Objectives: In patients with rheumatoid arthritis (RA) to explore the agreement at a joint level between tenderness, spontaneous patient reported joint pain, swelling and US synovitis.

Methods: 174 patients with established RA (mean (SD) age 52¹³ years, disease duration 10⁸ years, 82% women, 79% anti-CCP positive were assessed when they initiated bDMARD treatment and after 1, 2, 3, 6 and 12 months. An experienced study nurse assessed presence/absence of joint tenderness and swelling (wrist, MCP1–5, PIP2–3, elbow, knee, ankle and MTP1–5 bilaterally). The same 32 joints were assessed by use of a manikin for Patient Reported Spontaneous Joint Pain (PRSJP) the last day as well as US (GS and PD, both scored 0–3) by an experienced sonographer (HBH). Agreement at joint level was explored between categorical variables using Cohens kappa (US scores transformed to presence (PD score 1–3/GS score 2–3) versus absence (PD score 0/GS score 0–1), and in addition agreement between presence of tenderness/swelling and the different US scores were explored.

Results: A total of 4091 (baseline) and 22 885 (all visits) joints were assessed. Tender joints had moderate agreement with PRSJP and swollen joints, and lower with US synovitis. Swollen joints had high agreement with US synovitis (table 1), and US synovitis was found in 75% of swollen joints. There were no differences in agreement between results at baseline and all visits, or if subgroup analyses were performed of only finger joints. A clear relationship was found between increasing GS/PD scores and percentages of joints being swollen, but this association was not found for tender joints (table 2).

Abstract FRI0042 – Table 1. Kappa values for agreement between categorical variables at baseline (4091 joints)/all visits (22885 joints)

	PRSJP	Swollen joint	GS US	PD US
Tender joint	0.34/0.40	0.32/0.32	0.21/0.21	0.20/0.20
PRSJP		0.25/0.26	0.23/0.24	0.25/0.23
Swollen joint			0.57/0.56	0.56/0.54

Abstract FRI0042 – Table 2. At joint level; percentages of agreement between joints being tender and/or swollen and US synovitis (all visits, number of joints in parenthesis)

	GS=0 (n=13874)/PD=0 (n=18656)	GS=1 (n=4077)/ PD=1 (n=1888)	GS=2 (n=3079)/ PD=2 (n=1791)	GS=3 (n=1855)/ PD=3 (n=550)
Swollen joints	3.8%/7.9%	16.3%/45.7%	47.1%/70.1%	77.7%/86.7%
Swollen, but not tender joints	2.1%/4.4%	8.8%/28.2%	26.7%/42.0%	49.4%/51.8%
Tender joints	9.7%/12.7%	20.4%/27.5%	29.7%/33.1%	32.7%/39.3%
Tender, but not swollen joints	8.0%/9.1%	12.8%/10.0%	9.3%/4.8%	4.4%/3.8%

Conclusions: Tender joints had weak agreement with presence of US synovitis, while swollen joints had strong agreement. PRSJP had moderate/weak agreement with all the other assessments. Presence of swelling was highly associated with the degree of US synovitis, while this association was not found for tenderness. Our results raise questions regarding the prominent role of tender joint count in RA clinical composite scores for disease activity.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2236

FRI0043 TRENDS IN ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS. A 10- TO 20-YEAR FOLLOW-UP STUDY IN 3 CONSECUTIVE INCIDENCE COHORTS

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Background: The mortality rate in patients with rheumatoid arthritis (RA) has been estimated to be 1.5–1.6 compared to the general public. Moreover, RA patients are still not benefitting fully from the declining mortality rate that the general population has enjoyed and cardiovascular disease (CVD) continues to be a major concern.

Objectives: To examine the all-cause and CVD mortality in 3 consecutive cohorts of patients with incident RA, compared to population controls

Methods: The Oslo RA register (ORAR) was established in 1994. The inclusion criteria were a diagnosis of RA according to the 1987 ACR criteria and residency in Oslo. The register was updated annually until 2009, and validated for completeness.¹ In January 2012, 3328 patients were registered in ORAR. We grouped patients into 3 successive incidence cohorts; 1996(1994–1998), 2001 (1999–

2003) and 2006(2004–2008). For each patient we identified 5 historical population controls matched according to age at disease incidence, gender and postal code of residence. Patients and controls were linked to the Norwegian Cause of Death Registry. Counts were compared using chi² tests. The hazard ratio (HR) for survival was calculated using stratified cox-regression models adjusted for highest achieved level of education.

Results: 422, 477 and 459 patients in the 1996, 2001 and 2006 cohorts were matched to 2110, 2385 and 2295 controls respectively. 20, 15 and 10 years follow-up for 1996, 2001 and 2006 cohorts were available in 201, 292 and 311 patients respectively. Results are presented in the table 1.

	1996		2001		2006	
	ORAR	Controls	ORAR	Controls	ORAR	Controls
Age years mean (SE)	55.9 (0.8)	55.9 (0.4)	54.1 (0.7)	54.1 (0.3)	54.7 (0.7)	54.7 (0.3)
Female gender n (%)	308 (73.0)	1540 (73.0)	358 (75.1)	1790 (75.1)	328 (71.5)	1640 (71.5)
Deaths at 5 years n(%)	37 (8.8)	180 (8.5)	30 (6.3)	130 (5.5)	25 (5.5)	104 (4.5)
Deaths at 10 years n (%)	95 (22.5)	371 (17.6)*	78 (16.4)	297 (12.5)*	38 (12.2)	257 (11.2)
Deaths at 15 years n (%)	147 (34.8)	586 (27.8)*	82 (28.1)	482 (20.2)*		
Deaths at 20 years n(%)	88 (43.8)	801 (38.9)				
CVD deaths 5 years n(%)	20 (4.7)	57 (2.7)*	8 (1.7)	30 (1.3)	6 (1.3)	26 (1.1)
CVD deaths 10 years n (%)	39 (9.2)	128 (6.1)	28 (5.9)	74 (3.1)*	9 (2.8)	59 (2.6)
CVD deaths 15 years n (%)	57 (13.5)	210 (10.0)*	27 (9.2)	138 (5.8)		
CVD deaths 20 years n (%)	43 (21.4)	290 (13.7)*				
HR 5 year all-cause mortality (95% CI)	1.01 (0.71–1.44)		1.01 (0.67–1.51)		1.17 (0.75–1.81)	
HR 10 year all-cause mortality (95% CI)	1.27 (1.01–1.61)*		1.18 (0.91–1.52)		0.98 (0.69–1.40)	
HR 15 year all-cause mortality (95% CI)	1.39 (1.15–1.69)*		1.41 (1.10–1.83)*			
HR 20 year all-cause mortality (95% CI)	1.49 (1.16–1.90)*					
HR 5 year CVD mortality (95% CI)	1.68 (1.00–2.82)		1.13 (0.51–2.51)		1.20 (0.49–2.95)	
HR 10 year CVD mortality (95% CI)	1.49 (1.03–2.16)*		1.69 (1.07–2.69)*		0.97 (0.47–2.02)	
HR 15 year CVD mortality (95% CI)	1.55 (1.13–2.12)*		1.67 (1.05–2.65)*			
HR 20 year CVD mortality (95% CI)	2.27 (1.56–3.31)**					

*p<0.05.

Conclusions: RA patients with disease incidence in the period 1994–2003 had increased all-cause and CVD related mortality after 10–15 years of disease duration, compared to the population of Oslo. The increased mortality was not observed in the 2004–2008 cohort. Improved survival in recent years may be related to more effective therapies and earlier diagnosis, but further analyses are warranted.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5458

FRI0044 EXCEEDING PREDEFINED THRESHOLDS FOR MRI BONE OEDEMA AND EROSION AND HAQ-DI CAN PREDICT RELAPSE AFTER WITHDRAWAL OF ALL TREATMENT IN MTX-NAÏVE PATIENTS WITH RA IN REMISSION AFTER 12 MONTHS OF ABATACEPT THERAPY IN THE AVERT TRIAL

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Background: To assist in clinical decision making it is important to understand the factors, and their thresholds, that might predict relapse following treatment

withdrawal in patients with RA in remission. In a previous *post hoc* analysis of the AVERT trial (NCT01142726), in which several potential factors were assessed, erosions, synovitis and bone oedema scores on MRI and HAQ-DI scores in patients with DAS28 (CRP) <2.6 were associated with clinical relapse 6 and 12 months after complete drug withdrawal following 12 months of blinded treatment with abatacept +MTX or abatacept or MTX alone.^{1,2} Knowledge of the thresholds for these measures, above which relapse is more likely to occur, may aid clinical decisions about when to withdraw treatment in patients who have achieved remission.

Objectives: To evaluate *post hoc* the association between different thresholds of MRI and HAQ-DI scores at Month 12 and the risk of relapse at Months 18 and 24 in AVERT.

Methods: This analysis compared relapse event rates at Months 18 and 24 in patients with DAS28 (CRP) <2.6 but with differing severities of synovitis, bone oedema and erosion (assessed by MRI individual and combined scores) and HAQ-DI scores at Month 12. A relapse event was defined by the doubling of TJC28 and SJC28 and an increase in DAS28 (CRP) ≥ 1.2 relative to the Month 12 visit. Synovitis, bone oedema and erosion in the dominant hand and wrist MRI were scored using the OMERACT RAMRIS. Severity of each score was defined by cut-offs of >3 for synovitis, >2 for bone oedema, >7 for (weighted) combined synovitis and bone oedema, >5 for erosion and >0.5 for HAQ-DI. Univariate logistic models were conducted for comparisons and odds ratios (OR) with 95% CI and associated p values.

Results: All randomised and treated patients with DAS28 (CRP) <2.6 at Month 12 and relapse status available at Months 18 and 24 (n=155) were included. Among the overall study cohort at Month 12, 70 (45.2%) patients with DAS28 (CRP) <2.6 had a higher synovitis score (>3), 28 (18.1%) had a higher bone oedema score (>2), 39 (25.2%) had a higher combined score (>7), 73 (47.1%) had a higher erosion score (>5) and 42 (27.1%) had a higher HAQ-DI score (>0.5). Relapse events at Months 18 and 24 were significantly associated with supra-threshold MRI bone oedema, erosion and combined scores and with supra-threshold HAQ-DI score at Month 12 (figure 1). There was a trend toward association of relapse at Months 18 and 24 with high synovitis score (figure 1).

Abstract FRI0044 – Figure 1. Association Between Month 12 MRI and HAQ-DI Scores and Relapse Status at Months 18 and 24

Conclusions: It was possible to define MRI and HAQ-DI scores in patients with DAS28 (CRP) remission that were predictive of relapse 6 and 12 months after complete drug withdrawal in AVERT. Assessment of imaging and physical function, using predefined thresholds, in patients achieving remission may aid clinical decisions on when to withdraw therapy in MTX-naïve patients with RA.

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Disclosure of Interest: H. Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, J. Baker: None declared, M. Østergaard Grant/research support from: AbbVie, Bristol-Myers Squibb, Janssen, Merck, Speakers bureau: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Eli Lilly, Centocor, GSK, Hospira, Janssen, Merck, Mundipharma, Novartis, Novo Nordisk, Orion, Pfizer, Regeneron, Schering-Plough, Roche, Takeda, UCB, Wyeth, P. Emery Consultant for: AbbVie, Bristol-Myers Squibb, Merck, Pfizer, Roche, Lilly, Novartis, Samsung Bioepis, T. Huizinga Grant/research support from: EU and Dutch Arthritis Foundation, Consultant for: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Crescendo Bioscience, Novartis, Pfizer, Roche, sanofi-aventis, Schering-Plough, UCB, Eli Lilly, Speakers bureau: Abbott Laboratories, Biotest AG, Bristol-Myers Squibb, Novartis Pharmaceuticals Corporation, Pfizer Inc, Roche, sanofi-aventis, Schering-Plough, Y. Elbez Consultant for:

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DOI: 10.1136/annrheumdis-2018-eular.2117

FRI0045

EVALUATION OF SERUM PROTEIN LEVELS AT BASELINE AS PREDICTORS OF RESPONSE TO METHOTREXATE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS: RESULTS FROM SWEFOT TRIAL POPULATION

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Background: Methotrexate (MTX) is a standard first-line therapy option for patients with early rheumatoid arthritis (eRA). However, a substantial proportion of patients still do not respond to MTX.

Objectives: To identify biomarkers for prediction of response to MTX.

Methods: We analysed a group of patients (n=135) with eRA from the Swedish Pharmacotherapy (SWEFOT) trial population. Baseline serum levels of 177 proteins were profiled using 380 antibodies in a suspension bead array format. Median fluorescent intensity (MFI) levels of the proteins were subsequently analysed for association with achievement of low 28-joint disease activity score (DAS28 ≤ 3.2) after 3 months of MTX therapy (primary outcome). Proteins that remained significant in multivariate model were analysed using receiver operating characteristic (ROC) curve analysis for cut-off definition of MFI and categorisation into high and low categories. Proportion of patients with primary outcome between the generated categories were compared using Chi-squared test.

Results: In multivariate analysis, serum levels of two of the 177 proteins at baseline, matrix metalloproteinase 7 (MMP-7) and alpha-chain of fibrinogen (FGA) were significantly different among patients who achieved or not achieved low DAS28 at 3 months. ROC curve analysis revealed AUC of 0.692 for MMP-7 and 0.699 for FGA (p<0.001; figure 1A). ROC curve-based dichotomisation indicated that of patients with low versus high levels of either MMP-7 or FGA, 60% versus 24% and 58% versus 22%, respectively, achieved low DAS28 (p<0.001; figure 1B and C). Among patients with low categories of both proteins, 79% achieved low DAS28 at 3 months, while only 18% of those in high categories for both proteins (p<0.001; figure 1D).

Validation in the COMBINE cohort with available MMP-7 data (whose concentration was measured by different method) did not confirm results from the SWEFOT trial.

Abstract FRI0045 – Figure 1. Assessment of baseline levels of MMP-7 and FGA as predictors of LDA at 3 months. Receiver operating characteristic curve analysis and area under the curve of MMP-7 and FGA (A), proportion of patients achieving low DAS28 among groups dichotomised by MMP-7 (B), FGA (C) or using combination of MMP-7 and FGA (D).