Wk 52. An important endpoint for the evaluation of biologic treatment may be evaluation of change in DAS28 at Wk 12.
The Efficacy of Certolizumab Pegol Added to Methotrexate is Sustained Over 2 Years in the Treatment of Rheumatoid Arthritis

Edward Keystone (Mount Sinai Hospital, Toronto); Roy Fleischmann (University of Texas Southwestern Medical Center, Dallas); Joseph Smolen (University of Vienna, Vienna); Vibeke Strand (Stanford University, Palo Alto); Robert Landewé (University Hospital Maastricht, Maastricht); Bernard Combe (Hôpital Lapeyronie, 34295 Montpellier); Philip Mease (Seattle Rheumatology Associates, Seattle); Zainab Ansari (UCB, Slough); Niti Goel (UCB, Smyrna); Désirée Van der Heijde (Leiden University Medical Center, Leiden)

Objective:
Certolizumab pegol (CZP) 200 or 400 mg Q2W + MTX has been found to be significantly more effective than placebo + MTX in the treatment of rheumatoid arthritis (RA) over 52 weeks (RAPID1). Here we assess the efficacy of CZP + MTX over 100 weeks.

Methods:
Patients eligible to enter open-label (OL) treatment with CZP 400 mg Q2W + MTX were those who completed 52 weeks of double-blind treatment in RAPID1 (completers) or who withdrew at Wk 16 due to lack of ACR20 response (at Wks 12 and 14; withdrawers). This analysis focuses on CZP completers who entered the OL study (n = 243 for CZP 200 mg + MTX and n = 265 for CZP 400 mg + MTX) and were exposed to CZP for 100 wks (2 years) from BL. Efficacy analyses included degree of radiographic progression (assessed in hands, wrists, and feet using change from BL in modified total Sharp score [mTSS; linear extrapolation]), ACR20/50/70 responses (nonresponder imputation), ACR core component scores, and DAS28 (ESR) (LOCF). Treatment-emergent AEs (AEs after first study drug administration) were assessed at each visit in all patients.

Results:
95.8% of RAPID1 CZP completers reconsented and received OL CZP. Of these, 91.1% continued in the OL study through 100 wks or more. In this patient population, inhibition of radiographic joint damage progression was maintained throughout 2 years. Of completers originally in the CZP 200 mg and 400 mg groups, 72.4% and 77.3%, respectively were classified as non-progressors (mTSS change ≤0.5 units from BL) at 2 years. ACR20/50/70 responses, ACR core component scores and DAS28 were also sustained throughout 2 years in CZP completers. Benefits were comparable regardless of whether patients received CZP 200 mg or 400 mg through Year 1 based on their original randomization. No new safety signals emerged in the OL study.

Conclusion:
Inhibition of the progression of radiographic joint damage and improvements in RA signs and symptoms were sustained by CZP + MTX over 2 years with no new safety signals.
Benefit of Continuing Treatment Beyond 12 Weeks in Patients With Rheumatoid Arthritis Treated With Tocilizumab and DMARDs Who Had Previous Inadequate Responses to DMARDs or TNF Inhibitors

Edward Keystone (Mount Sinai Hospital, Toronto); Ani John (Roche, Nutley); Kar Wong (Everest Clinical Research Services, Inc., Markham)

Objective:
To assess the midterm course of patients (pts) with no or limited responses to treatment with tocilizumab (TCZ) and DMARDs, including methotrexate (MTX), at wk 12.

Methods:
This post hoc analysis used data from pts who participated in 4 phase 3 clinical trials and had previous inadequate responses to DMARDs (DMARD-IR; pooled data from OPTION, TOWARD, and LITHE) or tumor necrosis factor-α inhibitors (TNFi-IR, RADIATE). Pts were treated for 24 wks with TCZ (4 mg/kg or 8 mg/kg) and DMARDs/MTX. Proportions of non-responders (NR) in various disease activity parameters were determined (ACR20/50/70, LDAS [DAS28 ≤ 3.2], DAS28 remission [< 2.6]) at wk 12 but who achieved the respective responses at wk 24 (responders [R]).

Results:
Analysis included 2018 DMARD-IR pts and 331 TNFi-IR pts. Response rates at wk 12 for ACR20/50/70, LDAS, and DAS28 remission were numerically higher for DMARD-IR and TNFi-IR pts randomly assigned to TCZ 8 mg/kg than to TCZ 4 mg/kg. Of DMARD-IR pts, more in the TCZ 8 mg/kg (33%) than in the TCZ 4 mg/kg (25%) group who were ACR20 NR at wk 12 responded by wk 24. Similarly, of TNFi-IR pts, more in the TCZ 8 mg/kg (27%) than the TCZ 4 mg/kg (10%) group who were ACR20 NR at wk 12 responded by wk 24. High-level responses became more apparent after 24 wks of TCZ treatment for pts who had not achieved the respective level of responses at wk 12, with absolute response rates numerically higher for pts in the TCZ 8 mg/kg group than in the TCZ 4 mg/kg group.

Conclusion:
Substantial proportions of DMARD-IR and TNFi-IR pts who did not respond to 12 wks of treatment with TCZ and DMARDs achieved responses when treatment was continued for 24 wks. In the more difficult to treat TNFi-IR population, nearly 30% of pts not achieving ACR20 or LDAS after 12 wks of treatment with TCZ 8 mg/kg and DMARDs reached the respective responses by wk 24 with continued treatment. Clinicians should be aware that some pts will require more than 12 wks of TCZ treatment to achieve clinical benefit.
Open-Label Certolizumab Pegol Is Effective In Patients Who Withdrew From Double-Blind Treatment Due To Non-Response

Edward Keystone (Mount Sinai Hospital, Toronto); Désirée Van der Heijde (Leiden University Medical Center, Leiden); Joseph Smolen (University of Vienna, Vienna); Michael Weinblatt (Brigham & Women's Hospital, Boston); Tore Kvien (Diakonhjemmet Hospital, Oslo); Vibeke Strand (Stanford University, Palo Alto); Zainab Ansari (UCB, Slough); Niti Goel (UCB, Smyrna); Bernard Combe (Hôpital Lapeyronie, 34295 Montpellier)

Objective:
Double-blind treatment with certolizumab pegol (CZP) 200 mg or 400 mg Q2W + MTX significantly reduces RA signs and symptoms and inhibits radiographic progression compared with placebo (PBO) + MTX, as was demonstrated in the RAPID1 trial. The purpose of this study is to evaluate the efficacy of open-label (OL) CZP + MTX in patients who withdrew from double-blind treatment with either PBO or CZP.

Methods:
In the RAPID1 trial, patients who were ACR20 non-responders at Wks 12 and 14 were withdrawn from the trial at Wk 16 (as per protocol). This applied to 68.84%, 23.15%, and 18.97% of patients in the PBO, CZP 200 mg and CZP 400 mg arms, respectively. Of those, 95.0% (n=287) of patients reconsented and were enrolled in the OL study. Efficacy of CZP + MTX was assessed using ACR20/50/70 responder rates (using non-responder imputation based on enrollment in the OL portion of the trial), DAS28(ESR) and HAQ-DI (LOCF).

Results:
8% of PBO-treated patients and 16% of CZP-treated patients who withdrew at Wk 16 due to ACR20 non-response demonstrated transient ACR20 responses at Wk 8. PBO withdrawers and CZP 400 mg withdrawers switched to OL CZP rapidly achieved ACR20 responses which reached 63% and 54%, respectively; comparable to response rates in the double blind trial. Responses were sustained through Wk 100 or longer. ACR50 and 70 response rates, DAS28 and HAQ-DI scores saw similar trends for both the PBO and CZP withdrawers. Comparable benefits were observed in patients who received either CZP 200 mg or 400 mg for the first 16 weeks.

Conclusion:
Upon receiving OL CZP therapy, a subset of patients with ongoing active RA, who previously failed to respond to CZP or PBO in the double-blind phase, experienced rapid ACR20 responses. This data implies that response to CZP + MTX may be underestimated in a double-blind trial. The effect seen in this analysis may not be specific to CZP + MTX, but also might occur with other trial drugs. The data also supports an early switch to OL treatment in clinical trials. Patient and physician perceptions are influenced by the possibility of receiving placebo versus active treatment; these results may contribute to an understanding of how and why this happens.
A Faster Clinical Response to Certolizumab Pegol (CZP) Treatment is Associated With Better 52-Week Outcomes in Patients With Rheumatoid Arthritis (RA)

Edward Keystone (Mount Sinai Hospital, Toronto); Jeffrey Curtis (University of Alabama at Birmingham, Birmingham); Roy Fleischmann (University of Texas Southwestern Medical Center, Dallas); Philip Mease (Seattle Rheumatology Associates, Seattle); Dinesh Khanna (UCLA, Los Angeles); Joseph Smolen (University of Vienna, Vienna); G. Coteur (UCB Pharma, Brussels); Bernard Combe (Hôpital Lapeyronie, 34295 Montpellier)

Objective:
Certolizumab Pegol (CZP) is a PEGylated anti-TNF that has been shown to provide rapid improvements in the signs and symptoms of RA, physical function and relief of pain and fatigue when used in combination with methotrexate (MTX). The objective of our analysis was to determine if a faster response to CZP treatment was associated with better long-term outcomes in patients with active RA.

Methods:
In the RAPID1 clinical trial, patients treated with CZP 200 mg + MTX who had an ACR20 response or DAS28 change of ≥1.2 points from baseline (BL) at Wk 12 were divided into 2 subgroups depending on response at Wk 6: Wk 6 responders and WK 6 non-responders (responded at Wk 12). Using logistic regression, ACR20/50/70 response rates at Wk 52 were compared between responder subgroups; ANCOVA, adjusted for BL, was used to compare HAQ-DI, Pain-VAS and Fatigue Assessment Scale (FAS) at Wk 52.

Results:
The 2 subgroups in both analyses exhibited similar BL characteristics. The response to CZP treatment was rapid as the majority of Wk 52 responders achieved DAS28 or ACR20 responses by Wk 6. Wk 6 DAS28 and ACR20 responders had higher ACR20/50/70 response rates at Wk 52 than Wk 12 responders: Wk 6 DAS28 and ACR20 responders achieved 81.5/61.0/37.0 and 83.1/66.7/39.0 ACR20/50/70, respectively [P<0.001] vs Wk 12 responders. Wk 6 DAS28 responders also had a significantly greater improvement in Pain VAS than Wk 12 responders (-42.8 vs -34.3, respectively [P≤0.01]), but not in HAQ-DI or FAS at Wk 52. Wk 6 ACR20 responders also reported significantly greater improvements in Pain VAS vs Wk 12 responders (-44.8 vs -34.3 [P<0.001]), and HAQ-DI than Wk 12 responders (-0.87 vs -0.69, respectively [P≤0.05]) and but not FAS.

Conclusion:
A faster response to treatment is associated with better long-term outcomes at 52 wks in active RA patients treated with CZP + MTX. Rapid (Wk 6) responders had significantly higher ACR response rates and greater improvements in physical function and pain relief than later (Wk 12) responders. These observations underscore the importance of a rapid, 6-wk response in RA outcomes over 52 weeks. Furthermore, this is largely independent of whether ACR20 or DAS28 change ≥1.2 is used to assess response.
Long-term Efficacy of Tocilizumab in Rheumatoid Arthritis (RA) for up to 3.5 Years

J. Smolen (Medical University of Vienna, Vienna); Majed Khraishi (N/A, St-John's); Juan Gomez-reino (Universidad de Santiago de Compostela, Santiago de Compostela)

Objective:
Demonstrate efficacy of tocilizumab (TCZ) in RA patients (pts) for up to 3.5 years (y).

Methods:
Analysis includes all pts who received ≥1 dose of TCZ in the randomized controlled studies OPTION, AMBITION, RADIATE, and TOWARD, or in the long-term, open-label extensions of these studies (GROWTH95 and GROWTH96). Also included are all pts who received ≥1 dose of TCZ in LITHE, a 2-y controlled phase 3 study with 3-y follow-up. Pts were analyzed in 3 groups: inadequate responders to DMARDs (DMARD-IR), anti-TNF-IR pts, and monotherapy pts who never failed MTX (AMBITION). Outcomes, including ACR50/70, DAS28 remission rate (DAS28 ≤2.6), and low disease activity score (LDAS; DAS28 ≤3.2), were assessed every 12 wks from initial TCZ exposure to cutoff. Data are shown for a maximum of 180 wks, after which pt numbers were insufficient to draw conclusions. High clinical hurdles examined include proportions of pts with HAQ-DI=0, ≤1 SJC, and ≤1 TJC at 96 wks. Pts withdrawing from treatment were categorized as missing for all time points thereafter. Pts with insufficient data at a given time point were excluded from analysis for that time point.

Results:
Of the 3986 pts, approximately 4% discontinued due to insufficient therapeutic response and approximately 14% due to safety (including intercurrent illness) by cutoff. TCZ efficacy in DMARD-IR pts was demonstrated by increased numbers of pts achieving ACR50 and ACR70 up to wks 72 and 96, respectively, and maintenance of ACR70 for 24 consecutive wks, LDAS, and DAS28 remission up to wk 72. Thereafter, proportions increased further or were maintained with continued TCZ. The proportions of anti-TNF-IR and monotherapy pts achieving these end points increased or were maintained with continued TCZ. At 96 wks, proportions in the DMARD-IR, anti-TNF-IR, and monotherapy groups with HAQ=0 were 15%, 8%, and 23%, respectively; proportions with ≤1 SJC were 46%, 34%, and 55%, respectively; and proportions with ≤1 TJC were 37%, 23%, and 35%, respectively.

Conclusion:
TCZ efficacy was demonstrated with increasing numbers and/or proportions of pts achieving outcomes during long-term RA treatment. These data support TCZ as an effective, long-term treatment option in pts who are DMARD-IR or anti-TNF-IR, or who have not failed MTX.
The Electronic Version of the Psoriatic Arthritis Screening Questionnaire (EPASQ) Is An Effective Tool in Detecting Patients with Psoriatic Arthritis

Majed Khraishi (Nexus Clinical Research, St. John's); Jonathan Mong (Memorial University Of Newfoundland, St. John's)

Objective:
to examine the sensitivity and specificity of an electronic version of the PASQ and validate it against the original paper version.

Methods:
The electronic version of the PASQ (EPASQ) was developed using Adobe Creative Suite 4 software, and was based on the previous paper version of the PASQ. The EPASQ was programmed to provide a maximum of 15 points. The PASQ contained 10 differently weighted questions as well as a diagram where patients marked where they had or have had pain and or swelling. The same questions were included in the EPASQ in addition to a diagram with 68 joints plus the spine. The diagram and the questionnaire can be electronically marked and automatically scored. Validation was conducted using the questionnaires from 42 patients with confirmed PsA (mean disease duration 12 months). Questionnaires from 12 psoriasis patients without PsA were used as a control. Comparison of scores obtained from the manual and the electronic versions were conducted. A receiver operating curve (ROC) was determined for both the paper version as well as the electronic version.

Results:
The original PASQ, data was collected from 87 patients (58 with established PsA meeting the CASPAR criteria and 29 with psoriasis and no arthritis). Analysis of the PASQ score [AUC = 0.913, 95% C.I.: (0.833, 0.963), p = 0.0001] yielded an optimal cut-off score of 9, with 86.27% sensitivity and 88.89% specificity. A score of 8 would yield a sensitivity of 91.16% and a specificity of 77.78%. The EPASQ data was collected from a prospective cohort of 42 patients with early PsA, and from 12 psoriasis patients without PsA. All but two of the PsA patients scored 8 or more in the paper PASQ. Concordance of the paper and electronic scores was very high with only one patient who scored 7 in the paper PASQ and 11 in the EPASQ. The ROC Curve of the entire group yielded an optimal 97.62% sensitivity and 75.00% specificity for a cut-off score of 7.

Conclusion:
The electronic version of the PASQ is a simple self-administered and scored program with a high sensitivity and specificity. It can be an effective tool to screen for early and established
The Psoriatic Arthritis Screening Questionnaire (PASQ) Continues to Identify Psoriatic Arthritis (PsA) Patients With Change in Disease Activity

Majed Khraishi (Nexus Clinical Research, St. John's)

Objective:
Early detection and management of PsA may prevent serious joint damage and serious co-morbidities. We set to examine the reliability of the PASQ in detecting PsA over time and whether a change of score corresponds to disease activity

Methods:
Data collected from an early PsA cohort at baseline and 6 months. Patients scored the PASQ at screening and at 6 months interval as part of their assessments. The PASQ was developed to provide a maximum score of 15. It contained 10 differently weighted questions as well as a diagram where patients marked where they had or have had pain and or swelling (maximum score 5). Epidemiological, clinical and laboratory parameters were recorded in addition to the score of the PASQ at each visit. correlation of the score to disease activity and disability measures (such as DAS28, HAQ) was conducted utilizing SPSS 16

Results:
Fifty three patients with mean age (SD) of 48.1 (10.8) years were enrolled in the study. 62% were females. Nearly 65% of the patients had polyarticular involvement. Average duration of symptoms of PsA was 12.2 (9.2) months. At the time of this report, twenty eight patients had a repeat 6 months visit. The original PASQ data was collected from 87 patients and yielded an optimal score of 9, with 86.27% sensitivity and 88.89% specificity. In the early patients the optimal cutoff point was 7 with a sensitivity and specificity of 82% and 75% respectively. Patients mean total PASQ scores at baseline and 6 months were 10.7 (2.1) and 10.6 (2.1). 7 patients showed significant reduction in PASQ score: 12(2.2) vs. 9.3(1.9) (0&6 months respectively). All except one, scored higher than 7. These patients had higher baseline ESR (26.2 ±17 mm/hr) and CRP (11.5 ±6.4 mg/L) values compared to the rest of the cohort. Correlation with DAS 28 change and PASQ score was not detected however, The PASQ score at Baseline correlated significantly with age (p=0.034)

Conclusion:
The PASQ is a sensitive tool in detecting PsA even in patients with short disease duration (12 months). The test is consistent overtime and a change in disease activity did not reduce its ability to detect PsA. This is important especially in population based studies as many patients with PsA experience intermittent improvement of their symptoms
Proof of Concept Study: Is Body Mass Index a Useful Diagnostic Clue for Systemic Sclerosis

Roni Kraut (University of Alberta, Edmonton); Niall Jones (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

Objective:
To determine if Body Mass Index (BMI) may be a simple and useful clue for the diagnosis of Systemic Sclerosis (SSc), as multiple sites of organ involvement in these patients may predispose to lower BMIs compared to a healthy population.

Methods:
The Edmonton Scleroderma Registry maintains a longitudinal database on all referred patients with scleroderma in Northern Alberta. Examining only female patients to maintain homogeneity, we calculated and compared the BMIs of this cohort at their first registry visit to BMIs of Alberta women as last published by Statistics Canada in 2004. We sought to compare the percentage of patients in the following groups: BMI < 25 (normal), 25-30 (overweight), and >30 (obese).

Results:
Between 2005 & 2008, 47 females were registered. Median disease duration was 14 years. The average BMI was 24.09 kg/m², compared to a Canadian national average of 26.7 kg/m². In the registry, 66% of patients had a normal BMI, including 11 patients with a BMI < 20, 23% were overweight and 11% were obese. For the larger female Alberta cohort (N=1.164 million), only 47% had a normal BMI, with 30% overweight and 23% obese. Using Chi-Square Analysis, the difference between these groups was significant (p value = 0.0265). Further analysis showed a BMI of 30 may be a sensitive (89%) marker to rule out SSc (p=0.05), but not specific (23%).

Conclusion:
Further study for the utility of body mass index in the diagnosis of SSc is warranted. Future directions may include a prospective study, examining larger retrospective databases, and/or examining its use in patients with earlier disease.
Pancreatitis of the Joints: A Case of Pancreatitis, Panniculitis and Polyarthritis

Alison Kydd (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton); Carol Johnston (University of Alberta, Edmonton); Audric Moses (University of Alberta, Edmonton); Suki Dhillon (University of Alberta, Edmonton); Steven Katz (University of Alberta, Edmonton)

Case Report:
Objective: Pancreatitis, Panniculitis with Polyarthritis is an uncommon presentation of inflammatory arthritis. We present a case, demonstrate the radiological and synovial fluid findings. Case: A healthy 72 year old male presented with a 10 day history of painful swelling of the hands and feet requiring admission. The patient denied constitutional symptoms and had no abdominal pain. A peripheral hospital started prednisone and treated him for possible alcohol withdrawal. Vitals signs, neurologic and chest exams were normal. Abdominal exam revealed no tenderness, nor hepatosplenomegaly. Initial musculoskeletal exam revealed synovitis of the hands and feet. The patient had numerous raised 1-4cm in diameter erythematous fluctuant lesions over the distal extremities. Bloodwork showed hemoglobin of 109g/L and a leukocytosis of 54.2x10⁹/L. Alkaline phosphatase and lactate dehydrogenase were elevated at 154 IU/L and 397 IU/L. ESR was 74 mm/h and CRP was 262 mg/L. Immunologic studies were negative except for a weakly positive pANCA. Blood cultures showed an enterococcal bacteremia for which the patient was treated. Skin biopsy found diffuse dermal neutrophilic infiltrate and fat necrosis. Lipase and amylase were eventually tested and were elevated at 11,016 units/L and 2284 IU/L respectively. Synovial fluid analysis demonstrated a milky yellow fluid with a cell count of 60,000x10⁶/L, negative and positive birefringent crystals, negative culture, and positive for cholesterol. Detailed lipid analysis with gas chromatography showed high levels of lipid compared to a control; protein determination using mass spectroscopy showed elevated acute phase proteins. Despite biochemical resolution of his pancreatitis and glucocorticoids, the patient's arthritis worsened; serial X-rays showed the development of multiple osteolytic bone lesions about involved joints. Pamidronate was infused monthly without benefit. The patient was diagnosed with pancreatitis, panniculitis, with polyarthritis based on this presentation. Discussion: Although panniculitis occurs in approximately 2-3% of patients with pancreatitis, rarely these patients develop a destructive polyarthritis with extensive intraosseous fat necrosis leading to bone and joint destruction. No treatment including steroids has been beneficial for the arthritis except early intervention for the pancreatitis when possible. Detailed synovial analysis has not been previously well described prior to this patient. Conclusion: This is a rare presentation of a destructive arthritis, and pancreatitis should be considered in the differential diagnosis in patients presenting with unusual polyarthritis. Synovial fluid lipid analysis may be helpful in the diagnosis.
Objective:
Currently, there is limited research on the perspectives of LTC staff on attitudes, practices and beliefs regarding osteoporosis awareness, management and fracture prevention. The goal of this study is to determine how well nurses at LTC facilities are educated to properly administer bisphosphonates. A secondary question assessed was the nurse`s attitudes and beliefs regarding the role and benefits of vitamin D for LTC patients.

Methods:
Eight LTC facilities in Hamilton, Ontario were surveyed, and all front line staff who worked day shifts was offered a survey. A total 57 registered nurses were surveyed. A 21 item questionnaire was developed to assess existing management practices and specific osteoporosis knowledge areas.

Results:
The questionnaire assessed the nursing staff`s education to properly administer bisphosphonates by having them select all applicable responses from a list of options. These options included administering the drug before meals, after meals, with meals, given with other medications, separated from other medications, given with juice, with or without water, given with the patient sitting up, or while lying down. Only 52% of the nurses administered the drug properly, where they selected the options: (given before meals, with water, separated from all other medications, and in an upright position). If at least one incorrect option was selected, it was considered inappropriately administered. For nurses who administered bisphosphonates inappropriately, 10.4% gave bisphosphonates with other medications, 6.2% gave it after or with meals, and 2.1% each gave bisphosphonates while the resident was lying down, with juice, or without water. In assessing the attitudes regarding vitamin D, the questions were scored on a 7 point scale (1point=strongly disagrees, 7=strongly agrees). Of the 57 nurses surveyed, 68% strongly felt their patients should be prescribed vitamin D supplements. Specifically, 96.5% believed vitamin D improves calcium absorption, 40% believed it reduces falls, 42% believed it improved balance, and 68% believed it reduced fracture rates.

Conclusion:
Osteoporosis has a significant impact on morbidity and mortality, especially in the LTC setting. Although bisphosphonates are quite effective in reducing fracture rates and improving BMD values, it is only effective if properly administered. Alarmingly, only 52% of the nurses surveyed were administering the drug properly. In addition, only 68% of nurses felt their patients would benefit from vitamin D supplementation, and many were unaware of its benefits. In summary, although the education of health providers has improved since the mid-1990’s, this area still requires further attention and the subject of future quality-assurance research.
Incidence and Predictors of Hospitalization of Patients with Systemic Lupus Erythematosus

June Lee (University of Western Ontario, London); Janet Pope (University of Western Ontario, London); Christine Peschken (University of Manitoba, Winnipeg)

Objective:
Hospitalization has an impact on patient morbidity and plays a role in health care burden. Annual rates of hospitalization for lupus in some cohorts are as high as 30 to 40%. There have not been many recent studies looking at hospitalization of patients with SLE in Canada. The aim of this study was to look at the incidence of hospitalization of patients with systemic lupus erythematosus (SLE), the causes of hospitalization, and to determine any predictors of hospitalization.

Methods:
Data were collected as part of the 1000 Canadian Faces of Lupus, a prospective cohort study, where annual major lupus flares including hospitalizations for flares were recorded.

Results:
Of 1802 enrolled patients whose data was available, 60 reported hospitalization related to their SLE (3.3%). The most common causes of SLE-related hospitalization were hematologic (18.1%), serositis (16.8%), musculoskeletal (13.3%), and renal (12.0%); some were hospitalized for more than one of above reasons. The occurrence of hospitalization were significantly associated with being of Aboriginal descent (p<0.0005), having a higher co-morbidity burden as reflected in the Charlson Co-morbidity Index (p=0.042), and having greater disease activity as indicated by the SLAM-2 (SLE activity measure) (p=0.005). There was no significant relationship between hospitalization and gender, age, level of education, or marital status.

Conclusion:
The rate of hospitalization of patients with SLE was lower than expected, however this may indicate that the care of lupus is improving, that the cohort is biased towards healthy patients (however, 25% have had a MI or stroke) or that flares are more likely to be handled as an outpatient. Some hospitalizations may have been under ascertained (recall bias). The causes of hospitalization were varied and different than what other studies have shown (less for infection). Not surprisingly, several predictors of hospitalization are related to ethnicity and comorbidity and disease activity at their annual visit.
Development Of The 2009 Revised ACR Recommendations For The Management Of Osteoarthritis

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Objective:
To develop revised recommendations for the management of osteoarthritis of the hand, hip and knee.

Methods:
A list of pharmacological and non-pharmacological modalities commonly used to manage osteoarthritis (OA) of the knee, hip and hand as well as clinical scenarios were generated by a team of experts. A systematic review of the literature was undertaken to identify current scientific evidence concerning the benefits and harms for each modality. The search was conducted in MEDLINE (1950-2009), EMBASE (1980-2009) and The Cochrane Library (Issue 3, 2009). The quality of the evidence was appraised using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system and the evidence was summarized into the GRADE Summary of Findings table and Evidence profile. A panel of 16 clinical experts in primary care, rheumatology, orthopedics, rehabilitation and geriatrics was gathered to review the evidence and develop recommendations using the GRADE system.

Results:
Recommendations covered the use of 29 modalities. Modalities suggested for the management of hand OA were oral non-steroidal anti-inflammatory drugs (NSAIDs), tramadol, topical NSAIDs, capsaicin, trolamine salicylate, joint protection techniques, assistive devices, use of thermal agents and splints. Modalities recommended for the management of knee OA were land- and water-based exercises as well as weight loss for overweight patients. Other pharmacological and non-pharmacological modalities were also suggested for knee OA such as: acetaminophen, oral and topical NSAIDs, tramadol, intra-articular injections, medial wedge insoles for valgus knee OA, subtalar strapped lateral insoles for varus knee OA, medially-directed patellar taping, manual therapy, acupuncture, transcutaneous electrical nerve stimulation (TENS), walking aids, thermal agents and psychosocial interventions. Separate recommendations could not be made for hip OA because of limited scientific evidence.

Conclusion:
The 2009 revised American College of Rheumatology (ACR) recommendations for the management of OA were developed by a panel of experts using the GRADE method. Recommendations covered the use of 29 modalities, including both pharmacological and non-pharmacological modalities. Use of this method as well as clinical scenarios is an innovative strength of the present recommendations.
Transition From A Research-Based Anti-Sa ELISA To A Commercial Anti-Sa ELISA To Monitor Rheumatoid Arthritis Activity.

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Objective:
Anti-citrullinated peptide/protein antibodies (ACPA) are biomarkers for the diagnosis and prognosis of rheumatoid arthritis (RA). The prognostic value for disease persistence and severity was established with a research based anti-Sa ELISA and was shown five years ago to be better than that of anti-CCP2 and RF combined in early arthritis. Titer variations overtime are seen using the original in house anti-Sa ELISA but the assay was unstable and had to be performed soon after the plates were prepared. Can those results be reproduced with an assay destined for commercialization and if so, can the new assay be used for monitoring disease activity?

Methods:
We used two Euroimmun ACPA kits: the widely available anti-CCP2 ELISA and the prototypic commercial version of the anti-Sa ELISA. We compared them with the original “in house” anti-Sa ELISA on serial stored RA sera.

Results:
We used 69 serial sera: 50 were positive with the in house anti-Sa ELISA and their titers correlated with disease activity. The Euroimmmun anti-Sa kit showed 98.5% agreement with the original anti-Sa at the suggested cutoff level and a highly significant titer correlation (Spearman’s r = 0.9196, p < 0.0001). The Euroimmun anti-CCP2 kit showed 94.2% agreement with the in house ELISA at the suggested cutoff level. Titer correlations were impossible to calculate because 47.8% of the sera tested above the standard curve upper limit at the dilution suggested for anti-CCP2 clinical testing. Thus, when the three ELISAs are performed under usual clinical laboratory conditions, the first two show titer variations correlating with clinical activity over time. For monitoring purpose, Homemade =~ Euroimmun anti-Sa ELISA >> anti-CCP2 =~ 0.

Conclusion:
This pilot study shows that the transition from a “research” to a “commercial” anti-Sa ELISA was successful. It supports the view that the new anti-Sa ELISA being made available now to all clinicians and investigators can be compared to what has been published with the research based assay and will be useful for prognosis and disease monitoring purposes in real world conditions.
RA Diagnosis Clinic: An Experiment in Prioritizing Appointments for Suspected RA.

Cheryl Magnusson (Mary Pack Arthritis Program, Vancouver); David Collins (Gordon and Leslie Diamond Health Care Centre, Vancouver)

Objective:
Objective: To evaluate the wait time from GP referral to rheumatologist diagnosis after implementation of a rapid access RA diagnosis clinic (RAD).

Methods:
Methods: A clinic for rapid access to diagnosis and DMARDs for new onset inflammatory arthritis was developed and piloted in 2008. All Vancouver area rheumatologists are invited to refer suspected new RA patients who have been referred to their private practices (PP) and who have not yet been seen. Information which has been supplied by the referring GP is faxed to the clinic nurse. These referrals undergo nurse administered telephone screening to confirm 1) onset within one-year 2) symptoms and signs of inflammation and 3) no visit yet with a rheumatologist (ie waiting). Patients who pass the screen are seen by the clinic rheumatologist in the earliest clinic. The clinic rheumatologist does a full consultation, orders appropriate tests, makes a provisional diagnosis and prescribes DMARD as needed. Disease and medication education is provided by the clinic nurse. Those with probable or definite RA are booked to see the OT and PT. All patients, whether or not they pass the screen have consultation appointments booked with the PP rheumatologist who initially triaged the patient. A retrospective review of prospectively collected data was performed. From the patient record, wait times, diagnoses and DMARD prescription dates were extracted. The wait time was calculated using the date of the initial GP referral, and the dates of the RAD Clinic and PP rheumatologist attendances. Probable and definite RA were based on the rheumatologist diagnosis. If the patient was prescribed DMARD at the initial consultation visit, this was recorded as the DMARD start date.

Results:
Results for 2008-2009: Between October 1, 2008 and October 31, 2009, 32 clinics were held with mean 3 patients per clinic. Referrals came from 11 Vancouver area rheumatologists. There were 97 patients, 80 F and 17 M, who passed the screening and were seen in clinic. Fifty-nine were diagnosed with probable or definite RA. Fifty-six of 59 were started on DMARD at the clinic visit. The mean wait time was 31 days from GP referral to RAD clinic and 76.4 days from GP referral to PP rheumatologist.

Conclusion:
Conclusion: A RA diagnosis clinic provides early access to rheumatologist diagnosis, OT, PT and Nursing services, and reduces wait time for diagnosis and DMARD.
Objective:
To determine the validity of the generally held assumption that the lupus anticoagulant (LAC) is associated with adverse events late in pregnancy.

Methods:
We performed a Medline search for English-language articles involving human subjects between 1990 and 2009 with key terms including lupus anticoagulant, early and late fetal loss, pre-eclampsia, placental abruption, prematurity, intrauterine growth restriction (IUGR), HELLP and PPROM. Published studies were systematically reviewed and their quality assessed by evaluating the standardization of subjects, rigor of LAC testing, and clarity of defined outcomes.

Results:
Forty-three studies fulfilled criteria: 24 case-control, 12 cohort, 4 cross-sectional, 2 retrospective reviews and 1 meta-analysis. The studies varied substantially with respect to laboratory methodology, definition of early and late pregnancy loss, sample size (from 14 to 2195), and patient inclusion/exclusion criteria (with and without primary or secondary antiphospholipid syndrome). Thirty-five of 43 studies specifically referred to the LAC; 8 included LAC as part of a generalized antiphospholipid (aPL) assessment. Of the 25 LAC-specific studies that reported early and/or late pregnancy losses, 21 (84.0%) found an association with LAC. However, of those, only 3 specifically identified late losses: 2/3 found an association with LAC. LAC and IUGR were assessed in 11 studies: 1/11 found an association. Only 3 of 15 studies evaluating LAC and pre-eclampsia demonstrated a significant association. Two of 8 studies reviewing LAC and pre-term delivery found an association. No association between LAC with HELLP, PPROM, or placental abruption was found in any study.

Conclusion:
Despite its reputation as a risk factor for adverse events late in pregnancy, relatively few reports in the literature specifically report LAC prevalence among hundreds of studies on aPL and pregnancy outcome. Those that do, vary greatly with respect to study design, patient inclusion criteria, and definitions of early and late pregnancy loss. In contrast to current understanding, we found a fairly consistent association between LAC and early pregnancy loss, but were unable to confirm any consistent association between LAC and late pregnancy loss, pre-eclampsia, PPROM, placental abruption, or IUGR.
Case Report:
Objective: In view of the current decade’s dramatic increase in the incidence and severity of Clostridium difficile infections, it is an important pathogen to consider in the etiology of reactive arthritis. There have been 42 reported cases in the adult and pediatric literature since 1975. In this report, two more illustrative cases are presented, and the clinical and laboratory features of all the reported cases to date are reviewed.
Methods: Case reports of C. difficile associated reactive arthritis were collected using a PubMed search.
Results: In all reported cases, no other pathogen known to cause reactive arthritis was found and either the C. difficile culture or toxins, or both were positive in the stool. In adult cases, patients’ ages ranged from 20 to 72 years (mean 41 years), and the male to female ratio was 1:1. 61% (22/36 cases) were HLA-B27 positive. The mean time from the onset of diarrhea to onset of arthritis was 14 days (range -1 to 55 days), and the median duration of the arthritis was 42 days (range 7-730 days). The arthritis usually persisted even after the diarrhea had resolved. The pattern of joint involvement was usually oligoarticular or polyarticular with the majority being asymmetric and a significant proportion being migratory (6/38 cases). Most do not have eye involvement or urethritis. The average WBC in the synovial fluid was 22388/mm3, with a median PMN component of 80%. Conclusion: C. difficile appears now to be a well established cause of reactive arthritis and shares clinical characteristics with other reactive arthritides. However, the diagnosis may not be clear at the onset as there are reported cases in which no antibiotic has been given and those where the arthritis may have preceded the diarrhea. Effective antibiotics against C. difficile are the most important therapeutic intervention in this condition. The majority do well soon after the infection is treated.
Economic Modelling in Rheumatoid Arthritis in Real World Practice: The DAS has minimal impact on HRQOL data categorized by the HAQ score

Liam Martin (University of Calgary, Calgary); Anthony Russell (University of Alberta, Edmonton); Susan Barr (University of Calgary, Calgary); Sholter Dale (University of Alberta, Edmonton); Christopher Penney (University of Calgary, Calgary); Yan Charles (Institute of Health Economics, Edmonton); Walter Maksymowycz (University of Alberta, Edmonton)

Objective:
We aimed to assess the relationship between Health Related Quality of Life (HRQOL), the Health Assessment Questionnaire (HAQ), and the Disease Activity Score (DAS28) for use in economic modelling of HRQOL outcomes using data from real world practice.

Methods:
A Provincial prospective observational cohort study of consecutive RA patients starting anti-TNF therapy was started in 2004. The data is collected at baseline, 3 months, and every 6 months thereafter on patients receiving anti-TNF. Health-related quality of life is measured with the EQ-5D and single index scores were calculated using US value set for the EQ-5D. The clinical outcome measures were the HAQ and the DAS28 scores that were analyzed both as raw data and categorical data (HAQ using 0.5 unit intervals and DAS28 using cut points 3.2 and 5.1). We analyzed change in the mean EQ-5D index score in HAQ and DAS28 categories over time. We used regression model to analyze the impact of the HAQ and DAS28 scores on the EQ-5D index scores at baseline and 21 months. An intention-to-treat analysis was conducted during follow-up period.

Results:
778 patients started on anti-TNF with mean age 54.4 (SD 14.6) years, 69.8% of them being females. Twenty one month outcome data was available from 563 patients. At baseline the EQ-5D index score in the anti-TNF group was 0.483 and improved 0.281 units (p< 0.001; t-test) during follow up. The mean HAQ and DAS28 scores were 1.66, SD 0.63 and 5.91, SD 1.42, respectively, at the baseline and 0.80, SD 0.70 and 3.16, SD 1.49, at follow up, respectively. The results show that the EQ-5D index was consistently higher the better the HAQ index category the patient was in except for category 0 at baseline. After baseline the EQ-5D index decreased by increasing DAS28 categories. In the regression model the HAQ explained most of variance in the EQ-5D index scores while the DAS28 had little impact on the HRQOL, especially at the 21 months follow-up.

Conclusion:
Economic modeling to the anti-TNF medication is often based on DAS scores. Our study shows a significant change in the distribution of the EQ-5D values in different HAQ categories over time. This has to be addressed in the Quality Adjusted Life Year model at baseline and after starting anti-TNF therapy. After baseline, the DAS28 has minimal additional impact on HRQOL data categorized by the HAQ score and is therefore much less relevant for economic modelling than the HAQ.
The Sensitivity and Specificity of the GALS (Gait, Arms, Legs, Spine) Examination when used by Physiotherapists to Detect Rheumatoid Arthritis

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Objective:
To evaluate the sensitivity and specificity of the GALS examination for detecting rheumatoid arthritis (RA) when used by physiotherapists working in direct access settings and physiotherapy students.

Methods:
Participating healthcare professionals (HCP), including 2 rheumatologists, 2 physiotherapists (PT) and 2 physiotherapy students (PTS), were trained to perform the GALS exam and record their findings by viewing an instructional DVD and attending a hands-on training workshop. Three weeks following training, HCP performed the GALS on 48 study participants. Twenty-five participants were recruited through a local rheumatology practice and had previously been diagnosed with RA; Twenty-three participants without diagnoses of arthritis were recruited from a primary care family health centre. Each participant was assessed by a rheumatologist, PT and PTS using the GALS musculoskeletal screening exam. HCP recorded any gait abnormalities and abnormalities of the movement or appearance of the arms, legs and spine. If an abnormality was observed, HCP recorded the location and description of the abnormality (i.e. left hand, Heberden’s nodes) and whether a diagnosis of Inflammatory Arthritis or RA was suspected. HCP were told that the primary objective of the study was to investigate their level of agreement regarding findings on the GALS exam and were unaware that half of the study population had previously been diagnosed with RA. HCP were blinded to the medical history of the participants. Sensitivity and specificity were calculated to determine the ability of the GALS to detect RA when performed by PT and PTS.

Results:
Compared to the recruitment source (RA versus no arthritis), sensitivity and specificity varied from 50 to 77% and 75 to 100%, respectively. When compared to the findings of the rheumatologists’ GALS examination findings on the study day, sensitivity and specificity varied from 67 to 86% and 71 to 92%, respectively.

Conclusion:
These results suggest that the GALS exam may be a useful tool for PT to use to rule out the diagnosis of inflammatory arthritis in a direct access setting. Differences in level and type of clinical experience may contribute to the variation in sensitivity observed. Lower sensitivity in relation to the actual diagnosis likely reflects the clinical status of participants with RA whose disease was controlled with medication. The merits of introducing the GALS exam into primary care physiotherapy and physiotherapy curricula should be explored.
An Assessment of the Quality and Accuracy of the Referral Information Received at an Early Inflammatory Arthritis Clinic (EIA Clinic)

Lindsay Mcmillan (University of British Columbia, Calgary); Gary Morris (University of Calgary, Calgary); Christopher Penney (University of Calgary, Calgary); Liam Martin (University of Calgary, Calgary)

Objective:
To assess the quality and accuracy of the referral information on patients referred to an Early Inflammatory Arthritis Clinic (EIA Clinic)

Methods:
Referral data on patients who met inclusion criteria for the EIA Clinic at the Foothills Medical Centre between 4/2006 and 6/2009 were assessed. This information was obtained from the Referral Outcomes Data Worksheet and the patients’ charts. The worksheet is completed by the triage nurse based on the data received on the referral form. The rheumatologist receives the worksheet and all the referral information on each patient. The assessment compared the patients’ working diagnosis at referral with that of the rheumatologists; the quality of the history and reason for referral; completeness of laboratory/supporting data; triage (prioritization) category; and medication prior to clinic visit. The quality of history and reason for referral were evaluated as high, medium or low depending on completeness. The quality of laboratory/supporting data was reported as high, medium or low depending on the number of tests that were requested by the triage nurse. The appropriateness of the triage/prioritization category was determined based on the rheumatologist’s diagnosis. Medications used prior to the visit were recorded.

Results:
Two hundred and three patients were reviewed. The rheumatologist agreed with the referring diagnosis in 162 (79.8%) patients. Of the 121 patients referred with an inflammatory arthritis referral diagnosis, the rheumatologist agreed with the diagnosis in 100 (82.6%) patients. Of these patients 62 patients had rheumatoid arthritis. The quality of history and reason for referral was high in 139 (68.5%), medium in 57 (28.1%) and low in 7 (3.4%). The completeness laboratory/supporting data was high in 115 (56.7%), medium in 63 (31.0%), and low in 25 (12.3%). There were 175 referrals (87.1%) assessed as being appropriately triaged. Corticosteroid therapy was prescribed in 36 (18%) patients by the referring physician.

Conclusion:
These data show that the majority of patients are referred and triaged appropriately. There is high degree of agreement in regarding the diagnosis between the referring physicians and the rheumatologists. The quality of history and reason for referral is also high or medium. The quality of the laboratory/supporting data could be improved but was at a high or medium level in the majority. The one concern is that certain patients are prescribed corticosteroids prior to their assessment which can lead to a delay in making a diagnosis.
The Link between Rheumatoid Arthritis and Cigarette Smoke

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Objective:
Epidemiological studies in Rheumatoid Arthritis (RA) suggest a salient role of non-genetic factors in RA development most notably exposure to cigarette smoke (CS). In this study of three mouse strains that vary in their susceptibility to CS induced lung disease, we sought to investigate the effect of CS exposure on circulating levels of different RA biomarkers and to determine if a link exists between biomarker concentration and genetic susceptibility to Chronic Obstructive Pulmonary Disease (COPD).

Methods:
Sera from male AKR/J, A/J, and C57BL6 mice were exposed to either a room air control or CS from two unfiltered research cigarettes per day, for 5 days a week. This prescriptive regime was administered for different periods of time ranging from less than one month to 12 months in order to emulate both acute and chronic CS exposure. ELISA assays were established and then used to measure biomarkers in the serum. Such biomarkers include Rheumatoid Factor (subtypes IgM, IgA), Extracellular Heat Shock Protein 70 (eHsp70), and Autoantibodies to Hsp70 (subtypes IgM, IgA, IgG1, IgG2a).

Results:
We report that CS was associated with an induction of autoantibodies to the Fc portion of IgG also known as Rheumatoid Factor (RF). Our results suggest that RF is a potential biomarker for the development of COPD in mice with the strength of the induction corresponding well to susceptibility to COPD. Measurement of the level of circulating eHsp70, another prospective RA biomarker, revealed a dependence on age. Levels of eHsp70 dropped with increasing age in strains susceptible to COPD but rose with age in resistant strains. Most importantly, for the very first time we report that chronic CS can be associated with a break in tolerance and induction of IgG1 autoantibodies to Hsp70 but only in mice most susceptible to lung disease. This suggests that autoantibodies to Hsp70 could be a suitable potential biomarker and may contribute in part to the loss of eHsp70 noted in these mice with age.

Conclusion:
These studies suggest that in genetically susceptible strains of mice, CS induces eHsp70 leading to a break in tolerance to Hsp70 resulting in production of autoantibodies to Hsp70. These components in the form of an immune complex have the potential to activate RF producing B cells leading to the production of RF that could migrate to the joints and contribute to pathology and RA.
Association of Smoking and Rheumatoid Arthritis in First Nations

Gabriela Montes aldana (University of Manitoba, Winnipeg); Irene Smolik (University of Manitoba, RR149-800 Sherbrook St.); Hani El-gabalawy (University of Manitoba, Winnipeg)

Objective:
Smoking has been associated with rheumatoid arthritis (RA) in multiple populations. In particular there is a link between smoking and the RA autoantibodies rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). This data analysis explores that potential association between smoking and the presence of RA, RF, and ACPA in a First Nations (FN) population of RA probands (RA-pro) and first-degree relatives (FDR).

Methods:
RA-pro and FDR were recruited at the Arthritis Centre, University of Manitoba, and at rheumatology clinics held in northern FN communities. Participants were asked to fill out questionnaires, which included socio-demographic data, detailed smoking history, and health profile questions. RF and ACPA were detected by nephelometry and ELISA, respectively. Statistical analysis of the demographic, smoking, and autoantibody variables was conducted with SPSS version 16.0.

Results:
In total, RA-pro n=171, and FDR n=279 were included. Smoking rates were 87% in RA-pro and 83% in FDR (p=NS). Forty-one percent of FDR were RF positive, and 80% of those were smokers. Twenty-three percent of FDR were ACPA positive, and 88% of those were smokers. While only 4% of FDR were strongly positive (>40 IU) for both RF and ACPA, 91% of those individuals were also smokers. Univariate analysis suggested a trend towards association between years smoked and both RF and ACPA. ACPA positive FDR were significantly older than ACPA negative FDR (39 vs. 34 y/o, p=0.01). A logistic regression analysis model for the presence of RA autoantibodies, which included the input variables age, sex and years smoked, indicated that associations between RF, ACPA and the number of years smoked were reflective of the association of autoantibodies with age. Similarly, a significant difference observed between RA-pro and FDR in terms of years smoked could be accounted for on the basis of age alone.

Conclusion:
This First Nations population reported extremely high smoking rates exceeding 80%, irrespective of age and gender. These rates precluded a clear demonstration of the effects of smoking on either the development of RA autoantibodies or of RA itself. These observations do not preclude the presence of a biological association between RF, ACPA and smoking, particularly since the entire population is enriched for the disease predisposing HLA-DRB1 alleles which have been shown to interact with smoking in other populations. Our findings indicate that ACPA are more likely to be present in older FDR, who in turn have been smoking longer.
Wait time for Assessment in Early Inflammatory Arthritis Clinic

Dianne Mosher (University of Calgary, Calgary); Susan Barr (University of Calgary, Calgary); Nicole Fahlman (University of Calgary, Calgary); Avril Fitzgerald (University of Calgary, Calgary); Sharon Leclercq (University of Calgary, Calgary); Theresa Lupton (University of Calgary, Calgary); Gary Morris (University of Calgary, Calgary); Liam Martin (University of Calgary, Calgary); Christopher Penney (University of Calgary, Calgary)

Objective:
To assess the length of time from referral to clinic date in patients with early inflammatory joint disease using our central triage database in the Division of Rheumatology, University of Calgary.

Methods:
All referrals from 2006 to October 2009 to the Early Inflammatory Arthritis clinic were recorded in the central triage database. They were evaluated for length of time from referral to the receipt of adequate information to allow appropriate triage and also from referral to date seen. In addition we looked at the final diagnosis by the rheumatologist for the proportion of undifferentiated inflammatory arthritis, rheumatoid arthritis and other.

Results:
A total of 541 patients were seen at the Foothills hospital and Rockyview Hospital sites. 352 of these referrals had a diagnosis recorded in the database after being seen. 139 (39.5%) had rheumatoid arthritis, 58 (16.5%) had an undifferentiated inflammatory arthritis and 155 (44%) had other including crystalopathies, systemic lupus erythematosus, other connective tissue diseases, osteoarthritis, ankylosing spondylitis, psoriatic arthritis and fibromyalgia. The average wait for completion of information to allow triage was 7 days with a median of 0 days. The average wait to be seen in clinic was 25 days with a median of 20 days.

Conclusion:
The triage process and the establishment of an early inflammatory arthritis clinic at the University of Calgary has allowed for early access of patients with rheumatoid arthritis, undifferentiated inflammatory arthritis and other. This is within the four weeks recommended in the 2005 Standards for Arthritis Prevention and Care document of the Alliance for Canadian Arthritis Program.
Regional Variation of the Profile of Rheumatoid Arthritis Patients Treated with Infliximab in Canada – RemiTRAC Rheumatology

John Kelsall (Mary Pack Arthritis Center and St Paul's Hospital, Vancouver); Heidi Imhoff (Schering-Plough Canada Inc., Kirkland); John Sampalis (McGill University and University of Montreal, Westmount)

Objective:
The efficacy of Infliximab (IFX) in the management of Rheumatoid Arthritis (RA) is well established. The aim of the current analysis is to describe regional differences in the patient baseline characteristics and treatment effects in Canadian RA patients treated with IFX.

Methods:
RemiTRAC is an ongoing Canadian prospective observational study of patients treated with IFX that was initiated in 2002. Patients who were biologic naïve or had initiated treatment with a biologic within six months are enrolled in the cohort and are followed prospectively as per routine care. Baseline characteristics and treatment outcomes were compared for RA patients treated with IFX in the Maritimes and Quebec (QC+M), Ontario (ON) and the Western provinces (West).

Results:
A total of 663 RA patients were enrolled between 2002 and December 31, 2008 of which 161 were from QC+M, 307 from ON and 195 from West. Patient baseline characteristics differed between regions with patients from ON having a higher mean ESR and patients from West having a higher mean disease duration and longer morning stiffness compared to patients from the other regions. Patients from the West were treated with significantly more DMARDs before initiation of IFX treatment. Compared to the other provinces, more patients were treated with Leflunomide in Ontario while gold compounds were used more frequently in the West. Across all regions the vast majority of patients starting IFX had a high disease activity (DAS28>5.1). DAS28 and HAQ values after 6 and 12 months of treatment were lowest in QC+M and highest in ON. Regression analysis over time showed a significant improvement for all parameters observed (CRP, ESR, AM stiffness, HAQ, pain, patient and physician global assessment, tender and swollen joint count and DAS28 using CRP or ESR) for all regions with a higher decrease in CRP in ON when compared to QC+M.

Conclusion:
In the RemiTRAC study, patient profiles in Canada differed with patients from West having the longest disease duration and were treated with more DMARDs before initiation of IFX. All patients showed a significant response to IFX treatment with patients from QC+M reaching lowest DAS and HAQ values.
Factors Impacting Adherence to Therapy in Canadian Patients With Rheumatoid Arthritis: A Multicenter, Clinic-Based Cohort Study

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Objective:
To assess patient self-reported adherence to rheumatoid arthritis (RA) therapies in a real-world clinical setting using clinical, demographic, and functional covariates.

Methods:
Through PROGRESS, an adalimumab patient support program in Canada, patients with RA receiving adalimumab (N=250) completed a questionnaire on demographics, RA disease characteristics and status, current and past management of RA, medication adherence, and patient–physician interaction.

Results:
A total of 167 women and 83 men provided data. Mean age was 56.2 years, duration of RA was 13.2 years, Health Assessment Questionnaire (HAQ) score was 0.75, and duration of adalimumab therapy was 2.1 years. Most patients reported taking their medications as prescribed (90% for adalimumab and 84% for all RA medications). An association between presence of morning stiffness and increased RA medication adherence ($r=0.16$, $p<0.05$) was the only significant correlation between RA signs and symptoms and medication adherence. Approximately 90% of patients believed that RA medications would not work optimally unless always taken as prescribed; those with stronger beliefs had better RA medication adherence ($r=0.28$, $p<0.01$) and better adalimumab adherence ($r=0.17$, $p<0.05$). Greater adherence was associated with those who found adalimumab ($r=–22$, $p<0.01$) or all RA medications ($r=–0.20$, $p<0.01$) less difficult/complex to take. Approximately 92% of patients felt that being involved in their treatment decision would cause them to administer their medications as prescribed. Medication administration every other week rather than weekly was preferred for 87% of patients and 90% claimed that they preferred subcutaneous vs. intravenous administration. In PROGRESS, 91% were satisfied with the support they received, and patients more satisfied with it had better RA medication adherence ($r=0.14$, $p<0.05$). Having friends or family provide reminders led to greater adalimumab adherence ($r=0.17$, $p<0.01$) including adalimumab ($r=0.12$, $p<0.05$).

Conclusion:
These data highlight the important role of perceptions in terms of patient adherence to RA medications and may prove beneficial for educational interventions for RA patients and health care professionals.
Prevalence and Predictors of Vitamin D Insufficiency in Patients with Low Bone Mineral

Tripti Papneja (McMaster University, Edmonton); Ganesh Subramanian (McMaster University, Edmonton); Jonathan Adachi (McMaster University, Hamilton)

Objective:
Vitamin D insufficiency/deficiency is extremely common and may contribute to the development of osteoporosis. The objective of this study is to assess the prevalence and predictors of inadequate serum vitamin D levels in patients referred to specialty osteoporosis clinic for low bone mineral density in Hamilton, Canada.

Methods:
A retrospective chart review was performed in 89 patients with osteoporosis/osteopenia referred in 2006-2007. Three cut-offs of 25(OH)D levels were fixed: >75 nmol/L, 50-75 nmol/L (insufficiency) and < 50 nmol/L (deficiency).

Results:
The overall prevalence of vitamin D insufficiency was 36.0%, and vitamin D deficiency was 13.5%. Vitamin D levels were significantly higher in those taking vitamin D supplements compared to patients not taking vitamin D supplements (p = 0.0007). In addition, 32.3% of patients taking vitamin D supplements had vitamin D insufficiency and 6.5% had vitamin D deficiency. Logistic regression analysis showed that vitamin D status was significantly associated with age (p=0.004) and vitamin D supplementation (p=0.0001) and not with season or PTH levels. Vitamin D levels significantly increased with age (p=0.02). In addition, vitamin D supplementation also increased with age (p=0.02).

Conclusion:
This study indicates a high prevalence of vitamin D inadequacy in Canadian osteopenic/osteoporotic patients. Serum vitamin D levels correlate well with vitamin D supplementation. Supplementation is greater in older individuals and may reflect the educational efforts worldwide to prevent and treat osteoporosis in elderly populations. Even with supplementation, vitamin D deficiency/insufficiency occurs and suggests that ongoing laboratory monitoring may be required to optimize vitamin D dosing.
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*BMD Shows Osteoporosis in only 25% of Males with Known Fragility Fracture, Resulting in Significant Under-Treatment and Fracture Protection*

Viktoria Pavlova (McMaster, Ancaster); Juliana Tricta (McMaster, Hamilton); Maggie Larché (McMaster University, Hamilton); Karen Beattie (McMaster, Hamilton); George Ioannidis (St Joseph's healthcare, Hamilton); Jonathan Adachi (McMaster University, Hamilton); William Bensen (McMaster University, Hamilton)

**Objective:**
The primary objective of this study is to determine the proportion of males with a previous clinical fragility fracture recommended for treatment based on BMD alone, bone DESTINY and Osteoporosis Canada guidelines (OCG). Diagnosis of osteoporosis is generally perceived as a simple diagnosis and decision to treat driven primarily by BMD T-score. Fragility fracture is a major risk factor for a future fracture and should be trigger screening for diagnosis and consideration of therapy. Most studies of Osteoporosis have focused on postmenopausal women, however, older men are also at increased risk of fragility fractures. In the Ontario Fracture Program only 30% of people with fracture have a BMD in the osteoporotic range. Under-treatment of osteoporosis in men, particularly those who have sustained a fragility fracture, remains a significant problem.

**Methods:**
During the period of May 2006 to October 2009, 6,319 men over the age of 50 years underwent a DXA scan in the Hamilton area, Ontario. Men recommended for treatment included those with a BMD $\leq -2.5$, DESTINY fracture risk in the high or very high categories or a high fracture risk according to OCG. Bone DESTINY is a computerized fracture prediction tool that combines BMD, age, steroid use, propensity to fall, previous history of falls, fragility fracture and BMI $< 18.5$kg/m$^2$ while OCG included sex, BMD, age, history of fragility fracture and steroid use.

**Results:**
Of 6,319 males, 877 had a previous fragility fracture; 187 were 50-59 years old, 269 were 60-69 years old, 271 were 70-79 and 150 were $\geq 80$ years. The proportion of men in each age group who would be recommended for treatment by BMD alone, bone Destiny and OCG are shown in the Figure 1. To further improve sensitivity of the bone DESTINY fracture risk assessment tool, men in a moderate risk group identified by bone Destiny were also included as being recommended for treatment. These results support the notion that less than 30% of all men who had experienced a fragility fracture have a BMD in the osteoporotic range regardless of age.

**Conclusion:**
These results further underscore the limitations of BMD T-score alone in considering a male patient for osteoporosis treatment. Implementation of the Bone DESTINY fracture risk prediction tool appears to reduce the treatment gap such that a higher proportion of men with a fragility fracture are considered for treatment as compared to BMD alone or OCG.
Cardiovascular Disease Risk Profile in Patients with Systemic Lupus Erythematosus (SLE) without Past History of Cardiovascular Events

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Objective:
To determine the prevalence at baseline of the cardiovascular (CVD) risk factors in female subjects with SLE without past history of CVD in the Health Improvement and Prevention Program (HIPP).

Methods:
Our cohort consisted of 287 female, meeting at least 4 of the ACR classification criteria for SLE, without any past history of CVD. CVD risk profile including: family history, smoking, history of diabetes, menopausal status, systolic and diastolic blood pressure (SBP, DSP), body mass index (BMI), physical activity and serum levels of triglycerides (TG), total cholesterol (TC) and LDL and HDL-cholesterol, homocysteine and high sensitivity C-reactive protein (hsCRP) were documented for all patients. The use of lipid lowering and hypertensive medications was recorded. Hypertension was defined as SBP>130 and DBP>85. Patients with BMI>25 and >30 were considered overweight and morbidly obese, respectively. Serum TG>1.7mg/l; TC>5.5 mg/l; LDL>2.5; HDL< 0.9mg/l, homocysteine >13 and CRP>1 were considered abnormal and risk factors for CVD.

Results:
The mean (SD) age for the cohort was 43.6(13.1) years, SLE duration was 11.5(10.3) years, 38.6% (n=128) had family history of CVD, 23.2% (n=77) were smokers, 42.5% (n=141) had a sedentary lifestyle, 31% (n=103) were post-menopausal and 0.9% (n=3) had history of diabetes. The mean (SD) BMI was 25.8 (6.1), 34.5% were overweight and 18.1% were morbidly obese. The mean SBP and DSP were at 121.9mmHg (14.7) and 75.9 mmHg (11.1), respectively. 22.9% of the patients had abnormal SBP and 13% had abnormal DBP. The mean (SD) serum profile were as follows; triglycerides: 1.2(0.6) mg/dl, total cholesterol: 4.7(1.1) mmol/l, LDL-cholesterol: 2.6 (0.8) mmol/L, HDL-cholesterol:1.7 (0.6) mmol/L, TC/HDL ratio: 3.0(1.0), homocysteine: 10.1 (4.3)µmol/L and CRP: 3.2 (6.2) (mg/L). Abnormal serum levels were seen in 14.2 % for TG, 21.2% for TC, 50.8% for LDL, 2.7% for HDL, 16.7% for homocysteine and 62.7% for CRP. Thirty-one percent (n=104) were on antihypertensives and 6.6% (n=22) were on lipid lowering medications. The distribution of total CVD risk factors in the sample were as follows: 31% had only 1, 44% had between 2 - 4 and 25% had 5 or more.

Conclusion:
CVD risk factors are commonly seen in female patients with SLE. Given the high prevalence of CVD risk factors, immediate screening and interventions are needed for CVD risk reduction in this patient population.
Lupus In Asian Canadians: The 1000 Canadian Faces of Lupus Study

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Objective:
There are few reports of systemic lupus erythematosus (SLE) in North American Asians. We describe differences in disease expression, disease activity and damage between Asian (ASN) and Caucasian (CAU) SLE patients in a multicentre Canadian cohort.

Methods:
SLE patients were enrolled in a multi-centre cohort and followed annually. Sociodemographic factors, diagnostic criteria, disease activity, treatment, damage, and self-reported disease activity and health were collected. Patients reporting ASN or CAU ethnic origin were abstracted, results were compared between the two groups. Data from the last annual visit were analyzed, testing for differences in sociodemographic and clinical factors and patient reported measures between the two ethnic groups in univariate analyses; significant variables from univariate analyses were included in multivariate regression models.

Results:
1388 patients were studied, including 1113 CAU and 275 ASN. 330 patients reporting other ethnic backgrounds were excluded. Disease onset was younger (ASN= 22±12 yrs, CAU 33±15 yrs; p< 0.001) and disease duration (ASN= 9±8 yrs, CAU 14±11 yrs; p< 0.001) and age (ASN= 32±15 yrs, CAU 47±16 yrs; p< 0.001) were lower in ASN compared to CAU. Income was similar, but high school completion was higher in ASN (ASN 92%, CAU 84%; p=0.001). SLEDAI scores and number of ACR criteria met were similar. ASN had more frequent renal criteria (ASN 60%, CAU 34%; p< 0.001), less frequent arthritis criteria (ASN 64%, CAU 80%; p< 0.001). ASN were more frequently treated with prednisone (ASN 80%, CAU 64%; p< 0.001), cyclophosphamide (ASN 18%, CAU 12%; p=0.007) and mycophenolate (ASN 22%, CAU 10%; p< 0.001). Mean damage scores were higher in CAU; this difference disappeared after controlling for age and disease duration. SLAM scores were higher in CAU (ASN= 5.0±4.2, CAU 6.5±4.7; p< 0.001). Self-reported flares, fatigue, disease activity and symptom scores (SLAQ) were lower in ASN. SF-36 physical (PCS) and mental (MCS) component scores were higher in ASN. In multivariate analyses, Asian ethnicity remained a significant predictor of better PCS ($\beta$=3.3, 95% CI 0.5,6.1; p=0.02) and MCS ($\beta$=2.9, 95% CI 0.3,5.5;p=0.03) and lower SLAQ ($\beta$=-5.0, 95% CI -6,1.0; p=0.01) when age, disease duration, damage, immunosuppressives, ACR criteria met, education, and SLEDAI were included.

Conclusion:
Although lupus was at least as severe in ASN Canadians, (younger onset age, more renal involvement, and more exposure to immunosuppressives), ASN patients reported fewer disease flares, lower levels of disease activity and fatigue, and better PCS and MCS compared to CAU. Cultural attitudes may influence patient perceptions of disease activity and overall health.
Prognostic Value of Patient History, Radiography and Serology on Poor Outcomes in Undifferentiated Inflammatory Arthritis Patients

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Objective:
To determine the clinical outcome of undifferentiated inflammatory arthritis (UIA) patients enrolled in 2 Canadian early arthritis cohorts and the prognostic value of patient history, physical exam, serology, and radiography for poor patient outcomes.

Methods:
Data from patients (n=642) enrolled since Sept. 2003 were collected from the Toronto/Canadian Early Arthritis Cohorts (TEACH/CATCH). CATCH is a multi-centre observational prospective “real world” cohort of patients with early inflammatory arthritis (EIA). Inclusion criteria: age >16, symptom duration of 6-52 weeks of persistent synovitis, ≥2 effused joints or 1 swollen MCP/PIP + ≥1 of: + RF, + anti-CCP, AM stiffness >45 minutes, response to NSAIDs, or painful MTP squeeze test. UIA was defined as not meeting 1987 ACR classification criteria for rheumatoid arthritis (RA) or criteria for other rheumatological diagnoses. The proportion of patients developing a classifiable diagnosis over time (survival analysis) and hazard ratios (HR) for the prognostic value of baseline age, gender, smoking status, initial use of DMARDs, RF status, 2nd-5th MTP involvement (including erosions), in the progression of UIA to RA were calculated. The feet were evaluated in this study due to their under-representation in the current ACR criteria for RA diagnosis.

Results:
At baseline, 24.5% of patients in the cohort were UIA (n=138) with the following baseline characteristics: age 51.9±15.4 years, 74% female, symptom duration 6.1±3.7 months, and DAS28 of 2.8±2.0. Of those who were UIA at baseline, 64.1% remained UIA at 12 months, with the remainder developing RA and other rheumatological conditions. HRs for MTP tenderness and foot erosions in the progression of UIA to RA were 1.111 (CI 1.001-1.233) and 4.428 (CI 1.231-15.930), respectively.

Conclusion:
Early presence of MTP tenderness and erosions predicted which patients will develop RA. Thus, a thorough foot exam should be performed on UIA patients to predict prognosis and guide therapeutic treatment.
Longitudinal Measures in Cross-Over Trial Show Consistency in Improvement Across Outcomes Following an Interprofessional Education Program for Adults with Inflammatory Arthritis

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Objective:
Inflammatory arthritis is accompanied by chronic inflammation, pain and joint destruction. Patient education complements medical treatment by helping people learn to self-manage their disease. Systematic review of arthritis education trials reports only small short-term effects (disability, joint count). However, these may not be the most relevant outcomes for educational interventions. Objective: To examine the effect of an interprofessional, inflammatory arthritis education program (RxEd) on arthritis self-efficacy and other secondary outcomes.

Methods:
Non-randomized, wait-listed control (with cross-over) of RxEd program (I) among patients with inflammatory arthritis recruited from tertiary level arthritis care clinics. Data were collected at the beginning of the study (T1), immediately following I (T2), 6 months [T3, cross-over of control group (C) to receive I], immediately following I (T4) and 1 year (T5). Self-report questionnaires served as the data collection tool. Measures included demographics, disorder-related, Arthritis Self-Efficacy Scale (SE), arthritis knowledge [ACREU RA knowledge questionnaire (PK) and RxEd Content knowledge questionnaire (CK)], coping efficacy (CE), Readiness to Manage Arthritis (RMAQ) and Illness Intrusiveness (II). Analysis of longitudinal data included: Mean scores plotted over time and repeated measures ANOVA to assess cross-over effect.

Results:
42 persons participated in the study (I n=23; C n=19) and 93% follow-up at 1 year. No significant baseline differences were found for: demographics, disorder-related, SE, PK, CK, CE, RMAQ and II measures. Longitudinal plots over time revealed the following: Primary outcome: I group showed immediate effect (improved SE) after the intervention and sustained the effect at 1 year. C group showed no effect until cross-over (immediate improvement in SE which diminished over 6 months). Secondary outcomes: I group showed an immediate effect in uptake of arthritis knowledge (PK and CK) after the intervention that diminished slightly over 1 year while C group had no effect until cross-over (immediate increased knowledge that diminished slightly over 6 months). I group showed an increase in CE that continued to increase over 1 year while C group had no effect until cross-over (increased CE over 6 months). I group showed improved RMAQ and II at 6 months and maintained this at 1 year while C group had no effect until cross-over (improved RMAQ and II over 6 months). Repeated measures ANOVA (to be analyzed).

Conclusion:
Longitudinal measures reveal consistency in results across outcomes. There is evidence for the effectiveness of the "Prescription for Education" program in the improving arthritis self-efficacy and other secondary outcomes among persons with inflammatory arthritis.
A Proof of Concept Trial of Gleevec (Imatinib) in Active Diffuse Scleroderma (DSSc)

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Objective:
There has been interest in tyrosine kinase inhibitors in systemic sclerosis (SSc) due to the effects on PDGF, TGFbeta, adhesion molecules and other factors.

Methods:
We performed a 6 months proof of concept double blinded RCT of imatinib in active diffuse SSc with skin biopsies using 2mm biopsy on abdomen at time 0 and repeated beside original biopsy at 6 months; and plasma (0,3,6 months) analyzing PDGF, RANTES, E-Selectin, VCAM-1, ICAM-1, MMP-9, tPAI-1, IFN-gamma, IL-1alpha, IL-1beta, IL-4, 6, 10, 12p70, 13, 17; MCP-1,3, MIPs, CD40L, VEGF, TNFalpha, and TGFbeta, and patient and physician outcomes including HAQ, and modified Rodnan skin score (mRSS). We used 4:1 randomization and planned to enroll 20 patients, stratifying by presence or absence of stable background Methotrexate use. Novartis supplied imatinib and placebo for this investigator initiated study.

Results:
After enrolling 10 patients mean age (9 active and one placebo);7 Female, mean age 51, 3.1 years disease duration (0.5 to 6 years) and mRSS skin score: 32 (SD 8), 3 had tendon friction rubs, patient global 66 (on 100 mm VAS), MD global 46, and HAQ 1.7; we found poor tolerability and high AEs (5 had to stop due to AEs or interrupting dose including fluid retention, weakness, nausea, vomiting, chest pain, worsening anemia, and hair loss), only 4 patients completed the 6 months on study drug at recommended dose. There was also one SAE (active drug marked fluid retention) so we stopped enrolling further subjects. Using ITT analysis, at 6 months, we found: no difference in any parameter with all p values (none were near significance) including: skin score (6 months mRSS 30. P=0.6), CRP, ESR, MD global (36) and patient global (39), HAQ (1.5), tissue (skin biopsy) and plasma cytokines and other factors. The 6 months health transition was rated by two who dropped out as much worse, and one more as much worse, another worse, 4 the same and 2 better. The plasma and tissue cytokines in those on active treatment were not statistically different from 0 to 6 months except sVCAM-1(plasma p< 0.001) and sICAM-1 (tissue p=0.009).

Conclusion:
In relatively early active disuse SSc, imatinib was not well tolerated and did not change any clinical or skin biopsy parameters over 6 months. It is unlikely that imatinib will be a feasible treatment for early SSc with respect to modifying skin sclerosis or inflammation.
C-Reactive Protein (CRP) is Associated with High Disease Activity in SSc: Results from the Canadian Scleroderma Research Group (CSRG)

Janet Pope (University of Western Ontario, London); Sarah Harding (University of Western Ontario, London); Sarit Khimdas (University of Western Ontario, London); Ash Bonner (McMaster University, London); Murray Baron (McGill University, Montreal)

Objective:
It has been reported that elevated ESR in SSc increases morbidity and mortality. Little is known about the predictive value of the CRP in SSc.

Methods:
The CSRG is a large multi-site dataset comprised of annually assessed SSc patient physical exam and laboratory parameters. Statistical comparisons were made for CRP in early vs. late SSc, diffuse vs. limited, association with skin score and disease activity (MD and patient assessment of disease activity). CRP was drawn annually and normal is up to 8.0mg/L.

Results:
Nine hundred and thirty-eight (938) patients were analyzed, of whom 47% (413) had diffuse SSc and 41 were early diffuse patients (< 3 years from first non-Raynaud’s symptom). CRP was significantly associated overall with modified Rodnan Skin Score (mRSS r=0.2, P=0.04), MD (r=0.3, P=0.01) and patient global assessments (r=0.2, P=0.05) and ESR (r=0.4, P=0.01). The strongest correlations were for early diffuse SSc. The mean difference in CRP between tendon friction rubs (yes and no) (which is also a predictor of worse outcome) was significant for diffuse SSc.

Conclusion:
It appears that CRP is elevated in many SSc patients especially early diffuse SSc. It is associated with other active signs of disease such as tendon friction rubs and MD and patient global assessments. Interventions that lower CRP may be worth pursuing in active SSc.
Women’s College Hospital’s:
Osteoarthritis Nurse Navigator Demonstration Project

Ina Radziunas (Women's College Hospital, Toronto); Shelley Bouchard (Women's College Hospital, Toronto); Carolyn Franke (Women's College Hospital, Toronto)

Objective:
In Ontario, the current model of care delivery to individuals with osteoarthritis (OA) is inadequate to meet the current and future population needs. Beyond the surgical care of patients with OA, the role of nursing has been not been well developed. Yet, it is clear that the professional scope of nursing is ideally suited to play a major role in caring for patients living with OA. Funded through the Nursing Secretariat of the MOHLTC, the project aimed to: • define and maximize the role of nursing in the assessment and management of OA in an ambulatory care setting • implement a chronic disease management program for OA care, that integrates the role of the nurse within an interprofessional framework Furthermore, it was intended that the developed nursing role and framework be transferable to other regions where access to a multidisciplinary care is limited.

Methods:
To understand current issues, the project team conducted an environmental scan. Armed with the newly acquired knowledge, two distinct roles and intervention strategies were developed, one within the multidisciplinary OA team and the other external to the team. A Registered Nurse followed both groups at determined intervals to: • reinforce self-care approaches • manage perceptions and misperceptions about OA • align expectations and set goals • provide linkages to needed community resources • problem solve around health issues they were experiencing

Results:
It was determined through patient surveys that holistic, patient-centered nursing interventions did have a positive influence on patients’ ability to live with OA. Overall, it was shown that the nurse navigator role did meet the patients’ need for education, improved coordination of care, ongoing monitoring and support.

Conclusion:
After intensive review, it is apparent that nurses are well positioned to play an integral, comprehensive and collaborative role in future health care initiatives with this population. As the population ages and OA becomes a fact of life for millions of people, the role of nursing, the “untapped resource” should be considered in any health initiative seeking to provide comprehensive, holistic, patient-centered care.
Anti-TNF Therapy and the Risk of Serious Infection and Malignancy in Patients with Early Rheumatoid Arthritis: A Meta-Analysis of Randomized Controlled Trials

Scott Rieder (University of Western Ontario, London); Andrew Thompson (University of Western Ontario, London); Janet Pope (University of Western Ontario, London)

Objective:
To conduct a meta-analysis of the rates of serious infection and malignancy in patients with early rheumatoid arthritis who have were started on anti-TNF therapy and were naïve to DMARD/Methotrexate therapy.

Methods:
A systematic literature search was conducted through the summer of 2009. All studies included were randomized, double-blind, placebo-controlled of patients with early rheumatoid arthritis who were started on anti-TNF therapy without prior DMARD/Methotrexate use. Seven trials met our inclusion criteria that included 2648 patients receiving biologic therapy and 1391 patients receiving control therapy. All data extracted was from published trials.

Results:
A pooled odds ratio (Mantel-Haenszel methods with a continuity correction designed for sparse data) was calculated for serious infections (requiring hospitalization) and malignancies. The pooled odds ratio for serious infections was 1.17 (95% CI, 0.78-1.75) and for malignancies was 0.95 (95% CI, 0.48-1.87). There was no significant difference between the anti-TNF therapy and the control therapy in both serious infection rates and malignancy rates.

Conclusion:
While other meta-analyses have shown an increased risk of serious infection and malignancy in patients taking anti-TNF therapy, our results show that there is not an increased risk when the patients have early disease and haven’t previously failed DMARD/Methotrexate therapy.
Ultrasound Identification of a Thickened A3 Pulley as the Reason for a Trigger Finger in a 5 year old Girl with JIA

Johannes Roth (Children's Hospital of Eastern Ontario, Ottawa); Alessandra Bruns (Centre Hospitalier Universite de Sherbrooke, Sherbrooke); Roman Jurencak (Children's Hospital of Eastern Ontario, Ottawa); Emilio Filippucci (Università Politecnica di Marche, Jesi)

Case Report:
Introduction Musculoskeletal ultrasound has been shown to be a useful tool in diagnosis and evaluation of treatment response in adult rheumatology. Its use by pediatric rheumatologists is still in its infancy. The aim of this case report is to illustrate the potential for clinic based ultrasound as a non-invasive and rapid diagnostic method on the example of a five year old girl with the unusual finding of a thickened A3 pulley as the reason for a trigger finger. Patient and Methods A five year old girl with known rheumatoid factor positive polyarticular arthritis on methotrexate treatment presented with a new onset trigger finger of her second digit. On clinical exam a firm subcutaneous structure over the volar aspect of the PIP II was noted. An ultrasound exam was performed in clinic with an Esaote MyLab 70 equipped with a multifrequency linear probe at 18 MHz in grey scale mode and 9.1 and 14 MHz in Power Doppler mode to clarify the subcutaneous structure. Results Ultrasound exam of the entire second digit in comparison to the other fingers did show a thickening of the A3 pulley of the second digit with mild tenosynovitis of the underlying flexor digitorum tendons with evident Power Doppler signal. No joint effusion, nodules or other pathology were demonstrated. Discussion Whereas thickening of the A1 pulley is commonly seen in adults and much rarer in children as a cause of trigger fingers this report illustrated the unusual finding of a thickened A3 pulley as a cause for trigger finger in a child. Ultrasound was able to quickly and reliably identify the subcutaneous structure causing the trigger finger and guided the clinical management without any time delays.
Assessment of Muscle Function in Juvenile Idiopathic Arthritis

Johannes Roth (Children's Hospital of Eastern Ontario, Ottawa); Rainer Rawer (Novotec Medical, Pforzheim)

Objective:
Muscle function in children suffering from juvenile idiopathic arthritis (JIA) is an important secondary outcome parameter as it is important for physical function, joint function and the acquisition as well as maintenance of bone mass. Muscle function can be described by muscle force and power and both components need to be assessed to fully understand deficits that might be present. The aim of this study was to assess muscle force and power in children with JIA.

Methods:
In a cross sectional study, muscle force and power were assessed in 50 JIA patients (n=20 oligo, n=22 poly and n=8 systemic) on a Leonardo ground force plate during a two leg and one leg jump. Results of both force and power per kg were calculated as Z-scores, i.e. standard deviations of patients’ results as compared to results of 800 age matched healthy children. In addition the efficiency of the movement and the presence of differences between the right and the left leg were assessed. P-values were calculated comparing the mean of the JIA children with the healthy control group.

Results:
20 patients were oligoarticular, 22 polyarticular and 8 systemic JIA. 22 had active disease and 28 were in remission. Significant deficits of muscle power were found in oligoarticular, polyarticular and systemic JIA patients with a mean(SD) Z-score of -1.08 (0.94), -0.74 (1.31) and -1.65 (1.73) respectively. Comparing patients in remission with active arthritis the mean (SD) Z-score in the active arthritis group was -0.95 (0.97) and not significantly different from the remission group with -1.07 (1.48). For muscle force the oligoarticular JIA group's mean (SD) Z-score was -1.42 (1.20), for polyarticular patients it was -1.21 (1.20) and systemic patients -1.97 (2.07). The active disease group's mean (SD) Z-score was -1.07 (1.27) vs the remission group with -1.69 (1.40).

Conclusion:
This study shows significant deficits of muscle force and power in all subgroups of JIA with deficits in force being more significant than power. There were no differences in parameters of muscle function between patients in remission and patients with active disease indicating that these deficits might persist despite resolution of the disease. As muscle function is an important secondary outcome of JIA, both the assessment as well as therapeutic interventions might be necessary.
Inflammatory Arthritis Education Program outcomes: comparing patient satisfaction and attendance rates following transition from a three week program to a two week program.

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Objective:
The Arthritis Program (TAP) at Southlake Regional Health Centre in Newmarket, Ontario offers an interprofessional, patient centred, patient education program for Inflammatory Arthritis. Originally designed as twelve 3.5 hour classes over a 3 week period, the program has recently been reorganized into ten 4 hour classes over 2 weeks in an effort to make this valuable program more accessible to participants. The objective of this study was to evaluate behavioural outcomes and patient responses between the two class designs in order to evaluate if there are notable differences with respect to program duration.

Methods:
Response surveys were completed by patients at the end of each program and attendance data was gathered for both the 3 and 2 week classes. Patients were asked about reasons for being unable to attend, their preferred class start times, program length and class size, and overall satisfaction with knowledge gained from the classes. Data was collected and compared from the 3 week classes held September to December 2008 and the 2 week classes held January to June 2009. Chi square analysis was used where appropriate.

Results:
A total of 61.1% of patients booked for the 2 week classes (n = 221) attended vs. 52.1 % of patients booked for the 3 week class (n = 96), however this difference was not significant. A significant difference did exist for the proportion of attendees who ultimately attended 100% of their scheduled program classes (57.8% of 2 week class participants vs. 26.0% of 3 week class participants, p < 0.001). There were no significant differences between responses for preferred program length (both classes preferred the idea of a 10 class program over 2 weeks), satisfaction with program length and satisfaction with knowledge gained. Significantly more 3 week class participants (32.4% vs. 8.8%, p< 0.01) preferred a smaller class size (≤ 10 patients).

Conclusion:
Data is still being collected for the ongoing 2 week class participants in order to strengthen these preliminary results. Evidence suggests improved patient attendance with a 2 week program accompanied by no loss in perceived benefit and satisfaction with the program. These results are therefore intriguing in the context of future and ongoing inflammatory arthritis education and program development.
Abatacept Demonstrates Consistent Safety and Sustained Improvements in Efficacy Through 5 Years of Treatment in Biologic- Naïve Patients with RA

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Objective:
To assess the safety and efficacy of abatacept (ABA) in RA patients with inadequate response to methotrexate (MTX) over 5 years of the AIM trial.

Methods:
Patients completing the 1-year, randomized, double-blind (DB), placebo-controlled AIM trial (ABA [~10 mg/kg] or placebo, plus MTX) were eligible to enter the open-label long-term extension (LTE) period (ABA [~10 mg/kg] plus MTX). Safety was assessed for all patients who received ≥1 ABA dose. ACR20, 50 and 70 responses, and remission (DAS28 [CRP] < 2.6) are presented for all patients randomized to ABA (as-observed analysis).

Results:
Of 433 and 219 patients randomized and treated with ABA or placebo, respectively, 378 and 161 entered the LTE. A total of 266/378 patients (70.4%) originally randomized to ABA remained on treatment at Year 5, with annual drop-out rates of ~11, 12, 6, 7 and 8% through Years 1-5, respectively. A total of 37/378 patients (9.8%) discontinued due to adverse events (AEs) and 22 patients (5.8%) due to lack of efficacy. The types and incidence of AEs and serious AEs, respectively, were similar between the DB (303.4 and 17.7/100 patient-years) and cumulative period (combined DB + LTE; 242.3 and 13.9/100 patient-years). Incidence rates of infections and serious infections, respectively, were 90.5 and 4.2/100 patient-years in the DB, and 67.1 and 2.8/100 patient-years in the cumulative period. Over 5 years, malignancies were reported in 33 (5.6%) patients (including non-melanoma skin cancers, solid organ and hematologic malignancies). Autoimmune events and tuberculosis were reported in 49 (8.2%) and 3 (0.5%) patients, respectively. ACR response rates were maintained over 5 years. DAS28 remission was achieved by 25.4% (94/370) and 33.7% (90/267) of patients at Years 1 and 5, respectively.

Conclusion:
Safety of ABA was consistent over 5 years in patients with RA and an inadequate response to MTX, with no increase in incidence rates of safety events in the cumulative versus DB periods and no unexpected events observed. Improvements in ACR response rates were sustained through the LTE; these efficacy benefits were supported by high retention rates, with approximately 75% of patients initially randomized to ABA remaining on treatment at Year 5.
Consistent Safety and Sustained Improvement in Disease Activity and Treatment Response over 7 Years of Abatacept Treatment in Biologic-Naïve Patients with RA

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Objective:
To report seven-year outcome data for biologic-naïve patients treated with abatacept (ABA).

Methods:
This was a 7-year, long-term extension (LTE) of a 1-year, randomized, double-blind (DB), placebo-controlled Phase IIb trial of patients with an inadequate response to methotrexate (MTX). In the DB period, patients received ABA (10 or 2 mg/kg) or placebo, + MTX. During the LTE, patients received ~10 mg/kg ABA + MTX, every 4 weeks. Safety was assessed for patients who received ≥1 dose of ABA. Low Disease Activity State (LDAS: DAS28 [CRP] ≤ 3.2), remission (DAS28 [CRP] < 2.6) and ACR 70 were assessed for patients randomized to ABA 10 mg/kg with available data at the visit of interest (as-observed).

Results:
A total of 235 patients completed the DB period and 219 entered the LTE (ABA 10 mg/kg = 84, 2 mg/kg = 68 and placebo = 67). In total, 114/219 (52.1%) were ongoing at Year 7 (ABA 10 mg/kg = 42, 2 mg/kg = 37 and placebo = 35). Discontinuation due to lack of efficacy and for AEs was observed in 24/219 (11.0%) and 42/219 (19.2%) patients, respectively. The cumulative incidence of AEs, serious AEs and serious infections were 366.1/100, 17.4/100 and 3.18/100 patient-years, respectively, consistent with previous data. Malignancies were reported in 20 patients (7.0%; 24 events: 18 solid organ and 6 non-melanoma skin cancers). Autoimmune events (including psoriasis) and tuberculosis were reported in 13 (4.5%) and 0 patients, respectively. LDAS and remission were sustained/improved over 7 years (48.2 vs. 69.7% and 25.3 vs. 51.5%, at Years 1 vs. 7, respectively). By Year 7, 19/37 (51.4%) patients achieved ACR 70 vs. 24/83 (28.9%) at Year 1.

Conclusion:
Over 7 years, ABA provided sustained improvements in disease activity and ACR 70, and was well tolerated with no unexpected safety events. Together with the relatively high retention rates, this confirms the sustained clinical benefits of ABA in patients with RA and an inadequate response to MTX.
Nurse-led Triage in Musculoskeletal Care

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Objective:
In earlier work, we documented that most arthritis stakeholders endorse an approach to arthritis care that involved non-physicians in an integral way. There is some evidence that nurse-led triage of musculoskeletal patients might bring improvements in patient care. We undertook a realist synthesis to tabulate existing interventions related to nurse-led triage in musculoskeletal disease.

Methods:
A realist synthesis involves successive reviews of the literature and other forms of evidence, along with a detailed explanatory analysis focused on the context of variable regional effects and circumstances. The first step of our literature search employed MEDLINE(1959-2009), EMBASE(1980-2009), EMBASE Classic(1947-1979) and CINAHL(1982-2009). Search terms included: triage, rheumatology, referral and consultation, nurses, nurse's role, musculoskeletal diseases. Two team members screened the titles and abstracts of all potentially relevant citations, to exclude topics outside our area of interest. Data was extracted from the remaining articles, to establish whether the intervention was shown to be effective, and the context. Colloquial evidence was gathered by interviews with individuals involved with nurse-led triage for rheumatology referrals in Canada.

Results:
Our search yielded 2718 titles. After screening these, 29 full-text articles were shortlisted, from which only six were found to be relevant. In these six studies of nurse-led triage in musculoskeletal disease, reported benefits included decreased out-patient waiting times, high patient and physician satisfaction levels, greater morale and personal development of health professionals, more appropriate referrals, and greater efficiency. At centers where nurse-led triage of rheumatology referrals is in place in Canada, similar benefits have been noted in terms of efficiency. In preliminary results from one centre, over a 7-month period, approximately 95 patients were designated as highest priority and seen within 4 weeks. Of these, about 65% were truly inflammatory cases. The majority of these would not have been identified as priority from the consult alone, but required the intervention of the nurse triage specialist. At least one other centre, the relative number of referrals for inflammatory arthritis is increasing, due to the triage process.

Conclusion:
We found very few published examples of nurse-led triage in musculoskeletal disease. However, the literature that does exist has noted several potential benefits of this intervention. Existing examples of nurse-led triage for rheumatology care are operational in Canada. Further work is ongoing to evaluate other sources of data(e.g. ‘gray literature’, colloquial evidence) and to explore whether particular contextual factors are of importance for effective implementation of nurse-led triage.
Functional Assessment in Fibromyalgia: A Study of the Relation of 2 Functional Assessment Instruments to Each Other, and to the Tender Point Count.

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Objective:
Functional assessments are relevant in measuring the impact of fibromyalgia (FM) on patients with this condition, in following the effects of treatment, and as quantitative measures in reports to 3rd parties. We have administered the Fibromyalgia Impact Questionnaire (FIQ), and the Health Assessment Questionnaire (HAQ), to FM patients, seen over a 6 month period, on their first visit. We wished to determine: 1) the relation of these 2 instruments to each other; 2) whether using 2 instruments rather than 1 adds important information; 3) the relation between FIQ and HAQ, respectively, to the tender point count (TPC).

Methods:
All patients with FM, seen for a first consultation between March –August 2009, had a TPC, and, with the exclusion of those with a concurrent inflammatory arthritis and/or who could not read English, filled in FIQ and HAQ forms. Means (M) + 1 standard deviation (SD) were calculated, as were coefficients of correlation (r) between variables using parametric and non parametric statistics as appropriate.

Results:
We saw 54 patients, mean (SD) age 46.9 (11.43) years ; 52 were female; their disease duration was 9.7 ±7.15 years. Mean (SD) scores for the TPC, HAQ, and FIQ were 16.2 (2.03), 1.49 (0.50), and 69.19 (18.39) respectively. The correlation between clinical severity assessments HAQ and FIQ, was 0.677 (p < 0.001) with an r2 of 0.458. Correlations between TPC, and FIQ and HAQ, were -0.091 and 0.118, respectively and not significant (p>0.05). FIQ items 1-11 (part 1) had a 0.608 correlation with the HAQ (p<0.001; r2 =0.370). Interestingly, measures of mood disorders, as assessed by items 19 and 20 of FIQ, showed no significant correlation to TPC (r = 0.063, p>0.05).

Conclusion:
The FIQ and HAQ correlate but a value for r2 =0.458, suggests that HAQ is orthogonal to FIQ, and gives additional information on function. TPC does not correlate with either measure of function, and should not be used for that purpose. Surprisingly, TPC, reputedly a measure of distress, does not correlate with items 19 and 20 of FIQ, which assess anxiety and depression.
Sexual Functioning in Male Ankylosing Spondylitis Patients

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Objective:
Ankylosing Spondylitis (AS) is commonly associated with fatigue, pain, and stiffness, resulting in significant disability. Sexual functioning plays an important role as a contributor to quality of life factors. Sexual functioning in AS patients has not been studied extensively. This study assessed the sexual function of male AS patients and its correlation with various measures of disease activity and severity.

Methods:
The International Index of Erectile Function (IIEF) was used as a validated measure of sexual functioning, with a higher score reflecting better sexual function. Nocturnal Back Pain (NBP), Total Back Pain (TBP), BAS-G (Bath Ankylosing Spondylitis Global score), BASDAI (BAS Disease Activity Index), BASFI (BAS Functional Index), and ASQoL (AS Quality of Life) surveys were self-administered to randomly selected AS patients. A partial correlation that was adjusted for age was used to assess for correlation. Student t-test was used to compare morbidity measures between groups. P values less than 0.05 were considered significant.

Results:
45 Male AS patients were recruited, on whom 30 were on an anti-TNF agent and 15 were on NSAIDs. The mean age of the group was 40.3±11.1 years. According to the Sexual Health Inventory for Men (SHIM), a sensitive marker for erectile dysfunction (ED) constructed from the IIEF, 12 of the 35 patients with sexual activity had ED (mild ED=4, mild-moderate ED=0, moderate ED=6, and severe ED=2). Of the 45 patients, 5 were taking sildenafil or tadalafil and 2 had medical comorbidities affecting sexual function (beta-blocker use and medically-induced tardive dyskinesia). IIEF scores negatively correlated with NBP (rho=-0.564, p=0.001), TBP (rho=-0.593, p<0.001), BAS-G (rho=-0.596, p<0.001), BASDAI (rho=-0.591, p<0.001), BASFI (rho=-0.557, p=0.001), and ASQoL (rho=-0.569, p<0.001). Significant differences were found between patients with and without ED in regards to NBP (p=0.005), TBP (p=0.002), BAS-G (p=0.001), BASDAI (p<0.001), BASFI (p<0.001), ASQoL (p=0.001). The mean IIEF scores of patients on Biologics vs NSAIDs alone were 64.7 (+/-9.5) vs 49 (+/-18.9) respectively (p=0.037).

Conclusion:
Sexual dysfunction is common in AS patients and the strongest correlation was with the degree of pain experienced by the patient. Patients with ED had worse indicators of back pain severity compared to those without ED. Patients with sexual activity on biological therapy reported significantly higher IIEF scores, reflecting better sexual functioning, than those on non-biological therapy.
High Prevalence of Positive ANA (Anti Nuclear Antibody) Test in 823 Acute Hepatitis A patients.

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Objective:
Detection of anti-nuclear antibodies (ANA) is essential for diagnosing autoimmune diseases including autoimmune liver diseases. ANA test is also positive in chronic viral hepatitis of B or C (16 ~19%). Hepatitis A infections are usually mild, self-limiting but could result in fulminant hepatitis or autoimmune hepatitis type I. In this study, we evaluate the prevalence, titers and impact of autoantibodies in Korean patients with HAV infection.

Methods:
We retrospectively reviewed the electric medical records of 823 patients with acute hepatitis A at 3 University Hospital from January, 2008 to May, 2009. Acute viral hepatitis was confirmed by existence of IgM-HAV antibody. The presence and pattern of anti-nuclear antibody were assessed by indirect immunofluorescence on Hep-2 cells and mouse/kidney section.

Results:
Of the 823 patients with Hepatitis A, 442 (53.7%) had positive indirect immune-fluorescence tests of ANA. Notably, most of these patients (77%) showed a cytoplasmic or cytoskeletal pattern with filamentous staining of cytoplasmic fibers. In patients positive for autoantibodies, ALT, IgG and leukocyte count were significantly higher, while the increase in globulin was not statistically significant. In terms of titers, globulin was significantly higher in patients with >1:160 than with < 1:80.

Conclusion:
Our study demonstrated a high prevalence of anti-cytoplasmic autoantibodies in patients with acute hepatitis A. This data would be useful to aid interpretation of indirect immunofluorescence test in patients with acute hepatitis, especially in areas with a high prevalence of hepatitis A.
Tacrolimus for the Treatment of Active Rheumatoid Arthritis: A Meta-Analysis and Systematic Review

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Objective:
The aim of this study was to assess the efficacy and toxicity of tacrolimus in patients with active RA.

Methods:
The authors surveyed randomized controlled trials (RCT) and open-label studies that examined the efficacy and toxicity of tacrolimus in disease modifying anti-rheumatic drug (DMARD) and methotrexate (MTX)-resistant or intolerant patients with active RA patients using Medline, the Cochrane Controlled Trials Register, and by performing manual searches. Meta-analysis of RCTs was performed to determine treatment efficacy and toxicity outcomes. Results are presented as odds ratios (OR), weighted mean differences (WMD), or standardized mean differences (SMD). Open-label studies were included in the systematic review.

Results:
The four RCTs included 1014 DMARD-resistant or intolerant patients with DMARD-resistant or intolerant RA. Median follow-up duration was 6 months (range 16 to 28 weeks). ACR20 and ACR50 response rates were significantly higher in the tacrolimus 3 mg/day group than controls (OR 4.522, 95% CI 3.119 – 6.557, p < 0.001; and OR 2.956, 95% CI 1.120 – 7.807, p = 0.029), and efficacies in the tacrolimus 1.5 – 2 mg/day group showed a similar pattern. Patients treated with tacrolimus withdrew from treatment because of toxicities more frequently than controls, though this was not significant. All four open-label studies found that tacrolimus was safe, well-tolerated, and provided clinical benefits.

Conclusion:
Tacrolimus, at dosages of 1.5 – 3 mg/day, was found to be effective in DMARD-resistant or intolerant patients with active RA.
Prolonged serologically active clinically quiescent (SACQ) systemic lupus erythematosus (SLE): clinical and serologic features

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

Objective:
Some patients with SLE are clinically quiescent despite persistent serologic activity, and thus present a clinical dilemma. We aimed to determine the frequency of SACQ and its outcome in a large cohort of SLE patients followed prospectively at a single centre.

Methods:
Patients followed in the Lupus Clinic between July 1970 and April 2008 with visits no more than 18 months apart were identified. SACQ was defined as at least a two year sustained period without clinical activity and with persistent serologic activity (increased anti-dsDNA antibody by Farr assay and/or hypocomplementemia at each clinic visit), during which patients could be taking antimalarials, but not steroids or immunosuppressives. The characteristics of patients with a SACQ period and its features were analyzed. Anti-dsDNA levels were categorized as normal (≤7), low (8-20), moderately (21-50), or highly (>50) elevated. Results are presented using descriptive statistics. Comparisons were made using t-tests and chi-squared tests.

Results:
56/924 (6.1%) patients had SACQ periods (median 158 weeks, mean 204 weeks). These patients differed demographically from the remainder of the SLE population in terms of presenting SLEDAI-2K (7.34 vs. 10.1, p=0.01), and frequency of use of steroid (33.9% vs. 60.8%, p< 0.0001) and immunosuppressive (3.6% vs. 19.4%, p=0.0004) at first clinic visit. Median disease duration at the beginning of the SACQ period was 8.6 years. Thirteen patients had two or more SACQ periods. Median duration of the first SACQ period was 158 weeks. During this period, 35 patients (62.5%) had both elevated anti-dsDNA antibody and hypocomplementemia; thirteen (23.2%) and eight (14.3%) patients had isolated hypocomplementemia or elevated anti-dsDNA antibody, respectively. Among the 43 patients with elevated anti-dsDNA antibody at some point during the SACQ period, the median anti-dsDNA level was normal in five (11.6%), low in 25 (58.1%), moderate in nine (20.9%), and high in four (9.3%). Thirty-three patients (58.9%) flared (median 155 weeks); six (10.7%) became clinically and serologically inactive (median 236 weeks); 17 (30.4%) continued to be SACQ at their most recent visit (median 159 weeks). In patients who flared, the most common manifestations were arthritis (24.2%), mucous membrane involvement (18.2%) and sterile pyuria (18.2%).

Conclusion:
SACQ patients represent a small, clinically important group. Although 59% of SACQ patients flare they do so after median 3 years. Thus prudent therapy would be close observation to discern which SACQ patients will ultimately flare.
Evaluating Cardiac Risk in Inflammatory Arthritis Patients

Michelle Teo (University of Alberta, Edmonton); Daisy Hartmann (University of Alberta, Edmonton); Stephanie Keeling (University of Alberta, Edmonton)

Objective:
Objectives: Rheumatoid arthritis and associated inflammatory arthritides are independent risk factors for cardiovascular disease (CVD). While it is unclear how to manage these patients, cardiovascular risk stratification using existing scoring tools developed by cardiology is a starting point in evaluating cardiovascular risk. Study objectives included: (1) To evaluate the inflammatory arthritis patients in a university rheumatology practice and determine their cardiovascular risk according to existing risk stratification scores. (2) To determine if cardiovascular risk stratification occurs in a typical academic rheumatologist’s practice.

Methods:
Methods: A retrospective chart review of 440 inflammatory arthritis (seropositive rheumatoid arthritis, seronegative rheumatoid arthritis and psoriatic arthritis) patients attending the practices of nine rheumatologists at the University of Alberta Hospital was performed. A pre-specified case report form detailing patient demographics, traditional cardiac risk factors and variables for the Framingham 2008 and Reynold’s risk scores was used. Details of their arthritis, including seropositivity and medication use were collected.

Results:
Results: In this group of 440 patients (M:F = 117:323), 156 (35.5%) were CCP positive and 257 (58.4%) were RF positive. Complete Framingham risk scores were calculable for 3 (0.68%) patients, while the Reynold’s risk score was calculable for none of the patients. Common cardiac risk variables not recorded by a rheumatologist included (1) positive family history of MI 440 (100%) patients, (2) diabetes 421 (95.7%) patients, (3) lipids status 322 (73.2%) patients and (4) smoking status 275 (62.5%) patients. When documented, patients were noted to be on the following medications: ASA 34 (7.7%) patients, anti-hypertensives 80 (18.2%) patients and lipid lowering medications 41 (9.3%) patients. Medication use for traditional cardiac risks was not documented in the chart for the following: ASA 127 (28.9%) patients, anti-hypertensives 123 (28.0%) patients and lipid lowering medications 130 (29.5%) patients. From the available data, the average Framingham risk of having a general cardiovascular event in 10 years was 29.7% (3 patients). Cardiovascular events were recorded in 2 (0.45%) patients. Rheumatologists ordered cardiac evaluation for 10 (2.3%) patients.

Conclusion:
Conclusions: While cardiovascular risk reduction is a recognized goal in the inflammatory arthritis patient, this has not translated well into clinical practice after reviewing nine different rheumatologists. Even though cardiovascular risk stratification does not take into account the contribution of inflammatory arthritis to CVD risk, it is an important starting point from where further studies can identify inflammatory arthritis specific algorithms for reduction of CVD risk.
Prevalence of Vitamin D Insufficiency and Clinical Outcomes in Psoriatic Arthritis Patients

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Objective:
Hypovitaminosis-D seems to be pandemic in populations residing at higher latitude in North America during the winter months, where sun exposure is often inadequate to generate sufficient vitamin D. Low vitamin D level has been correlated with several autoimmune diseases and increased all-cause mortality. However no studies have determined the prevalence of vitamin D in Psoriatic arthritis (PsA) patients. We aimed to determine the prevalence of vitamin D deficiency and association with disease activity in PsA patients.

Methods:
This is a cross-sectional study conducted at a single centre from March-April 2009. Demographic, clinical and laboratory data were collected for each patients. Patients completed a vitamin D questionnaire developed to assess lifestyle determinant of Vitamin D. Skin class was determined by The Fitzpatrick classification. Serum 25(OH)D, creatinine, calcium, phosphorus and liver enzymes were measured on the day of the visit. 25(OH)D levels were categorized as deficient < 30, Insufficient 30 – 74 and Adequate >75 ng/ml. We evaluated the correlation between disease activity of psoriasis and PsA and vitamin D level. A multivariate linear regression model was used to evaluate the relationship between 25(OH)D levels and the demographic/lifestyle variables. 25(OH)D levels were adjusted for confounders collected from the vitamin D questionnaire.

Results:
One hundred ninety six patients with PsA were assessed (table 1). Vitamin D levels were adequate in 42%, insufficient in 52% and deficient in 6% of PsA patients. No clinically significant abnormalities were found in the liver or kidney laboratory tests. There was no correlation with level of vitamin D and disease activity (Psoriasis; PASI score and nails lesions, PsA; active, swollen and damage joints, enthesitis, dactylitis and tendonitis, and morning stiffness). We found a correlation between the vitamin D level use of phototherapy during last 3 months (less likely to be deficient, p=0.015), use of multivitamin (less likely to be deficient p=0.011) and use of vitamin D (less likely to be deficient, p< 0.001). No correlation could be found between vitamin D levels and skin tone, fibromyalgia, use of anti-inflammatory drugs, DMARD and biological agents.

Conclusion:
A high prevalence of vitamin D insufficiency among PsA patients was found. No correlation could be established between disease activity and vitamin D level. There was a correlation between lifestyle and demographic determinants; phototherapy during last 3 months and use of multivitamin and vitamin D, less likely to be deficient, and vitamin D levels.
Ability of Nonfasting and Fasting Triglycerides to Predict Coronary Artery Disease in Lupus patients

Zahi Touma (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

Objective:
Hypertriglyceridemia is a metabolic disorder associated with atherosclerosis. We have previously shown that there is no clinically significant difference in individual lupus patients in the levels of fasting triglycerides (FTG) and nonfasting triglycerides (NTG). We aimed to determine whether nonfasting triglycerides predict coronary artery disease (CAD) in lupus patients.

Methods:
Patients are followed at regular intervals (at 2-6 months) according to a standard protocol which includes: complete history and physical exam, SLE Activity Index (SLEDAI-2K), and Systemic Lupus International Collaborative Clinics Damage Index (SDI). Fasting lipid profile was measured once yearly and nonfasting was determined at all other visits. We included the entire patient cohort and all the values of TG available in our data. Time-dependent covariate survival analysis was conducted to determine the predictive ability of TG for CAD – whether fasting and nonfasting. Variables considered were: sex, age at diagnosis, age, SDI, SLEDAI-2K, smoker, glucocorticoid, anti-malarial, immunosuppressive drugs, cholesterol. Variables retained for multivariate analysis were selected through the variable reduction strategy (Harell) – selecting variables which alter the parameter estimate of TG by ±10% when included in the model. Using this variable selection, age, SDI, and immunosuppressive drugs were selected to be included in the models.

Results:
We identified 1289 patients since the date of the first TG available. Eighty eight percent of the patients were female. Five hundred forty one patients had elevated cholesterol level and the length of follow-up from the 1st TG to CAD was 8.82±8.19. One hundred eight patients (8.1%) developed CAD. We identified 89 events of CAD in 1137 patients in the nonfasting model and 35 events of CAD in 707 patients in the fasting model. The length of follow-up from first triglycerides to CAD was 8.82±8.10 years. Both nonfasting and fasting model showed ability of the variables to predict CAD; NTG and FTG predicted CAD (HR 1.80, 95% CI 1.10 to 2.93; p=0.02) and (HR 2.76, 95% CI 1.07 to 7.10; p=0.04) respectively.

Conclusion:
Both fasting and nonfasting TG predicted CAD in lupus patients. Nonfasting TG levels can be used in clinic to detect CAD event in lupus patients.
SLEDAI-2K 10 days versus SLEDAI-2K 30 days in a Longitudinal Evaluation

Zahi Touma (University of Toronto, Toronto); Murray Urowitz (University of Toronto, Toronto); Dominique Ibanez (University of Toronto, Toronto); Dafna Gladman (University of Toronto, Toronto)

Objective:
The SLEDAI (Systemic Lupus Erythematosus Activity Index) was developed in 1985 and is based on the presence of 24 features in 9 organ systems over the patient’s past 10 days. An updated version SLEDAI-2000 (SLEDAI-2K) was introduced and validated in 2002 again documenting findings in the past 10 days. Our objective was to evaluate SLEDAI-2K 30 days in a cross-sectional study design and over time and to compare with the original SLEDAI 10 days.

Methods:
In the first phase we enrolled 131 consecutive lupus patients seen at a single centre Lupus Clinic over 6 weeks. In the second phase 41 patients were followed at monthly intervals for 12 months. A complete history, physical examination and laboratory tests were performed to allow the determination of SLEDAI-2K. The SLEDAI-2K score was completed twice, once for a 10-day window and the second for a 30-day.

Results:
Among the 131 patients, 97 had a SLEDAI-2K of 0 and 34 patients had varying levels of disease activity (12 had SLEDAI-2K of 2; 11 had 4; 2 had 6; 3 had 8; 1 had 10; 2 had 12; 1 had 14 and 2 had 16). In all patients but one there was agreement between the SLEDAI-2K 10 and 30 days. 419 patient-visits in 41 patients were recorded. 268 patient-visits had varying levels of disease activity (3 patients-visits had SLEDAI-2K of 1; 133 had 2, 2 had 3, 68 had 4, 9 had 5, 35 had 6, 11 had 8, 4 had 10, 2 had 12 and 1 had 15). In all but 1 patient-visit there was an agreement between the SLEDAI-2K 10 and 30 days. This patient experienced skin rash as a minor lupus flare, however in the last 10 days prior to the visit his rash completely faded. This study confirmed that it is unusual to have a manifestation of active lupus present at -11 to -30 days prior to a visit and have complete resolution in the 10 days prior to the visit. SLEDAI-2K 30 days scores were concordant with SLEDAI-2K 10 days scores, both in patients in remission and in patients with a spectrum of disease activity levels followed monthly over 1 year.

Conclusion:
SLEDAI-2K 30 days was validated against SLEDAI-2K 10 days and may now be used in clinical studies and clinical trials to describe disease activity over the previous 30 days.
Certolizumab Pegol (CZP) Added to Methotrexate (MTX) Provides Lasting Improvements in Patient-Reported Outcomes (PROs) Over 2 Years

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Objective:
Based on results obtained from the RAPID1 trial, CZP 200 or 400 mg Q2W+MTX provided rapid, sustained, and clinically meaningful improvements in physical function and HRQoL, as well as reductions in arthritis pain and fatigue over 1 year. This analysis examines the impact of CZP + MTX on these PROs over 2 years.

Methods:
Patients who completed 1 year of double-blind CZP treatment (completers) and then continued with open-label CZP + MTX were included in this analysis. These patients had a minimum 2 yrs of CZP exposure from BL. Physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]), pain (Visual Analog Scale [VAS; 0-100 mm]), fatigue (Fatigue Assessment Scale [FAS, 0-10]), and HRQoL (SF-36) were assessed for changes from RAPID1 BL and percentage of patients achieving Minimum Clinically Important Differences (MCIDs). MCIDs are $\geq 0.22$ for HAQ-DI, $\geq 10$ for pain VAS, $\geq 1$ for FAS, $\geq 5$ points for the 8 SF-36 domains (Physical Functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, and Mental Health) and $\geq 2.5$ points for SF-36 physical and mental component summaries [PCS, MCS]).

Results:
At Wk 1, clinically-meaningful improvements to physical function as well as reductions in pain and fatigue were reported with CZP. For completers originally treated with CZP 200 mg + MTX, physical function (HAQ-DI) had improved on average by 0.79 points; pain relief averaged 39.5 points, and fatigue relief averaged 3.2 points, at Year 2. These patients also experienced mean improvements of 10.1 and 7.7 points for the PCS and MCS, respectively (Yr 2). At Wk 12, the first post-BL assessment of HRQoL was completed and improvements were reported with CZP. HRQoL levels approached US population norms in the Vitality and Mental Health domains. For all PROs, improvements were sustained through Year 2 (Wk 100) or longer. Comparable benefits were observed in completers who received CZP 400 mg + MTX in RAPID 1.

Conclusion:
CZP + MTX provided clinically meaningful improvements in physical function and HRQoL, and reduction of pain and fatigue, over 2 years. These improvements maintained average levels at least 3 times higher than the thresholds for meaningful improvement.
Under Utilization of DMARDs in Early Rheumatoid Arthritis: A Population-Based Study from the Ontario Biologics Research Initiative Comparing Rheumatology Care with Primary Care

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Objective:
Numerous studies have demonstrated the importance of earliest possible referral, diagnosis and initiation of DMARDs for RA. Primary care physicians function as gatekeepers for access to specialists and play an integral role in ensuring RA patients receive optimal early care. The OBRI represents a collaboration of rheumatologists, patients and researchers. Current research is aimed at delineating provincial practice patterns, and the real-world effectiveness and safety of anti-rheumatic therapies through administrative database linkages with the advantage of comprehensive health coverage that covers the entire population. We estimated the percentage of RA patients in Ontario exposed to DMARDs within the first year of diagnosis.

Methods:
We assembled an incident RA cohort from physician billing data for 1997-2006. We used a standard algorithm to identify 24,326 RA cases aged >65 years, based on >2 RA billing codes, >60 days apart but within 5 years. Drug exposures were obtained from pharmacy claims data. We followed subjects for 1 year, assessing if subjects had been exposed (defined as ≥1 prescription) to one or more DMARD (focusing on methotrexate, sulfasalazine, or hydroxychloroquine) within the first year of RA diagnosis. We assessed secular trends & differences for subjects who had received rheumatology care (defined as one or more rheumatology encounter) versus those who had not.

Results:
Overall 40% of the 24,326 seniors with new-onset RA identified over 1997-2006 were exposed to DMARD therapy within 1 year of diagnosis. This increased from 30% in 1997, to 55% in 2006. Only 55% of patients saw a rheumatologist. In 2006, the percentage of early RA patients on DMARDs for those who saw a rheumatologist was 70% compared to 20% for those that did not.

Conclusion:
Improvements in RA care have occurred but more efforts are needed. Particularly in patients who were not referred to a rheumatologist where only 20% receive a DMARD in the 1st year of diagnosis. This emphasizes the key role of rheumatologists. Current OBRI research will further delineate practice patterns, funding patterns, and the real-world effectiveness and safety of anti-rheumatic therapies.
Elevating Patients’ Knowledge on the Process to Access Publicly Funded Biologic Therapies: Benefits of Collaborative Research Efforts

Jessica Widdifield (University of Toronto, Toronto); Carter Thorne (Southlake Regional Health Care, The Arthritis Prog, Newmarket); Catherine Hofstetter (Canadian Arthritis Patient Alliance, Scarborough); Anne Lyddiatt (Ontario Biologics Research Initiative, Ingersoll); Patricia Pugh (UNIVERSITY HEALTH NETWORK, Toronto); Patricia Frank (UNIVERSITY HEALTH NETWORK, Toronto); Claire Bombardier (University of Toronto, Toronto)

Objective:
The Ontario Biologics Research Initiative (OBRI) is a collaboration of rheumatologists, consumers, researchers and other arthritis stakeholders. The goals of the OBRI are to determine the long term effectiveness and safety of biologic therapies as compared to traditional disease-modifying anti-rheumatic drugs (DMARDs) and to optimize access to quality care for Rheumatoid Arthritis patients. The OBRI is also providing valuable information to inform surveillance in usual care. To reduce the burden on physicians and ensure adequate data collection, patient questionnaires are administered by trained telephone interviewers. Interviewers have identified a need for information on access to publicly funded biologic therapies as the most pressing learning need of patients.

Methods:
To address these concerns, interviews were conducted with key informants to identify barriers and gaps in information on the process of accessing public reimbursement of biologic therapies. Informants included members of the Ontario Rheumatology Association (ORA), the Canadian Arthritis Patient Alliance (CAPA), the OBRI Consumer Advisory and Scientific committees, and the OBRI project interviewers.

Results:
Several areas were identified where patient information on the process of public reimbursement was lacking and thus contributed to additional delays to reimbursement approval. Questions identified from this needs assessment included: What options are available for access to expensive therapies? What is the process for public drug reimbursement? How are requests for reimbursement made? What are the roles and responsibilities of the patient and the rheumatologist in submitting reimbursement requests? Who is notified regarding decisions of reimbursement coverage? What is the duration of coverage? What is the process for coverage renewal? What other patient assistance programs are available? Findings from key informant interviews were used to develop a patient toolkit to address these questions. The toolkit is currently being piloted at the OBRI recruiting sites and will be available on association websites.

Conclusion:
In collaboration with the ORA and consumers, the OBRI represents a unique resource in elevating patients’ knowledge on the process to access publicly funded biologic therapies once prescribed by their rheumatologist. Future research will explore the toolkit’s impact and the usefulness of patient support programs.
The In Vitro Osteoclast Differentiation in Arthritis (IODA) Project: Osteoclastogenesis as a Marker of Presence and Activity of Disease in Arthritis

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Objective:
Osteoclasts play an important role in the pathophysiology of rheumatoid arthritis (RA) and osteoarthritis (OA). We hypothesized that in vitro osteoclast formation and activity correlate with disease presence in RA and OA patients and with disease activity in RA. We previously showed that cells from patients with RA exhibit higher bone resorption rates. Moreover, cells from patients with inactive RA have higher osteoclastogenesis rates than cells from patients with active RA or controls. We have now studied the OA cohort.

Methods:
A cohort of OA patients and controls were recruited from the outpatient rheumatology clinic at the Centre Hospitalier Universitaire de Sherbrooke. Peripheral blood monocytes were differentiated into osteoclasts in vitro. Multiple parameters were quantified including osteoclastogenesis, resorptive activity, survival (apoptosis) and the expression of cytokine receptors. We investigated which parameters could differentiate between patients with OA and controls (based on several attributes including demographics, clinical observations, lab tests and osteoclastogenesis). A descriptive (human-readable) classifier capable of discriminating these different patient groups was developed using alternating decision trees as the method that provided high-quality models. To ensure statistical validity, we imposed a 10-fold cross validation, and we measured accuracy, MCC (Matthews Correlation Coefficient), sensitivity and specificity of the generated classification model. We performed classical statistical analysis to validate the significance of the discovered markers.

Results:
The analyses revealed the following: 1) cells from patients with OA had lower apoptosis rates than controls; 2) protein expression of RANK and IL-1 receptor 1 and 2 was higher in controls than in OA patients; and 3) low apoptosis combined with low RANK/GAPDH values were associated with OA.

Conclusion:
The results indicate that parameters important to osteoclast biology correlate with the presence of OA. These studies are supported by CIHR, CAN and Pfizer Canada.
**Objective:**
Digital ulcers (DU) in systemic sclerosis (SSc) are common (up to 50% of patients) and can affect function. The self-reported impact of disease manifestations is worse for Raynaud's phenomenon (RP) and DU than breathing or intestinal problems associated with SSc. We studied patients with SSc enrolled in two RCTs using bosentan, which has been shown to prevent DU. Patients completed the Health Assessment Questionnaire (HAQ) at each study visit. Data were provided upon request by Actelion for this analysis.

**Methods:**
Data from the studies were pooled to determine the within patient differences of the HAQ, between groups, with and without DU, where 309 were enrolled in the two trials, of whom 133 were on placebo and 176 received bosentan. Patients were pooled irrespective of drug allocation. The patients were grouped by DU status at baseline and study end into: no DU at baseline and no DU at trial end, no DU at baseline and DU at trial end, DU at baseline and no DU at trial end, DU at baseline and DU at trial end. The components of the HAQ scores that are compared are overall disability, hand function, dressing, hygiene, and grip. The main outcome, difference in HAQ score between baseline and trial end in the 4 categories in a post hoc analysis (HAQ at baseline - HAQ at end of study), was calculated for each group.

**Results:**
The groups that had a different DU status at baseline than at end had greater change scores for the majority of the HAQ components compared to groups whose DU status remained constant throughout the trial. Those who had a baseline DU and none at end improved their HAQ scores (Overall -0.14 (0.43), Hand Function -0.22 (0.56), Dressing -0.42 (0.80), Hygiene -0.16 (0.69), Grip -0.08 (0.66)).

**Conclusion:**
Patients with a DU at baseline and no DU at trial end had improvements in all components of the HAQ. The cohort of patients with no DU at baseline and a DU at trial end had worsening of all but the grooming score, but numbers were small (N=10). The overall change in HAQ did not meet the minimal important difference (MID) of 0.22, but the Hand Function part of the HAQ seemed to be above the MID when DU were present and then healed. As expected, those patients with no change in DU status from baseline to trial end had no changes in HAQ.
Impaired Renal Function in Patients with Systemic Lupus Erythematosus (SLE) Predicts Cardiovascular Events

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Objective:
To determine whether impaired renal function predicts the development of cardiovascular diseases (CVD) in SLE patients.

Methods:
An inception cohort of 437 female was studied between 1970 and 2007. Renal function was assessed by calculating estimated glomerular filtration rate (eGFR, mL/min/1.73m2) using serum creatinine. Arterial thrombosis events (ATE) including myocardial infarction, angina, transient ischemic attacks, cerebral vascular accidents and other arterial events were documented. Disease activity was determined using SLE-Disease-Activity-Index (SLEDAI). Patients were classified into those with or without ATE (ATE, non-ATE) and further into ATEs that occurred within or after 3 years since the first visit. Comparisons were done using un-paired T-test, Wilcoxon test and one-way ANOVA. Multivariate Cox proportional hazard model was used to determine the associations.

Results:
437 females, mean age 35.5(13.9) yrs, followed for 11.3(8.24) yrs, with the baseline eGFR of 88.3(29.8) were studied. Of those, 13.5% died. Among the ATEs recorded up to 15 yrs after the first visit, 48% were ATE<3yr. ATE group had a significantly (P< 0.05) lower baseline eGFR [ATE: 73.7(26.2); non-ATE:90.5(29.7)] and were significantly older than non-ATE [ATE: 44.1(16.5); non-ATE: 34.4(13.1) yr]. In patients with ATE, there was no difference in baseline eGFR between those who were older or younger than the mean age of the group. ATE<3yr group had a significantly lower baseline eGFR [61.2(26.0)] than ATE>=3yr [82.6(22.7)]. In either ATE<3yr or ATE>=3yr, there was no difference in baseline eGFR between those older or younger than mean age of ATE group. Furthermore, those who were younger than the mean age and with ATE<3yr had significantly lower baseline eGFR [61.0(26.7)] than the corresponding age group in ATE>=3yr [78.9(25.5)]. The following variables were included in the multivariate model: age, baseline: eGFR, SLEDAI, cholesterol and systolic blood pressure. Baseline eGFR, age and SLEDAI were significantly associated with the risks of ATE (eGFR: Hazard Ratio (HR) =0.986, CI: 0.974-0.997; age: HR=1.032, CI: 1.012-1.052; SLEDAI: HR=1.041, CI:1.015-1.067). For a typical female with SLE, controlling for other risk factors, every 10 mL/min/1.73m2 increase of baseline eGFR decreased CVD risks by 14%, every 10-year increase in age increased CVD risks by 32%.

Conclusion:
Low baseline eGFR, older age and high baseline SLEDAI were significantly associated with risks and time of CVD. Aggressive management of renal diseases and CVD risk factors should begin from the early stages of SLE in order to prevent the development of CVD.
Description and Validation of a Clinical Test to Sort out Chronic Low Back Pain. A Pilot Study.

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Objective:
Assessing the precise origin of low back pain (LBP) is difficult. We set to design a simple clinical test to identify LBP as posterior (facet joint problem), anterior (disk-vertebra problem) or neither i.e. referred pain.

Methods:
Normal individuals (group A), active (group B) and inactive (group C) ankylosing spondylitis (AS) patients were studied by experienced and inexperienced physiotherapists (SB and MJM) and rheumatologists (OM and HAM), respectively. AS diagnosis and activity was based on Good Clinical Practice: pain pattern, medications, family history, BASFI, BASDAI, HLA B27 and MRI. The state of contraction of the lumbar paravertebral muscles was validated with surface electromyography (EMG). The t test compared the means at significance of p< 0.05.

Results:
We first elaborated the neurophysiological rationale and standardized the clinical test to establish its intra- and inter-observer reproducibility. The resulting M&M (Ménard & Morneau) test consists in a controlled-standardized lumbar extension with concomitant palpation of the lumbar paraspinal muscles to detect either relaxation (normal) or its absence (abnormal). Surface EMG (in μvolts/sec) confirmed the manual finding. In 44 tests, intra- and inter-observer reproducibility was 100% and 95.5%, respectively. The test was normal in 26/28 (92.8%) of group A and in 6/6 inactive AS in group C. It was positive in 10/10 active AS in group B. The EMG performed by an observer blinded to the M&M test showed: downward tracing-relaxation in group A and C and, flat-no relaxation or upward-contraction tracings in group B. The mean-individual-μvolts/sec difference between rest and full extension readings gave p< 2x10^-7 between groups A and B and groups B and C. There was no difference between groups A and C with p=0.06.

Conclusion:
The M&M test is an easy to learn and perform, reliable, reproducible, qualitative/semi-quantitative appreciation of the state of contraction of the lumbar para-vertebral muscles during extension of the lumbar spine. It stresses that the para-vertebral lumbar muscles normally relax during early lumbar extension and support the suggestion that the earliest objective manifestation of AS is the reflex contraction of the lumbar para-vertebral muscles during early lumbar extension. The M&M test should be evaluated as a screening test for AS in primary care and field studies and, with/without surface EMG as an objective outcome measure in clinical trials of AS.
High-Resolution Peripheral Quantitative Computed Tomography (HR-pQCT) Identification of Bony Damage in Rheumatoid Arthritis

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Objective:
To determine if high resolution peripheral quantitative computed tomography (HR-pQCT) can provide quantitative assessment of features of RA damage, in particular joint space narrowing, erosion quantity and volume, and periarticular bone density. HR-pQCT provides three-dimensional information on bony structures with an isotropic voxel size of 82 micrometers. Highly sensitive imaging techniques may assist physicians in identifying early lesions in RA which are amenable to intervention, or in quantifying the degree of existing damage.

Methods:
In this pilot study, patients with established RA and damage of the MCP or PIP joints by x-ray are recruited to undergo HR-pQCT (XtremeCT; Scanco Medical, Switzerland). Age and sex-matched control patients are screened to ensure they do not have an inflammatory arthritis or damage from osteoarthritis. A semi-automated segmentation method identifies bone based on changes in the gray scale, with manual correction of any errors made by the program. These images are used to create a three-dimensional reconstruction of the joint. Joint space width is calculated using Image Processing Language software, with the distance between each phalange measured by counting the number of voxels at the closest points. Methods to determine periarticular bone density and morphology will be based on existing protocols used in osteoporosis research. Erosions are counted visually and their location summarized.

Results:
Twelve RA patients and five control patients have been scanned to date. Average age is 47 years, 83% are female, 92% are right-handed and 72% of the RA patients are seropositive. All patients have received methotrexate and plaquenil, and the majority are biologic-naïve. Joint space narrowing occurs more frequently at the MCP joints than at the PIP joints.

Conclusion:
HR-pQCT allows more detailed imaging of RA damage compared to the current gold standard, x-ray. Quantification of important parameters of damage, such as joint space width, erosion quantity and periarticular bone density, are possible with HR-pQCT based on preliminary analysis.
The Safety and Effectiveness of Single and Repeat Dosing of Intra-Articular Anti-Tumour Necrosis Factor Treatment after a Lack of Sustained Response with Intra-Articular Steroids.

Justin Chia (University of Western Ontario, London); Janet Pope (University of Western Ontario, London)

Objective:
Recently, there have been case reports in inflammatory arthritis with intra-articular (ia) antiTNFs (adalimumab, etanercept, and infliximab). Although there have been positive results, most studies have had few patients, short follow up and no data on repeat injections with ia antiTNFs. We wanted to determine if ia adalimumab and etanercept yielded benefit in patients recalcitrant to steroid injections to determine the safety, efficacy, and durability of single and repeated ia anti-tumour necrosis factor (anti-TNF) treatment in active inflammatory synovitis.

Methods:
Using a retrospective chart review, patients were identified who had been previously injected with 40mg ia adalimumab or 50mg ia etanercept over a four year period. Indications for treatment were those with inflammatory arthritis with one or two active joints, no contraindications to anti-TNFs, and little durability with previous ia steroids. Background DMARDs were not changed and the anti-TNFs were mixed with triamcinolone and lidocaine and injected intra-articularly into knees, ankles, and one wrist.

Results:
Nineteen patients were followed: 14 receiving ia adalimumab, 4 receiving ia etanercept, and one receiving both. Six patients had ongoing biologic therapy. Ten had rheumatoid arthritis (RA), 5 had a seronegative arthropathy, 2 had psoriatic arthritis, one had Still’s disease, and one had mixed connective tissue disease overlapping with RA. Of the patients having received follow-up, 79% of patients that received ia adalimumab and 100% of those injected with ia etanercept had an improvement in joint symptoms, often lasting far longer than ia steroids alone. There was only one reported adverse event in a wrist post-ia adalimumab, which was a rebound inflammation after 6 weeks of relief that was not correlated with infection. In total, 19 knees, 12 ankles, and one wrist were injected with anti-TNFs; where 6 patients received repeated injections (2 people with 4 injections each and 4 with repeated or multiple joint injections)

Conclusion:
This is the first report of repeated ia adalimumab injections added to background treatment with no serious adverse events and prolonged benefit compared to previous ia steroids patients. Similar to previous case reports, we report that ia etanercept can also be effectively used for persistent discrete arthropathies despite DMARD treatment. Although not approved for this method of administration, ia anti-TNFs may be a cost effective and successful treatment of inflammatory arthritis with persistent synovitis of a joint that is recalcitrant to ia steroids.
Burning Mouth Syndrome: Case Presentation
Angeli Chopra (University of Alberta, Edmonton); Cheryl Cable (University of Alberta, Edmonton); Elaine Yacyshyn (University of Alberta, Edmonton)

Case Report:
Objective: Burning mouth syndrome or stomatodynia is an unusual patient presentation in rheumatology. We present a case, and review the differential diagnosis of this condition. Case: A 60 year old woman with known seropositive, CCP positive Rheumatoid Arthritis (RA) presented with a six week history of tingling or burning of her diffuse tongue. There had been no known triggers and nothing which improved or relieved her symptoms. She had been previously diagnosed with RA four years previously, and was well controlled on hydroxychloroquine monotherapy for the duration of her disease. She was treated with hydrochlorothiazide and thyroxine for hypertension and hypothyroidism, however there were no recent changes to her medications. She denied ocular symptoms, or symptoms of Sjogren’s syndrome. Examination showed no obvious oral or ocular abnormalities. Her rheumatologic exam showed no active synovitis, although second MCP tenderness. Laboratory investigations showed a normal CBC, liver function tests, and inflammatory markers (ESR 17mm/h, CRP 2.8 mg/L). She was referred to an oral pathologist, and was evaluated. She developed symptoms of dizziness, and was diagnosed with Type 2 Diabetes Mellitus. With initiation of metformin, her tongue symptoms resolved, however when her blood sugars are elevated she has recurrence of burning tongue symptoms. Diabetes is the diagnosis of her burning mouth symptoms. Discussion: Burning Mouth Syndrome (BMS) or stomatodynia is well reported in the dentistry literature, although few reports in rheumatology. The incidence in the general population has been described up to 15% population. The manifestations of Burning Mouth Syndrome, (burning of tongue and mucous membranes, taste alteration and pain in the oral area) are predominantly seen in women, particularly post menopausal. Burning typically involves the anterior two thirds of the tongue, lips and or and anterior hard palate. Etiologies of Burning Mouth Syndrome have been classified as: 1) oral/local 2) systemic 3) psychogenic or 4) idiopathic, also known as primary BMS. Evaluations should include a complete blood count, random blood glucose, ferritin, IgE, B12, ANA, ENA, H pylori, scintigraphy, salivary flow rates and candidial swab testing. Conclusion Burning mouth syndrome is a complex and multi-factorial condition. Systemic and metabolic causes for oral symptoms should be investigated as important diagnoses can be underlying. Further research needs to be done as to the exact extent of the incidence and prevalence in rheumatologic conditions such as sjogren’s and rheumatoid arthritis.