models using generalized linear models with binomial link function. In model 1 we adjusted for age, sex and cell counts, in model 2 we additionally adjusted for BMI. We report effect estimate(beta) per standard deviation (SD) change in protein levels with 95% Confidence Interval (CI) and nominal p-value (significance level<0.05) for each protein. All statistical analyses were performed in R version 3.5.2.

Results: We found in total 56 proteins that were significantly associated with one or more OA-outcomes at nominal level. Figure 1 illustrates the 19 significant associations for severity of hand OA ordered by significance level (most significant at top). We observed a very robust association between the level of circulating Cartilage acidic protein 1 (CRTAC1) and severity of OA in the knee ($\beta=0.16$, 95%CI 0.09-0.23, $p=0.000013$, FDR-corrected $P=0.0011$) hand ($\beta=0.086$, 95%CI 0.03-0.14, $p=0.00085$, FDR-corrected $P=0.0252$), while a similar trend was seen in hip ($\beta=0.08$, 95%CI -0.02-0.18, $p=0.12$), although power in hip was limited in our study. The association with CRTAC1 was also found for progression in knee ($\beta=0.21$, 95%CI 0.03-0.36, $p=0.0156$, FDR-corrected $P>0.2$) and hip ($\beta=0.18$, 95%CI -0.01-0.38, $p=0.0624$, FDR-corrected $P>0.9$). These associations were independent of BMI. Among the findings were several other promising biomarkers, e.g. MMP-10, which we observed to be associated with severity of hand OA ($\beta=-0.09$, 95%CI -0.15- -0.04, $p=0.00067$, FDR-corrected $P=0.0383$) and progression of knee OA ($\beta=-0.24$, 95%CI -0.42- -0.06, $p=0.0073$, FDR-corrected $P>0.1$). Additionally, COMP, a well-known biomarker for OA, was also found significant for OA severity in hand ($\beta=0.10$, 95%CI 0.05-0.16, $p<0.001$, FDR-corrected $P=0.0043$) and knee ($\beta=0.09$, 95%CI 0.02-0.17, $p=0.01$, FDR-corrected $P>0.2$).

Conclusion: We identified the CRTAC1 protein as a robust, promising biomarker for osteoarthritis severity and progression. This protein is a glycosylated extracellular matrix protein that is found in the interterritorial matrix of articular deep zone cartilage. This protein can also be used to distinguish chondrocytes from osteoblasts and mesenchymal stem cells in culture. This suggests that CRTAC1-levels reflects a cartilage-specific process in the joint. Such a biomarker might be useful for targeting the right patients for clinical trials and designing novel therapies for OA.

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OP0112 FACTORS ASSOCIATED WITH OSTEOPOROSIS CARE OF MEN: A REAL-LIFE STUDY ON A NATION-WIDE DATASET

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Background: Male osteoporosis is associated with an important clinical and economic burden worldwide. Notwithstanding that, undertreatment of men with osteoporosis is common. Understanding the factors associated with less osteoporosis care utilization might help define future intervention to improve access of men to osteoporosis care.

Objectives: The aim of the study was to describe the factors associated with osteoporosis care in men.

Methods: We conducted a retrospective analysis of a nation-wide cohort (DeFRA-Calculator database). DeFRA-Calculator is a tool that estimates the fracture risk considering clinical and densitometric risk factors, including the presence of prior hip or vertebral and non-vertebral or non-hip fractures. We compared the clinical characteristics of male individuals with an age matched cohort of women. Propensity score generation with 2:1 matching for female and male patients was performed matching the cohorts for age, generating propensity estimates with a logistic regression model.

Results: We analyzed a sample of 4,902 men at high risk of osteoporosis. We found that the factors associated to osteoporosis care utilization in men were: the presence of comorbidities (OR 1.939, 95% CI 1.799-2.090), adjuvant hormonal therapy for prostate cancer (OR 1.482, 95% CI 1.315-1.670), the presence of vertebral or hip fractures (OR 1.490, 95% CI 1.378-1.611) and glucocorticoid treatment (OR 2.573, 95% CI 2.274-2.832) (Table 1)

Conclusion: We found that men accessed osteoporosis care with more severe osteoporosis and/or with a diagnosis of secondary osteoporosis. Male osteoporosis remains largely underdiagnosed with a dramatic latency in osteoporosis care utilization compared to women.

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Table 1. Clinical and densitometric characteristics of the study population and age-matched cohort of women

	Men (n=4,902)	Women (n=9,804)	OR (95% CI) – p value
Age (±SD)	65.1 (±14.2)	65.1 (±14.2)	NS
BMI (±SD)	25.31 (±4.91)	24.07 (±4.85)	<0.0001
Lumbar spine T-score (±SD)	-2.13 (±1.37)	-2.51 (±1.15)	<0.0001
Osteoporosis at lumbar spine (%)	2,601 (53.1%)	5,948 (60.7%)	0.733 (0.684-0.785)
Femoral neck T-score (±SD)	-1.93 (±1.04)	-2.19 (±0.91)	<0.0001
Osteoporosis at femoral neck (%)	1,412 (28.8%)	3,936 (40.1%)	0.603 (0.560-0.649)
% 10-year risk of fracture (±SD)	22.77 (±21.05)	20.26 (±4.85)	<0.0001
Family history of fragility fracture (%)	891 (18.2%)	2,379 (24.3%)	0.693 (0.636-0.756)
Secondary osteoporosis (%)	2,415 (49.3%)	3,092 (31.5%)	2.108 (1.965-2.262)
Glucocorticoids ≥5 mg/day >3 months (%)	768 (17.4%)	694 (7.7%)	2.573 (2.274-2.832)
Glucocorticoids ≥5 mg/day ≥3 months <12 months (%)	74 (2.0%)	72 (0.9%)	2.357 (1.700-3.267)
Glucocorticoids ≥5 mg/day ≥12 months (%)	119 (3.2%)	138 (1.6%)	1.977 (1.543-2.534)
Adjuvant hormonal therapy for breast cancer or prostate cancer (%)	495 (12.0%)	766 (8.4%)	1.482 (1.315-1.670)
Comorbidities (%)	1,778 (36.3%)	2,225 (22.7%)	1.939 (1.799-2.090)
Rheumatoid arthritis (%)	303 (8.8%)	511 (6.3%)	1.439 (1.241-1.668)
Psoriatic arthritis (%)	59 (1.9%)	103 (1.3)	1.390 (1.006-1.919)
Systemic lupus erythematosus (%)	22 (0.7%)	77 (1.0%)	0.693 (0.431-1.115)
Systemic sclerosis (%)	9 (0.3%)	60 (0.8%)	0.364 (0.180-0.734)
Other rheumatic diseases (%)	173 (5.2%)	310 (3.9%)	1.354 (1.119-1.638)
Inflammatory bowel diseases (%)	144 (2.7%)	126 (1.6%)	2.773 (2.175-3.534)
Chronic obstructive pulmonary disease (%)	281 (8.3%)	277 (3.5%)	2.461 (2.074-2.920)
Diabetes (%)	441 (12.4%)	478 (5.9%)	2.238 (1.954-2.564)
Neurological diseases (%)	236 (7.0%)	260 (3.3%)	2.202 (1.837-2.639)
HIV infection (%)	110 (3.4%)	23 (0.3%)	11.603 (7.389-18.221)
Vertebral or hip fractures (%)	1,434 (29.3%)	2,130 (21.7%)	1.490 (1.378-1.611)
Non-vertebral, non-hip fractures (%)	534 (10.9%)	1,477 (15.1%)	0.689 (0.620-0.766)

OP0113 FEMALE REPRODUCTIVE FACTORS AND RISK OF JOINT REPLACEMENT ARTHROPLASTY OF KNEE AND HIP DUE TO OSTEOARTHRITIS IN POSTMENOPAUSAL WOMEN: A NATIONWIDE COHORT STUDY OF 1.36 MILLION WOMEN

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Background: Previous studies on the link between female reproductive factors and osteoarthritis (OA) have shown conflicting results.

Objectives: This study attempted to explore the association between reproductive factors and joint replacement arthroplasty of knee (TKRA) and hip (THRA) in a large nationwide population-based cohort of postmenopausal women.

Methods: 1,218,257 subjects who participated in national health examination in 2009 were included in the study. The study outcomes is incident THRA or TKRA

due to severe hip or knee OA. The association of reproductive factors and THRA or TKRA was evaluated using a multivariate-adjusted proportional hazards model. **Results:** During the mean follow-up duration of 8.2 years, 1,733 incident THRA cases and 65,108 incident TKRA cases were observed. Later age at menarche (aHR 1.12 in 13-14 years; aHR 1.24 in 15-16 years; aHR 1.32 in ≥ 17 years), longer breastfeeding (aHR 1.24 in < 6 months; aHR 1.24 in 6-12 months; aHR 1.50 in ≥ 12 months), HRT (aHR 1.06 in < 2 years; aHR 1.11 in 2-5 years; aHR 1.21 ≥ 5 years) and OC use (aHR 1.11 in < 1 year; aHR 1.17 ≥ 1 year) was associated with increased risk of TKRA for severe knee OA, while later age at menopause (aHR 0.93 in 45-49 years; aHR 0.89 in 50-54 years), longer reproductive span (aHR 0.91 in 30-34 years; aHR 0.87 in 35-39 years; aHR 0.91 in ≥ 40 years) was associated with decreased risk. With regard to THRA for severe hip OA, later menarche (aHR 1.21 ≥ 17 years), longer breastfeeding (aHR 1.39 in < 6 months; aHR 1.31 in ≥ 12 months), and HRT more than 5 years (aHR 1.49) were associated with higher risk. The association between reproductive factors and severe OA was more pronounced in underweight and younger subjects.

Conclusion: Our study found that shorter estrogen exposure was associated with higher risk of joint replacement therapy due to severe OA, and such association was more pronounced in underweight and younger subjects.

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Rheumatoid arthritis - biological DMARDs

OP0114

SHORT- AND LONGER-TERM RISKS FOR ACUTE CORONARY SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS STARTING TREATMENT WITH DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS. A COLLABORATIVE OBSERVATIONAL HEAD-TO-HEAD STUDY ACROSS FIVE NORDIC RHEUMATOLOGY REGISTERS

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Background: Rheumatoid Arthritis (RA) is associated with increased cardiovascular co-morbidity including acute coronary syndrome (ACS), partly due to effects of systemic inflammation. Disease-modifying anti-rheumatic drugs (DMARDs) may reduce RA disease activity, but act through several pathways and may themselves have an impact on cardiovascular risks. Whether the risks of ACS associated with biologic (b) and targeted synthetic (ts) DMARDs differ is still unknown.

Objectives: To assess and compare incidences of ACS during treatment of RA with etanercept (ETA), adalimumab (ADA), infliximab (INF), certolizumab pegol (CTZ), golimumab (GOL), rituximab (RIT), abatacept (ABA), tocilizumab (TCZ), baricitinib (BAR) or tofacitinib (TOF).

Methods: We defined and pooled treatment cohorts of patients starting any of the above treatments between 2008 and 2017 from clinical rheumatology registers in Denmark (DK), Finland (FI), Norway (NO), and Sweden (SE). One patient could contribute several treatment episodes. Age, sex, co-medication (methotrexate, prednisolone), number of previous b/tsDMARDs, CRP, comorbidities (cardiovascular (including ACS (defined as ICD-10: I20.0, I21.0-4, I21.9) and cerebrovascular disease, thromboembolic events, diabetes, hospitalized infection, cancer, kidney failure, COPD) and associated drugs were extracted and used as adjustment in Cox regression analyses comparing the incidence of ACS between treatments. We used several follow-up lengths (1, 2, and up to 5 years) and two different risk windows (ACS on drug [ending follow-up on treatment discontinuation] and ACS ever since treatment start [disregarding any treatment discontinuation]). We also stratified by age and number of previous b/tsDMARDs.

Results: We included 40850 treatment courses in 24083 patients (DK 7271, FI 3732, NO 1540, and SE 11540; around 75% women). ETA was the most common treatment (27%) whereas BAR and TOF comprised $< 1\%$, and the other DMARDs 6-14% each. The proportions with a history of ACS at treatment start ranged from 1.2% (NO) to 1.8% (DK).

We found 780 incident ACS events during 141 326 person-years (pyrs) in the 5-year follow-up time and "ACS ever since treatment start" risk window, resulting in a crude incidence rate of 5.5 events per 1000 pyrs. No event was recorded for BAR nor TOF, which also had the shortest follow-up. Adjusted hazard ratios (HR) increased slightly with longer follow-up times, but the two risk windows provided similar HRs. For the 5-year follow-up, RIT was associated with an increased risk of ACS compared to ETA (Table), while no association was observed for shorter follow-up times. Stratifying on age did not modify the associations. Separate analyses by number of previous b/tsDMARDs suggested that ABA (HR=1.8, 95% CI 1.0-3.3), INF (HR=2.2, 95% CI 1.0-4.6) and RIT (HR=1.9, 95% CI 1.1-3.4) were associated with increased risks of ACS compared to ETA in the subgroup of patients with two or more previous bDMARDs (Figure), whereas no differences were found among patients starting either drug as 1st/2nd bDMARD.

Table 1. Comparisons of risks for ACS during a 5-year follow-up since start of bDMARD treatment.

Drug	N events	pyrs	Crude incidence rate/ 1000 pyrs	HR (95% CI) ¹
ETA	175	35917	4.9	ref.
ADA	115	24093	4.8	1.0 (0.8-1.3)
CTZ	54	14158	3.8	0.9 (0.6-1.2)
GOL	40	9006	4.4	1.1 (0.8-1.5)
INF	106	17803	6.0	1.2 (0.9-1.5)
ABA	70	10795	6.5	1.1 (0.8-1.4)
RIT	158	16622	9.5	1.3 (1.0-1.6)
TCZ	62	12866	4.8	0.9 (0.5-1.2)
BAR	0	36		
TOF	0	30		

Pyrs: person-years; HR: hazards ratio¹ adjustment: see text.

Conclusion: In this cohort including $\geq 24,000$ patients followed for up to 5 years, the ACS incidence rate was 5.5/1000 pyrs, with RIT showing an increased risk compared to ETA. In clinical practice, the choice of bDMARD does not seem to influence ACS risk in the short term. In the longer term, differences in ACS risk between bDMARDs may reflect channeling to these, or truly differential effects in subpopulations of patients.

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Figure:
Comparisons of risks for ACS during a 5-year follow-up since start of bDMARD treatment, stratified on number of previous b/tsDMARDs:
Hazard ratio and 95% confidence intervals (with etanercept as reference)

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