Objectives: To investigate factors associated with the development of sepsis in patients with IMIDs using the Taiwanese National Health Insurance Research Database (NHIRD).

Methods: We identified all biologic-naïve patients with RA, AS, PsO, PsA, or CD/UC from the claim data via the NHIRD who started their first anti-TNF- α agent (etanercept (ETN), adalimumab (ADA) or golimumab (GOL)) between 2003 and 2017 as study subjects. The index date was the first date of anti-TNF- α prescription. Sepsis was defined based on the sepsis-3 definition. We identified sepsis patients using a validated ICD-9-CM coding system proposed by Angus et al, in which a diagnosis of bacterial/fungal infection with one or more acute organ dysfunction is required to define an episode of sepsis. All study subjects were followed up till the date of first hospitalization due to sepsis, 90 days after the last date of anti-TNF- α prescription, withdrawal from NHIRD or death, whichever came first. We used a Cox regression analysis to assess the associations of covariates with the risk of sepsis shown as hazard ratios (HRs) with 95% confidence interval (CIs). Covariates included anti-TNF- α agent, IMID, age, sex, insured amount, level of urbanization, disease duration, Charlson comorbidity index (CCI), a history of prior hospitalization due to sepsis within 3 months before the index date and medication use within 12 months before the index date and during the follow-up period.

Results: We identified 18105 biologic-naïve patients with IMIDs, including 8123 ETN users, 7623 ADA users and 2359 GOL users. The incidence rates (IRs) of sepsis in patients treated with ETN, ADA and GOL were 1080, 1181, and 617 per 10^5 years respectively. Multivariable regression analyses showed that factors associated with an increased risk of sepsis were use of ADA (ETN as reference: HR, 1.21; 95% CI, 1.02–1.42), male (HR, 1.24; 95% CI, 1.04–1.48), age (HR, 1.06; 95% CI, 1.05–1.07), CD/UC (HR, 2.35; 95% CI, 1.57–3.53), CCI (HR, 1.30; 95% CI, 1.23–1.38), prior sepsis (HR, 2.42; 95% CI, 1.78–3.29), prior use of sulfasalazine (HR, 1.25, 95% CI, 1.00–1.55), lower levels of urbanization (level III: HR, 1.37; 95% CI, 1.06–1.77; level IV: HR, 1.68, 95% CI, 1.35–2.10). Factors associated with a decreased risk of sepsis were use of GOL (ETN as reference: HR, 0.59; 95% CI, 0.39–0.84), use of methotrexate (HR, 0.78; 95% CI, 0.65–1.00), and higher insured amount (reference: $\leq$ 15480 NTD; 15480–28800 NTD: HR, 0.83; 95% CI, 0.68–0.99; 28800–45800 NTD: HR, 0.58; 95% CI, 0.45–0.74; $>$ 45800 NTD: HR, 0.33; 95% CI, 0.21–0.54).

Conclusion: Our study revealed that among biologic-naïve IMID patients initiating anti-TNF- α treatment, use of ADA, age, sex, CD/UC, CCI, prior sepsis, prior use of sulfasalazine and lower levels of urbanization were associated with an increased risk of sepsis, while use of GOL, use of methotrexate, and higher insured amount were associated with a decreased risk of sepsis.

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OP0070

THE RISK OF PRECANCEROUS LESIONS OF THE BREAST AND CERVIX UTERI IN PATIENTS WITH AUTOIMMUNE RHEUMATIC DISEASES: A NATIONWIDE POPULATION STUDY IN TAIWAN

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Background: Precancerous lesions are pathologically atypical tissues which share part of abnormal features of cancerous tissue under microscopic

examination but lack the ability of uninhibited growth and distant metastasis. Some of the measures to screen for precancerous tissues have gained popularity because supporting evidence indicates the beneficial effects on cancer incidence and mortality [1, 2]. However, the roles of these screenings and the risk of precancerous lesions in patients with autoimmune diseases have not been clarified. We aim to exam the risk of precancerous lesions among different autoimmune diseases.

Objectives: To determine whether the Taiwanese autoimmune rheumatic diseases (ARDs) patients have a higher risk of precancerous lesions of the breast and cervix uteri.

Methods: The Taiwan national breast cancer screening program provides biennially mammography for women above 45 years old or with a positive family history of breast cancer above 40 years old. The national cervical cancer screening program provides Pap smear test once every three years for women age above 30 years old. Using the National Health Insurance (NHI) database, we identified a cohort of 6 different groups of ARDs patients in Taiwan between 2004 and 2014. We linked the data from the national screening program of breast and cervical cancer and the NHI database to estimate the standardized incidence ratios (SIRs) of precancerous lesions (atypical lobular and ductal hyperplasia of the breast, carcinoma in situ of the breast, cervical intraepithelial neoplasia 1 to 3 of cervix uteri and carcinoma in situ of cervix uteri) in patients with ARDs compared with the general population.

Results: From 2004-2014, we identified 64,904 patients with autoimmune diseases. Table 1 shows the number of patients receiving the screening programs. The standardized incidence ratio (SIR) of precancerous lesion of the breast was elevated in patients with rheumatoid arthritis (SIR, 2.21; 95% CI, 1.21-3.46) and Sjögren syndrome (SIR, 5.77; 95% CI, 2.63-9.85). The incidence of precancerous lesion of cervix uteri was elevated in patients with surveyed ARDs compared with the normal population, particularly for patients with systemic lupus erythematosus (SIR 28.94; 95% CI, 24.52-33.70) and inflammatory bowel disease (SIR, 27.50; 95% CI, 7.40-56.32) (Table 2).

Table 2 Standardized incidence ratio (SIR) of precancerous lesion of the breast and cervix uteri in patients with autoimmune rheumatic diseases

	Precancerous lesion of Breast	Precancerous lesion of Cervix
	SIR (95% CI)	SIR (95% CI)
Rheumatoid arthritis	2.21 (1.21-3.46)	5.32 (4.25-6.50)
Systemic lupus erythematosus	1.34 (0.27-2.93)	28.94 (24.52-33.70)
Sjögren syndrome	5.77 (2.63-9.85)	8.32 (5.72-11.34)
Systemic sclerosis	6.45 (0.72-15.54)	7.93 (2.90-14.80)
Vasculitis	0.00	7.68 (1.54-16.83)
Inflammatory bowel diseases	0.00	27.50 (7.40-56.32)

Conclusion: Precancerous lesions in the breast and cervix uteri were higher in female patients with ARDs and they should receive stringent screening program.

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OP0071

PREDICTING PERSISTENT HIGH-DOSE OPIOID USE AFTER TOTAL KNEE REPLACEMENT

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Table 1 Breast screen and Pap smear test in patients with autoimmune rheumatic diseases

	Rheumatoid arthritis (n=28289)	Systemic lupus erythematosus (n=11609)	Sjögren syndrome (n=17647)	Systemic sclerosis (n=1489)	Vasculitis (n=3050)	Inflammatory bowel disease (n=2820)
Female patients	21199	9808	15785	1043	1225	1034
Breast screening (n, %)	6296 (29.70%)	1382 (14.09%)	4737 (30.01%)	276 (26.46%)	67 (5.47%)	215 (20.79%)
Pap smear (n, %)	12827 (60.51%)	6495 (66.22%)	9961 (63.10%)	670 (64.24%)	1114 (90.94%)	665 (64.31%)

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Background: Patients undergoing total knee replacement (TKR) are at increased risk of persistent opioid use and dependence

Objectives: To identify patients with persistent high-dose opioid use after TKR using group-based trajectory models (GBTM) and determine predictors of persistent high-dose opioid users using pre-TKR patient characteristics

Methods: Using US Medicare claims (2010-2014), we identified patients aged ≥ 65 years who underwent a TKR and had no history of cancer or high-dose opioid use (>25 mean morphine equivalents (MME)/day) in the year prior. All patients were continuously enrolled in Medicare for ≥ 360 days prior to and ≥ 30 days after the TKR. To determine opioid filling patterns after the surgery, patients were followed up to 360 days from the day of TKR. We modeled 12 monthly indicators of opioid prescription fills as a continuous (MME/day) variable using a censored normal GBTM and categorized patients into 4 groups. The primary outcome was persistent high-dose opioid use defined as patients in trajectory Group 3 (38.8 MME/day) or Group 4 (22.4 MME/day). We split the data into training (2010-2013 data) and test (2014 data) sets and used logistic regression to predict high-dose opioid use vs low-dose opioid use (Groups 1 and 2) as a binary outcome utilizing pre-TKR patient characteristics as candidate predictors using the least absolute shrinkage and selection operator (LASSO) regression for variable selection. A reduced model with only 10 pre-specified variables readily available for clinical use was also considered

Results: The final study cohort included 142,089 patients. The GBTM identified 4 distinct trajectories (Group 1- Short-term, low-dose, Group 2- long-term, low-dose, Group 3- medium-term, high-dose, Group 4-long-term, high-dose) of opioid use in the year after TKR (Figure). Using logistic regression and LASSO, we predicted the probability of persistent high-dose opioid use (N=17,171) (vs. low-dose opioid use) in the training set (N=101,810) for an AUC=0.80. The AUC in the test set (N=40,279) predicting high opioid use (N=5,893) was 0.77. The final model selected 33 variables and identified baseline history of opioid use as the strongest positive predictor of high-dose persistent opioid use. The reduced model with only ten predictors also performed equally well (AUC=0.77) (Table).

Conclusion: In this cohort of older patients with no history of cancer or high-dose opioid use at baseline, 16.2% became high dose (28.1 MME/day) opioid users during the year after TKR. Our prediction model with 10 readily available clinical factors may help identify patients at high risk of future adverse outcomes from persistent opioid use and dependence after TKR

Figure. Trajectories of opioid use patterns after TKR

Table. Predictors of persistent high-dose opioid use in the reduced model

Variable	Multivariable Odds Ratio (95% CI)	P-value
Predicting High dose vs. Low dose opioid use		
Age (in years)	0.94 (0.93-0.94)	<0.001
Females (Ref=Males)	0.99 (0.93-1.06)	0.78
White race (Ref=Other)	1.25 (1.04-1.50)	0.02
Baseline opioid use (MME/day)	1.22 (1.22-1.23)	<0.001
Substance use (Yes/No)	1.10 (1.02-1.20)	0.02
Benzodiazepine use (Yes/No)	1.22 (1.12-1.32)	<0.001
Anxiolytic use (Yes/No)	1.30 (1.19-1.43)	<0.001
Anticonvulsant use (Yes/No)	0.94 (0.87-1.03)	0.19
Antidepressant use (Yes/No)	1.03 (0.96-1.11)	0.36
NSAID use (Yes/No)	1.07 (1.00-1.14)	0.04

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OP0072

IDENTIFYING POLYMYALGIA RHEUMATICA RELAPSE AND ITS ASSOCIATIONS IN A RETROSPECTIVE COHORT

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Background: Polymyalgia rheumatica (PMR) relapse occurs frequently when tapering glucocorticoids (GC)¹. Some risk factors for varying definitions of relapse have been identified, although with conflicting results². Identification of relapse and its associations can help identify patients in need of tighter follow up or additional medication.

Objectives: To identify PMR GC-taper related relapse (proportion 1 and 2 years after starting treatment and per year of treatment) and candidate predictors, for a future prediction model.

Methods: In a retrospective cohort of new PMR patients, visiting our hospital from April 2008 – January 2018, all visits > 30 days after starting GC treatment and with > 2.5 mg oral prednisolone were used to identify substantial relapses. Relapse was defined in two ways: rheumatologist judgement (RJ) and treatment intensification (TI). Agreement between RJ and TI at visits was assessed. TI relapse was used going forward for treatment based prediction. The proportion of relapses after 1 and 2 years (cumulative incidence) and the amount of relapses per year of treatment (incidence rate (IR)), were assessed. Unadjusted associations with candidate predictors, present when starting GC treatment, were assessed using logistic and Poisson regression respectively.

Results: Data from 417 patients was used (figure 1). Relapse occurred at 405 and 325 (of 2455) visits based on RJ and TI respectively. TI relapse (cumulative incidence) after 1 and 2 years was 134 (32%) and 184 (44%) and IR was 0.35 per patient year. Unadjusted significant associations for the cumulative incidence were CRP and ESR at baseline, and symptom duration before treatment (table 1), but only CRP and ESR were significantly associated with yearly IR.

Table 1: Associations between predictors and relapse after 1 and 2 years of treatment and the amount of relapses per year of treatment.

Predictors	Within first year		Within first 2 years		Incidence rate	
	OR	CI	OR	CI	IRR	CI
Age – years	1.00	0.98	1.03	1.00	0.98	1.02
Sex – ref. Male	1.44	0.95	2.20	1.38	0.94	2.05
Medical history – ref. No						
- inflammatory	1.18	0.75	1.86	1.00	0.65	1.53
- malignancy	0.69	0.36	1.35	0.96	0.53	1.73
- cardiovascular	1.68	0.07	2.95	1.74	1.00	3.03
Smoking – ref. no, n=336						
Stopped	0.85	0.49	1.46	1.16	0.70	1.92
Yes	0.81	0.412	1.57	0.98	0.53	1.82
Symptom duration before baseline – per week, n=411	0.98	0.96	0.998	0.98	0.964	0.997
Clinical disease severity – score 0-8	0.93	0.82	1.07	0.93	0.82	1.05
(Suspected) presence of peripheral arthritis – ref. No	0.73	0.40	1.33	0.67	0.38	1.16
Presence of systemic symptoms – ref. No	0.78	0.51	1.19	0.84	0.57	1.25
CRP – per mg/L, n=363	1.01	1.00	1.01	1.01	1.00	1.01
ESR – per mm/h, n=396	1.02	1.01	1.03	1.02	1.01	1.03
Hb – per mmol/L, n=316	1.03	0.75	1.39	0.99	0.74	1.32
APR – ref. normal, n=376	0.99	0.41	2.40	0.79	0.34	1.83

Ref., reference category; Hb, haemoglobin; APR, acute phase reactants; CI, 95% confidence interval

Conclusion: PMR relapse while tapering GC occurs frequently, and some – although weak – associations were found. Longer symptom duration before treatment decreased chance of relapse, but did not increase the amount of relapses per year of treatment, potentially indicating a more self-limiting disease course. A uniform definition of relapse and identifying further predictors for a potential prediction model is needed to focus GC sparing agents for patients.