which was supplemented by hand-search. Titles and abstracts were screened by two independent reviewers, who subsequently evaluated and extracted data from full-text of selected articles. Pooled meta-analysis was performed using random-effects weighting.

Results: Of 1014 articles identified, 40 were selected for full-text review and 13 studies reporting on CVDs were included in the systematic review (Figure 1). The first was published in 2009 and five were published in 2018 or 2019 alone. The included studies were of varying quality in regards to satisfying the assumptions for MR design.

Overall, there was little evidence for a causal association between SU and risk of CVDs (Table 1). Random-effects meta-analysis revealed that SU was not significantly associated with risk of CVDs (OR=1.04; 95% CI=0.99-1.09) (Figure 2). 11 of the 13 studies reported null estimates for the effects of genetically-determined SU levels on CVDs. Two studies with small numbers of cases (N=125 and 222) reported significant associations, but these pertained to highly-specific subgroups.

Table 1. Summary of included studies. CAD: Coronary Artery Disease; CHD: Coronary Heart Disease; IHD: Ischaemic heart disease; MI: Myocardial Infarction; MR: Mendelian Randomization; PVD: Peripheral Vascular Disease; SNP: Single Nucleotide Polymorphism

First author; year	Number of SNPs analyzed	Outcome (n cases)	Power	MR criteria validated: 1. relevance 2. pleiotropy 3. confounding	Conclusion
Stark; 2009	10 separately	CAD (1,473)	30%-66%	1, 3	Null
Yang; 2010	8 combined	CHD (3,050)	<80%	1, 2, 3	Null
Palmer; 2013	1 (rs7442295)	IHD (3,742)	N/A	1, 2*, 3	Null
Kleber; 2015	8 combined	CAD (2,418)	N/A	1, 2, 3	Null
		PVD (295)			
Han; 2015	2 separately	CHD (1,146)	80%	1, 2*, 3	Null
Testa; 2015	1 (rs734553)	CVD events (CVD death, stroke, MI) (222)	N/A	1, 2*	Significant for CV events
White; 2016	31 combined	CAD (65,877)	83%	1, 2, 3	Null
Keenan; 2016	14 combined	CHD (54,501)	>80%	1, 2, 3	Null
		Stroke (14,779)			
Li; 2018	31 combined	IHD (9,467)	70%	1, 2, 3	Null
		MI (3,625)			
Li; 2019	31 combined	CHD (60,801)	N/A	1, 2, 3	Null
		MI (43,676)			
		Stroke (10,307)			
Macias-Kaufer; 2019	2 separately	CAD (704)	N/A	1, 2*, 3	Null
Efstathiadou; 2019	28 separately	CHD (184,305)	>80%	1, 2, 3	Null
		MI (54,162)			
		Stroke (514,791)			
Chiang; 2019	8 combined	CHD (125)	N/A	1, 2, 3	Significant for CHD
		Stroke (57)			

* Risk of pleiotropy (assumption 2) is low when utilizing few well-established SNPs

Fig. 2 : Pooled meta-analysis results.

Conclusion: Evidence from this systematic review does not support a causal role for SU levels and CVDs. As such, interventions targeting SU levels alone are unlikely to lower the risk of CVDs.

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FRI0533

SMOKING AS A PREDICTIVE FACTOR FOR SPONDYLOARTHRITIS RELATED UVEITIS: RESULTS FROM A SINGLE CENTRE CROSS-SECTIONAL STUDY.

E. Costa¹, D. Almeida^{2,3}, M. Cerqueira², J. Redondo Costa², A. R. Ribeiro², J. Neves². ¹Hospital de Braga, Rheumatology, Braga, Portugal; ²Hospital de Braga, Rheumatology, Braga, Portugal; ³Unidade Local de Saúde do Alto Minho, Rheumatology, Ponte de Lima, Portugal

Background: Although spondyloarthritis (SpA) is primarily a musculoskeletal condition, ocular involvement is an important clinical feature and contributes to the burden of disease. Acute anterior uveitis (AAU) is classically described as the most frequent extra-articular manifestation of SpA and in some cases the first clinical presentation. The prevalence of AAU varies according to the sub-type of SpA. In a systematic literature review, the mean prevalence of AAU was 32.7% and a positive association between HLA-B27 positivity, axial SpA, male sex and uveitis has been reported (1). More recently, some cross-sectional studies have described lower odds of spondyloarthritis-related uveitis (SpA-U) in smokers than in patients who are ex smokers or never smokers (2). Predictors of SpA-U are poorly defined in literature and the influence of smoking status remains controversial.

Objectives: To analyse the factors associated with uveitis in SpA patients in a Tertiary Rheumatology Center.

Methods: An observational cross-sectional study was performed including patients fulfilling the ASAS criteria for axial SpA with a follow-up visit between January and June 2019. Clinical patients' charts were reviewed and the following variables were considered: age, gender, history of uveitis (confirmed by ophthalmologist observation), number of AAU episodes, smoking status (never smoker or ever smoker), HLA-B27, disease duration, disease involvement (exclusively axial or axial and peripheral), history of enthesitis and syndesmophytes. History of AAU and associated variables were determined in this subset of patients.

Statistical analysis was performed with logistic regression model. P value <.05 was defined as statistically significant.

Results: The study included 164 patients (62.3% men) with median age of 44.0 years (IQR 37 to 54) and a median disease duration of 14.6 years (IQR 9.28 to 20.32). SpA diagnosis was ankylosing spondylitis in 70.7% cases and the remaining were non-radiographic axial SpA. HLA-B27 was positive in 84.8%, 31.1% of patients were ever smokers and 21% had both axial and peripheral joint involvement. Twenty four percent of patients had at least one AAU episode. Recurrence of uveitis occurred in 70% of patients. Ever smoking (OR=2.256; 95%CI [1.077-4.276]; p<.05) and syndesmophytes (OR=2.125; 95%CI [1.009-4.475]; p<.05) showed a statistically significant association with uveitis in univariate logistic regression. Although not statistically significant, a trend to association was found between smoking and recurrence of AAU (OR=2.235; 95%CI [0.973-5.135]; p=.058). In multivariate logistic regression only ever smoking was independently associated with uveitis (OR=2.542; 95%CI [1.007-6.420]; p<.05). We did not find association between presence of uveitis and gender, age, disease duration, disease involvement, HLA-B27 positivity and enthesitis.

Conclusion: Contrary to few cross-sectional studies showing a possible protective effect of smoking in SpA-U, and in line with new data from Zhao *et al* (3), we report a statistically significant independent association between history of smoking and uveitis. Nevertheless, we emphasize the need of more studies to confirm these findings.

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FRI0534

PATIENT-REPORTED MEASURES OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS VARY ACROSS THE NORDIC COUNTRIES, RESULTS FROM A NORDIC COLLABORATION

B. Delcoigne¹, S. Aarrestad Provan², H. B. Hammer², D. Di Giuseppe¹, T. Frisell¹, B. Glintborg³, G. Gröndal⁴, B. Gudbjörnsson⁵, M. L. Hetland³, B. Michelsen², D. Nordström^{6,7}, H. Relas⁷, N. Steen Krogh⁸, J. Askling¹. ¹KI, Stockholm, Sweden; ²DH Hosp., Oslo, Norway; ³DANBIO, Glostrup, Denmark; ⁴LUH, Reykjavik, Iceland; ⁵ICEBIO, Reykjavik, Iceland; ⁶UH, Helsinki, Finland; ⁷HU Hosp., Helsinki, Finland; ⁸Zitlab Aps, Frederiksberg, Denmark

Background: Disease activity in rheumatoid arthritis (RA) patients is measured through composite scores which are considered treatment targets and thus facilitate clinical decision making. Scores often combine a mix of objective and

subjective measures, and, although the latter (e.g. pain, patient's global, 28 tender joint count (TJC)) may be impacted by contextual and cultural factors, these clinical metrics are often assumed to be comparable across different settings and reflecting the RA disease.

Objectives: To explore whether there are systematic differences in patient-reported measures of RA disease activity (i.e. TJC and a measure of pain on a Visual Analog Scale (VAS)) across countries, at similar time-points in the course of the RA disease, taking objective measures of concomitant disease activity and other factors into account.

Methods: RA patients starting a first ever tumor necrosis factor inhibitor (TNFi) 2008 through 2017 were identified in rheumatologic registers in five Nordic countries. Data were pooled for analysis. Clinical metrics were retrieved at three time-points: at TNFi start, and after three and twelve months, irrespective of treatment. Baseline clinical variables distributions were compared between countries. The correlation between pain and patient's global VAS was calculated with the Pearson correlation coefficient (r). At each time-point the subjective measures (TJC and pain) were compared between countries and analyzed with linear models: (i) crude; (ii) adjusted for age, sex, birth decade, disease duration (DD), year of TNFi treatment start (year), C-reactive protein (CRP) and 28 swollen joint count (SJC)) from the time-point in question.

Results: A total of 23 796 RA patients were included (Table 1). At baseline, the significant differences between Nordic countries for TJC and pain (crude model) were slightly modified after adjustment but remained statistically significant (Table 2). Compared to baseline, the inter-countries differences were reduced at 3 and 12 months, but also were statistically significant (Figure 1).

Figure 1: Country-specific cross-tabulation of median values of subjective measures (y axis: TJC, Pain VAS) versus objective measures (x axis: CRP, SJC). Baseline TNFi start (upper panel) and at 3 months (lower panel).

Table 1. RA patients starting a first TNFi baseline characteristics, median [Interquartile range].

	Sweden	Denmark	Finland	Norway	Iceland
N (% female) [†]	13621 (75)	6701 (75)	1946 (73)	1113 (71)	415 (73)
CRP (mg/L) [‡]	6 [3-17]	9 [3-20]	8 [3-20]	6 [3-14]	8 [3-19]
Physician's global VAS [‡]	30 [14-50]	31 [19-47]	35 [20-50]	32 [23-45]	60 [43-70]
Patient's global VAS [‡]	50 [28-70]	67 [46-82]	50 [28-70]	48 [26-69]	71 [53-86]
Pain VAS [‡]	50 [26-70]	60 [37-76]	52 [30-71]	42 [23-65]	67 [49-79]
SJC [‡]	4 [1-8]	4 [1-7]	4 [1-9]	4 [1-7]	6 [3-11]
TJC [‡]	4 [1-9]	6 [3-11]	4 [1-10]	4 [1-9]	7 [4-12]
DAS28 [‡]	5 [3-5]	5 [4-5]	4 [3-5]	4 [3-5]	5 [4-6]

[†] Patient's global and pain correlation: $r=0.85$

[‡] χ^2 test; p -value=0.04

[‡] One-way ANOVA; all p -values < 0.001

Table 2. Mean crude and adjusted differences in baseline TJC and pain between countries, using the largest (Sweden) as reference.

	SE	DK	FI	NO	IS
Crude model					
TJC	ref	1.8	0.8	0.5*	3.7
Pain	ref	7.2	1.4 [†]	-4.0	11.1
Adjusted model [‡]					
TJC	ref	2.3	0.7	0.6**	2.4
Pain	ref	7.9	0.7 ^{NS}	-3.3	7.2**

All p -values <0.001 except: ^{NS} > 0.10; [†] < 0.10; * < 0.05; ** < 0.01

[‡] adjusted for age, sex, birth decade, year, DD, CRP, SJC

Conclusion: In this observational study of 23 796 RA patients from 5 Nordic countries starting 1st TNFi, patient-reported variables related to RA disease activity (pain VAS, TJC) varied across countries. These differences were not explained by differences in demographic (age, sex, birth decade, year) or objective RA

measures (DD, CRP, SJC). This implies a limit to the direct comparability of results obtained from subjective measures from different countries.

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FRIO535

NEWLY DETECTED HYPERTHYROIDISM WITH THERAPEUTIC INDICATIONS IN RHEUMATIC DISEASE PATIENTS AND HEALTHY CONTROLS IN JAPAN: A RETROSPECTIVE COHORT STUDY

S. Fukui¹, Y. Ikeda¹, G. Kidoguchi¹, T. Nakai¹, H. Ozawa¹, S. Kawaai¹, A. Koido¹, Y. Ohara¹, H. Shimizu¹, H. Tamaki¹, K. Yamaguchi¹, M. Okada¹. ¹St. Luke's International Hospital, Immuno-Rheumatology Center, Tokyo, Japan

Background: Thyroid disorders are known as common comorbidities of rheumatic diseases(RD) [1]. However, data regarding prevalence of hyperthyroidism with treatment indication in RD patients are limited.

Objectives: This study aims to reveal and compare the frequency of newly developed hyperthyroidism with treatment indication between RD patients and healthy controls (HC), and identify risk factors to identify patients whose thyroid function should be followed up carefully.

Methods: We retrospectively reviewed charts of RD patients and HC who had thyroid stimulating hormone (TSH) measured at least once between 2004 and 2018 from immuno-rheumatology center and preventive medicine center in St. Luke's International Hospital, Japan. We compared frequency of hyperthyroidism requiring treatment (TSH $\leq 0.1\mu\text{U/mL}$ or for which physicians started treatment) with Kaplan-Meier curve and log rank test. Cox regression multivariate analysis was performed to reveal risk factors for the new onset of hyperthyroidism with treatment indication in participants without treatment-indicated hyperthyroidism at initial assessments.

Table1. Patients characteristics and results of hyperthyroidism

	Rheumatic Disease (n = 2307)	Control (n = 78251)	p. value
Age(yr)	53.7 (16.2)	46.1 (11.9)	<0.001
Female (%)	1826 (79.2)	38632 (49.4)	<0.001
Rheumatoid arthritis (%)	1091 (47.3)	-	NA
Spondyloarthritis	161 (7.0)	-	NA
ANA associated disease (%)	944 (40.9)	-	NA
SLE(%)	363 (15.7)	-	NA
SS (%)	396 (17.2)	-	NA
PMDM(%)	104 (4.5)	-	NA
SSc (%)	222 (9.6)	-	NA
MCTD (%)	43 (1.9)	-	NA
Vasculitis (%)	202 (8.8)	-	NA
Others (%)	244 (10.6)	-	NA
Times of TSH measurement	2.0 [1.0, 5.0]	5.0 [3.0, 9.0]	<0.001
Follow up of TSH (days)	258.00 [0, 1315]	1992 [958, 3632]	<0.001
Baseline TSH ($\mu\text{U/mL}$)	2.28 (3.21)	2.15 (4.07)	0.137
$\leq 0.45 \mu\text{U/mL}$ (%)	86 (3.7)	1371 (1.8)	<0.001
$\leq 0.1 \mu\text{U/mL}$ (%)	29 (1.3)	389 (0.5)	<0.001
Baseline FreeT4 ($\mu\text{U/mL}$)	1.16 (0.24)	1.30 (0.20)	<0.001
$\geq 1.65 \mu\text{U/mL}$ (%)	17 (0.8)	2355 (3.0)	<0.001
TSH level in follow up			
$\leq 0.45 \mu\text{U/mL}$ (%)	231 (0.0)	3926 (5.0)	<0.001
$\leq 0.1 \mu\text{U/mL}$ (%)	84 (3.6)	1388 (1.8)	<0.001
Newly detected hyperthyroidism with treatment indication (%)	68 (2.9)	1350 (1.7)	<0.001
At initial assessment (%)	29 (1.3)	389 (0.5)	<0.001
In follow up (%)	39 (1.6)	961 (1.2)	<0.001
Treatment for hyperthyroidism (%)	21 (0.9)	325 (0.4)	0.002