Results: 202 patients were included, and 140 completed a 12-month-follow-up: 94.0% males, 90.3% Caucasian, mean (SD) age 56.7 (14.1) years, disease duration 8.0 (7.7) years, sUA level 494 (87) $\mu\text{mol/L}$, eGFR 78.0 (18.8) ml/min. 58.6% had college education, 76.9% were married/cohabiting, 18.3% had tophi.

Allopurinol had at baseline previously been used by 30.0% (54/180), colchicine by 51.8% (100/193) and NSAID by 78.6% (154/196).

70.0% (98/140) of the patients were flare-free between 6 and 12 months, and among patients with flares only 10.2% (4/39) were not at treatment target. 80.9% (106/131) were at treatment target at month 12 (sUA<360 or 300 $\mu\text{mol/l}$).

A number of variables at baseline were bivariate ($p<0.05$) related to a flare-free outcome: male gender, low BMI, no previous use of colchicine or NSAIDs, better physical function summary score (SF-36), low level joint pain during strongest attack ever, and high number (>5) of previous gout attacks.

In multivariate logistic regression analyses, also adjusting for age, and gender in the final model, a lower BMI (OR 0.90 per unit, 95% CI 0.83-0.99), low baseline serum urate (OR 0.99 per unit, 95% CI 0.99-1.00) and no previous use of colchicine (OR 4.0, 95% CI 1.6-10.2) predicted a flare-free period between months 6 and 12. When substituted for colchicine, also lack of NSAID use (OR 6.9, 95%CI 1.8-26.1) was a predictor of a flare-free period during this period.

Conclusion: Most patients (70%) did not experience flares during the second half of the first treat-to-target year during ULT. High baseline level of sUA, and high BMI decreased the chance of a flare free period, as did experience with colchicine or NSAID.

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SAT0452 VITAMIN D INSUFFICIENCY AND DEFICIENCY ARE ASSOCIATED WITH A HIGHER LEVEL OF SERUM URIC ACID: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Several studies have revealed a relationship between vitamin D status and a number of non-skeletal health conditions such as insulin resistance, metabolic syndrome, cardiovascular diseases, inflammatory diseases, infection and malignancy. The interaction between serum uric acid and vitamin D has also been observed. A study found that uric acid can suppress 1- α -hydroxylase in vitro and in vivo, leading to the reduction in the conversion of the storage form of 25-hydroxyvitamin D into the active form of 1,25-dihydroxyvitamin D [1]. In fact, several epidemiological studies have suggested that patients with vitamin D insufficiency and deficiency tend to have a higher level of serum uric acid compared to those with adequate vitamin D level although the results were inconsistent across the studies.

Objectives: To compare serum uric level between individuals with normal vitamin D level versus patients with vitamin D deficiency and vitamin D insufficiency.

Methods: A systematic review was conducted using MEDLINE and EMBASE database from inception to October 2018 to identify all studies that compared the level of serum uric acid between individuals with normal vitamin D level and patients with vitamin D insufficiency/deficiency. Eligible studies must be cohort or cross-sectional studies that consisted of two groups of adult participants, one with normal level of vitamin D (vitamin D level >30 ng/ml) and one with vitamin D insufficiency (vitamin D level 20-30 ng/ml) or vitamin D deficiency (vitamin D level of <20 ng/ml). Mean serum uric acid level and standard deviation of participants in each group were extracted from each study to calculate mean difference

(MD) between the groups. Pooled MD was then calculated by combining MDs of each study using random-effects model.

Results: A total of seven cross-sectional studies were eligible for the meta-analyses. Individuals with normal vitamin D level had a significantly lower serum uric acid level than patients with vitamin D insufficiency with the pooled MD of -0.33 mg/dL (95% CI, -0.61, -0.04) (figure 1) and also had a significantly lower serum uric acid level than patients with vitamin D deficiency with the pooled MD of -0.45 mg/dL (95% CI, -0.82, -0.08) (figure 2). The statistical heterogeneity was high with the I^2 of 78% and 89%, respectively. Funnel plots of both meta-analyses were fairly symmetric which did not suggest the presence of publication bias.

Conclusion: Both patients with vitamin D insufficiency and patients with vitamin D deficiency had a significantly higher level of serum uric acid compared to individuals with normal vitamin D level.

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Figure 1. Forest plot of the meta-analysis of vitamin D insufficiency versus normal vitamin D level

Forest plot of the meta-analysis of vitamin D deficiency versus normal vitamin D level

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Infection-related rheumatic diseases

SAT0453 JOINT MANIFESTATIONS OF WHIPPLE'S DISEASE: CLINICAL AND RADIOLOGICAL PRESENTATION OF 19 PATIENTS

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Background: Whipple's disease (WD) is a rare chronic systemic bacterial infection caused by *Tropheryma whippelii*. It affects middle-aged men with diarrhea, weight loss, fever and joint manifestations. It usually develops as oligoarthritis or polyarthritis of large joints. WD may mimic chronic inflammatory rheumatisms. Some studies and case reports show that immunosuppressive treatment can worsen WD¹.

Objectives: Clinical and radiological (radiograph, ultrasound (US), MRI) presentation of joint manifestations of WD.

Methods: This retrospective monocentric observational study was led in Strasbourg University Hospital, Reference Center for Rare Diseases and included patients with WD diagnosed between 2006 and 2017. Patients were included if they had joint manifestations, positive *T.whippelii* polymerase chain reaction in stools or/and saliva, positive *T.whippelii* polymerase chain reaction on duodenal biopsy and/or positive periodic acid-Schiff performed on duodenal biopsy and good evolution with antibiotics.

Results: Nineteen patients including fifteen men were included. The median age at diagnosis was 57. The median time from first symptoms to diagnosis was 60 months. Before the diagnosis of WD, 13 patients had immunosuppressive therapy.

Clinical presentation was: 11 polyarthritis, 3 oligoarthritis, 1 monoarthritis and 4 inflammatory polyarthralgia including 3 with axial pain. Wrists (15/19), ankles (11/19) and knees (10/19) were the most affected. The metacarpophalangeal joints were affected in 8 patients. Eight patients had diarrhoea and weight loss.

C-reactive protein median was 45 mg/l.

Feet and hands radiographies were performed for seventeen patients. Five patients had carpalitis and two patients had tarsitis. Two patients had unilateral sacroiliitis.

Hand and wrist US were performed for twelve patients. Ten patients had joint damage. We found 7 radiocarpal and intercarpal synovitis, including 5 with a positive power Doppler (PD) signal, in 5 patients. US showed one distal radio-ulnar synovitis with no PD signal. Four patients had metacarpophalangeal synovitis including 3 with a positive PD signal. Proximal inter-phalangeal synovitis with no PD signal was found for one patient. There was no involvement of distal interphalangeal joint. Four patients had unilateral tenosynovitis including 2 with a positive PD signal. Feet US were done for ten patients. US showed joint damage for six patients. Three patients had metatarsophalangeal synovitis including one with a positive PD signal. Ankle synovitis with no PD signal was found for two patients. US showed one tarsal synovitis with a positive PD signal. Two patients had tenosynovitis including one with a positive PD signal.

US showed joint abnormalities in 6 patients with normal X-rays.

Hands joints MRI were performed for three patients. Carpalitis was found for one patient. One patient had radio-ulnar synovitis with tenosynovitis. One patient had radio-ulnar synovitis with metacarpophalangeal synovitis. Six patients had one or two erosions on feet or hands: 2 on radiographs, 3 on US and 3 on MRI (including one shown by US).

Conclusion: Clinical and radiological (radiograph and US) joints manifestation in WD affect large joints. However, small joints can also be affected. Axial involvement is rare. WD can affect both joints and tendons. Erosions are rare and never exceed 2 per patient in our series. US can show joint damage whereas radiograph is normal. US should be systematic for patient with WD in order to improve knowledge about this disease and to distinguish it from autoimmune arthritis.

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SAT0454 RHEUMATIC FEVER IN A TERTIARY MEDICAL CENTER – 25 YEARS OF FOLLOW-UP

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Background: Rheumatic Fever (RF) occurs after a pharyngeal infection caused by group A-B-hemolytic streptococci, and is often classified as a connective tissue disease. RF mostly affect children and it's diagnosis is determined using the Jones criteria.

The incidence of **rheumatic fever** and **carditis** in relation to the number of hospitalized patients

Its principal clinical significance is causing carditis at the acute phase of the disease, and valvular impairment, leading to a significant hemodynamic disturbance, as a late sequela.

Despite being a completely preventable disease, Rheumatic fever continues to be the most common cause of acquired heart disease among children in developing countries. In developed countries, a sharp decline in ARF was seen in the last decades.

Objectives: To examine the number of cases of Rheumatic fever in Schneider Children's medical center, and to find whether it has declined during the years of its existence. In addition, to characterize the patient population during that period, determine the clinical characteristics of ARF, It's risk factors and assess the course of the disease and it's treatment. In addition, we will address the relapse rates, with an emphasis on cardiac relapses, with a correlation to preventive treatment.

Methods: A retrospective cohort study was conducted, by collecting data from medical records of patients with rheumatic fever who were admitted to the Schneider Medical Center from 1993 to 2017. A database was built based on these medical records in order to assess the incidence of rheumatic fever and rheumatic heart disease, and the relapse rates, by use of descriptive and survival analysis.

Results: A 402 cases with relevant diagnostic codes were examined during the follow-up period, of which 307 patients met the inclusion criteria. During the acute phase, 197 of the patients (64%) presented with arthritis, 159 patients (52%) with carditis, 47 patients (15%) with chorea, 16 patients (5.2%) with erythema marginatum, and 2 patients (0.7%) with subcutaneous nodules. Carditis was found in higher rates among Jewish patients than among Arabs. 31 patients (19.5%) developed severe carditis, 21 patients (13.2%) of whom developed heart failure signs, 5 were hospitalized in intensive care, and one died. There was a decrease in incidence of rheumatic fever and rheumatic heart disease during the study period. Thirty-two patients (12% of all patients with rheumatic fever) developed a relapse of the disease and 11 of whom (4 percent of all patients) developed a cardiac relapse.

Median follow-up time was 49 months, and relapse rate was 13.9% after 5 years of follow-up. 15% of the patients who received oral prophylaxis experienced relapse, compared to 9% of those who received intramuscular injection therapy.

The rate of recurrence among all patients with rheumatic fever was 2.8% after 2 years of follow-up, and about 7% after 8 years of follow-up. 10 (90.9%) of the 11 patients with cardiac recurrence were present with carditis during the initial disease, with 7 of them (63.6% of patients with cardiac recurrence) having isolated carditis and 3 of them had a combined involvement of arthritis and carditis (27.3% of Cardiac relapses). Only in one case (9.1% of patients with cardiac recurrence) was an isolated occurrence of arthritis in the initial presentation.

It was found that chorea is more common among females.

Conclusion: Despite the reduction in incidence of rheumatic fever and rheumatic heart disease during the study period, the disease remains a significant cause of general and cardiac morbidity among children despite being completely preventable, therefore, It should remain in the mind of every doctor, pediatricians in particular.

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SAT0455 A QUALITY IMPROVEMENT INTERVENTION TO INCREASE INFLUENZA AND PNEUMOCOCCAL VACCINATION RATES IN IMMUNOSUPPRESSED INFLAMMATORY ARTHRITIS PATIENTS

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Background: Disease-related immune dysfunction and medications cause immunosuppression in inflammatory arthritis (IA)(1). EULAR and Centers for Disease Control (CDC) recommend influenza and 23-valent pneumococcal polysaccharide (PPSV23) vaccination. Previous studies show sub-optimal coverage.

Objectives: To increase influenza (annual) and PPSV23 (5 yearly) vaccination in immunosuppressed IA patients through a multifaceted quality improvement intervention.

Methods: Between April and September 2017, IA patients completed an anonymous paper 23 question worksheet recording demographics, medical history, medications, vaccination knowledge, status and barriers. All patients on oral steroids, bDMARDs or immunosuppressant cDMARDs were included.

Simultaneously, we introduced staff education sessions, point-of-care paper "Arthritis and Infection Worksheets" and "Vaccination Advice Letters". In 2018, the clinic was re-assessed.

Results: 163 patients met inclusion criteria in 2017 and 262 in 2018. Patients were typical of an IA clinic (74% women, 45.4% ≥60 years old, 72.7% had RA, 61.1% on cDMARDs, 53.6% on methotrexate, 46.6% on bDMARDs, 23.1% on cDMARD plus bDMARD).

In 2017, 104 (65.4%) knew of the increased infectious risk of IA. In 2018, 168 (65.6%) were aware. Awareness of infection risk with medications increased from 111 (69.8%) to 172 (66.9%).

Table 1 shows vaccination rates. PPSV23 rates increased from 41.0% to 47.2% (P value=0.29, Pearson Chi squared), and influenza from 61.8% to 62.1% (P value=0.95, Pearson Chi squared).

Table 1. Vaccination Rates

Vaccination awareness was higher for influenza (Table 2). Most patients were informed of requirements and vaccinated by general practitioners (GPs), with <5% of patients vaccinated in hospital. In 2017, the most common reason for non-vaccination was lack of awareness. This decreased post intervention. 70% of patients had smart phone access. 78% were willing to use this for vaccination reminders.

Table 2. Vaccination awareness, provision and reasons for non-compliance

	Influenza		PPSV23	
	2017	2018	2017	2018
<u>Aware required</u>	128 (80.0%)	212 (81.9%)	60 (38.0%)	118 (46.8%)
<u>Aware of frequency</u>	133 (99.3%)	219 (99.1%)	59 (75.6%)	98 (65.8%)
<u>Source of awareness</u>				
GP	29 (23.0%)	44 (21.5%)	15 (23.1%)	27 (21.8%)
Hospital	0	12 (5.9%)	0	8 (6.5%)
Clinical Nurse Specialist	0	8 (3.9%)	0	1 (0.8%)
Public Health/Ward Nurse	6 (4.8%)	9 (4.4%)	1 (1.5%)	1 (0.8%)
Radio	5 (4.0%)	6 (2.9%)	0	0
Television				
<u>Site of last vaccine</u>				
GP	93 (78.8%)	149 (77.2%)	53 (89.8%)	98 (90.7%)
Work	7 (5.9%)	14 (7.3%)	0	0
Pharmacy	6 (5.1%)	3 (6.7%)	0	1 (0.9%)
Public Health Nurse	6 (5.1%)	10 (5.2%)	1 (1.7%)	3 (2.8%)
Hospital	4 (3.4%)	5 (2.6%)	3 (5.1%)	4 (3.7%)
Other	2 (1.7%)	2 (1.0%)	2 (3.4%)	3 (2.8%)
<u>Non-compliance reasons</u>				
Unaware	18 (36.7%)	26 (34.2%)	69 (82.1%)	94 (76.4%)
Fear of side effects	12 (24.5%)	18 (23.7%)	7 (8.3%)	10 (8.1%)
Too busy	6 (12.2%)	10 (13.2%)	0	1 (0.8%)
Cost	2 (4.1%)	2 (2.6%)	0 (0%)	1 (0.8%)
Other	13 (26.5%)	22 (28.9%)	8 (9.5%)	17 (13.8%)

Conclusion: This study shows suboptimal vaccination awareness and uptake. Our interventions increased PPSV23 and influenza vaccination rates. There is debate about who is responsible for vaccinations. Guidelines advocate specialists sharing responsibility with GPs. 57% of rheumatologists considered GPs responsible (2). Perhaps, we should take a more active approach.

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SAT0456 SERO-REACTIVITY TO GALACTOSE-ALPHA-1,3-GALACTOSE AND CLINICAL PRESENTATIONS OF PATIENTS SEEN IN A RHEUMATOLOGY OUTPATIENT PRACTICE

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Background: Anaphylactic reactions to cetuximab, a monoclonal antibody used in cancer therapy, were recognized in 2007 as a regional complication related to recognition of a protein epitope by IgE. This protein epitope was defined as galactose-alpha-1,3-galactose (alpha-gal), which is found in non-primate mammalian tissue. Reactivity to this epitope was also found to occur after meat consumption with manifestations including anaphylaxis, urticaria, or angioedema. Further study showed that reactivity was induced by tick bites from the Lone Star tick. Similar cases of reaction to red meat have been described in Australia in 2006, and more recently in Japan and various European countries. In our Rheumatology practices where patients often raise concerns about possible tick-borne illnesses, we have observed patients presenting with symptoms related to consumption of mammalian meat, but generally less severe, and with IgE reactivity to alpha-gal.

Objectives: We have characterized the range of presenting symptoms in our alpha-gal positive patients, and their response to dietary modification.

Methods: Patients referred to this Rheumatology practice who had known exposure or risk factors for tick exposure were tested for IgE antibodies against galactose-alpha-1,3-galactose (alpha-gal) using a standardized test administered by Viacor-IBT, and also tested for typical Rheumatologic markers, as indicated by their symptoms. Alpha-gal IgE levels varied from 0.38 to >100 kU/L (normal <0.35 kU/L).

Results: 147 patients were identified as positive for alpha-gal, and were recommended to avoid mammalian meat. Followup testing and evaluation was achieved in 38 patients, along with documentation of symptoms for improvement or persistence.

Clinical manifestations, laboratory findings, and reasons for referral in symptomatic alpha-gal positive patients were diverse. Dermatologic manifestations occurred in 9 including urticarial vasculitis, serpiginous urticarial rash, purpuric rash, psoriasiform rash, nummular eczema, and subcutaneous nodules.

Arthritic manifestations varied and included monoarthritis (one patient, with negative Lyme PCR of fluid), oligoarthritis in 2 patients, inflammatory polyarthritis in 10 who did not meet criteria for a diagnosis of RA, and polyarthralgia in 22. 15 patients were diagnosed with Rheumatoid Arthritis, and 13 with Spondyloarthritis.

28 patients were referred with positive ANA tests. 25 were felt to be false positive ANAs who did not meet criteria for any connective tissue disease. Anticardiolipin antibodies were present in 4 patients.

Surprisingly only 11 patients had a history of severe reaction to mammalian meat, and only one had been previously diagnosed with mammalian meat allergy

Of the 38 patients seen in followup, 10 reported symptom improvement with mammalian meat restriction.

Conclusion: Alpha-gal reactivity from tick bites is more common than Lyme disease or other tick-borne disease in our catchment area. The patients rarely recall distinct exposure to a Lone Star tick.

Manifestations are protean, and do not correlate with alpha-gal IgE level. Some patients are shown to improve with restriction of dietary mammalian meat. Somewhat surprisingly, other patients prefer to tolerate intermittent mild symptoms to maintain current dietary patterns.