drome (AECG 2002 and ACR/EULAR 2017) did not include major salivary glands ultrasononography (SGUS).
Objectives: The UTOPIA study was undertaken to determine if and how SGUS may improve the ACR/EULAR criteria.
Methods: Twenty four international experts in pSS evaluated on an internet-secure relational database 512 randomly realistic vignettes derived from 150 patients with suspected pSS included in the french DiapSS cohort. Each vignette contained sections on "history" (duration of the symptoms, gender, age), clinical symptoms (dry mouth, dry eyes and systemic manifestations), results of the SGUS evaluation (score > ou < to 2), and results of the major tests to diagnose pSS (Schirmer's test, ocular staining score (OSS), salivary flow, focus score on salivary biopsy, presence of anti-SSA antibodies). Each expert had to score the diagnosis of pSS as absent, unlikely, likely or present for 64 vignettes. Each vignette was evaluated by 3 experts. Diagnosis of pSS was obtained when at least 2 of 3 considered it as likely or present. Univariate and multivariate analysis (Wald test) were performed to evaluate the association between the SGUS criteria, the ACR/EULAR criteria and its different individual items with the diagnosis of pSS as defined by the experts. Data were then replicated on independent cohorts of suspicion of pSS.
Results: Univariate and multivariate analyses confirmed that ACR/EULAR criteria and SGUS were independently associated with the diagnosis of pSS. Disease duration, OSS and ocular dryness were not associated with the diagnosis of pSS. Only 6 variables were selected by logistic regression analysis: presence of anti-SSA (weight:4), focus score (weight:3), SGUS (weight:2), Schirmer's test (weight:1), dry mouth (weight:1) and salivary flow rate (weight:1). According to ROC curve analysis, a score of ≥5 had 96% Se and 84% Sp, compared with 90% Se and 84% Sp for the ACR/EULAR criteria. The corrected C statistic (AUC) for the new weighted score was 0.98.
Conclusions: Inclusion of the SGUS item in the ACR/EULAR criteria improves their diagnostic performance.
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OP0041 ALL-CAUSE, CARDIOVASCULAR AND MALIGNANCY RELATED MORTALITY IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A POPULATION-BASED STUDY

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Background: SLE is associated with increased risk of overall mortality; however morality trends due to specific causes including cardiovascular disease (CVD), malignancies or other causes are largely unknown.
Objectives: Our objective was to assess trends in cause-specific mortality among SLE patients between January 1, 1997 and December 31, 2012 in a general population-based context.
Methods: We conducted a population-based matched cohort on SLE patients diagnosed between January 1,1997 and December 31,2012 using an administrative health database from the province of British Columbia, Canada. We identified all incident cases of SLE and up to 10 non-SLE controls matched on sex, age, and calendar year of study entry. The cohort was divided into two cohorts based on year of SLE diagnosis (1997–2004 and 2005–2012). All-cause mortality and cause-specific incidence of death rates (IR) were calculated. Cox proportional hazard regression models were used to estimate the mortality hazard ratios (HR), adjusting for possible confounders (i.e. Charlson Comorbidity Index, number of outpatient visits, hospitalization, cardiovascular medications, glucocorticoids and NSAIDs at baseline).
Results: 4238 SLE and 42380 matched controls were studied. SLE patients had significantly increased all-cause mortality with HR 1.29 (95% CI, 1.15–1.46) and increased cause-specific mortality from CVD and other causes with HRs of 1.43 (95% CI, 1.15 -1.79) and 1.74 (95% CI, 1.46–2.09), respectively. The cohorts did not differ in the rate of death from malignancy. SLE patients had an approximately 2-fold increase in death from other causes in both early (HR 1.86 (95% CI 1.33–2.60)) and recent cohorts (HR 1.90 (95% CI 1.42–2.56)). There was no significant improvement in all-cause and cause-specific mortality trends between the two cohorts.
Conclusions: This study demonstrates that despite advances in therapy with novel biologic agents, there are no significant differences in all-cause and CVD mortality from SLE between early and recent cohorts. Death from other causes, which includes a composite of death related to for example renal disease and infections, remains high suggesting areas for future targeted research and therapy.
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OP0042 BACTEREMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FROM RELESSER REGISTRY: RISK FACTORS, CLINICAL AND MICROBIOLOGICAL CHARACTERISTICS AND OUTCOMES

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Background: According to RELESSER (Spanish Society of Rheumatology Lupus Registry) data, bacteremia is the main cause of death by infection in systemic lupus erythematosus (SLE). However, the available information about this severe infection in SLE patients remains scarce.
Methods: Retrospective, nested case-control study of SLE patients (ACR-97 criteria) with at least one bacteremic episode and random controls from RELESSER Registry. Descriptive, bivariate and multivariate analysis (logistic regression)
Results: 114 bacteremic episodes in 83 patients were recorded. Incidence rate: 2,7/ 1,000 patient-years (n total: 3658). At the time of the bacteremia: median age: 40.5 (8–90) years, 88.6% female, disease duration: 9.7 (IR16.7), median SELENA-SLEDAI: 4 (IR8), 66% with severe flare (SFI criteria), active nephritis: 16.7%, median SLICC/ACR DI: 3 (IR4), any comorbidity: 64% (McCabe-Jackson criteria: 28.1% rapidly or ultimately fatal), more frequently renal failure (15.8%) or diabetes (11.4%). SLE treatment at the time of bacteraemia: 88.6% corticosteroids (68,6%>10mg/day), 57% immunosuppressors (mycophenolate 17.5% and cyclophosphamide 12.3%), 27% antimalarials. 44.7% suffered invasive procedures, more frequently intravascular catheter (24.6%). The bacteremia was nosocomial in 35.1% and the source was more frequently urinary (27.2%). 64% developed systemic inflammatory response syndrome and 35% needed intensive care unit admission, with multiorganic failure in 22.8%. The most frequent microorganism was *E.coli* (29.8%) followed by *Staphylococcus aureus* (16.7%) (22% methicillin-resistant) and *Salmonella spp.* (10.5%). 16% of the gram-negative enteric bacilli were extended-spectrum b-lactamase positive. 17.5% were multidrug resistant. 68,4% started the antibiotherapy before blood culture results, resulting finally active in susceptibility testing in 56 cases (71.8%), indicating an appropriate empirical antibiotic therapy in 49%. The bacteremia-related mortality was 14%. The risk of death was higher in patients with severe sepsis (Pitt index >8) (OR: 13 (IC95%: 3.71–45.17). The bacteremia was recurrent in 26.3%. Associations with bacteremia in bivariate analysis (114 bacteremias vs 688 controls) are shown in Table 1. Antimalarials were protective. In the multivariate analysis (adjusted for disease duration), only elevated creatinine (OR 1.31 (95% CI 1.01–1.70), p=0.045), diabetes (OR 6.01 (95% CI 2.26–15.95), p=0.000), cancer (OR 5.32 (95% CI 2.23–12.70), p=0.000), immunosuppressors (OR 6.35 (95% CI 3.42–11.77), p=0.000), cyclophosphamide (OR 9.37 (95% CI 5.12–17.14), p=0.000) and SLICC/ACR DI (OR 1.65 (95% CI 1.31–2.09), p=0.000) remained statistically significant.
Conclusions: Bacteremia occurred mostly in active SLE, frequently in the context of a severe flare. Gram negative bacilli predominated, with high rate of multidrug resistance. The empiric treatment was inappropriate in a half of the cases. The

Abstract OP0041 – Table 1. Overall and cause-specific mortality in SLE patients compared to general population; HR, hazard ratio

Cohorts		All-Cause Deaths		CVD Deaths		Malignancy Deaths		Other Causes	
		Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)	Deaths	HR (95% CI)
Overall Cohort	SLE (n=4238)	411	1.29 (1.15–1.46)	104	1.43 (1.15–1.79)	95	0.80 (0.63–1.00)	212	1.74 (1.46–2.09)
	Non-SLE (n=42380)	2226	1	622	1	795	1	809	1
Female Cohort	SLE (n=3643)	323	1.34 (1.17–1.54)	75	1.40 (1.08–1.81)	77	0.81 (0.62–1.05)	171	2.05 (1.68–2.50)
	Non-SLE (n=36430)	1697	1	469	1	618	1	610	1
Male Cohort	SLE (n=595)	88	1.06 (0.81–1.39)	29	1.73 (1.10–2.71)	18	0.76 (0.44–1.30)	41	1.06 (0.70–1.62)
	Non-SLE (n=5950)	529	1	153	1	177	1	199	1
Early Cohort (1997–2004)	SLE (n=1678)	98	1.20 (0.96–1.51)	25	1.18 (0.76–1.82)	22	0.68 (0.42–1.09)	51	1.86 (1.33–2.60)
	Non-SLE (n=16780)	508	1	163	1	173	1	172	1
Recent Cohort (2005–2012)	SLE (n=2560)	137	1.13 (0.92–1.39)	25	0.89 (0.57–1.39)	33	0.66 (0.45–0.98)	79	1.90 (1.42–2.56)
	Non-SLE (n=25600)	622	1	179	1	260	1	223	1

TABLE 1		
	OR	*p*
SELENA-SLEDAI	1.10 (1.06-1.14)	<0.001
SLICC/ACR DI	1.27 (1.16-1.38)	<0.001
Elevated creatinine	2.08 (1.66-2.61)	<0.001
Active nephritis	3.52 (1.94-6.37)	=0.001
Hepatitis C	4.82 (1.89-12.27)	=0.002
Diabetes	3.87 (2.06-7.26)	=0.0001
Cancer	3.60 (2.01-6.42)	=0.000
Corticosteroids (Prednisone > 10mg/day)	1.81 (1.07-3.09)	=0.023
Immunosuppressors	11.44 (7.31-17.92)	=0.000
Antimalarials	0.39 (0.25-0.61)	=0.000
Renal Transplant	5.64 (2.63-12.1)	=0.000
Dialysis	0.39 (0.25-0.61)	=0.000

recurrence and mortality were high. Immunosuppressors use, comorbidity and damage were all associated to bacteraemia.

Disclosure of Interest: None declared

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OP0043 THE NUMBER OF CIRCULATING REGULATORY T CELLS IS REDUCED AND LOW-DOSE IL-2 SELECTIVELY STIMULATES ITS PROLIFERATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The imbalance of T help 17 cells (Th17)/regulatory T cells (Tregs) is considered to be a pivotal cause of autoimmune diseases[1], including systemic lupus erythematosus (SLE). However, previous reports[1,2] describing the respective changes of Tregs and Th17 cells in SLE patients were controversial because a few samples or diverse markers were used to identify Tregs with little consensus.

Objectives: To clarify the status of Tregs and Th17 in SLE, we investigated the frequencies of Tregs and Th17 cells on a large scale and whether those defects can be corrected by the supplementation of low-dose human recombinant interleukin-2 (IL-2).

Methods: Two hundred and thirty-five SLE patients (219 women and 16 men), with mean age of 37.80±14.00 years, were enrolled. The disease activity using European League Against Rheumatism (EULAR) criteria was judged for SLE patients with erythrocyte sedimentation rate (ESR) and SLEDAI scores. The frequencies of CD3+CD4+FOXP3+Treg cells and Th17 cells in peripheral blood from these patients were measured by flow cytometry. And low-dose IL-2 was used among 127 patients at a dosage of fifty WIU every day for five days. Immunological and clinical assessments were performed again at the end of IL-2 treatment. Ninety healthy volunteers, matched for patients' age and gender, were also included for the estimation of CD4+ T cell subsets.

Results: As compared to healthy controls (median of Treg cells: 33.09 cells/ul), the frequencies of circulating CD4+CD25+FOXP3+Treg cells were significantly decreased in SLE patients (median: 15.49 cells/ul, $P<0.001$). The median ratios of Th17/Tregs cells in patients were greatly higher than those of healthy volunteers [0.42 (0.19, 0.88) vs. 0.21 (0.15, 0.34), $P<0.001$]. There was not significantly different in circulating Th17 cell between two groups. Moreover, CD4+CD25+FOXP3+Treg cells were negatively correlated with ESR and SLEDAI score (r=-0.198, $P=0.01$; r=-0.25, $P=0.002$).While no obvious correlation was seen between Th17 cells and SLEDAI score. After IL-2 therapy in SLE, there was a four-fold increase in circulating CD4+CD25+FOXP3+Treg cells [43.73 (24.08,74.22) vs. 11.95 (7.51,20.34),$P<0.001$], whereas Th17 cells were increased slightly. The ratio of Th17/Tregs was decreased significantly in patients with IL-2 treatment [0.19 (0.09,0.41) vs. 0.52 (0.23,0.95),$P<0.001$], tended to balance and had no difference with healthy individual ($P=0.275$).

Conclusions: With the increase of disease activity,CD4+CD25+FOXP3+Treg cells were gradually reducing, while Th17 cells did not show a significant change, indicating that the reduction of Tregs but not the elevation of Th17 cells may be the major reason for imbalance of Th17/Tregs. It is speculated that SLE is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 selectively modulated the abundance of Tregs, which effectively induced autoimmune tolerance and further improved clinical symptoms.

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OP0044 ANTIBODIES ANTI-SACCHAROMYCES CEREVISIAE IN PRIMARY SJÖGREN'S SYNDROME: PREVALENCE, CLINICAL ASSOCIATIONS AND POSSIBLE CROSS-REACTIVITY WITH DISEASE SPECIFIC AUTOANTIGENS

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Background: Saccharomyces cerevisiae is a common yeast used in the food industry. Antibodies against the phosphopeptidomannan part of the cell wall of S. cerevisiae (ASCA) are a well established biomarker of Crohn's disease and have been assessed in several organ-specific and systemic autoimmune diseases (ADs) (1–2) Although the pathogenic significance of ASCA is not yet fully understood, the molecular mimicry of self-antigens in several associated ADs has been suggested as putative mechanism.

Objectives: Since to date ASCA have not been tested in primary Sjogren's syndrome (pSS), the purpose of this study was to assess these antibodies in a large cohort of pSS patients and investigate their significance as potentially helpful biomarker in a clinical setting.

Methods: One hundred and four patients with pSS according to the 2002 American European Consensus criteria and 30 healthy donors (HD) were enrolled. ASCA IgG+IgA were assessed in serum samples with ASCA screen dot (Alphadia sa/nv). T cell phenotyping was performed in paired peripheral blood samples by flow cytometry. To compare the aminoacid sequence of mannan of Saccharomyces cerevisiae and well characterized auto-antigens peculiar of pSS (52kD and 60kD Ro/SSA, La/SSB) we browsed the protein database of the National Center for Biotechnology Information (NCBI) and run the Basic Local Alignment Search Tool (BLAST).

Results: ASCA were detected in 5 out of 104 pSS patients, therefore the prevalence in our cohort is 4.8%. None of the ASCA$^+$ pSS patients displayed IBD or other autoimmune conditions that could account for ASCA positivity. ASCA$^+$ pSS patients displayed more frequently a reduction of C3 and C4 complement fractions as well as pulmonary, articular and cutaneous involvement (all $p<0.05$). Binary logistic regression revealed that ASCA$^+$ pSS patients display an odds ratio of 14 ($p=0.006$) to have cutaneous manifestations of pSS. All ASCA+ patients but only 39% of ASCA- patients displayed anti-Ro52, anti-Ro60 and anti-La autoantibodies together ($p=0.01$). No differences concerning T regulatory and Th17 cell proportion could be observed in ASCA$^+$ compared to ASCA$^-$ pSS patients. S. cerevisiae mannan displays a consistent similarity with 52kD and 60kD Ro/SSA, La/SSB autoantigens. The highest similarity was observed when aligning the mannan with 60kD Ro/SSA (identities 7/11, 64%; positives 8/11, 72%, E value 2.2.).

Conclusions: Our study assessed for the first time ASCA IgG+IgA with a highly specific immunoblot assay in a large cohort of pSS patients, showing that ASCA positivity identifies a peculiar clinical and serological pSS phenotype. In particular, ASCA$^+$ pSS patients display anti-Ro52, anti-Ro60 and anti-La antibodies, low complement and cutaneous involvement. The high similarity between S. cerevisiae mannan and Ro60/SSA autoantigen may suggest that: i. ASCA may bind pSS autoantigens, such as anti-Ro, as already postulated for other autoantigens (2); ii. ASCA may bind more likely Ro60 autoantigen rather than the Ro52 or La autoantigens in pSS. A possible pathogenic/prognostic significance of ASCA in pSS may therefore be speculated.

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OP0045 PREDICTORS OF PERSISTENT DISEASE ACTIVITY AND PERSISTENT LONG QUIESCENCE IN SYSTEMIC LUPUS ERYTHEMATOSUS – RESULTS FROM THE HOPKINS LUPUS COHORT

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Background: Systemic lupus erythematosus (SLE) is characterized by a diversity of disease activity.

Objectives: The aim of this study was to identify prognostic factors of persistent disease activity and persistent long quiescence using baseline demographics and clinical characteristics.

Methods: Patients enrolled in the Hopkins Lupus Cohort from 1987 to 2014, who had at least 3 visits per year during 3 years following cohort inclusion and available information on disease activity were included. Three major patterns of SLE disease activity over time (1 year intervals) based on the modified SLE Disease Activity Index have been previously described: long quiescent (LQ), chronic active (CA) and relapsing-remitting (RR) *(1)*. Based on maintenance of the aforementioned