Abstract SAT0692 – Table 1. General characteristics of RA-FDR women, n=882

Table 1. General characteristics of RA-FDR women, n=882		
	ACPA (+) 57 (6%)	ACPA (-) 825 (94%)
General characteristics		
Age, years, median (IQR)	52 (47-60)	45 (34-54) *
Education, years, median (IQR)	14 (13-16)	14 (13-15)
Caucasian, n(%)	51 (90)	770 (93)
Body mass index, kg/m ² , median (IQR)	24 (21-27)	23 (21-26)
Ever smoking, n(%)	32 (56)	378 (46)
Alcohol consumption, n (%)	43 (75)	651 (79)
Rheumatoid factor, n(%)	11 (19)	123 (15)
Reproductive characteristics		
Parous women, n(%)	38 (67)	465 (56)
Number of pregnancies, median (IQR)	2 (2-2)	2 (2-2)
Breastfeeding, [yes/no] n(%)	31 (54)	371 (45)
Breastfeeding, months, median (IQR)	1 (0-4)	0 (0-3)
0 month	26(46)	455(55)
1-7 months	22(39)	284(34)
≥7 months	9 (16)	86(10)

*p-value <0.05, univariable logistic regression.

Conclusions: Among women at risk of RA, breastfeeding was not associated with the presence of ACPA or antiCarP. Our results do not support a protective role of breastfeeding in the development of systemic autoimmunity associated with RA.

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SAT0693 GENETIC POLYMORPHISMS AND EFFICACY OF METHOTREXATE IN RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the DMARD of choice in the treatment of rheumatoid arthritis (RA). There is important variability in its therapeutic response. The identification of genetic factors related to the absorption, metabolism and action of MTX may facilitate a more efficient use.

Objectives: To study the effect of clinical characteristics and different single nucleotide polymorphisms (SNPs), related to the transport and metabolic pathways of MTX, on the therapeutic response of MTX in monotherapy in RA patients.

Methods: Observational study. Outcome variable: response to MTX (DAS-PCR <3.2). Study factors: SNPs of transport (ABCB1 C3435T), glutamation (GGH T16C and FPG G2782A), transmethylation (MTHFR C677T and MTHFR A1298C) and adenosine (AMPD1 C34T, ADA A534G, ITPA C94A). The association between SNPs and therapeutic response was analysed by logistic regression, assessing the allele independence (Hardy-Weinberg equilibrium) and interaction by sex. Different models of SNPs inheritance were analysed. Models were adjusted by the characteristics of the patient, of disease and of treatment. The haplotypes of the MTHFR SNPs (C677T and A1298C) were also analysed.

Results: Bivariate analysis showed lower probability of response with smoking (OR=0.37), erosions (OR=0.26), Mantoux (OR=0.20), disease activity (OR=0.08), previous DMARDs (OR=0.46) and doses of folic acid (OR=0.97), MTX (OR=0.87) and prednisone (OR=0.93), with higher response at a higher age at diagnosis (OR=1.05). In relation to the SNPs, the C/A genotype of the ITPA_C94A decreases the probability of response (OR=0.48) according to an overdominant inheritance model, and the C/C genotype of MTHFR_A1298C is also associated with a lower response according to a model of recessive inheritance (OR=0.18). An interaction between the GGH_T16C SNP and sex was observed, so that the C/C genotype increases the possibility of response in women (OR=2.95), but not in men.

In the adjusted models, only the effect of genotype C/C of MTHFR_A1298C is maintained (OR=0.14), irrespective of age, sex, smoking, alcohol, RF, anti-CCP, erosions, extra-articular manifestations, Mantoux, DAS28-CRP, previous

DMARDs, time to MTX, doses of folic acid, prednisone, MTX and route of administration. On the contrary, the association between the ITPA-C94A polymorphism and the response was not maintained nor the interaction effect of the C/C genotype of GGH_T16C observed in bivariate analysis. Finally, the CC haplotype of the combination MTHFR C677T and MTHFR A1298C is associated with a decrease in the response (OR=0.55) in the adjusted models, so it is an effect independent of the control variables. No interaction effects were observed by sex.

Conclusions: Genetic polymorphisms related to the transport and metabolism of MTX have little effect on the therapeutic response, or at least much lower than other patient (smoking), disease (activity, erosions), or treatment (number of previous DMARDs) characteristics.

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SAT0694 DETERMINANTS OF TRAJECTORIES OF MULTI-SITE PAIN IN KNEE OSTEOARTHRITIS: A 10.7-YEAR PROSPECTIVE STUDY IN OLDER ADULTS

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Background: Pain in osteoarthritis (OA) is very common especially in elderly and commonly occurs at multiple sites. Multi-site pain (MSP) has been shown to be associated with more severe symptoms and worse health-related quality of life compared to single-site pain. Limited evidence exists about understanding the course of MSP and its determinants.

Objectives: To identify distinct trajectories of MSP over 10.7 years in an older population, and to examine risk factors for identified trajectories.

Methods: 1099 participants (mean age 63 years) from the population-based Tasmanian Older Adult Cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. Knee radiographic OA was assessed by X-ray at baseline. Group-based trajectory modelling was applied to identify distinct trajectories of MSP. Multi-nominal logistic regression was used for the analyses with adjustment for potential confounders.

Results: Three distinct MSP trajectories were identified: a group of participants with 'no MSP' (11%), a group with 'fluctuating MSP' (38%), and a group with 'persistent MSP' over time (51%). In multivariable analyses with the 'no MSP' trajectory as reference, emotional problems and comorbidity were significantly associated with both 'fluctuating MSP' and 'persistent MSP' trajectory. In addition, female sex, being obese and radiographic knee OA predicted the trajectory of 'persistent MSP' in the whole population. Results were similar with emotional problems (relative risk [RR]: 2.57 for 'fluctuating MSP' and 5.70 for 'persistent MSP', both p<0.05), being obese (RR: 3.80 for 'persistent MSP', p=0.007) and comorbidity (RR: 2.45, p=0.010) in either 'fluctuating MSP' or 'persistent MSP' trajectory in those with radiographic knee OA.

Conclusions: MSP trajectories appear stable once established and can be predicted by factors both peripheral and central in origin.

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SAT0695 HOSPITALISATION RATES AMONG PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME: A POPULATION-BASED STUDY, 1995-2016

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Objectives: To determine rates and primary discharge diagnoses of hospitalisation in a cohort of patients with incident primary Sjögren's syndrome (pSS) compared to the general population.

Methods: This was a retrospective population-based cohort study focused on Olmsted County, Minnesota. The pSS cohort consisted of patients with incident pSS in the 1976–2015 period and was compared with a cohort of individuals without pSS matched 3:1 for age, sex and calendar year, randomly selected from the same population. Hospitalizations in 1995–2016 were examined. Discharge diagnoses were categorised using the Clinical Classifications Software for ICD-9-CM.

Results: A total of 385 hospitalizations occurred in the 160 patients with pSS during 1592 person-years of follow-up. Among 466 comparators, there were 899 hospitalizations during 4660 person-years of follow-up, resulting in a significantly higher rate of hospitalizations in patients with pSS (rate ratio [RR]:1.25, 95% CI:1.11–1.41). Rates of hospitalisation were increased among patients with pSS for endocrine, nutritional and metabolic diseases and immunity disorders

(RR:1.82, 95% CI:1.08–2.98), diseases of the musculoskeletal system and connective tissue (RR:1.49, 95% CI:1.05–2.05), and for injuries and poisoning (RR:1.46, 95% CI:1.01–2.06). While not significantly increased overall, hospitalizations for diseases of the circulatory system were significantly increased in patients with pSS aged ≥ 75 years (RR:1.54, 95% CI: 1.11–2.11).

Conclusions: Patients with pSS experienced higher rates of hospitalisation than the general population. Hospitalizations for endocrine/metabolic disorders, diseases of the circulatory system, diseases of the musculoskeletal system and connective tissue disorders, and injuries were more common among patients with pSS than comparators.

Disclosure of Interest: None declared

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SAT0696

ASSOCIATIONS BETWEEN ANTIBIOTICS FOR NON-TUBERCULOUS MYCOBACTERIAL INFECTION AND INCIDENT SJÖGREN'S SYNDROME: A NATIONWIDE, POPULATION-BASED CASE-CONTROL STUDY

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Background: We recently reported an association between Sjögren's syndrome (SS) and prior nontuberculous mycobacterial (NTM) infection which was defined as having a diagnosis of NTM with concurrent combinational antibiotics therapy for NTM infection. However, whether the increased risk of SS was attributed to NTM infection or antibiotics used to treatment NTM infection was unknown.

Objectives: To address the association between use of antibiotics which can be used to treat NTM infection and the risk of newly diagnosed SS.

Methods: Using a nationwide, population-based, claims dataset, 5751 newly diagnosed SS were identified, and we further excluded those (n=198) having a history of confirmed or suspected mycobacterial infection to avoid the confounding effect of NTM infection-associated incident SS as we previously identified. A total of 5,553 SS cases were enrolled and compared them with 83 295 non-SS controls matched (1:15) for age, sex, and their year of first SS diagnosis date. The association between the risk of incident SS and antibiotics was determined by calculating odds ratios (ORs) with 95% confidence intervals (CIs) using conditional logistic regression analysis.

Results: After adjusting for potential confounders, the risk of SS was increased in patients treated with new macrolides (aOR 1.95, 95% CI 1.80–2.11), fluoroquinolones (aOR 1.52, 95% CI 1.41–1.64), and tetracyclines (aOR 1.69, 95% CI 1.59–1.79) compared with those in non-SS controls after adjusting for CCI, bronchiectasis and *Helicobacter pylori* infection. Notably, we found that the association was consistent among each antibiotic in these three groups of antibiotics. In contrast to these three groups of antibiotics, usage of amikacin was found to have a negative association with incident SS (aOR 0.68, 95% CI 0.53–0.87).

	Model A	Model B
	aOR (95% CI)	aOR (95% CI)
New macrolide		1.95 (1.80–2.11)
Clarithromycin	1.84 (1.69–2.01)	
Azithromycin	2.07 (1.71–2.51)	
Aminoglycoside		0.68 (0.53–0.87)
Amikacin	0.58 (0.41–0.81)	
Streptomycin		
Kanamycin	0.83 (0.58–1.19)	
Fluoroquinolone		1.52 (1.41–1.64)
Ofloxacin	1.15 (1.01–1.32)	
Ciprofloxacin	1.34 (1.17–1.54)	
Levofloxacin	1.50 (1.22–1.85)	
Moxifloxacin	1.43 (1.30–1.56)	
Tetracycline		1.69 (1.59–1.79)
Doxycycline	1.59 (1.49–1.70)	
Minocycline	1.48 (1.35–1.62)	

Conclusions: New macrolides, fluoroquinolones and tetracyclines were associated with a higher incidence of SS, whereas usage of amikacin had a negative correlation. These findings indicated the need for vigilance of SS in prescribing

these antibiotics to treat NTM and other infectious diseases and warrant further mechanistic studies.

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SAT0697

ASSOCIATION BETWEEN TONSILLITIS AND NEWLY DIAGNOSED ANKYLOSING SPONDYLITIS: A NATIONWIDE, POPULATION-BASED, CASE-CONTROL STUDY

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Background: To date, two most commonly proposed environmental risk factors for ankylosing spondylitis (AS) include mechanical stress at the enthesis and infections. A recent Swedish study showed that childhood tonsillitis was associated with future development of AS. However, no Asian study has reported this association.

Objectives: To investigate the association between tonsillitis and the risk of newly diagnosed AS.

Methods: We used 2003–2012 data from the Taiwanese National Health Insurance Database to perform a nationwide, population-based, case-control study. We identified AS patients newly diagnosed from 2005 to 2012 as the study group and selected sex, age and the year of index date matched (1:6) non-AS individuals as controls. Using conditional logistic regression analysis after adjustment for potential confounders, including a history of periodontitis, appendicitis, and Charlson comorbidity index (CCI), we measured the association of AS risk with prior tonsillitis by calculating odds ratios (ORs) with 95% confidence intervals (CIs). Sensitivity analyses for the association between AS risk and tonsillitis were conducted by varying the definition of tonsillitis.

Results: We identified 37 002 incident AS cases and 2 22 012 matched non-AS controls. The risk of AS was associated with tonsillitis (OR, 1.80; 95% CI, 1.55–2.10) after adjustment for potential confounders. The association between AS risk and a history of tonsillitis remained significant by using various definitions of tonsillitis based on ICD9-CM Codes. Such associations were consistent across various subgroups stratified by age, sex, and a history of periodontitis or appendicitis.

Conclusions: The present study reveals an association between AS risk and prior tonsillitis.

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SAT0698

MORTALITY OF PATIENTS WITH DIAGNOSED RHEUMATOID ARTHRITIS (RA) IN GERMANY 2012: ANALYSIS OF CLAIMS DATA FROM 60 MILLION PEOPLE

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Background: Mortality data of RA patients in Germany are sparse. Recently, data on the prevalence and incidence of RA comprising about 75% of the German population became available.¹ In case of chronic diseases, it is possible to

Abstract SAT0697 – Table 1. Conditional logistic regression analyses for the association between covariates with AS risk

Covariate	Univariate analysis OR (95% CI)	Multivariable aOR (95% CI)	Multivariable aOR (95% CI)	Multivariable aOR (95% CI)	Multivariable aOR (95% CI)	Multivariable aOR (95% CI)	Multivariable aOR (95% CI)	Multivariable aOR (95% CI)
Tonsillitis	1.96 (1.68–2.28)	1.80 (1.55–2.10)						
Chronic tonsillitis and adenoiditis	1.99 (1.38–2.86)		1.83 (1.26–2.64)					
Acute tonsillitis	1.96 (1.67–2.31)			1.81 (1.53–2.13)				
Tonsillectomy	1.89 (1.36–2.61)				1.66 (1.19–2.31)			
Tonsillitis with tonsillectomy	2.06 (1.33–3.19)					1.90 (1.22–2.97)		
Chronic tonsillitis and adenoiditis with tonsillectomy	1.90 (1.19–3.03)						1.73 (1.08–2.79)	
Acute tonsillitis with tonsillectomy	4.00 (1.13–14.18)							4.10 (1.15–14.63)
Periodontitis	1.42 (1.38–1.45)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)	1.32 (1.29–1.36)
CCI ≥ 1	2.22 (2.15–2.29)	2.19 (2.12–2.26)	2.19 (2.13–2.26)	2.19 (2.12–2.26)	2.19 (2.12–2.26)	2.19 (2.13–2.26)	2.19 (2.13–2.26)	2.19 (2.13–2.26)
Appendicitis	1.36 (1.19–1.56)	1.31 (1.14–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)	1.31 (1.15–1.50)

estimate excess mortality of diseased people compared to non-diseased people if prevalence and incidence are known.

Objectives: To compute the mortality in RA patients in comparison to the population without RA in Germany, utilising claims data from 60 million people.

Methods: We used a mathematical relation between the age-specific prevalence, incidence and mortality to estimate the age- and sex-specific hazard ratio (HR) of mortality rates for patients with diagnosed RA compared to patients without RA.² Standardised mortality ratios (SMRs) for men and women were calculated using the sex-specific age distributions in Germany in 2012. In addition, we calculated years of lost life (YLL) for men and women aged 40 and 60 years with diagnosed RA.

Results: Estimation of sex-specific HR in the age range of 40 to 95 years is possible from the data in.¹ The age-specific HRs are elevated in both male and female RA patients (figure 1, left panel and right panel, respectively) with a particular increase in the younger. SMRs in the age range of 40 to 95 are 1.93 and 2.15 for men and women, respectively. YLL at age 40 are 12.0 and 7.5 years for men and women with RA, respectively. The associated YLLs at age 60 are 5.2 and 4.7 years.

Abstract SAT0698 – Figure 1. Age-specific HR for men (left) and women (right) in Germany 2012. Grey regions indicate the range of possible values.

Conclusions: Despite the limitation of the data source (claims data), an estimation of excess mortality in terms of the HR is possible and yields plausible results. The obtained SMRs are similar to comparable populations.³ At age 40 men with RA suffer more from reduced life expectancy than women with RA. At age 60 the difference in YLL between men and women with RA is virtually vanished.

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SAT0699

PREDICTION OF CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS USING A MULTI-BIOMARKER OF DISEASE ACTIVITY

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Background: The ACC/AHA recommends preventive strategies for patients with a high predicted risk of atherosclerotic cardiovascular disease (CVD). RA patients are at higher risk for CVD events, yet the role of systemic inflammation and the influence of traditional CVD risk factors is unclear with respect to risk prediction in RA.

Objectives: A simple and accurate algorithm for predicting CVD event risk that includes systemic inflammation might help risk assessment for RA patients and optimise preventive care.

Methods: We derived a U.S. cohort of RA patients with multi-biomarker disease activity (MBDA) test results linked to Medicare claims data. Patients had to have ≥ 1 year baseline with Medicare coverage prior to the first MBDA test. Exclusions were past MI, PCI/CABG, stroke, or cancer. Follow-up ended at the earliest of 1) CVD event; 2) other than CVD cause of death; 3) loss of coverage; or 4) 12/31/2014. The composite CVD event comprised of incident MI, stroke or fatal CVD event, using validated algorithms. MBDA scores were grouped as low (<30), moderate,^{30–44} and high (>44). Other predictors included demographics, healthcare utilisation, and comorbidities. Three separate models were developed using Cox regression. Model 1 included age, sex and race. Model 2 included age, sex, race, 9 comorbidities and CVD medication classes, plus interaction terms. Model 3 included age, sex, and race plus categorised MBDA score. We calculated the net reclassification index (NRI) for model 2 and 3 compared to model 1. We also plotted the observed vs. predicted probability of CVD event for each model, with risk categorised as low (<7.5), moderate ($7.5–15$) and high (≥ 15) per 1000 person-years based upon annualised ACC/AHA cutpoints.

Results: A total of 15,757 RA patients were included; mean (SD) age 68.6 (10.8) years, 80% female, 80% white. A total 209 CVD events occurred in 14 843 person years (1.41/100 py). The median (IQR) follow up time was 0.84 (0.41, 1.27) year. The maximum event time was at 2.7 year. All models had reasonable discrimination and calibration; model 3 was better than models 1 and 2 and observed vs predicted risk is shown (figure 1). The sum of the absolute difference between observed and predicted probability was 0.56, 0.57 and 0.33 for models 1, 2 and 3 respectively.

Compared to model 1, model 2 resulted in a positive overall NRI of 0.214 (non-event NRI=0.173, event NRI=0.041); model 3 resulted in positive overall NRI of 0.279 (non-event NRI=0.092, event NRI=0.187), consistent with more accurate CVD event classification.