Baseline characteristics

Baseline characteristics	MTX-Starters	Biologic-starters
N	686	346
Age, years	59 (49, 67)	59 (51, 67)
Female, N (%)	441 (64.3)	269 (77.8)
Disease duration, months	9 (4, 27)	72 (24, 180)
Smoking:		
Never	240 (35.5)	106 (30.6)
Former	265 (39.1)	163 (47.1)
Current	172 (25.4)	77 (22.3)
Swollen joint count (28)	5 (2, 10)	8 (5, 11)
Tender joint count (28)	5 (2, 11)	13 (9, 18)
CRP, mg/l	7 (3, 19)	10 (5, 26)
DAS28-CRP	4.2 (3.3, 5.2)	5.6 (5.2, 6.2)
HAQ	1.13 (0.50, 1.63)	1.63 (1.13, 2.00)
Pain VAS, mm	50 (26, 73)	69 (52, 78)
Fatigue VAS, mm	51 (24, 72)	71 (52, 85)
Anti-CCP+, N (%)	686 (100)	346 (100)
Anti-CCP titre	147 (48, 416)	138 (37, 492)

Anti-CCP = anti-cyclic citrullinated peptide antibody, CRP = C-reactive protein, DAS28 = Disease Activity Score (28), HAQ = Health Assessment Questionnaire, MTX = methotrexate, N = number, VAS = visual analogue scale

Disclosure of Interests: James Gwinnutt: None declared, Kimme Hyrich Grant/research support from: Grants to institution: BMS, Pfizer, UCB, Mark Lunt: None declared, Darren Plant: None declared, Nisha Nair: None declared, Anne Barton: None declared, Suzanne Verstappen: None declared

DOI: 10.1136/annrheumdis-2019-eular.4724

THU0669 GESTATIONAL AGE AT BIRTH AND THE RISK OF AUTOIMMUNE DISEASE

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Background: A preterm newborn has an immature immune system. Although preterm birth is associated with autoimmune hypothyroidism, it is unclear, whether it also could lead to an overall increased risk of autoimmune disease.

Objective: We assessed whether a shorter gestation increases the risk of special reimbursement for medication for hypothyroidism, rheumatic disease, or ulcerative colitis/Crohn's disease

Design/Methods: A total of 235 622 children were born in Finland from Jan 1987 to Sep 1990, according to the Medical birth register, which provided also gestational age (GA) at birth. Data were linked by help of the personal identity number. A register held by the Social Insurance Institution provided the data on special reimbursements. We calculated cumulative incidences within gestational age groups until December 2014 and tested statistical significance by the chi-squared –test.

Results: At the end of the follow-up, 1354 men and 2200 women had at least one of the specified autoimmune diseases.

The cumulative incidences differed by gestational age only regarding a 50% higher incidence for hypothyroidism among all subgroups of preterm women (P=0.05). No other clear patterns were seen regarding autoimmune diseases among preterm born or early term born subgroups.

Conclusion(s): Those born preterm develop hypothyroidism more often. However, the two other composite categories of autoimmune diseases were unrelated to gestational age pointing against an overall tendency toward autoimmune disease in preterm born young adults.

Cumulative incidence (1/100,000) of four groups of autoimmune diseases

	Hypoth ¹⁰⁴	Rheuma ²⁰²	UC&CD ²⁰⁸	n
Men				
0 <31	0	597	398	1005
1 32 or 33	263	658	395	760
2 34 to 36	206	494	762	4856
3 37	149	512	776	6057
4 38	140	504	625	15687
5 39 to 41	122	550	692	85753
6 >41	120	519	798	5010

	99 missing	0	512	448	1563
	Total	128	539	687	120690
	P-value	0.40	0.99	0.49	
	(Chi ²)				
Women	0 <31	649	519	389	771
	1 32 or 33	651	163	814	614
	2 34 to 36	771	795	675	4149
	3 37	502	929	799	5380
	4 38	537	975	692	14152
	5 39 to 41	460	1056	704	83712
	6 >41	278	1069	684	4678
	99 missing	474	880	609	1477
	Total	478	1021	702	114932
	P-value	0.05	0.16	0.95	
	(Chi ²)				

202 Disseminated connective tissue disorders, rheumatoid arthritis and other rheumatic diseases (A04.6, A39.8, A50.5, D76.0, D76.3, H20.1, H30, I33.0, I40.8, J84, K50.9, K51.9, K73.2, K74.3, K83.0, L40.5, M02, M05, M06, M08, M13.9, M30–M35, M45, M46.1, M46.9, M94.1, N03, N04, Q44.2).

104 Hypothyroidism

208 Ulcerative colitis or Crohn's disease

Disclosure of Interests: Petteri Hovi Consultant for: Pfizer, Paid instructor for: Pfizer, Suvi Alenius: None declared, Pieta Näsänen-Gilmore: None declared, Mika Gissler: None declared, Eero Kajantie: None declared
DOI: 10.1136/annrheumdis-2019-eular.8269

THU0670 PATERNAL USE OF METHOTREXATE AND CONGENITAL MALFORMATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Maternal exposure to methotrexate (MTX) during pregnancy is known to be teratogenic, but less is known about the risk due to paternal MTX exposure. Because of a theoretical teratogenic risk from paternal exposure, treatment recommendations advocate that men should discontinue MTX three months before conception and continue discontinuation during the partners' pregnancy. This may lead to suboptimal adherence to treatment, fear among the future parents and pregnancy termination.

Objectives: The aim was to systematically review and meta-analyze the collective data on paternal MTX exposure and the risk of congenital malformations.

Methods: We performed a systematic search in the databases – PubMed, Embase, Cochrane Central, and Cinahl – on March 1, 2018. We included studies with an English abstract that assessed major or all (both major and minor) malformations following any paternal exposure to MTX. Studies that included a control group were included in the meta-analysis. No time restriction was applied. Review Manager Version 5.3 was used for the meta-analysis.

Results: We identified 36 studies assessing the risk of congenital malformations following paternal exposure to MTX of which 20 contained original data. Five studies met the inclusion criteria for the meta-analysis: Three studies from Denmark had a major overlap in study populations, one study from Norway, and one German study. All studies were cohort studies using national registries except the German that used structured interviews and phone interviews. Because of the overlapping Danish studies, only the largest Danish study for each of the outcomes were included. We included a total of 265 fathers exposed to MTX and 1,004,834 controls in the meta-analysis investigating risk of major congenital malformations. Among the offspring of the MTX-exposed 7 (2.64%) had a major malformation compared to 33,816 (3.37%) among the unexposed. Pooled odds ratios were 1.02 (95% confidence interval [CI] 0.48-2.20) for major malformations and 1.02 (CI 0.62-1.66) for all malformations.

Conclusion(s): In this systematic review and meta-analysis, we found no association between preconceptional paternal MTX use and major or all congenital malformations. The current recommendations to avoid paternal MTX use before conception do not appear to be supported by evidence and paternal treatment with MTX could be continued when planning a pregnancy.

Disclosure of Interests: Thomas Bo Jensen: None declared, Mikkel Bring Christensen: None declared, Nicole Tsao: None declared, Seoyoung Kim

Grant/research support from: Pfizer, Bristol-Myers Squibb, Roche/Genentech and AbbVie., Jon Trærup Andersen: None declared
DOI: 10.1136/annrheumdis-2019-eular.1294

THU0671 PULMONARY INVOLVEMENT IN RHEUMATOID ARTHRITIS: PATTERNS AND EPIDEMIOLOGICAL CHARACTERISTICS FROM A MONOCENTRIC COHORT STUDY

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Background: Extra-articular manifestations (EAM) are not an uncommon finding in patients with Rheumatoid Arthritis (RA). Pulmonary involvement is a potential life-threatening EAM with deleterious effects on the quality of life and is reported in different occurrence among studies.

Objectives: To evaluate the frequency of pulmonary involvement in RA patients followed-up in a 15-years period.

Methods: 549 RA patients were diagnosed according to the ACR/EULAR classification criteria since 2003. A full clinical examination as well as a detailed laboratory and immunological evaluation has been carried-out at baseline. Furthermore, chest, hand and wrist but also feet radiographs had been obtained. All patients were followed-up at predefined times and were treated appropriately with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and/or biologic (b)DMARDs. Any laboratory abnormalities or comorbidities were recorded and investigated appropriately at every visit. In addition, the disease activity score (DAS) using the 28-joints count (DAS-28) was recorded.

Results: Initial evaluation revealed 15 patients as having pulmonary abnormalities. Thus, these patients were excluded. From the rest, 37 (6.7%) patients manifested lung involvement. There were 26 males and 11 females, with mean age of 62.9 ± 3.4 years and disease duration of 8.5 ± 2.2 years. 14 were smokers and 10 ex-smokers. Dry cough and dyspnea on exertion were the main pulmonary symptoms. High resolution computed tomography (HRCT) scan of the chest revealed interstitial lung disease (ILD). More specifically, 23 patients showed usual interstitial pneumonia (UIP), 10 patients had nonspecific interstitial pneumonia (NSIP), while 4 had a mixed pattern. Six patients died 4 years after ILD development. ILD was associated with high DAS-28, seropositivity and male gender.

Conclusion: ILD is not a frequent EAM in patients with RA, but it carries a poor prognosis with high morbidity and mortality and it is associated with RA disease activity and male gender. UIP is the most prevalent pattern of ILD in RA patients.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.4830

THU0672 PREVALENCE OF OSTEOPOROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A MULTICENTER COMPARATIVE STUDY OF THE FRAX AND WHO CRITERIA

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Background: Reduced bone mass or osteoporotic fracture are one of major complications in chronic inflammatory diseases including systemic lupus erythematosus (SLE). Fracture risk was found to be determined not only by conventional factors such as age and a lack of physical activity, but also by systemic inflammation, musculoskeletal symptoms, and administration of glucocorticoids.

Objectives: We evaluated the prevalence of osteoporosis and fracture risk in patients with systemic lupus erythematosus (SLE), and compared the fracture risk assessment tool (FRAX) criteria and bone mineral density (BMD) criteria established by the World Health Organization (WHO).

Methods: Data of 182 female patients with SLE were collected retrospectively in 5 hospitals between January 2012 and December 2016. The FRAX criteria for high-risk osteoporotic fractures were calculated including and excluding the scores in BMD, respectively. The high risk for fracture by FRAX criteria and BMD criteria by WHO was defined as 10-year probability of $\geq 20\%$ for major osteoporotic fracture or $\geq 3\%$ for hip fracture, and T score ≤ -2.5 or Z score ≤ -2.0 , respectively.

Results: The mean age was 51.1 ± 11.23 years, 114 (62.3%) were post-menopausal. Osteoporotic fractures were detected in 9 (4.9%) among the 127 patients taking T-L spine X-ray. The numbers of candidates for pharmacological intervention using the FRAX criteria with and without BMD

and the WHO criteria were 26 (14.2%), 23 (12.6%), and 51 (27.9%), respectively. Only 50–69.6% of the patients in the high-risk group using the FRAX criteria and the WHO criteria were receiving osteoporosis treatments. The following were associated with candidates for pharmacological intervention for fracture using the FRAX criteria without BMD and WHO criteria: Age (OR 1.422, 95% CI 1.22–1.659 and OR 1.157, 95% CI 1.083–1.236), and weight (OR 0.87, 95% CI 0.798–0.949 and OR 0.943, 95% CI 0.901–0.986), respectively. In addition, cumulative glucocorticoids dose (OR 1.073, 95% CI 1.024–1.123) was associated with candidates for pharmacological intervention for fracture using the FRAX criteria with BMD.

Conclusion: The proportion of SLE patients with a high risk of osteoporotic fractures by the FRAX criteria with and without BMD and the WHO criteria was 12.6%–27.9%. Among the candidate patients, only 50%–69.6% were taking osteoporotic medications. Independent risk factors for osteoporotic fractures in SLE patients were older age, lower weight and cumulative glucocorticoids dose.

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Disclosure of Interests: Jiwon Kim: None declared, Ju-Yang Jung: None declared, Hyoun-Ah Kim: None declared, Chang-Hee Suh Consultant for: Celltrion, Inc

DOI: 10.1136/annrheumdis-2019-eular.5454

THU0673 CARDIOVASCULAR DISEASE AS A RISK FACTOR FOR DEVELOPMENT OF RHEUMATOID ARTHRITIS – A DANISH FOLLOW-UP STUDY

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Background: It is well-established that patients with rheumatoid arthritis (RA) have higher risk for development of atherosclerotic cardiovascular diseases (CVD) than the general population (1). The evidence shows that a CVD burden is already notable at the onset of RA (2). It is well-known, that atherosclerosis is an inflammatory condition (3). Therefore, we hypothesize that atherosclerotic CVD is positively associated with subsequent development of RA.

Objectives: To examine the risk of developing RA in persons who have had CVD, defined as acute myocardial infarction (AMI) or ischaemic stroke while controlling for established shared risk factors.

Methods: We conducted a population-based cohort study within the Danish Diet, Cancer and Health (DCH) cohort. The cohort was recruited 1993-97 and included individuals aged 50 to 64 years, born in Denmark and living in geographically defined parts of Denmark. Data on lifestyle factors and anthropometric measurements were collected at enrolment into the DCH. Information on incident AMI (ICD-10 code: I21), ischemic stroke (ICD-10 code: I63) and RA (ICD-10 codes: M05, M06 combined with ATC codes for DMARDs) was obtained from nationwide administrative registers. Participants were followed until development of RA, death, loss to follow-up or October 2016, whichever came first. Data were analyzed using Cox's proportional hazards regression models with delayed entry and age as the underlying time scale and cardiovascular disease (CVD) as a time-varying exposure variable, stratifying by gender. Established shared risk factors - smoking, body mass index and waist circumference - were included in the multivariable analyses.

Results: Complete data were available on 53287 subjects (52% female) without a AMI, stroke or RA diagnosis prior to their enrolment into the DCH. Median age at entry into DCH was 56 years. During follow-up (median 21 years), 4,627 participants developed CVD (37% female) and 516 participants developed RA (69% female). The risk for developing RA was 30% higher in women with CVD than in women without CVD (adjusted hazard ratio (HR) 1.30 (95% CI 0.70-2.38)) (Table 1). In men, there was no clear association between CVD and development of RA (adjusted HR 0.73 (95% CI 0.34-1.58)).