interleukin-1 and interleukin-6, affect serotonin transporters in the brain and promote low stress tolerance and depression².

Objectives: To investigate the effect of orthopaedic surgery on the mental condition of patients with RA by assessing the Beck depression inventory II (BDI-II) and to investigate the factors associated with changes in the BDI-II.

Methods: A prospective cohort study was performed in 294 sites of primary elective surgery in 276 patients with structural damage due to RA. The average (range) age was 64^{19–89} years old, and the average (range) disease duration was 16^{1–60} years. The surgical site was the shoulder in 6 patients, elbow in 26, wrist in 74, hand in 63 (with wrist in 18), hip in 13, knee in 50, ankle in 12, and forefoot in 50. The BDI-II, EuroQol 5 dimensions (EQ-5D), Japanese version of the Stanford Health Assessment Questionnaire (J-HAQ), and disease activity score 28 using C-reactive protein⁴ (DAS28-CRP⁴) were assessed at the baseline and at 12 months after surgery. During the observational period, the number of patients using methotrexate (MTX), prednisolone (PSL), and biological disease-modifying anti-rheumatic drugs (bDMARDs) did not change significantly. The mean dose of MTX and PSL was reduced by 0.4 mg/w and 0.2 mg/d, respectively, at 12 months after surgery.

Results: In total, the mean BDI-II significantly improved from 13.0 to 11.5 at 12 months after surgery ($p<0.01$). The number of patients with depression (BDI-II ≥ 14) decreased from 42.8% to 34.8% (figure 1). A significant improvement in the BDI-II was noted in the elbow, wrist, hand, and forefoot surgeries ($p<0.05$). EQ-5D, J-HAQ, and DAS28-CRP⁴ also improved significantly ($p<0.01$)³. A multiple regression analysis showed that the magnitude of decrease in the BDI-II (Δ BDI-II) was independently related to the Steinbrocker's stage (95% confidence interval [CI]: 0.42, 2.39, $p=0.005$) and pain-visual analogue scale (VAS) (95% CI: 0.01, 0.10, $p=0.02$) at baseline and inversely related to matrix metalloproteinase-3 (MMP-3) (95% CI: -0.01 , -0.001 , $p=0.03$) at baseline. The BDI-II was correlated with the EQ-5D ($\gamma=-0.049$, $p<0.01$) and J-HAQ ($\gamma=0.387$, $p<0.01$) at 12 months after surgery.

Abstract THU0156 – Figure 1. Distribution of BDI-II at baseline and a postop. 12mos.

Conclusions: Depression was ameliorated by surgical intervention in patients with RA. The mental condition is associated with the quality of life and physical function.

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THU0157 ALTERED DNA-METHYLATION IN CHILDREN BORN TO MOTHERS WITH RHEUMATOID ARTHRITIS DURING PREGNANCY

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Background: Exposures during early life are associated with later-life health, which is referred to as the Developmental Origins of Health and Disease hypothesis¹. Epigenetic processes are thought to be one of the mechanisms underlying this hypothesis. DNA-methylation is the best studied and understood epigenetic modification. DNA-methylation of the fetus *in utero* may be influenced by multiple factors, including maternal disease².

Objectives: To determine whether the DNA-methylation profile of children born to women with RA is different from children born to women from the general

population. Furthermore to determine which pathways are associated with the significantly differentially methylated CpG sites.

Methods: For the current study, blood from 80 children with a mean age of 6.82 (SD=1.28) born to women with RA, who were followed prospectively during pregnancy and postpartum in the PARA-study³, was used to measure genome-wide DNA-methylation using the Infinium Illumina Human-Methylation 450 k BeadChip. DNA from 345 children with a mean age of 6.04 (SD=0.39) born to women from the population-based Generation R study⁴ were used as controls, also followed prospectively during pregnancy and postpartum. Linear mixed models were used to analyse differences in methylation between these groups. The models were corrected for age, BMI (SDS) and sex of the child, gestational age at delivery, maternal age, folic acid use during pregnancy, socioeconomic status, maternal smoking during pregnancy, white blood cell subtypes and technical batch.

Results: In total 770 CpGs were significantly different between the 2 groups at Bonferroni threshold $p=1.08 \times 10^{-7}$ (see table 1. for top 10 sites). In addition, pathway analysis resulted in 4 statistically significant enriched pathways. The top 2 pathways were the FOXO signalling pathway consisting of 16 genes ($p=3.39 \times 10^{-4}$) and mTOR signalling pathway consisting of 17 genes ($p=5.65 \times 10^{-4}$). These pathways are known for regulating the glucose and lipid metabolism, respectively.

Table 1 Top 10 methylation sites from the linear mixed model

CpG	P-value	Beta	SE	Nearby gene ($\pm$ bp)	Chr	Bp	Location*
(Effect size)							
cg07786668	4.75*10 ⁻³³	0.027	0.002	ZFXH3(-10142)	16	73092391	-
cg06642177	1.29*10 ⁻²⁹	0.028	0.002	SLC2A12(-122529)	6	134496341	-
				SGK1(+142878)			
cg08867893	5.68*10 ⁻²⁷	0.017	0.001	ZNF365(+221)	10	64134160	-
cg20116574	4.89*10 ⁻²³	0.024	0.002	NCOA5(+435)	20	44718168	Promoter
cg06778273	9.33*10 ⁻²³	0.021	0.002	TNFRSF18(+4995)	1	1137117	-
				TTL10(+27808)			
cg21160472	8.45*10 ⁻²²	0.015	0.001	ATF3(+119)	1	212782112	Promoter
cg01067849	4.09*10 ⁻²⁰	0.011	0.001	WRNIP1(-102)	6	2765587	Promoter
cg06656994	5.88*10 ⁻¹⁹	0.051	0.005	FAM163A(+903)	1	179713176	Enhancer
cg14810343	1.36*10 ⁻¹⁸	0.013	0.001	CXXC5(-127)	5	139028149	-
cg01458961	3.47*10 ⁻¹⁸	0.032	0.003	PPP3CA(-822)	4	102269425	-

* Location in promoter, gene, enhancer or other/unknown (-)

SE= standard error; bp=base pair; Chr= chromosome

Conclusions: This study demonstrates that children born to women with RA have a different methylation profile compared with children born to mothers from the general population.

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THU0158 INCREASED PROGRESSION OF ATHEROSCLEROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS IS PARTIALLY REFLECTED BY DISEASE SEVERITY AT THE TIME OF DIAGNOSIS- 11-YEAR PROSPECTIVE FOLLOW-UP

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Background: Patients with Rheumatoid arthritis (RA) have increased mortality and morbidity due to cardiovascular disease (CVD) compared to general population. While it has been established that atherosclerosis is increased, there is much yet to reveal about the underlying cause. Contributing factors, such as

inflammation, traditional CVD risk factors and metabolic disease have been suggested, but no full explanation is currently present.

Objectives: In this prospective case-control study, we investigated how the progression of subclinical atherosclerosis is associated with CVD risk factors and parameters of inflammation in patients with RA compared with matched controls.

Methods: By the time of diagnosis, patients from northern Sweden diagnosed with early RA are consecutively recruited into an ongoing prospective study. From these, a subgroup aged ≤ 60 years was consecutively included for ultrasound measurements of intima media thickness (IMT) of a. carotis communis at inclusion (T0) (n=79), after 5 years (T5) (n=71) and after 11 years (T11) (n=55). 44 age-sex-matched controls were included and 31 could be reevaluated at T11. Pharmacological treatment, previous CVD, markers of inflammation, lipid status, blood pressure, body mass index as well as measurements of disease activity were registered. Any previous CV events were verified by medical records. European Systematic Coronary Risk Evaluation (SCORE) and Reynolds Risk Score were calculated and Larsen score (of hands and feet) were registered. IMT progression rate (Δ IMT T0-T11) was calculated by subtracting baseline values from IMT after eleven years follow up.

Results: IMT increased significantly between T0 and T11 among patients with RA (IMT T0: 0.51 (0.12) T11: 0.68 (0.16) $p < 0.0001$) and controls (IMT T0: 0.54 (0.12) T11: 0.63 (0.13) $p < 0.0001$). There was a higher progression rate between T0 and T11 in the RA group compared with the controls ($p < 0.05$). In simple regression models, IMT T11 was significantly associated with several traditional CVD risk factors as well as Larsen score at T0 among RA patients (table 1). Moreover, in simple regression models Δ IMT T0-T11 was significantly associated with Larsen score and age at T0 (both $p < 0.01$) among patients with RA. A multiple regression model, with Δ IMT T0-T11 as dependent variable, including traditional CVD risk factors at T0 (age, systolic blood pressure (BP), cholesterol and smoking), resulted in a R^2 of 0.32 where age and cholesterol ($p < 0.01$ for both) were significantly associated with Δ IMT T0-T11. When also adding CRP and Larsen score the R^2 increased to 0.50 and age ($p < 0.05$) and Larsen score ($p < 0.01$) were significantly associated with IMT T11.

Abstract THU0158 – Table 1. Simple regression models among 55 patients with RA with IMT after 11 years of follow up as the dependent variables.

Variable	IMT T11		
	β	95% CI	p
Age, T0	0.104/year	0.071–0.136	<0.001
Systolic BP, T0	0.035/ mmHg	0.009–0.061	0.009
SCORE, T0	0.534/unit	0.261–0.807	<0.001
Reynolds risk score, T0	0.182/unit	0.048–0.315	0.009
Larsen score, T0	0.122/unit	0.004–0.239	0.043
DAS 28, T0	–0.236/unit	–0.771– 0.298	0.364

Conclusions: In this prospective study, we found that there was an increased progression of atherosclerosis among RA patients, compared with controls, eleven years after diagnosis, and that this increase is associated with Larsen score and age at baseline.

Disclosure of Interest: None declared

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THU0159 BARRIERS TO RHEUMATOID ARTHRITIS TREATMENT OPTIMISATION: REAL-WORLD DATA FROM THE ARTHRITISPOWER REGISTRY

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Background: Few research studies have investigated treatment (Tx) goals in rheumatoid arthritis (RA) from the patients' (pts) perspective, including factors preventing achievement of Tx targets and reasons why pts tolerate sub-optimal disease control.

Objectives: To identify barriers to Tx optimisation, using real-world data from the ArthritisPower registry. Secondary objectives were to understand pts' Tx goals and why pts tolerate active disease.

Methods: This was an observational, cross-sectional sub-study of pts in the ArthritisPower registry. Pts were aged ≥ 19 years, had physician-diagnosed RA, no change to Tx within 3 months of baseline, and had access to a computer/smartphone. Pt-reported outcomes (PROs) included pain, fatigue, sleep, physical function, and general health. Pts also completed an online survey on barriers to Tx escalation, and were classified into 3 groups based on physician and pt attitudes to Tx change (change not offered, change offered and accepted, change offered

and rejected). Disease activity was reported using Routine Assessment of Patient Index Data 3 (RAPID3) scores.

Results: 257 pts met the inclusion criteria (table 1). 195/257 (76%) pts were treated with DMARDs (non-biologic or biologic). 180/257 (70%) pts had high disease activity by RAPID3 (median 18.0 on 0–30 scale), of which only 67/180 (37%) were offered a Tx change at their last physician visit. Most of these pts accepted the Tx change (48/67 [72%]). There were few differentiating factors in demographics, RA-related features, and background therapy among pts who were offered a Tx change versus not. Most pts (33/44 [75%]) who intensified Tx did so because their symptoms remained bad or worsened, whereas only 16/44 (36%) changed because they did not reach pre-defined Tx goals. The most common reason (21/32 [66%]) for deciding not to change therapy was the rheumatologist's satisfaction with the current therapy; pt concerns related to safety of the new therapy were less common (8/32 [25%]). There was a weak correlation between the RAPID3 score and pts' self-reported perception of their own disease activity. The majority of pts (176/257 [69%]) valued being actively involved in making decisions with their doctor about Tx.

Abstract THU0159 – Table 1. Patient demographics at baseline

	Demographics		
	Survey participants (N=257)	High disease activity (n=180)	Moderate or low disease activity, or near remission (n=77)
Age, mean years (SD)	51.9 (11.0)	51.1 (10.8)	53.7 (11.3)
Females, n (%)	236 (91.8)	167 (92.8)	69 (89.6)
Ethnicity, n (% white)	231 (89.9)	157 (87.2)*	74 (96.1)*
Years since diagnosis, mean (SD)	11.4 (9.9)	10.9 (9.2)	12.4 (11.3)
PRO scores, median (IQR)			
RAPID3	15.0 (12.0–19.0)	18.0 (15.0–20.0)*	9.0 (6.0–11.0)*
Pain	63.2 (60.0–66.9)	65.7 (62.7–67.6)*	58.7 (54.5–61.5)*
Fatigue	64.0 (58.7–68.0)	64.0 (62.3–69.3)*	57.1 (50.7–62.5)*
Physical function	37.3 (33.9–40.7)	36.3 (32.5–38.6)*	42.6 (38.8–45.9)*
Sleep	59.4 (54.3–63.0)	61.2 (55.8–64.8)*	55.8 (50.4–61.9)*

*Statistical significance between patient groups, $p < 0.05$; p values were nominal in nature and should be interpreted in an exploratory manner. Chi square tests were used to compare patient groups. IQR: Interquartile range; PRO: patient reported outcome; RAPID3: Routine Assessment of Patient Index Data 3; SD: standard deviation.

Conclusions: Despite treat-to-target recommendations,¹ about two-thirds of RA pts with high disease activity in this sample were not offered a Tx change by their rheumatologist. Only a minority changed because they had not met predefined targets for disease control. Pts commonly followed their rheumatologist's decision that no Tx change was needed and placed greater importance on their doctor's Tx goals than their own. These findings suggest that pts may be more deferential to their physicians' satisfaction with poor RA disease control than is appropriate. Encouraging pts (not just physicians) to overcome the status quo by changing medications and striving for low disease activity/remission may be worthwhile, but traditional metrics (e.g. RAPID3) may not reflect the most relevant target for pts' goals for therapy.

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THU0160 JUXTA-ARTICULAR BONE HEALTH AFFECTS NEW CAROTID PLAQUE FORMATION INDEPENDENT WITH GLUCOCORTICOID THERAPY IN POSTMENOPAUSAL PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic and systemic inflammatory disease.

The incidence of cardiovascular (CV) disease is increased in patients with RA, compared with the general population, which is related to the fact that atherosclerosis has an inflammatory etiology.