Supplementary Material

This document contains supplementary information for Westerlind et al Remission, response, retention and persistence to treatment with disease modifying agents in patients with rheumatoid arthritis – a study of harmonised Swedish, Danish and Norwegian treatment cohorts"

Contents

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Supplementary methods

Health care in the Nordic countries

Health care in the Nordic countries are publicly funded and tax-based. Patients with RA are typically managed in specialised rheumatology (hospital-based clinics or other outpatient facilities) and private care is negligible. For the individual patient, the costs for care and drugs are reimbursed above a threshold of around 200 euro per year (Sweden), 574 euros per year or less depending on income (Denmark), and 294 euros per year (Norway).

Data collection in Sweden

In Sweden, we used the following RA data sources and other registers to define the source populations with RA: i) The EIRA study of newly diagnosed RA aged 18 through 70 years of age, ongoing since 1996[1, 2]. In total, 4603 RA cases were included in EIRA during the study period (through 31st of December 2020), ii) the national Swedish Rheumatology Quality of Care register (SRQ). Initiated in the mid 1990ies SRQ currently covers around 85-90% of all patients with RA in the country[3]. Patients are monitored longitudinally and as part of routine clinical care. At visits, the rheumatologist enters information on RA disease activity and treatment, and the patient enters information on selected disease activity measures (e.g., pain on the visual analogue scale) and pre-defined patient reported outcome measures (PROMs). In addition, we used information from iii) the SRQ biobank (SRQb) that was created in 2012 and has been open for individuals with RA followed in SRQ (i.e., all patients in SRQb are also in SRQ). SRQb specifically patients with incident disease and patients starting (or who recently started) a biologic or targeted synthetic disease modifying anti-rheumatic drug (DMARD). SRQb currently holds blood samples for around 5,000 patients. iv) the Swedish National Patient Register (NPR) that contains information on hospitalisations and visits in specialty care (such as rheumatology) since 2001; v) the Swedish Prescribed Drug Register (PDR) that contains information on all dispensed drugs since July 2005; vi) The Swedish Total Population Register (TPR) that contains information on residency, migration and death since 1961.
While EIRA and SRQ served to identify patients with RA and clinical and treatment data, SRQb served to define sub-cohorts of the treatment cohorts identified from SRQ, based on available blood samples. The NPR, PDR and TPR provided data through which we could assess vital status and residency during follow-up for remission, and also quality assure information on treatment status as otherwise defined in SRQ.

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The following sub-cohorts were created for each of the four Swedish treatment cohorts: i) EIRA patients diagnosed with RA 2006 or later, ii) EIRA patients with available genotyping data, iii) SRQ patients diagnosed 2006 or later, and iv) SRQ patients included in SRQb (i.e., with an available blood sample stored in SRQ biobank) irrespective of its timing relative to the start of the treatment in question, v) SRQ patients included in SRQb with a stored blood sample taken at most 90 days after start of the treatment in question, and vi) SRQ patients included in SRQb with a stored blood sample taken more than 90 days after start of the treatment in question (exemplified in Supplementary Figure S1).

Data collection in Denmark

In Denmark, the nationwide registry, DANBIO, covers >90% of RA patients and >95% of the biological DMARD treated patients in routine care (N=22,500 RA patients). It started in year 1999, mainly targeting biological DMARD treated patients but now includes RA patients irrespective of treatment within both primary and secondary care (i.e. rheumatology private practise and hospital). The structure is quite similar to the Swedish SRQ with longitudinal monitoring in routine care and similar characteristics and outcomes are included, including DMARD treatment, effectiveness and monitoring of adverse safety events. Patients enter PROMs through an online system – either in the waiting areas or, since 2020, remotely from home by PC or other electronic devices. Similar to SRQ, DANBIO is approved as national quality registry and patient consent is not required. The completeness of the follow-up data is monitored by audits and yearly reports. For this study, we used the following sources to define the RA populations and treatment cohorts: i) adult patients monitored in DANBIO and treated with the respective DMARD of interest, ii) Patients monitored in DANBIO and with blood-samples available for biomarker analyses. Since 2015, sampling for the Biomarker protocol within the Danish Rheumatologic Biobank (DRB) infrastructure could occur after informed patient consent[4-6]. Sampling can occur at any timepoint during follow-up in routine care (a single cross-sectional sampling, or longitudinal multiple sampling in case a new DMARD is started). iii) The Danish National Patient Registry (DNPR), v) The Danish prescribed drug registry (DPDR), iv) The Danish civil registry (DCR). Thus, the RA cohorts and clinical data were identified in DANBIO, patients with sampling for DRB represented sub-cohorts, and information from DNPR, DPDR and DCR was used to assess deaths and emigrations during follow-up, as well as relevant information on comorbidities and treatments.

As data on symptom duration RA was missing for a subset of the DANBIO cohort, those starting methotrexate as their first ever DMARD are presented as the main cohorts, with filtration on early RA presented as sub-cohorts.

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Data collection in Norway

In Norway we included patients from several cohorts, including the NORDMARD study which is an observational study including patients with inflammatory joint diseases[7]. NORDMARD recruits from about a third of the population in Norway, was initiated in 2000 and collects blood samples from 2012. In the present study we included RA patients initiating i) first ever anti-TNFi treatment, ii) rituximab treatment. Blood samples were taken when patients initiated a biological DMARD as well as after three months. From the early RA NORVEAC observational cohort[8], we included patients initiating methotrexate using data from eight consecutive visits. From the ARCTIC strategy clinical trial[9], we included patients initiating i) methotrexate and ii) first ever TNFi. Patients with per protocol insufficient response to methotrexate had TNFi treatment added. Thus, all patients initiating TNFi were previously included in the methotrexate naïve group. We used data from the first eight visits. From the ULRABIT cohort[10] we included i) TNFi naïve and ii) patients initiating rituximab with results from all six visits. From all cohorts we used results from blood samples, clinical and laboratory assessments and in addition comprehensive ultrasound examinations in two cohorts (ARCTIC and ULRABIT). Importantly, in Sweden and Denmark, all patient data were registered prospectively and as part of the data collections in each data source, with dates for e.g., treatment start and stop defined as the actual calendar dates rather than status at any pre-defined visit number. In Norway, all cohorts were followed according to pre-scheduled visits. No information was available on early RA status.

Further, we divided the NORDMARD cohort into RA patients included between year 2000 and 2011 for whom no blood samples were available, and a cohort included from 2012 of patients initiating TNFi or rituximab (about half with blood samples). For the other Norwegian data sources, no sub-cohorts were of relevance.

Cohort overlap

Because of the longitudinal nature of the RA data sources, one and the same patient could contribute to more than one treatment cohort and sub-cohort. For instance, a patient included in SRQ at RA diagnosis and who first started methotrexate monotherapy, then added TNFi, and at a later time point initiated treatment with rituximab would be eligible for all three treatment cohorts.

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Supplementary Table S1. Cumulative filtration criteria for the methotrexate (MTX) treatment cohorts

Country	Sweden			Denmark		Norway		
Source cohort	**EIRA**	**SRQ**	**SRQ biobank**	**DANBIO**	**DRB**	**NORDMARD**	**ARCTIC**	**NORVEAC**
Cumulative criteria								
All patients with RA in data source during study period	4,603	60,752	5,650	37,863	4,576	5016	230	434
As above + all initiations of MTX	4,041	50,451	5,005	26,599	3,338	2670	230	408
As above + MTX as first DMARD	3,244	36,718	3,760	12,493	1,286	1783	230	404
As above + MTX as first DMARD in early RA	2,428	17,385	1,930	5,484*	594*	NA	220	345
As above + blood sample available in source cohort, ever	2,127	NA	1,930	NA	594	NA	220	100
As above + blood sample within 90 days of MTX start	2,127	NA	582	NA	66	NA	NA	NA

NA: not relevant for cohort

*Information on RA symptom duration was not uniformly collected in DANBIO and DRB. Numbers here presented refer to those with known information on RA duration, and, among those, with less than 12 months of RA symptom duration.

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Supplementary Table S2 Definitions of outcome measures used for this study

Outcome	Definition
Remission	
(original) ACR/EULAR Boolean remission	TJC(28) ≤1, SJC(28) ≤1, PGA (0-100) ≤10, CRP≤1mg/dl
(revised) ACR/EULAR Boolean remission	TJC(28) ≤1, SJC(28) ≤1, PGA (0-100) ≤20, CRP≤1mg/dl*
SDAI remission	SDAI ≤ 3.3 SDAI is based on TJC(28)+SJC(28)+PGA(0-10)+EGA(0-10)+CRP(mg/dL)
ACR/EULAR 3 item Boolean remission	TJC(28) ≤1, SJC(28) ≤1, CRP ≤1mg/dL
DAS28 remission	DAS28 < 2.6 or DAS28CRP < XX.
No swollen joints	SJC(28) = 0
Patients global VAS remission	PGA (0-100) ≤ 10
Response	
EULAR response	Either fulfilling a or b a. DAS28ESR_0 – DAS28ESR_x ≥1.2 and DAS28ESR_x ≤ 3.2 b. DAS28CRP_0 – DAS28CRP_x ≥1.2 and DAS28CRP_x ≤ 3.2 where _0 denotes the start of treatment and _x denotes the month for evaluation.
Treatment	
Retention	Staying on the treatment until the time-point of evaluation
Persistence	Staying on the treatment until the time-point of evaluation with no additional DMARD added

* Exploratory analysis, only used in the SRQ cohort

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, EGA - evaluator's global assessment, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, PGA – patient's global assessment, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, TJC(28) – tender 28 joint count, VAS – visual analogue scale

Supplementary Table S3. RA patients initiating methotrexate as the first ever DMARD. Characteristics of sub-cohorts (available for the Swedish EIRA, SRQ, and SRQb, and the Danish DANBIO and DRB cohorts) and their outcome measures at 3, 6 and 12 months.

Country	Sweden					Denmark	
Source cohort	EIRA		SRQ	SRQ biobank		DANBIO	DRB
Sub-cohort	Treatment start 2006-2020	With genotyping data available	Treatment start 2006-2020	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	Early RA	Early RA
N patients	1549	2127	12853	356	1252	5484	594
Characteristics at treatment start							
N women (%)	1071 (69%)	1469 (69%)	8676 (68%)	231 (65%)	878 (70%)	3546 (65%)	369 (62%)
Median age at inclusion (IQR)	59 (48,66)	57 (46,64)	62 (51,71)	64 (53,74)	59 (47,68)	63 (52,72)	59 (49,68)
Median calendar year of inclusion (IQR)	2011 (2008,2015)	2007 (2004,2011)	2014 (2010,2017)	2017 (2015,2018)	2013 (2010,2016)	2016 (2013, 2018)	2014 (2013, 2016)
Median disease duration (IQR)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0, 0)	0 (0, 0)
Seropositive disease * (%)	999 (66%)	1426 (68%)	7953 (63%)	184 (53%)	798 (65%)	3460 (65%)	404 (70%)
Current smoker (%)	271 (23%)	496 (25%)	1795 (16%)	51 (15%)	196 (16%)	567 (27%)	71 (31%)
Co-treatment with oral steroids (%)	900 (58%)	1011 (48%)	7209 (56%)	193 (54%)	618 (49%)	743 (14%)	96 (16%)
Visit-based clinical data							
Clinical data at treatment start							
Median SJC(28) (IQR)	8 (4,12)	8 (5,12)	7 (4,11)	6 (3,10)	7 (3,10)	4 (2, 8)	4 (2, 8)
Median TJC (IQR)	7 (3,12)	7 (4,12)	6 (3,10)	6 (2,10)	6 (3,10)	6 (3, 11)	6 (2, 10)
Median CRP (IQR)	11 (4,25)	13 (6,31)	12 (5,30)	10 (4,24)	10 (5,27)	11 (4, 27)	11 (4, 27)
Median ESR (IQR)	27 (15,43)	27 (15,45)	27 (14,46)	28 (15,48)	25 (14,43)	NA	NA
Median Patient global VAS (IQR)	50 (31,69)	50 (30,69)	53 (33,72)	49 (30,70)	52 (34,72)	62 (37, 81)	65 (34, 83)
Median HAQ (IQR)	1.00 (0.63,1.38)	1.00 (0.63,1.38)	1.00 (0.50,1.50)	1.00 (0.63,1.50)	1.00 (0.63,1.50)	0.88 (0.38, 1.50)	0.88 (0.38,1.50)
Treatment outcomes at three months							
Retention (%)	1315 (98%)	1868 (99%)	9230 (97%)	303 (96%)	974 (97%)	4311 (98%)	474 (98%)
Persistence (%)	1264 (95%)	1859 (99%)	9141 (97%)	297 (94%)	955 (96%)	4183 (95%)	457 (94%)
EULAR good response	654 (54%)	796 (45%)	4042 (53%)	176 (64%)	406 (49%)	1507 (50%)	140 (38%)
Treatment outcomes at six months							
Retention (%)	1085 (93%)	1617 (93%)	6321 (92%)	206 (92%)	764 (92%)	3369 (94%)	393 (94%)
Persistence (%)	942 (81%)	1366 (79%)	5568 (81%)	182 (82%)	642 (77%)	2929 (82%)	328 (78%)
-EULAR good response	572 (56%)	755 (49%)	2592 (46%)	111 (57%)	298 (43%)	1098 (50%)	120 (42%)
Treatment outcomes at twelve months							
Retention (%)	1169 (89%)	1735 (90%)	7652 (88%)	251 (86%)	941 (89%)	3743 (89%)	454 (86%)

Persistence (%)	917 (70%)	1321 (68%)	6092 (70%)	193 (66%)	690 (65%)	2932 (70%)	319 (61%)
EULAR good response	589 (51%)	800 (47%)	3202 (45%)	123 (47%)	346 (39%)	1284 (51%)	152 (46%)

* Seropositivity defined as diagnosed with ICD code M05.8 or M05.9 and seronegative defined as diagnosed with M06.0 or M06.8 (and, if available, negative for antiCCP and IgM RF)

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, VAS – visual analogue scale

Supplementary Table S4. Missing data for the methotrexate cohorts. Numbers are N missing (%)

Country	Sweden								Denmark				Norway		
Source cohort	EIRA			SRQ		SRQ biobank			DANBIO		DRB		NOR-DMARD	ARCTIC	NOR-VEAC
(Sub)-cohort	EIRA	Treatment start 2006-2020	Genotyped	SRQ	Treatment start 2006-2020	SRQ biobank	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	DANBIO	Early RA	DRB	Early RA	NOR-DMARD	ARCTIC	NOR-VEAC
N patients	2428	1549	2127	17385	12853	1930	356	1252	12493	5484	1286	594	1783	230	404
Characteristics at treatment start															
N women	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (0)	0 (0)	1 (0)
Age at inclusion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (0)	0 (0)	0 (0)
Calendar year of inclusion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Disease duration	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Seropositive disease	52 (2)	26 (2)	42 (2)	423 (2)	320 (2)	43 (2)	10 (3)	25 (2)	407 (3)	171 (3)	49 (4)	18 (3)	0 (0)	0 (0)	0 (0)
Current smoker	396 (16)	381 (25)	173 (8)	3428 (20)	1623 (13)	27 (1)	5 (1)	17 (1)	7930 (64)	3377 (62)	803 (62)	367 (62)	11 (1)	0 (0)	17 (4)
Co-treatment with oral steroids	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	86 (5)	0 (0)	0 (0)
Visit-based clinical data															
Clinical data at treatment start															
Registered visit	37 (2)	33 (2)	26 (1)	1182 (7)	1105 (9)	156 (8)	15 (4)	115 (9)	2370 (19)	771 (14)	208 (16)	71 (12)	0 (0)	0 (0)	0 (0)
SJC(28)	68 (3)	62 (4)	52 (2)	1512 (9)	1383 (11)	191 (10)	27 (8)	134 (11)	2819 (23)	936 (17)	258 (20)	92 (16)	6 (0)	0 (0)	4 (1)
TJC(28)	68 (3)	62 (4)	52 (2)	1541 (9)	1404 (11)	195 (10)	27 (8)	137 (11)	2837 (23)	950 (17)	258 (20)	93 (16)	13 (1)	0 (0)	3 (1)
CRP	62 (3)	48 (3)	50 (2)	1611 (9)	1408 (11)	201 (10)	23 (6)	147 (12)	3185 (26)	1098 (20)	302 (24)	116 (20)	65 (4)	0 (0)	3 (1)
ESR	112 (5)	76 (5)	88 (4)	1883 (11)	1615 (13)	227 (12)	40 (11)	154 (12)	NA	NA	NA	NA	139 (8)	1 (0)	4 (1)
Patient global VAS	115 (5)	93 (6)	85 (4)	2525 (15)	2223 (17)	265 (14)	32 (9)	193 (15)	3787 (30)	1414 (26)	326 (25)	131 (22)	40 (2)	0 (0)	2 (0)
HAQ	156 (6)	113 (7)	118 (6)	3275 (19)	2874 (22)	351 (18)	42 (12)	261 (21)	4287 (34)	1659 (30)	368 (29)	151 (25)	31 (2)	230 (100)	23 (6)
Treatment outcomes at three months															
Available visit	291 (12)	212 (14)	243 (11)	4418 (25)	3383 (26)	358 (19)	39 (11)	253 (20)	3051 (24)	1077 (20)	237 (18)	109 (18)	0 (0)	0 (0)	0 (0)

Retention	291 (12)	212 (14)	243 (11)	4418 (25)	3383 (26)	358 (19)	39 (11)	253 (20)	3051 (24)	1077 (20)	237 (18)	109 (18)	221 (12)	0 (0)	58 (14)
Persistence	291 (12)	212 (14)	243 (11)	4418 (25)	3383 (26)	358 (19)	39 (11)	253 (20)	3051 (24)	1077 (20)	237 (18)	109 (18)	221 (12)	0 (0)	58 (14)
Response															
EULAR Good response	451 (19)	341 (22)	353 (17)	6600 (38)	5271 (41)	605 (31)	83 (23)	421 (34)	6464 (52)	2471 (45)	563 (44)	230 (39)	392 (22)	2 (1)	267 (66)
Remission															
ACR/EULAR Boolean	371 (15)	266 (17)	297 (14)	5343 (31)	4132 (32)	451 (23)	56(16)	316 (25)	3680 (30)	1335 (24)	290 (23)	128 (22)	294 (16)	1 (0)	75 (19)
SDAI	410 (17)	303 (20)	323 (15)	5757 (33)	4532 (35)	514 (27)	77 (22)	344 (27)	4891 (39)	1886 (34)	415 (32)	177 (30)	439 (25)	2 (1)	88 (22)
ACR/EULAR 3-item Boolean	339 (14)	244 (16)	275 (13)	4956 (29)	3810 (30)	413 (21)	50 (14)	289 (23)	3714 (30)	1340 (24)	301 (23)	129 (22)	310 (17)	1 (0)	80 (20)
DAS28	358 (15)	261 (17)	285 (13)	5243 (30)	4074 (32)	443 (23)	54 (15)	310 (25)	4437 (36)	1655 (30)	365 (28)	154 (26)	353 (20)	2 (1)	250 (62)
SJC(28)=0	312 (13)	230 (15)	251 (12)	4718 (27)	3649 (28)	391 (20)	45 (13)	273 (22)	3639 (29)	1310 (24)	291 (23)	124 (21)	273 (15)	1 (0)	78 (19)
Patient global VAS ≤ 10	334 (14)	244 (16)	270 (13)	4990 (29)	3871 (30)	415 (22)	47 (13)	293 (23)	3984 (32)	1462 (27)	329 (26)	142 (24)	309 (17)	1 (0)	74 (18)
Treatment outcomes at six months															
Available visit	484 (20)	382 (25)	395 (19)	7258 (42)	5985 (47)	665 (34)	133 (37)	422 (34)	4607 (37)	1897 (35)	370 (29)	175 (30)	0 (0)	0 (0)	0 (0)
Retention	484 (20)	382 (25)	395 (19)	7258 (42)	5985 (47)	665 (34)	133 (37)	422 (34)	4607 (37)	1897 (35)	370 (29)	175 (30)	265 (15)	21 (9)	98 (24)
Persistence	484 (20)	382 (25)	395 (19)	7258 (42)	5985 (47)	665 (34)	133 (37)	422 (34)	4607 (37)	1897 (35)	370 (29)	175 (30)	265 (15)	21 (9)	98 (24)
Response															
EULAR Good response	700 (29)	521 (34)	577 (27)	8882 (51)	7239 (56)	860 (45)	161 (45)	558 (45)	7952 (64)	3277 (60)	719 (56)	306 (52)	625 (35)	22 (10)	294 (73)
Remission															
ACR/EULAR Boolean	637 (26)	463 (30)	531 (25)	8209 (47)	6645 (52)	759 (39)	147 (41)	484 (39)	5518 (44)	2310 (42)	468 (36)	218 (37)	520 (29)	22 (10)	132 (33)
SDAI	658 (27)	483 (31)	547 (26)	8381 (48)	6801 (53)	794 (41)	155 (44)	508 (41)	6605 (53)	2767 (51)	575 (45)	256 (43)	655 (37)	24 (10)	141 (35)
ACR/EULAR 3-item Boolean	619 (25)	451 (29)	517 (24)	7991 (46)	6478 (50)	735 (38)	143 (40)	468 (37)	5616 (45)	2346 (43)	479 (37)	215 (36)	543 (30)	23 (10)	135 (33)
DAS28	625 (26)	457 (30)	519 (24)	8137 (47)	6604 (51)	753 (39)	147 (41)	478 (38)	6210 (50)	2599 (47)	532 (41)	238 (40)	586 (33)	22 (10)	272 (67)

SJC(28)=0	590 (24)	436 (28)	488 (23)	7808 (45)	6355 (49)	716 (37)	140 (39)	455 (36)	5546 (44)	2295 (42)	468 (36)	211 (36)	500 (28)	21 (9)	132 (33)
Patient global VAS ≤ 10	598 (25)	438 (28)	497 (23)	7951 (46)	6451 (50)	732 (38)	142 (40)	467 (37)	5720 (46)	2388 (44)	483 (38)	223 (38)	520 (29)	22 (10)	129 (32)
Treatment outcomes at twelve months															
Available visit	279 (11)	233 (15)	191 (9)	4941 (28)	4151 (32)	334 (17)	64 (18)	194 (15)	3055 (25)	1294 (24)	142 (11)	69 (12)	0 (0)	0 (0)	0 (0)
Retention	279 (11)	233 (15)	191 (9)	4941 (28)	4151 (32)	334 (17)	64 (18)	194 (15)	3055 (25)	1294 (24)	142 (11)	69 (12)	170 (10)	46 (20)	85 (21)
Persistence	279 (11)	233 (15)	191 (9)	4941 (28)	4151 (32)	334 (17)	64 (18)	194 (15)	3055 (25)	1294 (24)	142 (11)	69 (12)	170 (10)	46 (20)	85 (21)
Response															
EULAR Good response	548 (23)	405 (26)	428 (20)	7129 (41)	5787 (45)	571 (30)	97 (27)	356 (28)	7271 (58)	2965 (54)	612 (48)	267 (45)	724 (41)	46 (20)	305 (75)
Remission															
ACR/EULAR Boolean	483 (20)	352 (23)	379 (18)	6311 (36)	5090 (40)	462 (24)	85 (24)	275 (22)	4502 (36)	1903 (35)	311 (24)	149 (25)	630 (35)	46 (20)	145 (36)
SDAI	521 (21)	390 (25)	406 (19)	6584 (38)	5348 (42)	502 (26)	99 (28)	295 (24)	5446 (44)	2305 (42)	395 (31)	190 (32)	767 (43)	46 (20)	152 (38)
ACR/EULAR 3-item Boolean	470 (19)	340 (22)	368 (17)	6085 (35)	4905 (38)	436 (23)	79 (22)	263 (21)	4538 (36)	1915 (35)	315 (25)	151 (25)	667 (37)	46 (20)	145 (36)
DAS28	476 (20)	347 (22)	372 (17)	6248 (36)	5047 (39)	461 (24)	85 (24)	274 (22)	5006 (40)	2115 (39)	344 (27)	164 (28)	689 (39)	46 (20)	274 (68)
SJC(28)=0	446 (18)	321 (21)	344 (16)	5934 (34)	4796 (37)	423 (22)	77 (22)	255(20)	4433 (36)	1872 (34)	307 (24)	144 (24)	609 (34)	46 (20)	143 (35)
Patient global VAS ≤ 10	456 (19)	330 (21)	354 (17)	6064 (35)	4892 (38)	441 (23)	80 (22)	262 (21)	4603 (37)	1938 (35)	323 (25)	152 (26)	626 (35)	46 (20)	143 (35)
Retention and persistence based on recorded start/stop dates															
Retention															
Month 3	1 (0)	1 (0)	1 (0)	26 (0)	21 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	24 (1)	4 (2)	0 (0)
Month 6	20 (1)	20 (1)	1 (0)	324 (2)	296 (2)	14 (1)	0 (0)	0 (0)	247 (2)	129 (2)	11 (1)	6 (1)	43 (2)	8 (3)	0 (0)
Month 12	52 (2)	46 (3)	7 (0)	932 (5)	856 (7)	44 (2)	0 (0)	0 (0)	779 (6)	400 (7)	20 (2)	11 (2)	76 (4)	19 (8)	0 (0)
Month 36	193 (8)	172 (11)	32 (2)	3251 (19)	2980 (23)	343 (18)	106 (30)	110 (9)	2615 (21)	1256 (23)	116 (9)	54 (9)	194 (11)	177 (77)	0 (0)
Persistence															
Month 3	1 (0)	1 (0)	1 (0)	26 (0)	21 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	24 (1)	4 (2)	0 (0)
Month 6	20 (1)	17 (1)	1 (0)	324 (2)	296 (2)	14 (1)	0 (0)	0 (0)	230 (2)	117 (2)	11 (1)	6 (1)	43 (2)	8 (3)	0 (0)
Month 12	52 (2)	31 (2)	7 (0)	932 (5)	856 (7)	44 (2)	0 (0)	0 (0)	678 (5)	342 (6)	19 (2)	11 (2)	76 (4)	18 (8)	0 (0)
Month 36	193 (8)	105 (7)	32 (2)	3251 (19)	2980 (23)	343 (18)	106 (30)	110 (9)	2022 (16)	970 (18)	72 (6)	35 (6)	194 (11)	161 (70)	0 (0)

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, VAS – visual analogue scale

Supplementary Table S5. Patients with early RA initiating methotrexate as the first ever DMARD. Remission outcomes during one year and retention and persistence during three years of follow-up for the sub-cohorts.

Country	Sweden								Denmark				Norway		
Source-cohort	EIRA			SRQ		SRQ biobank			DANBIO		DRB		NOR-DMARD	ARCTIC	NOR-VEAC
(Sub-) cohort	EIRA	Treatment start 2006-2020	With genotype data available	SRQ	Treatment start 2006-2020	SRQ biobank	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	DANBIO	Early RA	DRB	Early RA	NOR-DMARD	ARCTIC	NOR-VEAC
N patients	2428	1549	2127	17385	12853	1930	356	1252	12493	5484	1286	594	1783	230	404
Remission at three months															
ACR/EULAR	342 (17%)	261 (20%)	288 (16%)	2029 (17%)	1728 (20%)	274 (19%)	74 (25%)	161 (17%)	1324 (15%)	714 (17%)	126 (13%)	67 (14%)	118 (8%)	65 (28%)	74 (22%)
SDAI	383 (19%)	298 (24%)	330 (18%)	2114 (18%)	1765 (21%)	287 (20%)	80 (29%)	164 (18%)	1987 (26%)	1011 (28%)	192 (22%)	95 (23%)	158 (12%)	84 (37%)	94 (30%)
ACR/EULAR 3-item Boolean	655 (31%)	504 (39%)	553 (30%)	4354 (35%)	3646 (40%)	568 (37%)	145 (47%)	339 (35%)	3853 (44%)	1864 (45%)	371 (38%)	180 (39%)	315 (21%)	104 (45%)	152 (47%)
DAS28	787 (38%)	602 (47%)	670 (36%)	4924 (41%)	4046 (46%)	666 (45%)	167 (55%)	397 (42%)	3356 (42%)	1638 (43%)	321 (35%)	154 (35%)	383 (27%)	124 (54%)	73 (47%)
SJC(28)=0	746 (35%)	571 (43%)	628 (33%)	4799 (38%)	3977 (43%)	663 (43%)	176 (57%)	381 (39%)	3699 (42%)	1707 (41%)	493 (50%)	234 (50%)	406 (27%)	144 (63%)	184 (56%)
Patient global VAS ≤ 10	562 (27%)	404 (31%)	485 (26%)	3333 (27%)	2667 (30%)	432 (29%)	102 (33%)	264 (28%)	1906 (22%)	977 (24%)	181 (19%)	84 (19%)	292 (20%)	90 (39%)	111 (34%)
Remission at six months															
ACR/EULAR	355 (20%)	255 (23%)	296 (19%)	1440 (16%)	1103 (18%)	220 (19%)	55 (26%)	134 (17%)	1146 (16%)	556 (18%)	102 (12%)	54 (14%)	127 (10%)	73 (35%)	75 (28%)
SDAI	392 (22%)	289 (27%)	334 (21%)	1603 (18%)	1235 (20%)	225 (20%)	57 (28%)	133 (18%)	1684 (29%)	811 (30%)	152 (21%)	75 (22%)	169 (15%)	94 (46%)	96 (37%)
ACR/EULAR 3-item Boolean	664 (37%)	475 (43%)	569 (35%)	3199 (34%)	2443 (38%)	431 (36%)	92 (43%)	272 (35%)	3157 (46%)	1471 (47%)	299 (37%)	154 (41%)	309 (25%)	123 (59%)	155 (58%)
DAS28	750 (42%)	520 (48%)	659 (41%)	3544 (38%)	2584 (41%)	457 (39%)	101 (48%)	284 (37%)	2722 (43%)	1298 (45%)	253 (34%)	126 (35%)	370 (31%)	135 (65%)	76 (58%)
SJC(28)=0	730 (40%)	519 (47%)	630 (38%)	3618 (38%)	2741 (42%)	492 (41%)	109 (50%)	302 (38%)	2416 (35%)	1072 (34%)	353 (43%)	164 (43%)	446 (35%)	160 (77%)	187 (69%)

Patient's global VAS ≤ 10	526 (29%)	352 (32%)	455 (28%)	2268 (24%)	1631 (25%)	305 (25%)	73 (34%)	180 (23%)	1621 (24%)	792 (26%)	151 (19%)	74 (20%)	288 (23%)	99 (48%)	104 (38%)
Remission at twelve months															
ACR/EULAR	393 (20%)	271 (23%)	351 (20%)	1911 (17%)	1473 (19%)	254 (17%)	60 (22%)	160 (16%)	1450 (18%)	710 (20%)	144 (15%)	84 (19%)	149 (13%)	85 (46%)	83 (32%)
SDAI	443 (23%)	305 (26%)	394 (23%)	2194 (20%)	1651 (22%)	285 (20%)	73 (28%)	177 (18%)	2213 (31%)	1077 (34%)	232 (26%)	130 (32%)	212 (21%)	117 (64%)	114 (45%)
ACR/EULAR 3-item Boolean	748 (38%)	529 (44%)	667 (38%)	4164 (37%)	3166 (40%)	517 (35%)	106 (38%)	324 (33%)	3922 (49%)	1826 (51%)	386 (40%)	202 (46%)	380 (34%)	135 (73%)	167 (64%)
DAS28	821 (42%)	561 (47%)	730 (42%)	4462 (40%)	3321 (43%)	560 (38%)	120 (44%)	358 (37%)	3527 (47%)	1668 (50%)	357 (38%)	174 (40%)	428 (39%)	151 (82%)	85 (65%)
SJC(28)=0	817 (41%)	559 (46%)	720 (40%)	4600 (40%)	3486 (43%)	589 (39%)	127 (46%)	377 (38%)	2224 (28%)	901 (25%)	344 (35%)	144 (32%)	525 (45%)	156 (85%)	210 (80%)
Patient global VAS ≤ 10	535 (27%)	348 (29%)	479 (27%)	2688 (24%)	1976 (25%)	344 (23%)	81 (29%)	218 (22%)	2079 (26%)	991 (28%)	224 (23%)	120 (27%)	273 (24%)	106 (58%)	107 (41%)
Retention and persistence based on recorded start/stop dates															
Retention															
Month 3	2370 (98%)	1509 (97%)	2077 (98%)	16849 (97%)	12421 (97%)	1870 (97%)	339 (95%)	1216 (97%)	11970 (96%)	5274 (96%)	1228 (95%)	575 (97%)	1635 (93%)	226 (100%)	386 (96%)
Month 6	2231 (93%)	1415 (93%)	1968 (93%)	15855 (93%)	11649 (93%)	1779 (93%)	320 (90%)	1177 (94%)	11210 (92%)	4941 (92%)	1154 (91%)	539 (92%)	1461 (84%)	210 (95%)	367 (91%)
Month 12	2105 (89%)	1324 (88%)	1884 (89%)	14613 (89%)	10606 (88%)	1667 (88%)	307 (86%)	1120 (89%)	9962 (85%)	4370 (86%)	1070 (85%)	500 (86%)	1195 (70%)	174 (82%)	325 (80%)
Month 36	1762 (79%)	1056 (77%)	1658 (79%)	11145 (79%)	7700 (78%)	1232 (78%)	192 (77%)	896 (78%)	6345 (64%)	2722 (64%)	783 (67%)	365 (68%)	697 (44%)	NA	151 (37%)
Persistence															
Month 3	2309 (95%)	1464 (95%)	2021 (95%)	16415 (95%)	12108 (94%)	1794 (93%)	329 (92%)	1165 (93%)	11460 (92%)	5034 (92%)	1160 (90%)	539 (91%)	1635 (93%)	221 (98%)	374 (93%)
Month 6	1892 (79%)	1252 (82%)	1659 (78%)	14047 (82%)	10443 (83%)	1499 (78%)	284 (80%)	985 (79%)	9935 (81%)	4350 (81%)	970 (76%)	446 (76%)	1461 (84%)	200 (90%)	333 (82%)
Month 12	1589 (67%)	1049 (69%)	1411 (67%)	11633 (71%)	8577 (71%)	1190 (63%)	236 (66%)	785 (63%)	7940 (67%)	3457 (67%)	750 (59%)	357 (61%)	1195 (70%)	158 (75%)	251 (62%)
Month 36	1065 (48%)	664 (46%)	1004 (48%)	7526 (53%)	5327 (54%)	647 (41%)	127 (51%)	444 (39%)	4327 (41%)	1840 (41%)	439 (36%)	212 (38%)	697 (44%)	NA	100 (25%)

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, VAS – visual analogue scale

Supplementary Table S6. RA patients initiating TNF inhibitors as the first ever biological DMARD. Characteristics of additional Swedish and Norwegian sub-cohorts.

Country	Sweden					Norway	
Source cohort	EIRA		SRQ	SRQ biobank		NOR-DMARD	
Sub-cohort	Treatment start 2006-2020	With genotype data available	Treatment start 2006-2020	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	Treatment start 2012-2021	Treatment start 2012-2021 and blood sampled
N patients	1226	1517	21992	626	1716	811	224
Characteristics at treatment start							
N women (%)	942 (77%)	1157 (76%)	16602 (75%)	464 (74%)	1322 (77%)	571 (71%)	161 (72%)
Median age at inclusion (IQR)	55 (43,64)	55 (43,63)	57 (46,65)	57 (46,67)	56 (45,64)	55 (43,64)	54 (40,65)
Median calendar year of inclusion (IQR)	2012 (2009,2016)	2009 (2006,2014)	2010 (2005,2016)	2017 (2015,2018)	2012 (2010,2014)	2016 (2014,2019)	2016 (2014,2017)
Median disease duration (IQR)	2 (0,7)[+]	3 (1,7)[+]	3 (0,7)[+]	2 (0,5)[+]	3 (0,8)[+]	4 (1,9)	5 (1,10)
Seropositive disease* (%)	946 (78%)	1175 (78%)	16186 (77%)	413 (67%)	1274 (75%)	632 (78%)	172 (77%)
Current smoker (%)	259 (23%)	349 (24%)	2585 (14%)	75 (12%)	219 (13%)	91 (16%)	24 (16%)
Co-treatment with oral steroids (%)	556 (45%)	647 (43%)	9619 (44%)	248 (40%)	758 (44%)	312 (40%)	92 (43%)
Visit-based clinical data							
Clinical data at treatment start							
Median SJC(28) (IQR)	6 (3,9)	6 (3,10)	6 (3,10)	4 (2,7)	6 (3,9)	2 (0,6)	2 (0,6)
Median TJC(28) (IQR)	6 (3,10)	6 (3,10)	6 (3,10)	5 (2,8)	6 (3,10)	3 (1,7)	3 (1,7)
Median CRP (IQR)	7 (3,17)	9 (4,22)	10 (4,28)	6 (3,15)	9 (4,23)	5 (2,11)	4 (2,9)
Median ESR (IQR)	20 (11,33)	21 (12,36)	23 (12,40)	17 (9,30)	18 (9,33)	14 (7,25)	13 (7,22)
Median Patient Global VAS (IQR)	54 (32,72)	55 (33,72)	59 (40,75)	54.5 (34,73)	57 (36,73)	45 (22,66)	42 (20,67)
Median HAQ (IQR)	0.88 (0.41,1.25)	1 (0.5,1.38)	1.13 (0.63,1.63)	0.88 (0.5,1.25)	1 (0.5,1.38)	0.5 (0.13,0.86)	0.38 (0.13,0.85)
Treatment outcomes at three months							
Retention (%)	821 (94%)	1056 (94%)	13570 (95%)	415 (97%)	1045 (94%)	569 (90%)	180 (93%)
Persistence (%)	819 (94%)	1052 (94%)	13514 (95%)	415 (97%)	1041 (94%)	534 (85%)	171 (89%)
EULAR good response	362 (51%)	438 (46%)	4943 (42%)	168 (51%)	414 (47%)	194 (39%)	60 (38%)
Treatment outcomes at six months							
Retention (%)	603 (82%)	832 (85%)	9901 (84%)	201 (72%)	829 (80%)	407 (69%)	130 (73%)
Persistence (%)	588 (80%)	806 (82%)	9546 (81%)	196 (71%)	803 (78%)	378 (65%)	127 (72%)
EULAR good response	298 (48%)	379 (44%)	3796 (38%)	89 (39%)	336 (40%)	149 (42%)	46 (41%)
Treatment outcomes at twelve months							
Retention (%)	650 (70%)	904 (74%)	11027 (73%)	253 (64%)	929 (66%)	365 (59%)	123 (65%)
Persistence (%)	622 (67%)	854 (70%)	10267 (68%)	244 (61%)	878 (62%)	321 (52%)	114 (60%)
EULAR response (Good vs moderate/none)	328 (44%)	425 (42%)	4450 (36%)	109 (36%)	387 (34%)	140 (45%)	49 (48%)

* Seropositivity defined as diagnosed with ICD code M05.8 or M05.9 and seronegative defined as diagnosed with M06.0 or M06.8 (and, if available, negative for antiCCP and IgM RF)

[+]calculated on the subset of patients starting TNFi treatment in year 2006 or later
Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, DRB – Danish Rheumatologic Biobank, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, TJC(28) – tender 28 joint count, VAS – visual analogue scale

Supplementary table S7 describing missing data for the TNFi sub-cohorts. Numbers are missing (%).

Country	Sweden								Denmark		Norway					
Source cohort	EIRA			SRQ		SRQ biobank			DANBIO	DRB	NOR-DMARD			ULRABIT	NOR-VEAC	ARCTIC
(Sub-) cohort	EIRA	Treatment start 2006-2020	With genotype data available	SRQ	Treatment start 2006-2020	SRQ biobank	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	DANBIO	DRB	NOR-DMARD	Treatment start 2012-2021	Treatment start 2012-2021 and blood sampled	ULRABIT	NOR-VEAC	ARCTIC
Patients	1628	1226	1517	22486	21992	2674	626	1716	9312	2127	2036	811	224	141	96	52
Characteristics at treatment start																
Women	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	9 (0)	3 (0)	1 (0)	0 (0)	0 (0)	0 (0)
Age at inclusion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (0)	3 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Calendar year of inclusion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Disease duration	0 (0)+	0 (0)+	0 (0)+	0 (0)+	0 (0)+	0 (0)+	0 (0)+	0 (0)+	381 (4)	56 (3)	307 (15)	288 (36)	95 (42)	0 (0)	0 (0)	0 (0)
Seropositive disease	14 (1)	12 (1)	12 (1)	1006 (4)	988 (4)	39 (1)	9 (1)	26 (2)	346 (4)	80 (4)	0 (0)	0 (0)	0 (0)	46 (33)	0 (0)	0 (0)
Current smoker (%)	126 (8)	120 (10)	60 (4)	3572 (16)	3503 (16)	51 (2)	10 (2)	35 (2)	5805 (62)	1276 (60)	269 (13)	256 (32)	71 (32)	50 (35)	6 (6)	0 (0)
Co-treatment with oral steroids (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	90 (4)	40 (5)	10 (4)	0 (0)	0 (0)	0 (0)
Visit-based clinical data																
Clinical data at treatment start																
Registered visit	113 (7)	101 (8)	100 (7)	2226 (10)	2172 (10)	288 (11)	85 (14)	155 (9)	759 (8)	99 (5)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
SJC (28)	166 (10)	141 (12)	148 (10)	3360 (15)	3278 (15)	377 (14)	104 (17)	214 (12)	944 (10)	137 (6)	102 (5)	88 (11)	23 (10)	0 (0)	4 (4)	0 (0)
TJC (28)	171 (11)	144 (12)	153 (10)	3393 (15)	3312 (15)	383 (14)	104 (17)	218 (13)	959 (10)	141 (7)	106 (5)	88 (11)	23 (10)	0 (0)	4 (4)	0 (0)
CRP	164 (10)	136 (11)	145 (10)	3416 (15)	3333 (15)	370 (14)	97 (15)	215 (13)	994 (11)	151 (7)	131 (6)	71 (9)	21 (9)	0 (0)	3 (3)	0 (0)
ESR	220 (14)	186 (15)	197 (13)	3995 (18)	3900 (18)	455 (17)	133 (21)	255 (15)	NA	NA	279 (14)	165 (20)	27 (12)	0 (0)	7 (7)	0 (0)
Patient Global VAS	183 (11)	150 (12)	166 (11)	4043 (18)	3943 (18)	483 (18)	112 (18)	312 (18)	1104 (12)	150 (7)	99 (5)	72 (9)	13 (6)	0 (0)	1 (1)	0 (0)

HAQ	256 (16)	208 (17)	235 (15)	4868 (22)	4744 (22)	602 (23)	141 (23)	378 (22)	1353 (15)	194 (9)	102 (5)	71 (9)	10 (4)	0 (0)	8 (8)	52 (100)
Treatment outcomes at three months																
Available visit	434 (27)	355 (29)	399 (26)	7923 (35)	7749 (35)	909 (34)	197 (31)	609 (35)	1773 (19)	270 (13)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retention	434 (27)	355 (29)	399 (26)	7923 (35)	7749 (35)	909 (34)	197 (31)	609 (35)	1773 (19)	270 (13)	337 (17)	180 (22)	31 (14)	3 (2)	28 (29)	15 (29)
Persistence	434 (27)	355 (29)	399 (26)	7923 (35)	7749 (35)	909 (34)	197 (31)	609 (35)	1773 (19)	270 (13)	337 (17)	180 (22)	31 (14)	141 (100)	26 (27)	15 (29)
Response																
EULAR response	623 (38)	513 (42)	569 (38)	10480 (47)	10234 (47)	1272 (48)	294 (47)	826 (48)	3252 (35)	568 (27)	614 (30)	314 (39)	67 (30)	5 (4)	76 (79)	15 (29)
Remission																
ACR/EULAR	527 (32)	423 (35)	482 (32)	9171 (41)	8964 (41)	1070 (40)	243 (39)	704 (41)	2306 (25)	378 (18)	483 (24)	255 (31)	44 (20)	3 (2)	59 (61)	15 (29)
SDAI	554 (34)	447 (36)	506 (33)	9593 (43)	9376 (43)	1115 (42)	259 (41)	728 (42)	3116 (34)	576 (27)	617 (30)	315 (39)	59 (26)	4 (3)	60 (62)	16 (31)
ACR/EULAR 3-item Boolean	503 (31)	405 (33)	460 (30)	8771 (39)	8579 (39)	1025 (38)	227 (36)	679 (40)	2428 (26)	412 (19)	495 (24)	258 (32)	47 (21)	3 (2)	59 (61)	15 (29)
DAS28	520 (32)	420 (34)	476 (31)	9052 (40)	8847 (40)	1058 (40)	240 (38)	697 (41)	2792 (30)	487 (23)	529 (26)	269 (33)	49 (22)	5 (4)	70 (73)	15 (29)
SJC (28)=0	481 (30)	390 (32)	441 (29)	8450 (38)	8265 (38)	983 (37)	219 (35)	653 (38)	2404 (26)	405 (19)	469 (23)	249 (31)	46 (21)	3 (2)	59 (61)	15 (29)
Patient global VAS ≤ 10	495 (30)	399 (33)	455 (30)	8654 (38)	8461 (38)	996 (37)	218 (35)	664 (39)	2449 (26)	406 (19)	490 (24)	256 (32)	43 (19)	3 (2)	57 (59)	15 (29)
Treatment outcomes at six months																
Available visit	582 (36)	490 (40)	535 (35)	10443 (46)	10205 (46)	1177 (44)	348 (56)	684 (40)	2918 (31)	494 (23)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retention	582 (36)	490 (40)	535 (35)	10443 (46)	10205 (46)	1177 (44)	348 (56)	684 (40)	2918 (31)	494 (23)	396 (19)	225 (28)	47 (21)	27 (19)	20 (21)	22 (42)
Persistence	582 (36)	490 (40)	535 (35)	10443 (46)	10205 (46)	1177 (44)	348 (56)	684 (40)	2918 (31)	494 (23)	396 (19)	225 (28)	47 (21)	141 (100)	18 (19)	22 (42)
Response																
EULAR response	721 (44)	600 (49)	660 (44)	12369 (55)	12073 (55)	1461 (55)	397 (63)	878 (51)	4922 (53)	943 (44)	947 (47)	456 (56)	113 (50)	28 (20)	78 (81)	22 (42)
Remission																
ACR/EULAR	670 (41)	553 (45)	614 (40)	11544 (51)	11270 (51)	1339 (50)	376 (60)	794 (46)	4190 (45)	791 (37)	822 (40)	402 (50)	88 (39)	28 (20)	61 (64)	22 (42)
SDAI	688 (42)	571 (47)	629 (41)	11771 (52)	11497 (52)	1381 (52)	386 (62)	822 (48)	4815 (52)	952 (45)	947 (47)	458 (56)	100 (45)	28 (20)	63 (66)	22 (42)

ACR/EULAR 3-item Boolean	654 (40)	541 (44)	600 (40)	11271 (50)	11010 (50)	1296 (48)	370 (59)	765 (45)	4325 (46)	832 (39)	849 (42)	414 (51)	92 (41)	28 (20)	63 (66)	22 (42)
DAS28	659 (40)	548 (45)	603 (40)	11453 (51)	11180 (51)	1329 (50)	376 (60)	786 (46)	4582 (49)	876 (41)	868 (43)	418 (52)	93 (42)	28 (20)	76 (79)	22 (42)
SJC(28)=0	637 (39)	533 (43)	583 (38)	11041 (49)	10786 (49)	1266 (47)	368 (59)	742 (43)	4310 (46)	818 (39)	820 (40)	409 (50)	91 (41)	28 (20)	61 (64)	22 (42)
Patient global VAS ≤ 10	652 (40)	543 (44)	596 (39)	11215 (50)	10949 (50)	1300 (49)	373 (60)	765 (45)	4278 (46)	800 (38)	816 (40)	397 (49)	86 (38)	27 (19)	60 (62)	22 (42)
Treatment outcomes at twelve months																
Available visit	343 (21)	296 (24)	294 (19)	7144 (32)	6987 (32)	634 (24)	229 (37)	303 (18)	1834 (20)	247 (12)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Retention	343 (21)	296 (24)	294 (19)	7144 (32)	6987 (32)	634 (24)	229 (37)	303 (18)	1834 (20)	247 (12)	302 (15)	194 (24)	34 (15)	38 (27)	3 (3)	29 (56)
Persistence	343 (21)	296 (24)	294 (19)	7144 (32)	6987 (32)	634 (24)	229 (37)	303 (18)	1834 (20)	247 (12)	302 (15)	194 (24)	34 (15)	141 (100)	2 (2)	29 (56)
Response																
EULAR response	567 (35)	478 (39)	505 (33)	9954 (44)	9727 (44)	1071 (40)	327 (52)	590 (34)	4868 (52)	915 (43)	1065 (52)	501 (62)	121 (54)	141 (100)	74 (77)	29 (56)
Remission																
ACR/EULAR	504 (31)	423 (35)	443 (29)	8992 (40)	8792 (40)	903 (34)	298 (48)	469 (27)	4158 (45)	786 (37)	969 (48)	463 (57)	100 (45)	141 (100)	49 (51)	29 (56)
SDAI	533 (33)	450 (37)	471 (31)	9318 (41)	9112 (41)	949 (35)	308 (49)	498 (29)	4631 (50)	913 (43)	1067 (52)	506 (62)	110 (49)	141 (100)	52 (54)	30 (58)
ACR/EULAR 3-item Boolean	483 (30)	405 (33)	424 (28)	8705 (39)	8511 (39)	867 (32)	292 (47)	444 (26)	4201 (45)	801 (38)	988 (49)	468 (58)	104 (46)	141 (100)	50 (52)	29 (56)
DAS28	492 (30)	416 (34)	433 (29)	8881 (39)	8683 (39)	895 (33)	297 (47)	463 (27)	4407 (47)	830 (39)	1002 (49)	471 (58)	105 (47)	141 (100)	65 (68)	29 (56)
SJC(28)=0	462 (28)	392 (32)	405 (27)	8433 (38)	8244 (37)	833 (31)	285 (46)	422 (25)	4169 (45)	793 (37)	959 (47)	459 (57)	102 (46)	141 (100)	50 (52)	29 (56)
Patient global VAS ≤ 10	475 (29)	404 (33)	416 (27)	8582 (38)	8390 (38)	856 (32)	285 (46)	444 (26)	4206 (45)	785 (37)	968 (48)	456 (56)	98 (44)	41 (29)	48 (50)	29 (56)
Retention and persistence based on recorded start/stop dates																
Retention																
Month 3	2 (0)	2 (0)	1 (0)	13 (0)	12 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	82 (4)	66 (8)	9 (4)	12 (9)	0 (0)	8 (15)
Month 6	21 (1)	20 (2)	10 (1)	363 (2)	352 (2)	29 (1)	15 (2)	0 (0)	121 (1)	20 (1)	128 (6)	102 (13)	17 (8)	27 (19)	0 (0)	11 (21)
Month 12	44 (3)	41 (3)	22 (1)	948 (4)	925 (4)	76 (3)	41 (7)	0 (0)	358 (4)	59 (3)	204 (10)	163 (20)	26 (12)	80 (57)	0 (0)	16 (31)
Month 36	210 (13)	196 (16)	144 (9)	3842 (17)	3744 (17)	424 (16)	273 (44)	46 (3)	983 (11)	153 (7)	374 (18)	281 (35)	73 (33)	140 (99)	0 (0)	35 (67)
Persistence																

Month 3	2 (0)	2 (0)	1 (0)	13 (0)	12 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	81 (4)	65 (8)	9 (4)	141 (100)	0 (0)	9 (17)
Month 6	21 (1)	19 (2)	10 (1)	363 (2)	352 (2)	29 (1)	15 (2)	0 (0)	118 (1)	20 (1)	126 (6)	100 (12)	16 (7)	141 (100)	0 (0)	12 (23)
Month 12	44 (3)	36 (3)	22 (1)	948 (4)	925 (4)	76 (3)	41 (7)	0 (0)	351 (4)	58 (3)	198 (10)	157 (19)	24 (11)	141 (100)	0 (0)	18 (35)
Month 36	210 (13)	170 (14)	144 (9)	3842 (17)	3744 (17)	424 (16)	273 (44)	46 (3)	943 (10)	149 (7)	309 (15)	217 (27)	68 (30)	141 (100)	0 (0)	48 (92)

[+]calculated on the subset of patients starting TNFi treatment in year 2006 or later

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, VAS – visual analogue scale

Supplementary Table S8. RA patients initiating TNF inhibitors as the first ever biological DMARD. Characteristics of Swedish, Danish and Norwegian treatment sub-cohorts at the start of TNFi. Remission outcomes during one year and retention and persistence during three years of follow-up.

Country	Sweden								Denmark		Norway					
Source cohort	EIRA			SRQ		SRQ biobank			DANBIO	DRB	NOR-DMARD			ULRABIT	NOR-VEAC	ARCTIC
(Sub-) cohort	EIRA	Treatment start 2006-2020	With genotype data available	SRQ	Treatment start 2006-2020	SRQ biobank	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	DANBIO	DRB	NOR-DMARD	Treatment start 2012-2021	Treatment start 2012-2021 and blood sampled	ULRABIT	NOR-VEAC	ARCTIC
N patients	1628	1226	1517	22486	21992	2674	626	1716	9312	2127	2036	811	224	141	96	52
Remission at three months																
ACR/EULAR	165 (15%)	147 (18%)	154 (15%)	1476 (11%)	1443 (11%)	250 (16%)	68 (18%)	145 (14%)	627 (9%)	188 (11%)	194 (12%)	118 (21%)	51 (28%)	18 (13%)	11 (30%)	11 (30%)
SDAI	187 (17%)	160 (21%)	173 (17%)	1586 (12%)	1548 (12%)	256 (16%)	82 (22%)	144 (15%)	1033 (17%)	293 (19%)	243 (17%)	140 (28%)	57 (35%)	26 (19%)	14 (39%)	10 (28%)
ACR/EULAR 3-item Boolean	367 (33%)	306 (37%)	336 (32%)	3871 (28%)	3784 (28%)	610 (37%)	178 (45%)	353 (34%)	2167 (31%)	566 (33%)	454 (29%)	264 (48%)	87 (49%)	43 (31%)	21 (57%)	19 (51%)
DAS28	420 (38%)	348 (43%)	388 (37%)	4642 (35%)	4530 (34%)	685 (42%)	189 (49%)	414 (41%)	1917 (29%)	518 (32%)	488 (32%)	262 (48%)	88 (50%)	48 (35%)	13 (50%)	27 (73%)
SJC(28)=0	410 (36%)	340 (41%)	375 (35%)	4438 (32%)	4336 (32%)	678 (40%)	195 (48%)	396 (37%)	3840 (56%)	969 (56%)	542 (35%)	293 (52%)	96 (54%)	33 (24%)	21 (57%)	26 (70%)
Patient global VAS ≤ 10	279 (25%)	225 (27%)	263 (25%)	2825 (20%)	2762 (20%)	408 (24%)	94 (23%)	255 (24%)	1132 (16%)	344 (20%)	371 (24%)	183 (33%)	71 (39%)	51 (37%)	17 (44%)	13 (35%)
Remission at six months																
ACR/EULAR	135 (14%)	106 (16%)	128 (14%)	1122 (10%)	1095 (10%)	185 (14%)	30 (12%)	130 (14%)	543 (11%)	153 (11%)	185 (15%)	100 (24%)	44 (32%)	28 (25%)	13 (37%)	8 (27%)
SDAI	152 (16%)	125 (19%)	145 (16%)	1277 (12%)	1255 (12%)	192 (15%)	34 (14%)	133 (15%)	880 (20%)	266 (23%)	239 (22%)	122 (35%)	49 (40%)	30 (27%)	19 (58%)	11 (37%)
ACR/EULAR 3-item Boolean	310 (32%)	235 (34%)	292 (32%)	2979 (27%)	2921 (27%)	429 (31%)	82 (32%)	292 (31%)	1781 (36%)	487 (38%)	417 (35%)	201 (51%)	77 (58%)	49 (43%)	27 (82%)	15 (50%)
DAS28	354 (37%)	268 (40%)	338 (37%)	3492 (32%)	3429 (32%)	480 (36%)	85 (34%)	338 (36%)	1591 (34%)	459 (37%)	454 (39%)	219 (56%)	82 (63%)	54 (48%)	15 (75%)	19 (63%)
SJC(28)=0	344 (35%)	263 (38%)	321 (34%)	3511 (31%)	3439 (31%)	489 (35%)	101 (39%)	324 (33%)	2516 (50%)	630 (48%)	520 (43%)	241 (60%)	90 (68%)	42 (37%)	28 (80%)	20 (67%)
Patient global VAS ≤ 10	233 (24%)	178 (26%)	223 (24%)	2064 (18%)	2016 (18%)	282 (21%)	42 (17%)	201 (21%)	908 (18%)	251 (19%)	326 (27%)	152 (37%)	56 (41%)	50 (44%)	15 (42%)	11 (37%)
Remission at twelve months																
ACR/EULAR	178 (16%)	138 (17%)	171 (16%)	1547 (11%)	1510 (11%)	243 (14%)	45 (14%)	168 (13%)	700 (14%)	217 (16%)	180 (17%)	82 (24%)	37 (30%)	24 (24%)	23 (49%)	9 (39%)

SDAI	223 (20%)	166 (21%)	215 (21%)	1778 (14%)	1732 (13%)	281 (16%)	57 (18%)	192 (16%)	1183 (25%)	338 (28%)	253 (26%)	113 (37%)	53 (46%)	35 (35%)	24 (55%)	14 (64%)
ACR/EULAR 3-item Boolean	400 (35%)	299 (36%)	380 (35%)	3926 (28%)	3829 (28%)	572 (32%)	119 (36%)	384 (30%)	2207 (43%)	603 (45%)	409 (39%)	185 (54%)	69 (57%)	50 (50%)	34 (74%)	14 (61%)
DAS28	426 (38%)	322 (40%)	405 (37%)	4345 (32%)	4238 (32%)	620 (35%)	129 (39%)	424 (34%)	1963 (40%)	553 (43%)	436 (42%)	192 (56%)	74 (62%)	48 (48%)	24 (77%)	17 (74%)
SJC(28)=0	433 (37%)	328 (39%)	407 (37%)	4547 (32%)	4440 (32%)	673 (37%)	143 (42%)	451 (35%)	2126 (41%)	538 (40%)	510 (47%)	221 (63%)	87 (71%)	48 (48%)	36 (78%)	19 (83%)
Patient global VAS ≤ 10	266 (23%)	199 (24%)	258 (23%)	2484 (18%)	2426 (18%)	350 (19%)	59 (17%)	245 (19%)	1097 (21%)	329 (25%)	309 (29%)	132 (37%)	49 (39%)	41 (41%)	26 (54%)	11 (48%)
Retention and persistence based on recorded start/stop dates																
Retention																
Month 3	1506 (93%)	1134 (93%)	1406 (93%)	20886 (93%)	20430 (93%)	2483 (93%)	582 (93%)	1596 (93%)	8464 (91%)	1951 (92%)	1756 (90%)	670 (90%)	201 (93%)	129 (100%)	65 (68%)	40 (91%)
Month 6	1323 (82%)	975 (81%)	1250 (83%)	18089 (82%)	17690 (82%)	2108 (80%)	486 (80%)	1363 (79%)	7135 (78%)	1655 (79%)	1436 (75%)	525 (74%)	165 (80%)	114 (100%)	56 (58%)	36 (88%)
Month 12	1119 (71%)	818 (69%)	1060 (71%)	14864 (69%)	14551 (69%)	1694 (65%)	384 (66%)	1108 (65%)	5685 (63%)	1363 (66%)	1113 (61%)	383 (59%)	129 (65%)	61 (100%)	46 (48%)	24 (67%)
Month 36	646 (46%)	460 (45%)	621 (45%)	8810 (47%)	8637 (47%)	885 (39%)	134 (38%)	660 (40%)	3355 (40%)	911 (46%)	614 (37%)	168 (32%)	58 (38%)	NA	17 (18%)	NA
Persistence																
Month 3	1488 (92%)	1122 (92%)	1390 (92%)	20672 (92%)	20220 (92%)	2458 (92%)	580 (93%)	1577 (92%)	8351 (90%)	1932 (91%)	1749 (89%)	663 (89%)	198 (92%)	129 (100%)	63 (66%)	42 (98%)
Month 6	1276 (79%)	951 (79%)	1206 (80%)	17382 (79%)	17000 (79%)	2047 (77%)	481 (79%)	1315 (77%)	6895 (75%)	1608 (76%)	1409 (74%)	498 (70%)	158 (76%)	114 (100%)	53 (55%)	39 (98%)
Month 12	1057 (67%)	784 (66%)	1003 (67%)	13838 (64%)	13544 (64%)	1609 (62%)	374 (64%)	1040 (61%)	5290 (59%)	1276 (62%)	1078 (59%)	349 (53%)	121 (60%)	61 (100%)	42 (44%)	31 (91%)
Month 36	571 (40%)	416 (39%)	549 (40%)	7590 (41%)	7444 (41%)	799 (36%)	126 (36%)	591 (35%)	2890 (35%)	808 (41%)	569 (33%)	141 (24%)	53 (34%)	NA	16 (17%)	NA

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, TJC(28) – tender 28 joint count, VAS – visual analogue scale

Supplementary Table S9. Characteristics of RA patients initiating rituximab in the Swedish, Danish and Norwegian sub-cohorts.

Country	Sweden					Norway	
Source cohort	EIRA		SRQ	SRQ biobank		NOR-DMARD	
Sub-cohort	Starting treatment 2006-2020	With genotype data available	Starting treatment 2006-2020	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	Treatment start 2012-2021	Treatment start 2012-2021 and blood sampled
N patients	427	414	5141	347	476	175	75
Characteristics at treatment start							
N women (%)	335 (78%)	324 (78%)	3892 (76%)	257 (74%)	359 (75%)	133 (77%)	59 (79%)
Median age at inclusion (IQR)	61 (51,68)	61 (51,68)	63 (53,71)	63 (53,71)	62 (53,69)	58 (49,67)	57 (51,66)
Median calendar year of inclusion (IQR)	2014 (2010,2017)	2014 (2010,2016)	2013 (2010,2016)	2017 (2015,2018)	2012 (2011,2014)	2014 (2013,2016)	2015 (2014,2016)
Median disease duration (IQR)	6 (3,10) [+]	6 (3,11) [+]	5 (2,9) [+]	6 (2,12) [+]	6 (2,10) [+]	11 (5,21)	9 (5,17)
Seropositive disease* (%)	369 (88%)	357 (87%)	4392 (88%)	290 (86%)	405 (86%)	166 (95%)	72 (96%)
Current smoker (%)	126 (31%)	127 (31%)	639 (14%)	45 (14%)	60 (13%)	24 (23%)	12 (29%)
Co-treatment with oral steroids (%)	215 (50%)	206 (50%)	2505 (49%)	160 (46%)	226 (47%)	101 (61%)	40 (56%)
Visit-based clinical data							
Clinical data at treatment start							
Median SJC(28) (IQR)	6 (3,9)	6 (3,9)	6 (3,9)	5 (2,7)	5 (3,9)	4 (2,7)	4 (2,6)
Median TJC(28) (IQR)	6 (3,10)	6 (3,10)	6 (3,10)	5 (2,9)	5 (2,10)	5 (2,10)	6 (2,10)
Median CRP (IQR)	8 (3,23)	8 (3,23)	11 (4,28)	7 (4,18)	10 (5,25)	8 (2,20)	8 (2,16)
Median ESR (IQR)	24 (13,42)	24 (13,42)	27 (14,46)	21 (10,39)	24 (12,42)	25 (12,39)	26 (13,38)
Median Patient Global VAS (IQR)	59.5 (38,75)	59 (38,75)	61 (42,76)	59 (33,74)	60 (37,75)	52 (34,76)	62 (33,71)
Median HAQ (IQR)	1.13 (0.75,1.5)	1.13 (0.75,1.5)	1.25 (0.88,1.75)	1.13 (0.75,1.63)	1.13 (0.63,1.63)	0.75 (0.38,1.13)	0.88 (0.38,1.13)
Treatment outcomes at three months							
Retention (%)	231 (92%)	219 (91%)	2426 (95%)	135 (96%)	221 (96%)	118 (98%)	56 (100%)
Persistence (%)	220 (87%)	215 (90%)	2336 (91%)	132 (94%)	220 (96%)	110 (91%)	50 (89%)
EULAR good response	48 (25%)	47 (26%)	451 (24%)	29 (28%)	38 (21%)	27 (25%)	14 (27%)
Treatment outcomes at six months							
Retention (%)	221 (88%)	219 (88%)	2729 (91%)	160 (91%)	286 (91%)	114 (90%)	55 (96%)
Persistence (%)	198 (79%)	205 (82%)	2544 (85%)	156 (89%)	276 (88%)	102 (80%)	47 (82%)
EULAR good response	53 (27%)	55 (28%)	626 (27%)	38 (31%)	88 (36%)	42 (40%)	19 (38%)
Treatment outcomes at twelve months							
Retention (%)	273 (81%)	265 (82%)	3085 (82%)	174 (77%)	344 (83%)	116 (88%)	52 (93%)
Persistence (%)	242 (72%)	238 (73%)	2780 (74%)	166 (73%)	321 (78%)	102 (77%)	43 (77%)
EULAR good response	66 (27%)	66 (28%)	788 (28%)	43 (28%)	108 (33%)	45 (43%)	23 (49%)

* Seropositivity defined as diagnosed with ICD code M05.8 or M05.9 and seronegative defined as diagnosed with M06.0 or M06.8 (and, if available, negative for antiCCP and IgM RF)

[+]calculated in the subset of patients starting Rituximab treatment in year 2006 or later Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, TJC(28) – tender 28 joint count, VAS – visual analogue scale

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Supplementary table S10 describing missing data for the rituximab cohorts. Numbers are N missing (%)

Country	Sweden								Denmark		Norway			
Source cohort	EIRA			SRQ		SRQ biobank			DANBIO	DRB	NOR-DMARD			ULRABIT
(Sub-) cohort	EIRA	Treatment start 2006-2020	With genotype data available	SRQ	Treatment start 2006-2020	SRQ biobank	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	DANBIO	DRB	NOR-DMARD	Treatment start 2012-2021	Treatment start 2012-2021 and blood sampled	ULRABIT
Patients	432	427	414	5232	5141	942	347	476	1462	346	411	175	75	43
Characteristics at treatment start														
Women	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1)	2 (1)	0 (0)	0 (0)
Age at inclusion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1)	2 (1)	0 (0)	0 (0)
Calendar year of inclusion	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Disease duration	0 (0) [+]	0 (0) [+]	0 (0) [+]	0 (0) [+]	0 (0) [+]	0 (0) [+]	0 (0) [+]	0 (0) [+]	51 (4)	9 (3)	53 (13)	52 (30)	25 (33)	1 (2)
Seropositive disease	6 (1)	6 (1)	4 (1)	128 (2)	123 (2)	16 (2)	8 (2)	6 (1)	65 (4)	20 (6)	0 (0)	0 (0)	0 (0)	26 (60)
Current smoker	18 (4)	18 (4)	10 (2)	633 (12)	604 (12)	35 (4)	16 (5)	14 (3)	658 (45)	128 (37)	71 (17)	69 (39)	33 (44)	11 (26)
Co-treatment with oral steroids	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	23 (6)	10 (6)	3 (4)	0 (0)
Visit-based clinical data														
Clinical data at treatment start														
Registered visit	69 (16)	68 (16)	67 (16)	760 (15)	751 (15)	128 (14)	53 (15)	51 (11)	67 (5)	5 (1)	0 (0)	0 (0)	0 (0)	0 (0)
SJC(28)	86 (20)	85 (20)	83 (20)	1070 (20)	1045 (20)	198 (21)	77 (22)	88 (18)	136 (9)	15 (4)	19 (5)	16 (9)	7 (9)	0 (0)
TJC(28)	86 (20)	85 (20)	83 (20)	1079 (21)	1054 (21)	199 (21)	77 (22)	89 (19)	137 (9)	17 (5)	18 (4)	16 (9)	7 (9)	0 (0)
CRP	84 (19)	83 (19)	81 (20)	989 (19)	964 (19)	166 (18)	66 (19)	74 (16)	127 (9)	17 (5)	15 (4)	12 (7)	5 (7)	0 (0)
ESR	106 (25)	105 (25)	103 (25)	1160 (22)	1134 (22)	198 (21)	76 (22)	95 (20)	NA	NA	30 (7)	21 (12)	7 (9)	0 (0)
Patient global VAS	90 (21)	89 (21)	86 (21)	1241 (24)	1209 (24)	213 (23)	87 (25)	96 (20)	146 (10)	13 (4)	17 (4)	15 (9)	5 (7)	0 (0)
HAQ	109 (25)	107 (25)	105 (25)	1485 (28)	1451 (28)	268 (28)	108 (31)	125 (26)	197 (14)	22 (6)	19 (5)	15 (9)	4 (5)	0 (0)
Treatment outcomes at three months														
Available visit	178 (41)	175 (41)	174 (42)	2626 (50)	2585 (50)	514 (55)	207 (60)	246 (52)	386 (26)	51 (15)	0 (0)	0 (0)	0 (0)	0 (0)

Retention	178 (41)	175 (41)	174 (42)	2626 (50)	2585 (50)	514 (55)	207 (60)	246 (52)	386 (26)	51 (15)	107 (26)	54 (31)	19 (25)	1 (2)
Persistence	178 (41)	175 (41)	174 (42)	2626 (50)	2585 (50)	514 (55)	207 (60)	246 (52)	386 (26)	51 (15)	107 (26)	54 (31)	19 (25)	43 (100)
Response														
EULAR response	241 (56)	238 (56)	234 (57)	3300 (63)	3242 (63)	619 (66)	243 (70)	298 (63)	684 (47)	124 (36)	136 (33)	66 (38)	24 (32)	1 (2)
Remission														
ACR/EULAR	207 (48)	204 (48)	201 (49)	2955 (56)	2905 (57)	561 (60)	225 (65)	267 (56)	520 (36)	81 (23)	115 (28)	57 (33)	19 (25)	1 (2)
SDAI	214 (50)	211 (49)	207 (50)	3046 (58)	2996 (58)	580 (62)	228 (66)	279 (59)	684 (47)	132 (38)	147 (36)	71 (41)	22 (29)	1 (2)
ACR/EULAR 3-item Boolean	196 (45)	193 (45)	191 (46)	2836 (54)	2788 (54)	547 (58)	220 (63)	261 (55)	548 (38)	95 (28)	120 (29)	58 (33)	19 (25)	1 (2)
DAS28	204 (47)	201 (47)	198 (48)	2927 (56)	2879 (56)	554 (59)	223 (64)	264 (55)	630 (43)	113 (33)	128 (31)	60 (34)	20 (27)	1 (2)
SJC(28)=0	190 (44)	187 (44)	185 (45)	2769 (53)	2724 (53)	534 (57)	217 (63)	254 (53)	554 (38)	95 (28)	119 (29)	59 (34)	20 (27)	1 (2)
Patient global VAS ≤ 10	199 (46)	196 (46)	194 (47)	2853 (55)	2807 (55)	541 (57)	217 (63)	258 (54)	563 (39)	87 (25)	126 (31)	64 (37)	20 (27)	1 (2)
Treatment outcomes at six months														
Available visit	175 (41)	175 (41)	164 (40)	2179 (42)	2134 (42)	396 (42)	172 (50)	161 (34)	363 (25)	62 (18)	0 (0)	0 (0)	0 (0)	0 (0)
Retention	175 (41)	175 (41)	164 (40)	2179 (42)	2134 (42)	396 (42)	172 (50)	161 (34)	363 (25)	62 (18)	99 (24)	48 (27)	18 (24)	2 (5)
Persistence	175 (41)	175 (41)	164 (40)	2179 (42)	2134 (42)	396 (42)	172 (50)	161 (34)	363 (25)	62 (18)	99 (24)	48 (27)	18 (24)	43 (100)
Response														
EULAR response	232 (54)	231 (54)	220 (53)	2915 (56)	2856 (56)	529 (56)	223 (64)	234 (49)	705 (48)	134 (39)	151 (37)	71 (41)	25 (33)	2 (5)
Remission														
ACR/EULAR	204 (47)	204 (48)	192 (46)	2548 (49)	2494 (49)	463 (49)	197 (57)	199 (42)	558 (38)	100 (29)	133 (32)	60 (34)	21 (28)	2 (5)
SDAI	213 (49)	213 (50)	201 (49)	2638 (50)	2584 (50)	476 (51)	202 (58)	204 (43)	701 (48)	148 (43)	165 (40)	74 (42)	24 (32)	2 (5)
ACR/EULAR 3-item Boolean	197 (46)	197 (46)	186 (45)	2423 (46)	2371 (46)	443 (47)	190 (55)	187 (39)	582 (40)	110 (32)	140 (34)	63 (36)	22 (29)	2 (5)
DAS28	203 (47)	203 (48)	191 (46)	2531 (48)	2478 (48)	461 (49)	197 (57)	198 (42)	646 (44)	125 (36)	142 (35)	65 (37)	23 (31)	2 (5)
SJC(28)=0	192 (44)	192 (45)	181 (44)	2359 (45)	2308 (45)	434 (46)	190 (55)	180 (38)	590 (40)	111 (32)	134 (33)	63 (36)	23 (31)	2 (5)
Patient global VAS ≤ 10	194 (45)	194 (45)	182 (44)	2429 (46)	2376 (46)	441 (47)	189 (54)	187 (39)	576 (39)	104 (30)	139 (34)	64 (37)	20 (27)	2 (5)
Treatment outcomes at twelve months														

Available visit	93 (22)	92 (22)	90 (22)	1389 (27)	1366 (27)	226 (24)	120 (35)	62 (13)	236 (16)	32 (9)	0 (0)	0 (0)	0 (0)	0 (0)
Retention	93 (22)	92 (22)	90 (22)	1389 (27)	1366 (27)	226 (24)	120 (35)	62 (13)	236 (16)	32 (9)	80 (19)	43 (25)	19 (25)	6 (14)
Persistence	93 (22)	92 (22)	90 (22)	1389 (27)	1366 (27)	226 (24)	120 (35)	62 (13)	236 (16)	32 (9)	80 (19)	43 (25)	19 (25)	43 (100)
Response														
EULAR response	180 (42)	179 (42)	174 (42)	2331 (45)	2288 (45)	404 (43)	192 (55)	149 (31)	700 (48)	140 (41)	165 (40)	70 (40)	28 (37)	8 (19)
Remission														
ACR/EULAR	142 (33)	141 (33)	136 (33)	1909 (36)	1876 (36)	324 (34)	168 (48)	105 (22)	572 (39)	116 (34)	146 (36)	62 (35)	24 (32)	8 (19)
SDAI	152 (35)	151 (35)	146 (35)	2017 (39)	1984 (39)	354 (38)	178 (51)	122 (26)	695 (48)	149 (43)	174 (42)	77 (44)	27 (36)	8 (19)
ACR/EULAR 3-item Boolean	132 (31)	131 (31)	128 (31)	1768 (34)	1735 (34)	297 (32)	158 (46)	91 (19)	591 (40)	123 (36)	147 (36)	63 (36)	24 (32)	8 (19)
DAS28	141 (33)	140 (33)	135 (33)	1897 (36)	1865 (36)	322 (34)	166 (48)	105 (22)	635 (43)	129 (37)	154 (37)	63 (36)	24 (32)	8 (19)
SJC(28)=0	130 (30)	129 (30)	126 (30)	1714 (33)	1684 (33)	288 (31)	155 (45)	85 (18)	589 (40)	119 (34)	143 (35)	63 (36)	24 (32)	8 (19)
Patient global VAS ≤ 10	131 (30)	130 (30)	125 (30)	1802 (34)	1771 (34)	297 (32)	156 (45)	92 (19)	598 (41)	118 (34)	149 (36)	65 (37)	24 (32)	8 (19)
Retention and persistence based on recorded start/stop dates														
Retention														
Month 3	0 (0)	0 (0)	0 (0)	11 (0)	11 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	14 (3)	6 (3)	1 (1)	1 (2)
Month 6	10 (2)	10 (2)	9 (2)	81 (2)	81 (2)	12 (1)	8 (2)	0 (0)	13 (1)	4 (1)	25 (6)	13 (7)	6 (8)	3 (7)
Month 12	15 (3)	15 (4)	13 (3)	196 (4)	196 (4)	28 (3)	20 (6)	1 (0)	39 (3)	10 (3)	44 (11)	28 (16)	10 (13)	26 (60)
Month 36	71 (16)	71 (17)	65 (16)	988 (19)	987 (19)	182 (19)	123 (35)	20 (4)	169 (12)	49 (14)	97 (24)	60 (34)	25 (33)	43 (100)
Persistence														
Month 3	0 (0)	0 (0)	0 (0)	11 (0)	10 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	14 (3)	6 (3)	1 (1)	43 (100)
Month 6	10 (2)	9 (2)	9 (2)	81 (2)	75 (1)	12 (1)	8 (2)	0 (0)	13 (1)	4 (1)	24 (6)	12 (7)	5 (7)	43 (100)
Month 12	15 (3)	13 (3)	13 (3)	196 (4)	177 (3)	28 (3)	20 (6)	1 (0)	39 (3)	10 (3)	42 (10)	26 (15)	9 (12)	43 (100)
Month 36	71 (16)	56 (13)	65 (16)	988 (19)	810 (16)	182 (19)	123 (35)	20 (4)	157 (11)	48 (14)	NA	NA	NA	43 (100)

[+]calculated in the subset of patients starting Rituximab treatment in year 2006 or later

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, VAS – visual analogue scale

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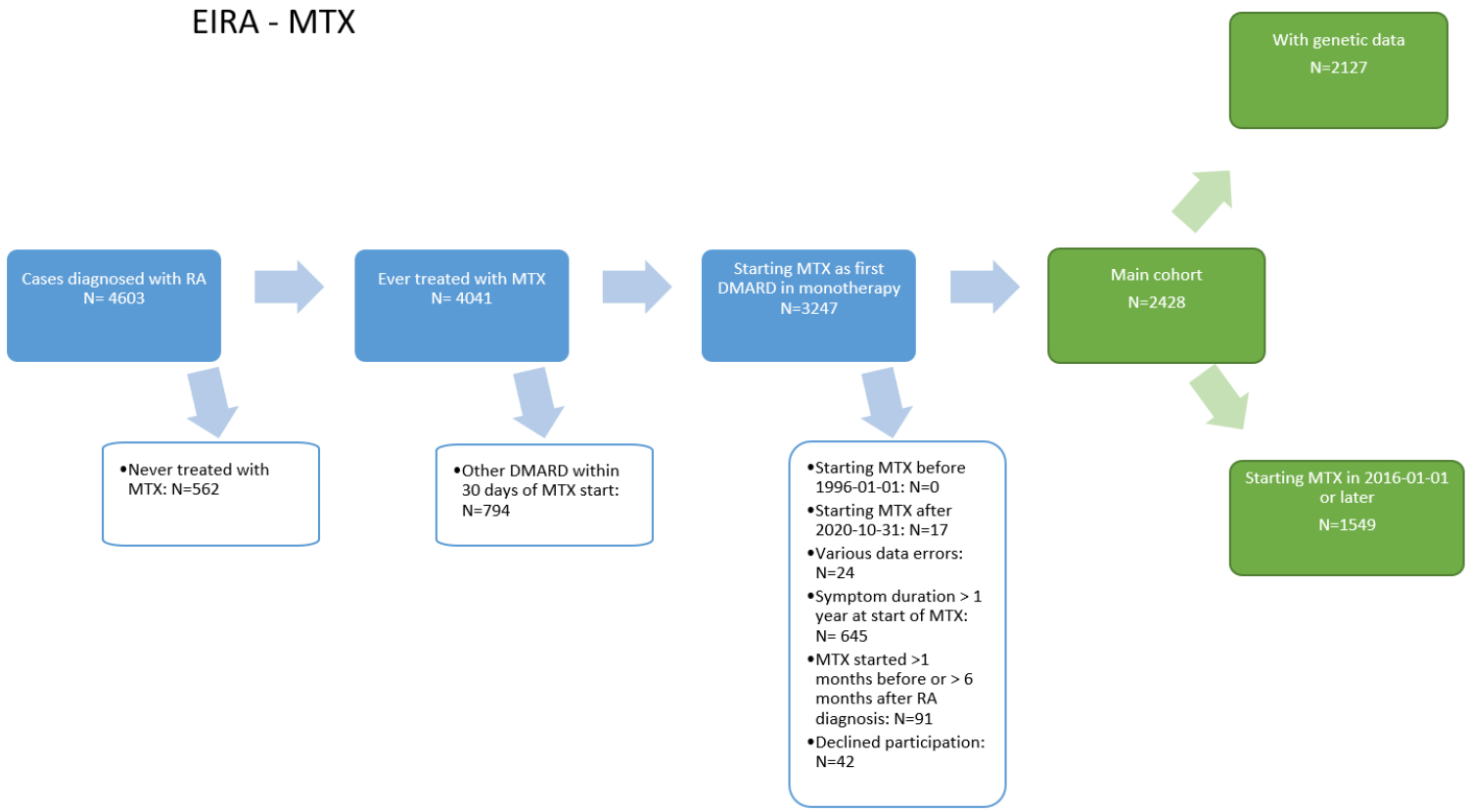
Supplementary Table S11. RA patients initiating rituximab. Characteristics of Swedish, Danish and Norwegian sub-cohorts at the start of rituximab. Remission outcomes during one year and retention and persistence during three years of follow-up.

Country	Sweden								Denmark		Norway			
Source cohort	EIRA			SRQ		SRQ biobank			DANBIO	DRB	NOR-DMARD			ULRABIT
(Sub-) cohort	EIRA	Starting treatment 2006-2020	With genotype data available	SRQ	Starting treatment 2006-2020	SRQ biobank	Blood sample ≤90 days before treatment start	Blood sample >90 days after treatment start	DANBIO	DRB	NOR-DMARD	Treatment start 2012-2021	Treatment start 2012-2021 and blood sampled	ULRABIT
N patients	432	427	414	5232	5141	942	347	476	1462	346	411	175	75	43
Remission at three months														
ACR/EULAR	14 (6%)	14 (6%)	14 (7%)	94 (4%)	91 (4%)	23 (6%)	12 (10%)	9 (4%)	24 (3%)	11 (4%)	20 (7%)	8 (7%)	4 (7%)	2 (5%)
SDAI	13 (6%)	13 (6%)	13 (6%)	117 (5%)	114 (5%)	24 (7%)	11 (9%)	13 (7%)	63 (8%)	21 (10%)	27 (10%)	13 (12%)	7 (13%)	3 (7%)
ACR/EULAR 3-item Boolean	44 (19%)	44 (19%)	43 (19%)	393 (16%)	387 (16%)	76 (19%)	28 (22%)	42 (20%)	188 (21%)	63 (25%)	43 (15%)	21 (18%)	9 (16%)	4 (10%)
DAS28	49 (21%)	48 (21%)	46 (21%)	435 (19%)	427 (19%)	89 (23%)	31 (25%)	52 (25%)	154 (19%)	46 (20%)	58 (20%)	24 (21%)	13 (24%)	5 (12%)
SJC(28)=0	62 (26%)	62 (26%)	59 (26%)	594 (24%)	584 (24%)	115 (28%)	45 (35%)	60 (27%)	559 (62%)	148 (59%)	73 (25%)	30 (26%)	16 (29%)	5 (12%)
Patient global VAS ≤ 10	34 (15%)	34 (15%)	29 (13%)	247 (10%)	241 (10%)	56 (14%)	21 (16%)	31 (14%)	72 (8%)	21 (8%)	54 (19%)	19 (17%)	11 (20%)	11 (26%)
Remission at six months														
ACR/EULAR	19 (8%)	18 (8%)	17 (8%)	171 (6%)	166 (6%)	50 (10%)	15 (10%)	28 (10%)	47 (5%)	8 (3%)	21 (8%)	12 (10%)	8 (15%)	1 (2%)
SDAI	18 (8%)	18 (8%)	17 (8%)	183 (7%)	176 (7%)	50 (11%)	16 (11%)	28 (10%)	96 (13%)	24 (12%)	30 (12%)	21 (21%)	14 (27%)	3 (7%)
ACR/EULAR 3-item Boolean	48 (20%)	47 (20%)	44 (19%)	557 (20%)	539 (19%)	145 (29%)	51 (32%)	73 (25%)	212 (24%)	56 (24%)	65 (24%)	37 (33%)	20 (38%)	5 (12%)
DAS28	51 (22%)	49 (22%)	49 (22%)	622 (23%)	596 (22%)	146 (30%)	46 (31%)	82 (29%)	183 (22%)	43 (19%)	77 (29%)	38 (35%)	16 (31%)	7 (17%)
SJC(28)=0	66 (28%)	65 (28%)	63 (27%)	762 (27%)	740 (26%)	166 (33%)	55 (35%)	91 (31%)	500 (57%)	126 (54%)	98 (35%)	49 (44%)	24 (46%)	8 (20%)
Patient global VAS ≤ 10	32 (13%)	30 (13%)	30 (13%)	345 (12%)	329 (12%)	80 (16%)	21 (13%)	50 (17%)	93 (10%)	20 (8%)	51 (19%)	23 (21%)	13 (24%)	10 (24%)
Remission at twelve months														

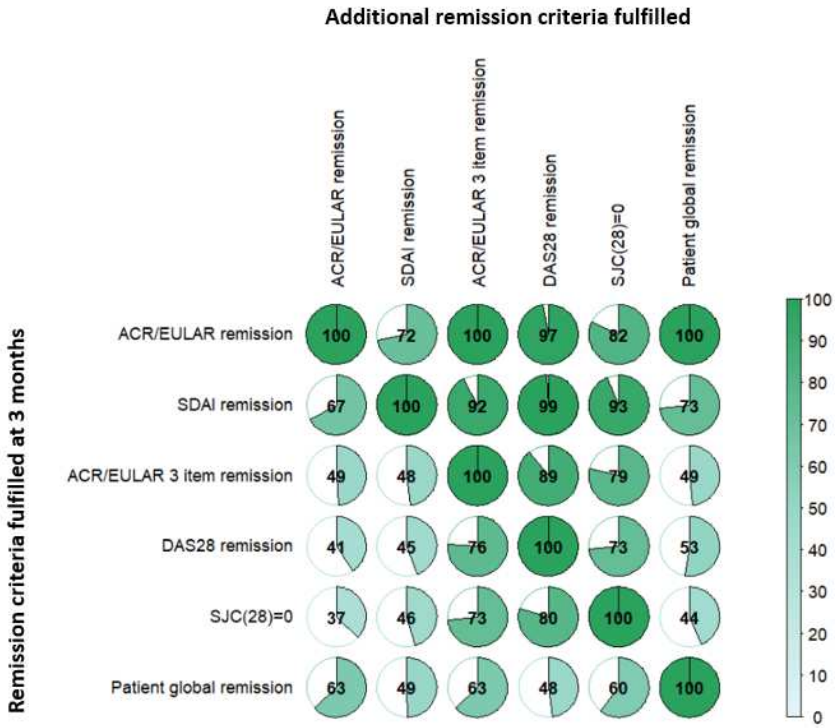
ACR/EULAR	22 (8%)	21 (7%)	21 (8%)	188 (6%)	183 (6%)	59 (10%)	16 (9%)	35 (9%)	42 (5%)	16 (7%)	25 (9%)	16 (14%)	12 (24%)	3 (9%)
SDAI	20 (7%)	19 (7%)	18 (7%)	239 (7%)	227 (7%)	68 (12%)	20 (12%)	42 (12%)	89 (12%)	33 (17%)	40 (17%)	26 (27%)	15 (31%)	4 (11%)
ACR/EULAR 3-item Boolean	67 (22%)	66 (22%)	63 (22%)	714 (21%)	695 (20%)	182 (28%)	53 (28%)	107 (28%)	218 (25%)	65 (29%)	67 (25%)	39 (35%)	22 (43%)	3 (9%)
DAS28 remission	71 (24%)	68 (24%)	69 (25%)	754 (23%)	732 (22%)	170 (27%)	48 (27%)	101 (27%)	176 (21%)	53 (24%)	75 (29%)	38 (34%)	19 (37%)	5 (14%)
SJC(28)=0	79 (26%)	78 (26%)	74 (26%)	962 (27%)	934 (27%)	231 (35%)	59 (31%)	145 (37%)	485 (56%)	119 (52%)	108 (40%)	58 (52%)	29 (57%)	7 (20%)
Patient global VAS ≤ 10	42 (14%)	40 (13%)	38 (13%)	388 (11%)	376 (11%)	95 (15%)	23 (12%)	62 (16%)	94 (11%)	30 (13%)	58 (22%)	31 (28%)	16 (31%)	9 (26%)
Retention and persistence based on recorded start/stop dates														
Retention														
Month 3	397 (92%)	392 (92%)	379 (92%)	4932 (94%)	4854 (95%)	903 (96%)	333 (96%)	457 (96%)	1261 (86%)	308 (89%)	385 (97%)	165 (98%)	74 (100%)	42 (100%)
Month 6	365 (86%)	360 (86%)	350 (86%)	4549 (88%)	4472 (88%)	825 (89%)	297 (88%)	424 (89%)	1138 (79%)	273 (80%)	350 (91%)	150 (93%)	67 (97%)	40 (100%)
Month 12	322 (77%)	317 (77%)	310 (77%)	3919 (78%)	3850 (78%)	721 (79%)	240 (73%)	387 (81%)	948 (67%)	228 (68%)	296 (81%)	127 (86%)	60 (92%)	17 (100%)
Month 36	184 (51%)	179 (50%)	179 (51%)	2358 (56%)	2305 (55%)	444 (58%)	99 (44%)	297 (65%)	550 (43%)	145 (49%)	189 (60%)	76 (66%)	35 (70%)	NA
Persistence														
Month 3	389 (90%)	376 (88%)	372 (90%)	4875 (93%)	4687 (91%)	892 (95%)	328 (95%)	454 (95%)	1242 (85%)	305 (88%)	382 (96%)	162 (96%)	73 (99%)	42 (100%)
Month 6	341 (81%)	328 (78%)	328 (81%)	4342 (84%)	4147 (82%)	796 (86%)	288 (85%)	408 (86%)	1092 (75%)	264 (77%)	340 (88%)	140 (86%)	61 (87%)	40 (100%)
Month 12	290 (70%)	279 (67%)	278 (69%)	3606 (72%)	3432 (69%)	672 (74%)	225 (69%)	359 (76%)	891 (63%)	218 (65%)	284 (77%)	115 (77%)	51 (77%)	17 (100%)
Month 36	147 (41%)	141 (38%)	142 (41%)	2046 (48%)	1950 (45%)	397 (52%)	93 (42%)	263 (58%)	498 (38%)	133 (45%)	170 (52%)	65 (52%)	29 (52%)	NA

[+]calculated in the subset of patients starting Rituximab treatment in year 2006 or later

Abbreviations: ACR – American Congress of Rheumatology, CRP – C-reactive protein, DAS28 – disease activity score 28 joints, DMARD – disease modifying anti-rheumatic drug, ESR – erythrocyte sedimentation rate, EULAR – European Alliance of Associations for Rheumatology, SDAI – simplified disease activity index, SJC(28) - swollen 28 joint count, TJC(28) – tender 28 joint count, VAS – visual analogue scale



Supplementary Figure S1. Example of data extraction and nesting of sub-cohorts within the EIRA study.



Supplementary Figure S2 Percentages of patients in the SRQ MTX cohort that at month 3 fulfilled a remission criteria (rows), and also fulfilled another remission criteria (columns). E.g. 72% of the patients fulfilling ACR/EULAR remission also fulfilled SDAI remission, while 37% of the patients with no swollen joints also fulfilled ACR/EULAR remission.