Conclusion: There is an association between use of certain types of antibiotics and the diagnosis of AS, but no dose-response gradient. These data do not support a causal effect of cumulative antibiotic use on the development of AS. More research is needed on the impact of microbiome disturbance on the risk of developing AS.

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OP0068

INCIDENCE AND PREVALENCE OF RHEUMATOID ARTHRITIS IN DENMARK: A NATIONWIDE POPULATION-BASED STUDY INVESTIGATING THE EFFECT OF FOUR DIFFERENT CASE DEFINITIONS

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Background: The incidence rate (IR) and point prevalence (PP) of rheumatoid arthritis (RA) in Denmark is largely unknown. Two challenges in estimating the “true” IR and PP using nationwide registry data are the choice of the RA case definition, and the denominator used, i.e. the exact amount of person years (PY) or census count data.

Objectives: To investigate the incidence and prevalence of RA in the adult Danish population using four different case definitions and two different denominator strategies.

Methods: Nationwide register-based cohort study. Patients with RA between 1996 and the end of 2016 were identified using the Danish National Patient Registry (DNPR) and information on DMARD prescriptions were obtained through linkage with the Danish National Prescription Registry. Age and sex standardised incidence and prevalence of RA were calculated in different ways: we estimated the IR (denominator = actual recorded number of PY in each year using migration and vital data) and the incidence proportion (IP) (denominator = census count data); and the PP (%) of RA was calculated for years 2000, 2009, 2011 and 2016. The four case definitions were: Model A, a first time RA diagnosis (ICD-10: M05-06) in DNPR and a redeemed prescription of a conventional DMARD in the following year¹; Model B, an RA diagnosis recorded twice in DNPR within 90 days with both records originating from a department of rheumatology or general internal medicine²; Model C, any RA diagnosis recorded in DNPR with a DMARD prescription redeemed in the year before or after the diagnosis; Model D, similar to Model A but with the additional requirement that cases had no registered ICD code for inflammatory diseases prior to the RA diagnosis¹.

Results: The overall IR of RA from 1996 to 2016 based on model A was 35.2 (95%CI 34.8 to 35.6) per 100,000 PY while the IP was 34.7 (95%CI 34.3 to 35.1) per 100,000 individuals. The age standardised IR was higher for women than for men (Figure 1), and this was observed across all age groups. The IR peaked at age 70 to 74 in both men and women. Regardless of which case definition was used, the temporal trend showed a peak in IR in 2010 followed by a plateau (Figure 2). The overall PP estimate for all four models increased from 2000 to 2016, data shown for Model A in Table 1.

Table 1. Point prevalence (PP) of rheumatoid arthritis in years 2000, 2009, 2011 and 2016 based on Model A				
	2000	2009	2011	2016
	N = 5906 70.3 % women	N = 15037 70.9 % women	N = 17363 71.0 % women	N = 22991 70.3 % women
	PP (%) (95% CI)	PP (%) (95% CI)	PP (%) (95% CI)	PP (%) (95% CI)
All	0.16 (0.15 to 0.16)	0.37 (0.36 to 0.37)	0.41 (0.41 to 0.42)	0.52 (0.51 to 0.52)
Women	0.21 (0.20 to 0.22)	0.50 (0.49 to 0.51)	0.57 (0.56 to 0.58)	0.71 (0.70 to 0.72)
Men	0.10 (0.10 to 0.11)	0.23 (0.22 to 0.23)	0.25 (0.25 to 0.26)	0.32 (0.31 to 0.33)

Conclusion: A peak in the IR of RA was observed in 2010, regardless of which case definition was used. We believe this was due to introduction of the new EULAR/ACR diagnostic criteria at that time. IP estimates were systematically lower than IRs calculated using exact migration and vital data as denominator. The PP increased over time regardless of which case definition we used. We conclude that the choice of RA case definition had a larger influence than the choice of denominator.

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OP0069

FACTORS ASSOCIATED WITH THE RISK OF SEPSIS IN PATIENTS WITH IMMUNE-MEDIATED INFLAMMATORY DISEASES TREATED WITH ANTI-TUMOR NECROSIS FACTOR-ALPHA: A NATIONWIDE, POPULATION-BASED COHORT STUDY

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Background: Anti-TNF-α agents have been proven to be effective for patients with immune-mediated inflammatory diseases (IMIDs) including rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), Crohn's disease (CD) and ulcerative colitis (UC). Prior studies have shown an increased risk of infection in IMID patients treated with anti-TNF-α but limited studies investigated factors associated with the development of sepsis in patients with IMIDs.

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%)