Table 1. Data on incident SpA patients between 2010-14, divided into two groups depending on whether bDMARDs were introduced (group B) or not (group A). Pain medication and DMARD use during the whole first year after the ID are shown.

	Group A N=2741	Group B N=836	p-value
Age, mean (SD)	39 (13)	38 (11)	0.16
Proportion of females,%	53	49	0.048
Pain medication,%			
Paracetamol	21.1	24.9	0.020
NSAID	71.9	78.5	<0.001
Opioid	18.2	33.0	<0.001
DMARDs			
None	3.6	0.2	
Methotrexate	29.9	53.8	<0.001
Sulphasalazine	84.5	78.6	<0.001
Prednisolone	33.8	47.0	<0.001
Other csDMARDs	6.5	9.8	<0.001
bDMARDs	0	58.0	..

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FRI0373 5-YEARS TREATMENT EFFECT OF TNF ALPHA INHIBITOR IN EARLY AXIAL SPONDYLOARTHRITIS AND ASSOCIATED FACTORS: AN INVERSE PROBABILITY WEIGHTING ANALYSIS OF THE DESIR COHORT

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Background: Only scarce data is available on the long-term treatment effect in a real-life setting (i.e. effectiveness) of TNFi in early axial SpA forms and its predisposing associated factors; furthermore, unbiased evaluation of treatment effect in non-randomized clinical trials is challenging, and new methods have been developed to overcome prescription bias.

Objectives: a) to estimate the probability to initiate a TNFi over 5 years of follow up in real life setting using novel statistical methods to overcome prescription bias; b) to determine the long-term effectiveness of first TNFi and its predictive factors.

Methods: Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naïve patients early axial spondyloarthritis. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist's. The probability to initiate a TNFi was estimated by the Kaplan Meier Method, assuming non informative dropouts. Effectiveness of the first TNFi was defined as the probability to reach an ASAS40 response in both groups (TNFi vs. any other treatment) after at least 10months of exposure. To evaluate treatment effect and overcome prescription bias repeatedly occurring over time, we have applied an iterative method based on inverse propensity score (PS) weighting using a marginal structural model, that allows the integration of the repeated weights derived from the propensity score at each visit (i.e. the probability to receive the treatment at each visit). The structural model used for this analysis was a PS-weighted cox regression, to estimate the probability to present an ASAS40 response after at least 10 months of treatment. Factors predicting first TNFi effectiveness, were explored by Cox (univariate and then multivariate) regression models.

Results: Of the 708 patients included in the analysis, 258 patients initiated a first TNFi during the first five years of follow up. The probability to initiate a TNFi treatment was 41.3% [95%CI 37.2-45.1]. Among the 258 patients who received a first TNFi, 163 (63.2%) were exposed for at least 10 months. On the original data, ASAS40 response was observed in 50/163(30.7%) vs. 58/450(12.9%) patients from the TNFi and usual care groups, respectively. The likelihood of an ASAS40 response was greater in the TNFi exposed group (HR= 3.3[95%CI 2.9-3.8], p <0.0001). Male gender (HR=1.5[95%CI 1.1-2.1]), HLAB27+ (HR= 1.4 [95%CI 1.1-2.0]) and the presence of at least one objective sign of inflammation

(MRI or CRP) or structural damage (radiographic sacroiliitis) (HR= 1.7 [95%CI 1.2-2.4]) were jointly predictive of an improved outcome.

Conclusion: Our study, applying novel statistical techniques to overcome prescription bias, confirms the 5-year effectiveness of TNF alpha inhibitors (TNFi) in patients with early axial Spondyloarthritis (axSpA), and we confirm that male gender, with HLAB7 positive and the presence of at least one objective sign of inflammation or structural damage are more frequently associated with such effectiveness.

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FRI0374 THE RISK OF INFECTION BY TUMOR NECROSIS FACTOR INHIBITORS AND ITS ASSOCIATED FACTORS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULT FROM KOREAN NATIONAL HEALTH INSURANCE DATA

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Background: Tumor necrosis factor inhibitors (TNFi) are effective in patients who do not respond to non-steroidal anti-inflammatory drugs, or disease modifying anti-rheumatic drugs, and have been widely used in patients with ankylosing spondylitis (AS). However, there is some evidence that treatment with TNFi can increase the risk of infection in patients with AS.

Objectives: The aim of this study was to investigate the risk of infection in patients with AS treated with TNFi.

Methods: Data was obtained from insurance claims database of the Health Insurance Review & Assessment Service (HIRA) in South Korea. Patients who have been prescribed a TNFi such as etanercept (ETN), adalimumab (ADA), golimumab (GLM), and infliximab (IFX) to treat AS from 1 July 2012 to 30 June 2017 were enrolled. We evaluated the incidence rate (IR) and hazard ratio (HR) of serious infections including pneumonia, tuberculosis, and herpes zoster in each TNFi treatment group by using cox proportional hazard model. We further analyzed the HR of infection by sex.

Results: A total of 2,515 patients were included in the study, and they were prescribed ETN (n=528), ADA (n=914), GLM (n=628), or IFX (n=445). The IRs of serious infection were 1668.63, 1489.88, 1457.58, and 1399.16 per 1,000 person years (pys) in ETN, ADA, GLM, and IFX treated groups, respectively. There was no significant difference in HR of serious infection between the TNFi groups. In the subgroup analysis of major infections, there was no difference in the HR of pneumonia between TNFi groups. However, the HR of tuberculosis with IFX group was significantly higher than that with ETN (adjusted HR 8.95, 95% CI: 1.12-71.4). In herpes zoster infection, there was no difference between TNFi groups in all patients, but the adjusted HRs significantly increased with GLM (adjusted HR 15.40, 95% CI: 1.64-144.34) and IFX (adjusted HR 10.02, 95% CI: 1.12-89.9) treatment as compared to ETN in female patients.

Conclusion: Patients receiving IFX had a higher risk of contracting tuberculosis than those receiving ETN. Moreover, the risk of herpes zoster was higher in female patients treated with GLM and IFX than in those treated with ETN in Korea.

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FRI0375 SITE-SPECIFIC EFFECTIVENESS OF TNF INHIBITORS FOR ENTHESITIS IN DMARD-NAIVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Enthesitis is a hallmark of spondyloarthritis (SpA), with substantial impact on quality of life. Although pathophysiological mechanisms of enthesitis may include both mechanical and autoimmune features, improvements upon initiation of TNF-inhibitors (TNFi) across individual enthesitis sites have not been reported in real-world patients with axial spondyloarthritis (axSpA).

Objectives: To investigate the effectiveness of TNFi in axSpA patients without prior DMARD treatment at specific enthesitis sites, including spine, thoracic cage, Achilles tendon and the plantar fascia.

Methods: This was a retrospective cohort study using the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry. AxSpA patients initiating TNFi without previous DMARD (biologic or conventional synthetic DMARD [csDMARD]) use and with available Maastricht Ankylosing Spondylitis Enthesitis Score, modified to include the plantar fascia, (MASES) at start of treatment ('baseline') and after 6 months ($\pm$ 3 months) of follow up were included. Presence of enthesitis was defined as at least 1 inflamed enthesitis. Among patients with any enthesitis present at baseline, the number of patients with enthesitis at each MASES site was assessed at baseline and the 6 month follow up. Fisher's exact test was used to assess significant enthesitis resolution at each enthesitis site between baseline and 6-month follow up. The Holm-Bonferroni method was used for multiplicity correction of p-values.

Results: 781 DMARD-naïve patients with axSpA who initiated TNFi were identified. At baseline, patients (57% male) were a median of 40 (interquartile range [IQR]) = 31-50 years of age with a median disease duration of 9 (IQR = 3-18) years and median Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) of 3.4 (IQR = 2.8-3.9) at treatment initiation. A subgroup of 160 TNFi patients had active enthesitis at baseline (MASES: mean = 4.14, standard deviation [sd] = 2.87) and a 6-month follow-up visit with MASES available (MASES: mean = 2.07, sd = 2.82), with a mean MASES reduction at the follow-up visit of 2.07 (sd = 3.06). At the 6-month follow up, complete enthesitis resolution was observed for 72 (45.0%) of patients. Enthesitis resolution was most frequent at the following sites: the costochondral sternum, the costochondral joint, the lumbar vertebra, the pelvic crest, and spina iliaca posterior (Figure 1). Limited resolution of enthesitis was observed in the spina iliaca anterior, plantar fascia, and the Achilles tendon.

Conclusion: Our results suggest that for real-world DMARD-naïve axSpA patients, TNFi are generally effective for resolving enthesitis. Significant

resolution was observed for enthesitis of the spine and thoracic cage though resolution was more limited for plantar fascia or Achilles tendon enthesitis. Lower limb entheses are more prone to mechanical strain and may therefore require alternative or more prolonged therapy.

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FRI0376 DIFFERENCES IN PHYSICAL ACTIVITY BETWEEN AXIAL SPONDYLOARTHRITIS PATIENTS WITH AND WITHOUT PHYSICAL THERAPY

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Background: Physical activity (PA) according to public health guidelines is effective and safe for people with rheumatic and musculoskeletal diseases, including axial spondyloarthritis (axSpA), and should be promoted by healthcare providers.¹ In axSpA, in particular high intensity aerobic PA is beneficial, yet this was found to be incompletely implemented in physical therapy programs.² Studies describing aerobic PA in axSpA patients with and without physical therapy are lacking.

Objectives: To describe the amount, frequency and intensity of aerobic PA in axSpA patients with and without physical therapy treatment.

Methods: A survey, which included questions on patient characteristics, current physical therapy use (individual or group), PA (Short QUEStionnaire to ASess Health-enhancing PA (SQUASH)) and health status (Assessment of Spondyloarthritis International Society Health Index (ASAS HI)), was sent by postal-mail to 458 axSpA patients registered in three hospitals in the Netherlands. From the SQUASH, besides amount (minutes/week) of all PA and meeting the PA guideline (≥ 30 minutes $\geq$ moderate PA on ≥ 5 days/week; yes/no), also the amount and frequency (sessions/week) of moderate and vigorous intensity aerobic PA during commuting and leisure (including sports) were extracted. Differences in PA behaviour between patients with and without current physical therapy were analyzed with the Mann-Whitney U or Chi-square test, where appropriate.

Results: The questionnaire was returned by 206 axSpA patients (response rate: 45%) of whom 200 completed the SQUASH correctly. Overall, 64% met the PA guideline. Half of the patients were using physical therapy (n=99; 77 individual, 11 group and 11 both); these patients had a significantly longer disease duration. Regarding overall PA, there were no differences in the total amount and the proportion meeting the guideline between patients with and without physical therapy. For moderate intensity aerobic PA, both the amount and frequency were significantly greater in the group with physical therapy, whereas for vigorous intensity aerobic PA there were no differences between the groups (Table 1).

Conclusion: More than half of people with axSpA were physically active according to public health PA guidelines. People using physical therapy engaged in significantly more moderate intensity, but not high intensity aerobic PA than those without physical therapy. These results indicate that high intensity aerobic PA should be more intensively advocated and implemented, also in physical therapy treatment.

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