and 31 patients. Patients with incident RA in 2000–09 had markedly lower cumulative incidence of any CVD events than patients diagnosed in 1990s and 1980s (Figure). Hazard ratios (HR) for any CVD events demonstrated significant reduction in CVD events among patients with incident RA in 2000s compared with incident RA in 1980s (HR: 0.52; 95% confidence interval (CI): 0.32–0.86) and a reduction approaching significance compared with incident RA in 1990s (HR: 0.65; 95% CI: 0.40–1.05). Patients with incident RA in 2000s were compared with 405 patients without RA in 2000s who experienced 30 CVD events during follow-up. Patients with incident RA in 2000s had no excess in CVD events over subjects without RA (HR: 0.88, 95% CI: 0.53–1.46). Results were similar for MI, stroke and CHD deaths when examined separately.

Figure. Cumulative incidence of any CVD event in RA and non-RA patients by decade of RA incidence/index.

Conclusion: Our findings show a dramatic reduction in incidence of major CVD events in RA in recent decades. The gap in CVD occurrence between RA patients and the general population may be closing. These findings may reflect increased awareness, improved primary CVD prevention and more optimal RA disease management in recent years. More studies are needed to understand the reasons and implications of these trends.

REFERENCES:

- [1] Myasoedova E, et al. *J Rheumatol* 2017, 44(6):732-9.
- [2] Kerola AM, et al. *Clin Exp Rheumatol* 2015, 33(3):391-8.
- [3] Lacaille D, et al. *Ann Rheum Dis* 2017, 76(6):1057-63.

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FRI0655

THE IMPACT OF PREGNANCY ON STRUCTURAL PROGRESSION IN PREMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

Deshire Alpizar-Rodriguez¹, Frauke Förger², Axel Finckh¹, On behalf the physicians of the Swiss Clinical Quality Management Program for Rheumatoid Arthritis. ¹University of Geneva, Division of Rheumatology, Geneva, Switzerland; ²University Hospital and University of Bern, Department of Rheumatology, Immunology and Allergology, Bern, Switzerland

Background: Disease activity often improves during pregnancy and worsens at the postpartum period [1]. The long-term effect of pregnancy on radiographic joint damage progression among premenopausal women with RA has been barely studied.

Objectives: The aim of this study was to analyse the impact of pregnancy on radiographic progression in premenopausal women with RA.

Methods: This is an observational cohort study of RA patients included in the Swiss Clinical Quality Management in Rheumatoid Arthritis (SCQM-RA). Patients enrolled are followed-up yearly and have radiographic assessments at regular intervals. Information about female reproductive factors, such as pregnancies, breastfeeding and hormonal treatment were retrospectively retrieved using a questionnaire. For this analysis we included premenopausal women with at least two radiographic assessment and full information on reproductive factors. The primary outcome was the rate of radiographic progression (Ratigen erosion score). We analysed the radiographic progression between premenopausal women with at least one pregnancy and those with no pregnancies. Baseline time was the first radiographic assessment. We used a multilevel regression model for longitudinal data, adjusted for potential confounders, such as baseline age, disease duration, DAS-28 and treatment.

Results: Among 1966 women who were interviewed, 430 premenopausal women with sequential radiographic assessments during follow-up were

analysed. Half of premenopausal women had at least one pregnancy. Women with at least one pregnancy were older than nulliparous (median of 41 vs 36 years, $p<0.001$) and had longer disease duration (median of 3.4 vs 2.6 years, $p=0.04$) (Table 1). During follow-up, the rate of radiographic progression was lower in women with pregnancies than in nulliparous women [(0.9% (95% CI: 0.0 to 1.9) vs 2.1% (95% CI: 0.9 to 3.1) over 10 years, respectively, $p=0.04$, Figure 1]. In a sub-analysis, the rate of radiographic progression appeared to be lower during the 13-year period after first pregnancy than after this period [(0.2% (95% CI: -0.8 to 1.3) vs 2.6% (95% CI: 1.3 to 3.9) over 13 years, respectively, $p=0.003$]. We found no difference in the rate of radiographic progression between women with a single pregnancy and multiparous women.

Conclusion: In premenopausal women with RA, joint damage progressed more rapidly in nulliparous women than in women with at least one pregnancy. However, we cannot make any definite causal inference, since it is well possible that women renouncing getting pregnant might be patients with more severe disease. Radiographic progression appeared to increase the longer the time since pregnancy.

REFERENCES:

- [1] Ince-Askan H, et al. *J Rheumatol* 2016;43 :22-5.

Table 1. Baseline characteristics of premenopausal women of SCQM cohort

General and disease characteristics	Women with pregnancies n=213	Nulliparous women n=217
Age, years, median(IQR)	41 (36-45) *	36 (29-43)
Ever smoking, n (%)	56 (26)	66 (30)
Alcohol consumption, n (%)	129 (61)	112 (52)
Disease duration, years, median (IQR)	3.4 (0.6-8.0) *	2.6 (0.4-7.4)
Seropositive (ACPA or RF positive), n (%)	175 (82)	180 (83)
DAS 28, median(IQR)	3.6 (2.6-4.9)	3.6 (2.4-4.8)
HAQ-DI, median (IQR)	0.6 (0.3-1.3)	0.6 (0.3-1.3)
Erosion score, %, median (IQR)	1.0 (0.3-4.9)	1.4 (0.1-5.0) *
DMARD treatment, n (%)	181 (85)	186 (86)
Biologic treatment, n (%)	70 (33)	72 (33)

*p-value <0.05. DAS28: 28-joint Disease Activity Score ESR; HAQ-DI: Health Assessment Questionnaire –Disability Index; DMARD: disease-modifying antirheumatic drugs.

Figure 1. Change in RA Disease Progression and pregnancies

Rating score is expressed in percentage [%], 95% CI are displayed as vertical lines.

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FRI0656

ENVIRONMENTAL AND ATMOSPHERIC FACTORS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A REGRESSION ANALYSIS

George Stojan¹, Frank Curriero², Anton Kvit², Michelle A. Petri¹. ¹Johns Hopkins University Medical School, Baltimore, United States of America; ²Johns Hopkins Bloomberg School of Public Health, Baltimore, United States of America

Background: Understanding the role of environmental exposures in the development of SLE and their association with SLE activity may help identify modifiable risk factors and potential etiological mechanisms

Objectives: We hypothesized that changes in fine particulate matter (PM_{2.5}) concentration, ozone concentration, temperature, resultant wind, relative humidity, and barometric pressure are predictive of organ specific flares in lupus.

Methods: 1628 patients who fulfill 4 of the 11 ACR or SLICC classification criteria for SLE were included in the analysis. The data ranged from 1999 to 2017. Maximum distance between visits was 110 days with 1-month time aggregation units. Disease activity was expressed as Physician Global Estimate (PGA), taken at

every patient visit. A flare was defined as a PGA score increase of 1 point or more compared to the previous visit. Environmental and atmospheric data was obtained from the EPA, including PM2.5 and ozone concentration, temperature, residual wind, relative humidity, and barometric pressure. The average values of each factor 10 days prior to patient visit was calculated. Univariate and multivariate models were built in order to study the association of these variables with lupus disease activity. The models were adjusted for age, sex, income, racial distribution, and rural vs. urban patient residence. Multivariate logistic regression was used to identify significant determinants associated with lupus flares. Regression was performed for each organ flare outcome. Regression inference was based on generalized estimating equations (GEE) to account for the time repeated outcomes. Standard regression techniques on model building and evaluation were followed, including but not limited to performing both univariate and multivariate regressions, coefficient significance, collinearity, confounding, variable interactions and reductions in model AIC.

Results: Rash, serositis, hematologic, and joint flares were statistically significantly associated ($p<0.05$) with an increase in temperature in univariate and multivariate analysis. Renal flares were negatively associated with increases in temperature ($p<0.05$) in univariate and multivariate analysis.

PM2.5 concentration was significantly associated ($p<0.001$) with rash, joints, serositis, neurologic, pulmonary, and hematologic flares in univariate and multivariate analysis.

Ozone concentration, residual wind, and relative humidity were significantly associated with lupus flares in univariate analysis only, while barometric pressure had no associations.

Conclusion: There is a strong association between changes in PM2.5 concentration and temperature 10 days prior to patient visit and organ specific lupus activity at the visit. These data could add an important aspect to lupus trials, the outcomes of which may be affected by so far unrecognized environmental factors, and ultimately it could allow predictive modelling of lupus flares which would revolutionize the approach to treatment.

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FRI0657

METABOLIC SYNDROME PRECEDES THE ONSET OF HIP AND KNEE PAIN AND THE RISK IS NOT MODIFIED BY DIET OR CHANGES IN BMI

Max Yates^{1,2}, Jordan Tsigarides³, Shabina Hayat⁴, Robert Luben⁴, Jack Dainty¹, Kay-Tee Khaw⁴, Nick Wareham⁵, Alex Macgregor¹. ¹University of East Anglia, Norwich Medical School, Norwich, United Kingdom; ²Ipswich Hospital ESNEFT, Rheumatology, Ipswich, United Kingdom; ³Norfolk and Norwich University Hospital, Rheumatology, Norwich, United Kingdom; ⁴University of Cambridge, Department of Public Health and Primary Care, Cambridge, United Kingdom; ⁵University of Cambridge, MRC Epidemiology Unit, Cambridge, United Kingdom

Background: Excess weight and components of the metabolic syndrome have been associated with knee osteoarthritis (OA). However, the precise timing of when this risk operates in the natural history of the disease is unknown. An understanding of the sequence in which risk factors operate in OA is important for delivering effective preventative interventions.

Objectives: We examined longitudinal data from a large prospective population-based cohort to assess the association between metabolic syndrome components and the subsequent development of either knee or hip over 10 years of follow-up.

Methods: Known risk factors data were obtained at enrolment to the EPIC-Norfolk cohort between 1993 and 1997. Data were available on anthropometric variables, smoking status and lipid metabolites. Knee and hip pain were self-reported at 18 months, 3 and 10 years when respondents answered whether they had had pain in their knee or hip on most days in the preceding month. Metabolic syndrome components were defined in line with the Alberti formula. Logistic regression was used to investigate metabolic syndrome components: waist circumference (men >102cm, women >88cm), low HDL (men <1mmol/L, women <1.3mmol/L), high triglycerides (>1.7mmol/L) and their association to incident pain and any effect-modification of dietary patterns and changes in BMI over time.

Results: Amongst 20,517 respondents (age at enrolment 59.7 years (SD 9.2), 56.5% female) there were 3,886 who reported knee pain and 2,467 who reported hip pain at 18 months. By the end of follow-up there were 2619 who had developed incident knee pain and 1752 who had

developed incident hip pain. In a logistic model adjusted for age and sex, significant associations were seen for incident pain for ever-smoking (knee: odds ratio 1.22, 95% CI 1.11, 1.33 $p<0.001$), (hip: odds ratio 1.21, 95% CI 1.08, 1.35 $p=0.001$) and obesity (knee: OR = 1.70 95% CI 1.51, 1.91 $p<0.001$), (hip: OR = 1.68 95% CI 1.47, 1.92 $p<0.001$). After adjustment for obesity, components of the metabolic syndrome associated with pain included waist circumference (knee: OR = 1.17 95% CI 1.03, 1.33 $p=0.019$), (hip: OR = 1.37 95% CI 1.17, 1.59 $p<0.001$) and for knee pain, low HDL (OR = 1.15 95% CI 1.05, 1.27 $p=0.003$) and high triglycerides (OR = 1.10 95% CI 1.00, 1.21 $p=0.043$). These association were not modified by dietary patterns nor changes in weight over the follow-up interval.

Conclusion: This longitudinal analysis shows that metabolic syndrome is a predictor for the future onset of hip and knee pain over an interval of 10 years and the risk is not modified by diet or subsequent weight change. These data suggest that preventative strategies need to be targeted early in the disease course, and should include a range of measures including smoking cessation and those that prevent the onset of metabolic syndrome.

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FRI0658

INCIDENCE AND PREVALENCE OF VACCINE PREVENTABLE INFECTIONS IN ADULT PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIIRD): A SYSTEMIC LITERATURE REVIEW INFORMING THE 2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR VACCINATION IN ADULT PATIENTS WITH AIIRD

Victoria Furer¹, Christien Rondaan², Marloes W. Heijstek³, Ulf Müller-Ladner⁴, Sander van Assen², Jacob M. van Laar³, Marc Bijl², Ori Elkayam¹. ¹Tel Aviv University, Tel Aviv-Yafo, Israel; ²University of Groningen, Groningen, Netherlands; ³Utrecht University, Utrecht, Netherlands; ⁴University of Giessen, Gießen, Germany

Background: Despite the well-established fact of a high burden of infections among patients with autoimmune inflammatory rheumatic diseases (AIIRD)¹, little evidence is available regarding the real incidence and prevalence of vaccine preventable infections (VPI) in this population.

Objectives: To update the evidence on the incidence and prevalence rates of VPI in patients with AIIRD and compare the data to the general population when available.

Methods: A systematic literature review was performed using Medline, Embase, and Cochrane library, from October 2009 to August 2018. Search terms were defined for AIIRD and VPI. Observational studies including cohort studies for incidence rates and cross-sectional studies for prevalence rates were included, as well as systematic reviews of cohort studies and meta-analyses. The primary outcome was the incidence or prevalence of VPI in the adult AIIRD population. Meta-analysis was performed when appropriate.

Results: The search identified 3876 records, out of which 63 met the inclusion criteria. Data on the following VPI rates was retrieved and analyzed: influenza (incidence; $n=4$), pneumococcal disease (incidence; $n=7$), hepatitis B virus (HBV) (incidence and prevalence; $n=10$), herpes zoster (HZ) (incidence; $n=29$), human papilloma virus (HPV) (incidence and prevalence; $n=13$). For influenza, limited data pointed to an increased incidence (409.33 vs 306.12 cases per 100,000 patient-years in patients with rheumatoid arthritis (RA) vs controls, respectively) and influenza-related complications in patients with AIIRD. Data on pneumococcal disease, available mainly for patients with systemic lupus erythematosus (SLE), showed a substantially increased risk in all age groups compared to controls (incidence rate ratio (IRR) 4.7, 95% confidence interval (CI) 3.7-6.0). For HZ, an increased risk was observed across all patients with AIIRD in comparison to the general population: pooled incidence rate ratio 2.4, 95% CI 2.05-2.76, with the highest incidence rate (IR) observed in inflammatory myositis (pooled IR 35.98, 95% CI 32.33-39.64), followed by SLE (pooled IR 18.87, 95% CI 8.7-29.64), and RA (pooled IR 11.64, 95% CI 9.37-13.91). Studies on HPV mainly investigated the SLE population in the Latin America and Asia: HPV pooled prevalence 26%, 95% CI 17%-36% and pooled prevalence ratio 1.58, 95% CI 0.74-3.36 in comparison with the general population. In RA, limited data showed a similar prevalence of HPV in patients and controls: pooled prevalence ratio 0.72, 95% CI 0.46-1.12. For hepatitis B virus, pooled prevalence of hepatitis B surface antigen in patients with AIIRD was similar to the general population, 3%, 95% CI 1%-5%.

Conclusion: Current evidence shows an increased risk of vaccine-preventable infections in patients with AIIRD, emphasizing that prevention of infections is essential in these patients.

REFERENCES:

[1] Falagas ME, Manta KG, Betsi GI, et al. Clin Rheumatol 2007;26(5):663-70.

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FRI0659

REMISSION PERSISTENCE IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHRITIS UNDER BIOLOGIC TREATMENT

Pedro Ávila-Ribeiro^{1,2}, Joao Eurico Fonseca^{1,2}, Elsa Vieira-Sousa^{1,2}. ¹Hospital de Santa Maria, CHULN, Centro Académico de Medicina de Lisboa, Portugal, Serviço de Reumatologia e Doenças Ósseas Metabólicas, Lisbon, Portugal; ²Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Portugal, Unidade de Investigação em Reumatologia, Lisbon, Portugal

Background: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) under biologic treatment are increasingly achieving prolonged remission and tapering treatment is becoming standard practice. However, the optimal timing to start tapering remains unclear and predictors of loss of remission (LOR) are missing. Guidelines disagree on whether to wait for 6 or 12 months of sustained remission before tapering.

Objectives: To determine whether longer sustained remission (6 versus 12 months) influences subsequent LOR rates and to identify predictors of LOR.

Methods: We used the Rheumatic Diseases Portuguese Register (Reuma.pt), to identify RA, PsA and axSpA patients on stable biologic treatment in a single center and retrospectively analyze those who achieved sustained remission for at least 6 and 12 months. Survival analysis was used to characterize stability of remission and identify predictors of LOR. The Cox proportional hazards regression was stratified by diagnosis and adjusted for age, gender, smoking, baseline disease activity, type of biologic, previous switches and starting year of biologic treatment.

Results: 195 patients (100 RA, 51 PsA and 44 AxSpA) of 1078 patients (785 RA, 116 PsA, 177 axSpA) registered in Reuma.pt at a single center and treated with biologics between 1999 and 2018, had at least one remission period with a minimal duration of 6 months. This corresponded to 310 individual remission periods longer than 6 months, 232 of which (74.8%) were longer than 12 months. Median remission time (since the start of remission period) was 78.6 weeks overall vs. 99.0 weeks for patients with a minimum 12 months remission (difference in median survival: 20.4 weeks). PsA patients showed significantly longer remission periods ($p<0.0001$), followed by axSpA and RA. We identified active smoking (HR 1.96, $p=0.008$ for the total population; HR 1.53, $p=0.20$; HR 7.42, $p=0.01$, HR 0.74, $p=0.79$ for RA, PsA and axSpA, respectively), and infliximab use (HR 2.23, $p=0.005$ for the total population; HR 4.07, $p<0.001$, HR 3.20, $p=0.36$, HR 0.62, $p=0.62$ for RA, PsA and axSpA, respectively; subcutaneous TNF inhibitors (TNFi) used as index category) to be significantly associated with LOR. A sensitivity analysis excluding infliximab patients further suggested female gender (HR 3.21, $p=0.005$) and duration of disease until first biologic (HR 1.05, $p=0.031$) as important co-variables.

a)

b)

Figure 1. – time to loss of remission considering a single flare (a) vs. persistent flare (b), all patients (minimum 150 days in remission). Number of failure events indicated in parenthesis

a)

b)

Figure 2. – time to loss of remission considering a single flare (a) vs. persistent flare (b), only patients with minimum 320 days in remission. Number of failure events indicated in parenthesis.