Abstract OP0227 – Table 2 Association between glucocorticoids and methotrexate with post-operative hospitalised infection among abatacept treated patients, logistic regression model

	Adjusted OR (95% CI)	p-value
Average glucocorticoid dose		
None (n = 764)	Reference	-
≤5mg (n = 454)	1.32 (0.88–1.98)	0.18
5–10mg (n = 232)	2.40 (1.54–3.73)	< 0.001
>10mg (n = 67)	1.73 (0.74–4.06)	0.21
Methotrexate use (n = 573)	0.97 (0.68–1.38)	0.86

Included in the reduced multivariable model but not shown: abatacept stop timing, age, disability, sex, race, median household income, surgery type, chronic kidney disease, surgeon volume. Tested but excluded ($p > 0.2$): osteonecrosis, diabetes, congestive heart failure, asthma/COPD, obesity, Charlson score, previous biologic, hospitalizations, hospitalized infections, number outpatient visits, hospital volume, skilled nursing facility residence, extra-articular RA, region, urban, antibiotics/NSAIDs/opioids past 90 days, year.

Conclusions: Holding intravenous abatacept for ≥ 4 weeks (one dosing interval) was not associated with a lower risk of hospitalised infection, prosthetic joint infection, or 30 day readmission. Glucocorticoid use even at 5–10 mg per day was associated with significantly greater risk of post-operative infection.

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- [1] Goodman SM, et al. ACR/AAHKS Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty. *Arthritis & Rheum* 2017;69:1538–1551.

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OP0228

COMPARATIVE RISK OF BIOLOGIC THERAPIES AND RISK OF GLUCOCORTICOID IN PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING ELECTIVE ARTHROPLASTY

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Background: Patients with RA undergoing major surgery are at high risk for infection. Different biologic DMARDs may be associated with different infection risks.

Objectives: Goals were 1) to compare post-operative infection risk after arthroplasty in patients with RA exposed to different biologics, and 2) examine associations between glucocorticoid use and post-operative infection.

Methods: A retrospective cohort study using U.S. Medicare data from 2006–September 2015 evaluated adults with ≥ 2 ICD9 codes for RA undergoing elective inpatient primary or revision total knee or hip arthroplasty. Eligible patients received an infusion or prescription for abatacept, adalimumab, etanercept, infliximab, or tocilizumab within 8 weeks or a rituximab infusion within 16 weeks of surgery. Patients with hip fracture, malignancy, pre-existing infection, or non-elective surgery were excluded. Average glucocorticoid dose in the 3 months before surgery was calculated from oral prescriptions. Logistic or Cox regression evaluated associations between biologic exposure and post-operative outcomes: 1) hospitalised infection within 30 days (from discharge diagnoses, PPV >80%), 2) rate of prosthetic joint infection (PJI, ICD9 996.66) within 1 year, and 3) 30 day readmission among patients with discharge to home, skilled nursing facility, or inpatient rehab. Propensity scores based on the probability of receiving a specific biologic treatment were used to balance confounders across treatment groups using inverse probability weighting. Similar analyses were used to evaluate associations between glucocorticoid dose and outcomes in the same cohort, using inverse probability weighted analyses based on the probability of being in each glucocorticoid treatment category.

Results: Among 7929 surgeries in 7138 patients, there were 717 (9.0%) hospitalised infections within 30 days of surgery (most commonly urinary, skin/soft tissue, and pneumonia), 192 (2.8/100 person-years) PJI within 1 year, and 465/7554 (6.2%) 30 day readmissions. There was no significant difference in the risk of

hospitalised infection, PJI, or 30 day readmission across biologic treatment groups (table 1). Glucocorticoid dose >10 mg/day (mean 13.5 ± 3.5 mg/day) was associated with a significantly greater risk of hospitalised infection [aOR 2.37 (1.63–3.44)] and prosthetic joint infection [aHR 2.04 (1.09–3.84)] compared to no glucocorticoid use (table 1). Patients with glucocorticoid dose >10 mg also had a numerically greater risk of 30 day readmission that did not reach statistical significance [aOR 1.61 (0.99–2.61)] (table 1).

Abstract OP0228 – Table 1 Associations between preoperative biologic exposure or glucocorticoid dose and post-operative outcomes

	30-day hospitalized infection	1-year prosthetic joint infection	30-day readmission***
	N (%)	N (inc/100py)	N (%)
	aOR (95% CI)	aHR (95% CI)	aOR (95% CI)
Associations with biologic exposure before surgery			
Abatacept (n = 1369)	126 (9.2)	Reference	92/1296 (7.1)
Adalimumab (n = 1284)	108 (8.4)	0.86 (0.63–1.18)	78/1225 (6.4)
Etanercept (n = 1836)	173 (9.4)	1.03 (0.79–1.35)	112/1767 (6.3)
Infliximab (n = 2798)	249 (8.9)	0.96 (0.75–1.24)	143/2673 (5.4)
Rituximab (n = 337)	33 (9.8)	1.10 (0.69–1.75)	21/314 (6.7)
Tocilizumab* (n = 305)	28 (9.2)	1.01 (0.62–1.63)	19/279 (6.8)
Associations with average glucocorticoid dose before surgery			
None (n = 3966)	342 (7.8)	Reference	107/2045 (5.2)
≤5mg (n = 1915)	205 (9.6)	1.18 (0.98–1.42)	90/1026 (8.8)
5–10mg (n = 1033)	121 (11.0)	1.28 (1.01–1.62)	51/530 (9.6)
>10mg (n = 281)	49 (16.1)	2.37 (1.63–3.44)	13/132 (9.9)

Adjusted odds ratios (aOR) and hazard ratios (aHR) from logistic and Cox regression with inverse probability weights, with separate analyses for biologics and glucocorticoids. *Tocilizumab (n = 305) compared to abatacept (n = 941) year 2011–2015 only. **Excluded from adjusted analyses because of inadequate outcomes. ***Readmissions assessed among those with discharge to home, rehabilitation facility, or skilled nursing facility. Inc/100py = incidence per 100 person years. Bolded values are statistically significant with $p < 0.05$.

Conclusions: Risk of hospitalised infection, prosthetic joint infection, and readmission after arthroplasty was similar in patients with RA treated with different biologics. In contrast, glucocorticoid use, especially >10 mg/day, was associated with greater risk of hospitalised infection and PJI.

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OP0229

THE ASSOCIATION OF BIOLOGIC DRUG-LEVELS WITH INFECTION RISK: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICS REGISTER FOR RHEUMATOID ARTHRITIS

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Background: High dose tumour necrosis factor inhibitor (TNFi) drugs are associated with an increased serious infection (SI) risk. It is feasible that high biologic levels predict dose-dependent adverse events such as SI. No registries have systematically evaluated the effect of drug levels on infection risk.

Objectives: To assess the effect of biologic drug levels in rheumatoid arthritis (RA) patients on (i) all infections (AI) (ii) SI (infections requiring hospitalisation, IV antibiotics or lead to death)

Methods: Patients recruited to both the British Society for Rheumatology Biologics Register-RA (safety data) and the Biologics in RA Genetics and Genomics Syndicate (serological samples) were included. Both are large national prospective RA cohorts. Biologic drug levels were measured at 3/6/12 months after biologic initiation and stratified as low/normal or high drug levels (HL) as per thresholds defined using concentration-effect curves for each drug. The risk of first and total infections within the first year was analysed. Events occurring on drug or within 90 days of last dose were included. The risk of an event was compared between low/normal vs HL groups using Cox proportional-hazard models. Factors affecting both drug levels and infection risk were adjusted for in the models.

Results: 703 patients (286 etanercept, 179 adalimumab, 120 certolizumab, 104 tocilizumab and 14 infliximab) had clinical data and serological samples. 74% were women, mean (SD) age 58¹² years, on a first biologic (89%). The crude rate/1000 pyrs was 314 and 464 for AI; 54 and 76 for SI in the low/normal and HL groups respectively. The adjusted hazard ratio for AI within the first year differed significantly between the two groups with the HL group having 50 percent higher risk of AI (HR: 1.51; 95% CI: 1.14, 2.01) (table 1). The most common types of AI in the HL group were lower (34%) and upper (16%) respiratory tract infections, urinary tract infections (15%), skin infections including shingles (8%).

Abstract OP0229 – Table 1

	Low/normal drug level (n=241)	High drug levels (n=462)
All events with follow up censored at 1 year (95% CI)		
All infections (n)	63	232
Crude rate (/1000 pyrs)	314 (245–401)	464 (408, 528)
Unadjusted HR	Ref	1.44 (1.09, 1.91)*
Adjusted HR †	Ref	1.51 (1.14, 2.01)*
Serious infections (n)	11	38
Crude rate (/1000 pyrs)	54 (30–98)	76 (55–104)
Unadjusted HR	Ref	1.36 (0.70–2.67)
Adjusted HR†	Ref	1.17 (0.58–2.30)
First event within 1 st year (95% CI)		
All infections (n)	46	150
Crude rate (1000 pyrs)	229 (172–256)	300 (256–352)
Unadjusted HR	Ref	1.24 (0.89–1.73)
Adjusted HR †	Ref	1.26 (0.91–1.78)
Serious infections (n)	6	22
Crude rate (/1000 pyrs)	29 (13–67)	44 (28–67)
Unadjusted HR	Ref	1.39 (0.56–3.44)
Adjusted HR†	Ref	1.26 (0.50–3.16)

*p<0.05 † Adjusted for age, gender, DAS score, methotrexate use

Abstract OP0229 – Figure 1 All infection Nelson-Aalen cumulative hazard estimates

Conclusions: RA patients with high biologic drug levels have a higher risk of infection. Monitoring drug levels may be helpful in prediction of infection. In disease remission patients with HL, biologic dose tapering may lower infection risk.

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OP0230

PREDICTORS OF HYPOGAMMAGLOBULINEMIA DURING RITUXIMAB MAINTENANCE THERAPY IN RHEUMATOID ARTHRITIS: A 12-YEAR LONGITUDINAL MULTI-CENTRE STUDY

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Background: Rituximab (RTX) is an anti-CD20 monoclonal antibody that selectively depletes B-cell population. One of the drawbacks of a prolonged peripheral B-cell depletion is the suppression of protective antibodies and an increased risk for infectious events. However, few long-term data are available on predictors for the development of low levels of serum immunoglobulins in patients receiving repeated courses of RTX.

Objectives: We aimed at the identification of predictors for hypogammaglobulinemia occurrence in RA patients long-term treated with RTX in a 'real-life' setting.

Methods: Multicenter longitudinal observational usual care study including RA patients according to ACR 1987 and/or ACR/EULAR 2010 classification criteria followed and treated with RTX. A previous study assessing the safety profile of RTX in patients with RA reported a median follow-up of 30 months.¹ Therefore, we decided to include RA patients on RTX maintenance therapy, after a minimal exposition of 30 months. Serum protein electrophoresis was performed before each RTX infusion. Hypogammaglobulinemia and severe hypogammaglobulinemia were defined as total gammaglobulin <6 g/L and <4 g/L, respectively. Safety monitoring included the collection of all adverse events (AE) in particular severe infections.

Results: 134 patients met inclusion criteria: 113 female subjects (84.3%); mean age 52.1±11.4 years. Mean follow-up was 79.5±24.6 months and analysis was based on 854.9 patient-years (pt-yrs). Mean RTX cumulative dose was 12.0 ±4.9 g. Hypogammaglobulinemia (<6 g/L) occurred during the follow-up period in 23 patients (2.7 events per 100 pt-yrs), leading to an incidence of 17.1%. The mean time to development of hypogammaglobulinemia was 64±23 months. A total of 9.7% of patients had severe infections (1.5 events per 100 pt-yrs). Patients who developed hypogammaglobulinemia were more likely to experience severe infections (26.1% vs 6.3%, p=0.033). Univariate Cox analysis identified age over 65 years (HR 4.28 [95% CI: 0.92 to 19.97], p<0.001), low gammaglobulin levels prior the first RTX infusion (<8 g/L) (HR 7.35 [95% CI: 1.82 to 29.68], p<0.001) as predictors of protective factor (HR 0.26 [95% CI: 0.08 to 0.87], p=0.03).

Conclusions: Our results show that gammaglobulin levels of less than 8 g/L at baseline is a strong independent risk factor for developing subsequent hypogammaglobulinemia, whereas concomitant MTX therapy seems to be a protective factor in RA patients treated long-term with RTX. Identifying such predictors will raise clinicians' awareness and allow more tailored monitoring of RA patients long-term treated with RTX.

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Disclosure of Interest: None declared

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OP0231

GASTRO-INTESTINAL PERFORATIONS AMONG RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGIC DMARDS: A NATIONWIDE SWEDISH COHORT STUDY

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Background: Use of glucocorticosteroids and NSAIDs for the treatment of RA has been associated with an increased risk of gastrointestinal (GI) perforations. The introduction of disease modifying agents, such as methotrexate or tumour necrosis factor inhibitors (TNFi) provided a seemingly safer treatment option, but the safety of other types of biologics relative to TNFi remains unclear.

Objectives: To estimate the incidence of gastro-intestinal perforations among Swedish RA patients treated with TNFi and non-TNFi biologics, and compare it with the incidence among bionative patients with RA and a matched general population comparator group.

Methods: We performed a register-based cohort study, including all Swedish RA patients, with follow-up between 2010 and 2015. For these, all treatment initiations with biologic disease modifying anti-rheumatic drugs were identified through the Swedish Rheumatology register (SRQ), and grouped by class into TNFi and non-TNFi drugs (10 857 and 5823 treatment starts). Biologics naïve patients with RA were identified by recorded diagnosis in the Swedish National Patient Register (NPR), since 2001 (n=54,732). Five general population controls were matched to