

SUPPLEMENTAL MATERIAL**Supplemental table 1.** List of registers used.

Register	Description
Education register (UREG)	Founded in 1985 by Statistics Sweden (SCB). Covers highest level of educational attainment for each citizen.
National Cancer Register	Founded in 1958. Covers the whole population. Newly detected cancer (diagnosed at clinical, morphological or other laboratory examinations or autopsies) are compulsory to report.
National Patient Register (NPR)	Founded in the 1960s. Mandatory participation from all counties since 1984. Covers all in-patient care in Sweden since 1987. Since 2001 it also covers out-patient visits from specialized care from both private and public care-givers. Primary health care is not included.
National Prescribed Drug Register (PDR)	Founded in July 2005. Contains all prescribed drugs dispensed at pharmacies.
Swedish Rheumatology Quality Register (SRQ)	Founded in 1995. Covers information on diagnosis/ inclusion date, symptom duration, disease activity and treatment.
Total Population Register (RTB)	Founded in 1968 by Statistics Sweden (SCB). Covers information on the whole population concerning birth, death, area of residence, immigration, emigration etc.

Supplemental table 2. Time periods used for comorbidity and antirheumatic drug data in each table and figure.

	Comorbidity data		Anti-rheumatic drug data		
	From 5 years before to RA diagnosis	From 5 years before to 12 months after RA diagnosis	At RA diagnosis	12 months after RA diagnosis	36 months after RA diagnosis
Table 1			X		
Table 2	X	X			
Table 3		X		X	
Figure 2	X		X	X	
Figure 3		X		X	
Figure 4		X		X	
Figure 5	X	X	X	X	X
Suppl table 6	X	X			
Suppl table 7	X		X	X	
Suppl table 8	X		X	X	
Suppl table 9		X		X	
Suppl table 10		X		X	
Suppl table 11		X		X	
Suppl table 12		X		X	
Suppl table 13	X	X	X	X	X
Suppl table 14	X		X		
Suppl figure 2			X		

Supplemental table 3. ICD-10 and ATC codes used for exclusion of patients^a.

Diagnoses	ICD-10 codes
Rheumatoid arthritis	M05, M06.0, M06.2-M06.3, M06.8-M06.9, M12.3
Other arthritis	M13
Psoriatic arthritis	L40.5, M07.0, M07.1, M07.3
Ankylosing spondylitis	M45
Juvenile arthritis	M08-M09
Inflammatory spondylopathies	M46.0-M46.1, M46.8-M46.9
SLE	M32.0-M32.1, M32.8-M32.9
PMR	M35.3

Drugs	ATC codes
Abatacept	L04AA24
Adalimumab	L04AB04
Anakinra	L04AC03
Apremilast	L04AA32
Baricitinib	L04AA37
Belimumab	L04AA26
Canakinumab	L04AC08
Certolizumab pegol	L04AB05
Etanercept	L04AB01
Golimumab	L04AB06
Chloroquine	P01BA01
Leflunomide	L04AA13
Methotrexate	L04AX03
Sodium aurothiomalate	M01CB01
Hydroxychloroquine	P01BA02
Auranofin	M01CB03
Secukinumab	L04AC10
Sulfasalazine	A07EC01
Tocilizumab	L04AC07
Tofacitinib	L04AA29
Ustekinumab	L04AC05

^aPatients were excluded if they had any of these diagnoses registered >12 months before RA diagnosis or any of these drugs prescribed >1 months before RA diagnosis in SRQ (Swedish Rheumatology Quality register). ICD-10, International Classification of Diseases, 10th revision; ATC, Anatomical Therapeutic Chemical Classification.

Supplemental table 4. Comorbidity categories and diagnoses with corresponding ICD-10 and/or ATC codes used to capture each comorbidity.

Comorbidity categories	Diagnoses	ICD-10 codes	ATC codes
Cardiovascular	Ischaemic heart disease	I20-I25	
	Acute coronary syndrome	I200, I21-I22	
	Heart failure	I50	
	Atrial fibrillation	I48	
Non-cardiac vascular	Peripheral vascular diseases	I65-I66, I70-I72, I739, I74	
	Lipid lowering drugs		C10
	Stroke	I60-I64	
	Transient ischaemic attack	G45	
	Thromboembolic venous disease	I26, I80-I82	
	Hypertension	I10-I15	
Respiratory	Chronic obstructive pulmonary disease	J43-J44	
	Chronic interstitial pulmonary disease	J84	
	Asthma	J45	
Gastrointestinal	Inflammatory bowel disease	K50-K51	
	Esophageal, gastric and duodenal disease	K20-K23, K25-K27, K29	
	Biliary disease	K80-K81	
	Chronic liver disease	K70-K76	
Psychiatric	Depression	F32-F33	
	Antidepressant drugs		N06A
	Anxiety disorder	F40-F41, F43	
	Psychosis	F20-F29	
	Dementia (antidementia drugs)	F00-F03, G30-G31	N06D
Chronic kidney	Chronic kidney disease	I12-I13, N03-N05, N07, N18, Q61	
Infectious	Hospitalisation due to infectious diseases	A00-B99, G00-G02, G042, G05-G07, H66-H67, J00-J22, J32, J340, J36, J838, J390-J391, J85-J86, L00-L08, M00-M01, M462-M465, M86, N10, N300, N390	
Endocrine	Type 1 diabetes (insulin) ^a	E10	A10A
	Type 2 diabetes (glucose-lowering drugs) ^b	E11	A10B
	Thyroid disease (thyroid and antithyroid preparations)	E038-E039, E050-E053, E055-E059	H03A, H03B
Malignant	Cancer	C00-C97, D00-D09	
Neurological	Parkinson's disease	G20	
	Multiple sclerosis	G35	
	Epilepsy	G40-G41	
	Polyneuropathies and nerve, nerve root and plexus disorders	G50-G59, G60-G65	
Fractures^c	Fractures of hip/spine/leg	M485, M489, M800A, M800E-F, M800J-K, M843E-G, S120-S127, S220-S221, S32, T021, T08, S72, S821-	

S824, S827

^aFor considered as having type 1 diabetes you had to have the E10 diagnosis, no E11 diagnosis, prescription of insulin and no prescription of glucose-lowering drugs. ^bFor considered as having type 2 diabetes you had to have the E11 diagnosis or prescription of glucose-lowering drugs and no E10 diagnosis. ^cInformation on fractures was only used for the Rheumatic Disease Comorbidity Index. ICD-10, International Classification of Diseases 10th revision; ATC, Anatomical Therapeutic Chemical Classification.

Supplemental table 5. Rheumatic Disease Comorbidity Index.

Comorbidity groups	Lung disease Heart Attack Other Cardiovascular disease Stroke Hypertension Diabetes Fracture (of hip/spine/leg) Depression Cancer Gastrointestinal ulcer Other stomach problems
Formula	2 x lung disease + [2 x (heart attack, other cardiovascular disease, or stroke), or 1 x hypertension + fracture + depression + diabetes + cancer + (ulcer or stomach problem)]

See methods and reference [20-22].

Supplemental table 6. Number of comorbidity categories at baseline and at 12 months after diagnosis.

Number of comorbidity categories	At diagnosis n (%)	At 12 months n (%)
0	6057 (44.9)	5151 (38.5)
1	3725 (27.6)	3738 (28.0)
2	2168 (16.1)	2402 (18.0)
≥3	1555 (11.5)	2082 (15.6)
Total	13505	13373

Supplemental table 7. Number and proportions of patients on the different treatments categories at RA onset and at 12 months, divided in the different comorbidity categories.

Comorbidity categories	MTX monotherapy			Non-MTX csDMARDs			MTX + other csDMARDs			b/tsDMARDs			No treatment		
	0 m	12 m	Δ	0 m	12 m	Δ	0 m	12 m	Δ	0 m	12 m	Δ	0 m	12 m	Δ
All patients, n (%)	9178 (68.0)	8282 (61.3)	-896 (-6.7 ^b)	768 (5.7)	869 (6.4)	101 (0.7 ^a)	101 (0.8)	777 (5.8)	676 (5.0 ^b)	339 (2.5)	1799 (13.3)	1460 (10.8 ^a)	3119 (23.1)	1778 (13.2)	-1341 (-9.9)
Cardiovascular, n (%)	758 (63.4)	711 (59.5)	-47 (-3.9 ^a)	82 (6.9)	77 (6.4)	-5 (-0.5)	9 (0.8)	57 (4.8)	48 (4.0 ^b)	20 (1.7)	96 (8.0)	76 (6.3 ^b)	326 (27.3)	254 (21.3)	-72 (-6.0 ^b)
Non-cardiac vascular, n (%)	2549 (69.0)	2359 (63.8)	-190 (-5.2 ^b)	189 (5.1)	217 (5.9)	28 (0.8)	16 (0.4)	160 (4.3)	144 (3.9 ^b)	69 (1.9)	374 (10.1)	305 (8.2 ^b)	872 (23.6)	585 (15.8)	-287 (-7.8 ^b)
Malignant, n (%)	359 (61.8)	368 (63.3)	9 (1.5)	48 (8.3)	40 (6.9)	-8 (-1.4)	5 (0.9)	30 (5.2)	25 (4.3 ^b)	3 (0.5)	46 (7.9)	43 (7.4 ^b)	166 (28.6)	97 (16.7)	-69 (-11.9 ^b)
Endocrine, n (%)	1820 (69.4)	1624 (61.9)	-196 (-7.5 ^b)	153 (5.8)	149 (5.7)	-4 (-0.1)	12 (0.5)	131 (5.0)	119 (4.5 ^b)	60 (2.3)	354 (13.5)	294 (11.2 ^b)	579 (22.1)	365 (13.9)	-214 (-8.2 ^b)
Gastrointestinal, n (%)	558 (63.5)	508 (57.8)	-50 (-5.7 ^a)	46 (5.2)	50 (5.7)	4 (0.5)	5 (0.6)	49 (5.6)	44 (5.0 ^b)	20 (2.3)	122 (13.9)	102 (11.6 ^b)	250 (28.4)	150 (17.1)	-100 (-11.3 ^b)
Infectious, n (%)	513 (61.7)	474 (57.0)	-39 (-4.7)	62 (7.5)	65 (7.8)	3 (0.3)	4 (0.5)	38 (4.6)	34 (4.1 ^b)	16 (1.9)	91 (10.9)	75 (9.0 ^b)	237 (28.5)	164 (19.7)	-73 (-8.8 ^b)
Chronic kidney, n (%)	50 (47.6)	41 (39.1)	-9 (-8.5)	12 (11.4)	10 (9.5)	-2 (-1.9)	0 (3.8)	4 (3.8)	4 (3.8 ^a)	4 (3.8)	15 (14.3)	11 (10.5 ^b)	39 (37.1)	35 (33.3)	-4 (-3.8)
Neurological, n (%)	656 (70.6)	556 (59.9)	-100 (-10.7 ^b)	31 (3.3)	51 (5.5)	20 (2.2 ^a)	3 (0.3)	52 (5.6)	49 (5.3 ^b)	19 (2.1)	135 (14.5)	116 (12.4 ^b)	220 (23.7)	135 (14.5)	-85 (-9.2 ^b)
Psychiatric, n (%)	1310 (66.7)	1143 (58.2)	-167 (-8.5 ^b)	108 (5.5)	135 (6.9)	27 (1.4)	5 (0.3)	107 (5.5)	102 (5.2 ^b)	42 (2.1)	286 (14.6)	244 (12.5 ^b)	498 (25.4)	292 (14.9)	-206 (-10.5 ^b)
Respiratory, n (%)	413 (56.8)	341 (46.9)	-72 (-9.9 ^b)	84 (11.6)	93 (12.8)	9 (1.2)	3 (0.4)	39 (5.4)	36 (5.0 ^b)	18 (2.5)	110 (15.1)	92 (12.6 ^b)	209 (28.8)	144 (19.8)	-65 (-9.0 ^b)
No comorbidity, n (%)	4133 (68.3)	3711 (61.3)	-422 (-7.0 ^b)	340 (5.6)	395 (6.5)	55 (0.9 ^a)	63 (1.0)	391 (6.5)	328 (5.5 ^b)	189 (3.1)	887 (14.6)	698 (11.5 ^b)	1332 (22.0)	673 (11.1)	-659 (-10.9 ^b)

Δ = change in drug use in number and percentage. Comorbidity data from RA diagnosis is used for both drug data at 0 and 12 months. The results were calculated on 13 505 patients both at 0 and 12 months. ^aP value <0.05, ^bP value <0.01 (0.05/5 treatment groups, corrected for multiple testing), otherwise non-significant results, calculated by X² test.

Supplemental table 8. Methotrexate monotherapy and total methotrexate use at RA diagnosis and at 12 months, divided by comorbidity categories.

Comorbidity categories	MTX	MTX	MTX	MTX
	monotherapy 0 m	total 0 m	monotherapy 12 m	total 12 m
All patients, n	9178	9548	8282	10382
(%)	(68.0)	(70.7)	(61.3)	(76.9)
Cardiovascular, n	758	781	711	834
(%)	(63.4)	(65.4)	(59.5)	(69.8)
Non-cardiac vascular, n	2549	2617	2359	2772
(%)	(69.0)	(70.8)	(63.8)	(75.0)
Malignant, n	359	365	368	426
(%)	(61.8)	(62.8)	(63.3)	(73.3)
Endocrine, n	1820	1871	1624	1998
(%)	(69.4)	(71.3)	(61.9)	(76.2)
Gastrointestinal, n	558	574	508	634
(%)	(63.5)	(65.3)	(57.8)	(72.1)
Infectious, n	513	527	474	565
(%)	(61.7)	(63.3)	(57.0)	(67.9)
Chronic kidney, n	50	52	41	50
(%)	(47.6)	(49.5)	(39.1)	(47.6)
Neurological, n	656	674	556	700
(%)	(70.6)	(72.6)	(59.9)	(75.3)
Psychiatric, n	1310	1342	1143	1446
(%)	(66.7)	(68.4)	(58.2)	(73.7)
Respiratory, n	413	427	341	445
(%)	(56.8)	(58.7)	(46.9)	(61.2)
No comorbidity, n	4133	4359	3711	4783
(%)	(68.3)	(72.0)	(61.3)	(79.0)

Comorbidity data from RA diagnosis is used for both drug data at 0 and 12 months. The results were calculated on 13 505 patients both at 0 and 12 months. MTX, methotrexate. MTX total, methotrexate +/- combination with cs/b/tsDMARDs.

Supplemental table 9. Association of comorbidity categories and antirheumatic treatment categories, in relation to methotrexate, at 12 months after RA diagnosis.

COMORBIDITY CATEGORIES	RA TREATMENT		CRUDE	ADJUSTED FOR SEX AND AGE	FULL MODEL*
Number of observations			13 373	13 373	13 373
		n (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Cardiovascular	MTX monotherapy	858 (62.1)	Reference	Reference	Reference
	Non-MTX csDMARDs	89 (6.4)	0.98 (0.76 to 1.27)	1.18 (0.91 to 1.53)	1.19 (0.76 to 1.88)
	MTX + other csDMARDs	66 (4.8)	1.02 (0.76 to 1.36)	1.17 (0.88 to 1.57)	1.17 (0.71 to 1.94)
	b/tsDMARD	125 (9.0)	0.73 (0.59 to 0.90)	0.93 (0.75 to 1.15)	0.92 (0.65 to 1.31)
	No treatment	244 (17.7)	1.23 (1.04 to 1.46)	1.29 (1.08 to 1.54)	1.30 (0.95 to 1.78)
Non-cardiac vascular	MTX monotherapy	2802(64.6)	Reference	Reference	Reference
	Non-MTX csDMARDs	251 (5.8)	0.70 (0.58 to 0.85)	0.88 (0.72 to 1.07)	0.88 (0.69 to 1.13)
	MTX + other csDMARDs	198 (4.6)	0.69 (0.56 to 0.85)	0.85 (0.68 to 1.05)	0.84 (0.65 to 1.10)
	b/tsDMARD	465 (10.7)	0.72 (0.62 to 0.83)	1.04 (0.89 to 1.21)	1.05 (0.88 to 1.26)
	No treatment	619 (14.3)	0.91 (0.79 to 1.05)	0.96 (0.83 to 1.11)	0.98 (0.82 to 1.16)
Malignant	MTX monotherapy	509 (65.3)	Reference	Reference	Reference
	Non-MTX csDMARDs	48 (6.2)	0.86 (0.63 to 1.18)	0.96 (0.70 to 1.31)	0.96 (0.66 to 1.39)
	MTX + other csDMARDs	36 (4.6)	0.81 (0.56 to 1.15)	0.89 (0.62 to 1.27)	0.88 (0.58 to 1.33)
	b/tsDMARD	61 (7.8)	0.59 (0.45 to 0.77)	0.69 (0.52 to 0.91)	0.69 (0.51 to 0.95)
	No treatment	126 (16.2)	1.10 (0.89 to 1.36)	1.13 (0.92 to 1.40)	1.10 (0.85 to 1.41)
Endocrine	MTX monotherapy	1717 (62.1)	Reference	Reference	Reference
	Non-MTX csDMARDs	161 (5.8)	0.90 (0.74 to 1.10)	0.89 (0.73 to 1.09)	0.90 (0.72 to 1.11)
	MTX + other csDMARDs	142 (5.1)	0.97 (0.78 to 1.20)	0.98 (0.79 to 1.21)	0.97 (0.77 to 1.23)
	b/tsDMARD	382 (13.8)	1.22 (1.06 to 1.41)	1.24 (1.07 to 1.43)	1.23 (1.05 to 1.45)
	No treatment	365 (13.2)	0.98 (0.85 to 1.13)	0.98 (0.85 to 1.12)	0.98 (0.84 to 1.14)
Gastrointestinal	MTX monotherapy	632 (58.5)	Reference	Reference	Reference
	Non-MTX csDMARDs	69 (6.4)	1.01 (0.77 to 1.32)	1.02 (0.78 to 1.34)	1.04 (0.75 to 1.45)
	MTX + other csDMARDs	55 (5.1)	1.01 (0.75 to 1.36)	1.03 (0.77 to 1.39)	1.02 (0.71 to 1.46)

	b/tsDMARD	153 (14.2)	1.25 (1.03 to 1.52)	1.29 (1.06 to 1.57)	1.28 (1.01 to 1.63)
	No treatment	172 (15.9)	1.20 (0.99 to 1.44)	1.20 (1.00 to 1.44)	1.21 (0.96 to 1.52)
Infectious	MTX monotherapy	631 (56.5)	Reference	Reference	Reference
	Non-MTX csDMARDs	85 (7.6)	1.17 (0.91 to 1.51)	1.22 (0.95 to 1.58)	1.22 (0.94 to 1.58)
	MTX + other csDMARDs	47 (4.2)	0.86 (0.63 to 1.18)	0.90 (0.65 to 1.23)	0.90 (0.65 to 1.24)
	b/tsDMARD	136 (12.2)	1.09 (0.89 to 1.34)	1.16 (0.95 to 1.43)	1.19 (0.97 to 1.46)
	No treatment	217 (19.4)	1.48 (1.24 to 1.76)	1.49 (1.25 to 1.78)	1.47 (1.23 to 1.75)
Chronic kidney	MTX monotherapy	65 (42.2)	Reference	Reference	Reference
	Non-MTX csDMARDs	13 (8.4)	2.17 (1.18 to 4.01)	2.32 (1.26 to 4.30)	2.34 (1.26 to 4.34)
	MTX + other csDMARDs	7 (4.6)	1.48 (0.67 to 3.28)	1.56 (0.70 to 3.44)	1.57 (0.71 to 3.48)
	b/tsDMARD	21 (13.6)	1.95 (1.18 to 3.24)	2.11 (1.27 to 3.51)	2.09 (1.25 to 3.48)
	No treatment	48 (31.2)	3.12 (2.12 to 4.60)	3.17 (2.15 to 4.67)	3.25 (2.20 to 4.81)
Neurological	MTX monotherapy	686 (60.5)	Reference	Reference	Reference
	Non-MTX csDMARDs	66 (5.8)	0.91 (0.69 to 1.20)	0.90 (0.68 to 1.19)	0.90 (0.69 to 1.19)
	MTX + other csDMARDs	62 (5.5)	1.01 (0.76 to 1.34)	1.00 (0.75 to 1.34)	0.99 (0.74 to 1.32)
	b/tsDMARD	159 (14.0)	1.16 (0.96 to 1.41)	1.17 (0.96 to 1.42)	1.19 (0.98 to 1.44)
	No treatment	161 (14.2)	1.12 (0.93 to 1.35)	1.11 (0.92 to 1.34)	1.10 (0.91 to 1.34)
Psychiatric	MTX monotherapy	1356 (58.6)	Reference	Reference	Reference
	Non-MTX csDMARDs	165 (7.1)	1.18 (0.97 to 1.45)	1.06 (0.86 to 1.30)	1.08 (0.82 to 1.41)
	MTX + other csDMARDs	131 (5.7)	1.09 (0.87 to 1.36)	1.00 (0.80 to 1.30)	0.98 (0.73 to 1.33)
	b/tsDMARD	340 (14.7)	1.29 (1.11 to 1.50)	1.13 (0.97 to 1.32)	1.12 (0.91 to 1.37)
	No treatment	321 (13.9)	1.14 (0.98 to 1.32)	1.10 (0.95 to 1.28)	1.12 (0.92 to 1.35)
Respiratory	MTX monotherapy	450 (48.1)	Reference	Reference	Reference
	Non-MTX csDMARDs	122 (13.1)	3.05 (2.44 to 3.82)	3.18 (2.53 to 4.01)	3.29 (2.12 to 5.11)
	MTX + other csDMARDs	46 (4.9)	1.27 (0.92 to 1.76)	1.33 (0.96 to 1.84)	1.30 (0.77 to 2.19)
	b/tsDMARD	147 (15.7)	1.85 (1.51 to 2.26)	1.99 (1.62 to 2.45)	1.89 (1.34 to 2.67)
	No treatment	170 (18.2)	1.70 (1.40 to 2.06)	1.71 (1.41 to 2.08)	1.83 (1.32 to 2.53)
No comorbidity	MTX monotherapy	3177 (61.7)	Reference	Reference	Reference
	Non-MTX csDMARDs	334 (6.5)	1.01 (0.81 to 1.26)	0.93 (0.75 to 1.16)	0.93 (0.74 to 1.16)
	MTX + other csDMARDs	46 (4.9)	1.06 (0.84 to 1.34)	0.98 (0.77 to 1.24)	0.98 (0.77 to 1.25)

b/tsDMARD	147 (15.7)	<i>1.23 (1.05 to 1.45)</i>	1.08 (0.92 to 1.28)	1.08 (0.91 to 1.28)
No treatment	531 (10.3)	0.94 (0.79 to 1.10)	0.92 (0.78 to 1.09)	0.92 (0.78 to 1.09)

*Adjusted for sex, age, smoking, educational level, serological status, Rheumatic Disease Comorbidity Index. Results calculated by multinomial logistic regression. We included patients where there was missing data on smoking: 1938 patients (14.5%), educational level: 88 patients (0.7%) and serological status: 374 patients (2.8%), in the full model. Significant results in italic. Reference, methotrexate was used as the reference drug.

Supplemental table 10. Comparison of logarithmic binomial regression and multinomial logistic regression for results with odds ratios above 3 in supplemental table 9

Chronic kidney disease: MTX vs No treatment	Results
Odds ratios (using multinomial logistic regression)	3.25 (2.20-4.81)
Relative risk (using log binomial regression)	3.16 (2.14-4.67)

Respiratory diseases: MTX vs Non-MTX csDMARDs	
Odds ratio (using multinomial logistic regression)	3.29 (2.12-5.11)
Relative risk (using log binomial regression)	3.22 (2.41-4.29)

All results showing full model, i.e. adjusted for sex, age, smoking, educational level, serological status, Rheumatic Disease Comorbidity Index.

Supplemental table 11. Association of comorbidity categories and antirheumatic treatment categories, in relation to methotrexate, at 12 months after RA diagnosis, stratified by age.

Comorbidity categories	RA treatment	Full model* <65 years (n: 7815)		Full model* ≥65 years (n:5558)	
		n (%)	OR (95%)	n (%)	OR (95%)
Cardiovascular	MTX monotherapy	150 (54.4)	Reference	708 (66.5)	Reference
	Non-MTX csDMARDs	19 (6.9)	1.92 (0.87 to 4.23)	70 (6.3)	0.84 (0.48 to 1.49)
	MTX + other csDMARDs	25 (9.1)	2.40 (1.13 to 5.09)	41 (3.7)	0.78 (0.39 to 1.55)
	b/tsDMARDs	57 (20.7)	1.66 (0.99 to 2.76)	68 (6.2)	0.64 (0.39 to 1.06)
	No treatment	25 (9.1)	1.17 (0.61 to 2.25)	219 (19.8)	1.15 (0.79 to 1.67)
Non-cardiac vascular	MTX monotherapy	867 (60.8)	Reference	1935 (66.5)	Reference
	Non-MTX csDMARDs	87 (6.1)	1.07 (0.75 to 1.52)	164 (5.6)	0.72 (0.52 to 1.01)
	MTX + other csDMARDs	97 (6.8)	1.05 (0.74 to 1.48)	101 (3.5)	0.62 (0.41 to 0.94)
	b/tsDMARDs	229 (16.1)	0.96 (0.75 to 1.22)	236 (8.1)	1.27 (0.93 to 1.73)
	No treatment	147 (10.3)	0.90 (0.68 to 1.19)	472 (16.2)	1.07 (0.85 to 1.35)
Malignant	MTX monotherapy	143 (57.2)	Reference	366 (69.1)	Reference
	Non-MTX csDMARDs	17 (6.8)	1.28 (0.70 to 2.35)	31 (9.7)	0.78 (0.49 to 1.24)
	MTX + other csDMARDs	16 (6.4)	1.17 (0.63 to 2.18)	20 (3.8)	0.72 (0.41 to 1.26)
	b/tsDMARDs	34 (13.6)	0.89 (0.58 to 1.38)	27 (5.1)	0.59 (0.37 to 0.94)
	No treatment	40 (16.0)	1.55 (0.99 to 2.42)	86 (16.2)	0.95 (0.70 to 1.29)
Endocrine	MTX monotherapy	708 (55.6)	Reference	1009 (67.6)	Reference
	Non-MTX csDMARDs	80 (6.3)	1.03 (0.76 to 1.41)	81 (5.4)	0.80 (0.59 to 1.09)
	MTX + other csDMARDs	80 (6.3)	1.02 (0.74 to 1.39)	62 (4.2)	0.95 (0.66 to 1.38)
	b/tsDMARDs	260 (20.4)	1.36 (1.11 to 1.66)	122 (8.2)	1.08 (0.83 to 1.42)
	No treatment	146 (11.5)	1.13 (0.88 to 1.44)	219 (14.7)	0.88 (0.72 to 1.08)
Gastrointestinal	MTX monotherapy	269 (54.0)	Reference	363 (62.3)	Reference
	Non-MTX csDMARDs	40 (8.0)	1.62 (1.01 to 2.61)	29 (5.0)	0.71 (0.44 to 1.14)
	MTX + other csDMARDs	28 (5.6)	1.06 (0.64 to 1.77)	27 (4.6)	1.01 (0.60 to 1.70)
	b/tsDMARDs	99 (19.9)	1.34 (0.98 to 1.85)	54 (9.3)	1.22 (0.83 to 1.79)
	No treatment	62 (12.5)	1.33 (0.90 to 1.96)	110 (18.9)	1.17 (0.87 to 1.56)
Infectious	MTX monotherapy	207 (52.0)	Reference	424 (59.1)	Reference
	Non-MTX csDMARDs	33 (8.3)	1.25 (0.83 to 1.87)	52 (7.2)	1.15 (0.82 to 1.61)
	MTX + other csDMARDs	19 (4.8)	0.71 (0.43 to 1.16)	28 (3.9)	1.21 (0.79 to 1.87)
	b/tsDMARDs	75 (18.8)	1.13 (0.85 to 1.51)	61 (8.5)	1.29 (0.94 to 1.76)
	No treatment	64 (16.1)	1.49 (1.09 to 2.03)	153 (21.3)	1.34 (1.07 to 1.68)
Chronic kidney	MTX monotherapy	15 (42.9)	Reference	50 (42.0)	Reference
	Non-MTX csDMARDs	5 (14.3)	3.63 (1.28 to 10.3)	8 (6.7)	1.83 (0.84 to 3.96)
	MTX + other csDMARDs	3 (8.6)	1.87 (0.53 to 6.60)	4 (3.4)	1.46 (0.51 to 4.15)
	b/tsDMARDs	5 (14.3)	1.19 (0.43 to 3.33)	16 (13.5)	2.83 (1.55 to 5.17)
	No treatment	7 (20.0)	2.53 (1.00 to 6.41)	41 (34.5)	3.04 (1.96 to 4.72)
Neurological	MTX monotherapy	382 (58.7)	Reference	304 (62.9)	Reference
	Non-MTX csDMARDs	41 (6.3)	0.97 (0.68 to 1.39)	25 (5.2)	0.90 (0.58 to 1.38)
	MTX + other csDMARDs	41 (6.3)	0.88 (0.61 to 1.27)	21 (4.4)	1.17 (0.72 to 1.89)
	b/tsDMARDs	108 (16.6)	1.01 (0.79 to 1.29)	51 (10.6)	1.62 (1.16 to 2.25)
	No treatment	79 (12.1)	1.04 (0.79 to 1.37)	82 (17.0)	1.23 (0.94 to 1.61)
Psychiatric	MTX monotherapy	791 (54.1)	Reference	565 (66.5)	Reference
	Non-MTX csDMARDs	113 (7.7)	1.47 (1.00 to 2.17)	52 (6.1)	0.86 (0.58 to 1.28)
	MTX + other csDMARDs	103 (7.0)	1.30 (0.88 to 1.93)	28 (3.3)	0.62 (0.37 to 1.03)
	b/tsDMARDs	276 (18.9)	1.22 (0.94 to 1.58)	64 (7.5)	0.88 (0.62 to 1.25)

	No treatment	180 (12.3)	1.29 (0.95 to 1.76)	141 (16.6)	1.01 (0.78 to 1.30)
Respiratory	MTX monotherapy	152 (42.0)	Reference	298 (52.0)	Reference
	Non-MTX csDMARDs	47 (13.0)	<i>4.59 (2.28 to 9.24)</i>	75 (13.1)	<i>2.70 (1.53 to 4.76)</i>
	MTX + other csDMARDs	26 (7.2)	<i>2.31 (1.11 to 4.83)</i>	20 (3.5)	<i>0.73 (0.34 to 1.54)</i>
	b/tsDMARDs	83 (22.9)	<i>2.14 (1.32 to 3.47)</i>	64 (11.2)	<i>1.74 (1.05 to 2.89)</i>
	No treatment	54 (14.9)	<i>2.67 (1.49 to 4.78)</i>	116 (20.2)	<i>1.56 (1.05 to 2.32)</i>
No comorbidity	MTX monotherapy	2233 (58.0)	Reference	944 (72.7)	Reference
	Non-MTX csDMARDs	273 (7.1)	1.16 (0.86 to 1.57)	61 (4.7)	0.69 (0.47 to 1.01)
	MTX + other csDMARDs	281 (7.3)	1.04 (0.76 to 1.41)	62 (4.8)	0.88 (0.57 to 1.36)
	b/tsDMARDs	670 (17.4)	1.08 (0.88 to 1.33)	96 (7.4)	1.16 (0.82 to 1.65)
	No treatment	395 (10.3)	0.90 (0.70 to 1.14)	136 (10.5)	0.93 (0.71 to 1.23)

*The full model was adjusted for sex, age, smoking, educational level, serological status, Rheumatic Disease Comorbidity Index. Results calculated by multinomial logistic regression. We included patients where there was missing data on smoking, educational level and serological status in this model. Significant results in italic. Reference, methotrexate (MTX) was used as the reference drug.

Supplemental table 12. Number and proportions of patients on the different treatments categories for each comorbidity category, at one year after RA-diagnosis, divided by seropositivity.

Comorbidity categories	MTX monotherapy			Non-MTX csDMARDs			MTX + other csDMARDs			b/tsDMARDs			No treatment		
	Sero-pos	Sero-neg	p-value	Sero-pos	Sero-neg	p-value	Sero-pos	Sero-neg	p-value	Sero-pos	Sero-neg	p-value	Sero-pos	Sero-neg	p-value
All patients, n (%)	5656 (61.1)	2399 (62.1)	0.31	532 (5.8)	217 (5.6)	0.23	613 (6.6)	234 (6.1)	0.76	1369 (14.8)	392 (10.1)	<0.0001	1085 (11.7)	624 (16.1)	<0.0001
Cardiovascular, n (%)	526 (58.3)	308 (61.5)	0.24	62 (6.9)	25 (5.0)	0.16	42 (4.7)	22 (4.4)	0.82	98 (10.9)	25 (5.0)	0.0002	175 (19.4)	121 (24.2)	0.036
Non-cardiac vascular, n (%)	1780 (62.8)	949 (64.4)	0.32	159 (5.6)	85 (5.8)	0.84	129 (4.6)	63 (4.3)	0.67	349 (12.3)	111 (7.5)	<0.0001	416 (14.7)	266 (18.1)	0.004
Malignant, n (%)	313 (62.7)	181 (63.3)	0.88	27 (5.4)	19 (6.6)	0.48	21 (4.2)	13 (4.6)	0.82	48 (9.6)	12 (4.2)	0.0059	90 (18.0)	61 (21.3)	0.26
Endocrine, n (%)	1145 (61.0)	522 (61.9)	0.65	111 (5.9)	47 (5.6)	0.73	96 (5.1)	42 (5.0)	0.88	288 (15.3)	85 (10.1)	0.0002	237 (12.6)	147 (17.4)	0.0009
Gastrointestinal, n (%)	431 (58.2)	184 (53.3)	0.13	45 (6.1)	21 (6.1)	0.99	36 (4.9)	19 (5.5)	0.65	109 (14.7)	42 (12.2)	0.26	120 (16.2)	79 (22.9)	0.008
Infectious, n (%)	431 (54.7)	188 (53.6)	0.72	60 (7.6)	24 (6.8)	0.64	35 (4.4)	12 (3.4)	0.42	101 (12.8)	34 (9.7)	0.13	161 (20.4)	93 (26.5)	0.023
Chronic kidney, n (%)	45 (42.9)	21 (37.5)	0.51	10 (9.5)	2 (3.6)	0.17	6 (5.7)	1 (1.8)	0.24	16 (15.2)	4 (7.1)	0.14	28 (26.7)	28 (50.0)	0.003
Neurological, n (%)	434 (59.9)	237 (60.8)	0.77	50 (6.9)	16 (4.1)	0.059	43 (5.9)	19 (4.9)	0.46	107 (14.8)	45 (11.5)	0.14	91 (12.6)	73 (18.7)	0.0056
Psychiatric, n (%)	912 (57.3)	409 (60.1)	0.21	122 (7.7)	38 (5.6)	0.076	91 (5.7)	36 (5.3)	0.69	256 (16.1)	76 (11.2)	0.0024	212 (13.3)	122 (17.9)	0.0045
Respiratory, n (%)	322 (45.4)	120 (50.6)	0.16	98 (13.8)	22 (9.3)	0.069	35 (4.9)	10 (4.2)	0.65	115 (16.2)	28 (11.8)	0.10	139 (19.6)	57 (24.1)	0.14
No comorbidity, n (%)	2293 (61.6)	811 (62.2)	0.69	247 (6.6)	79 (6.1)	0.47	233 (6.3)	94 (7.2)	0.23	597 (16.0)	153 (11.7)	0.0002	351 (9.4)	166 (12.7)	0.0007

Missing information on seropositivity/seronegativity: 384 (2.8%). Comorbidity data from one year after RA diagnosis is used. The results were calculated on 13 505 patients. P values calculated by χ^2 test. Seropos, seropositive. Seroneg, seronegative.

Supplemental table 13. Number and proportions of patients on methotrexate monotherapy at RA onset, 12 and 36 months after RA diagnosis, divided in the different comorbidity categories.

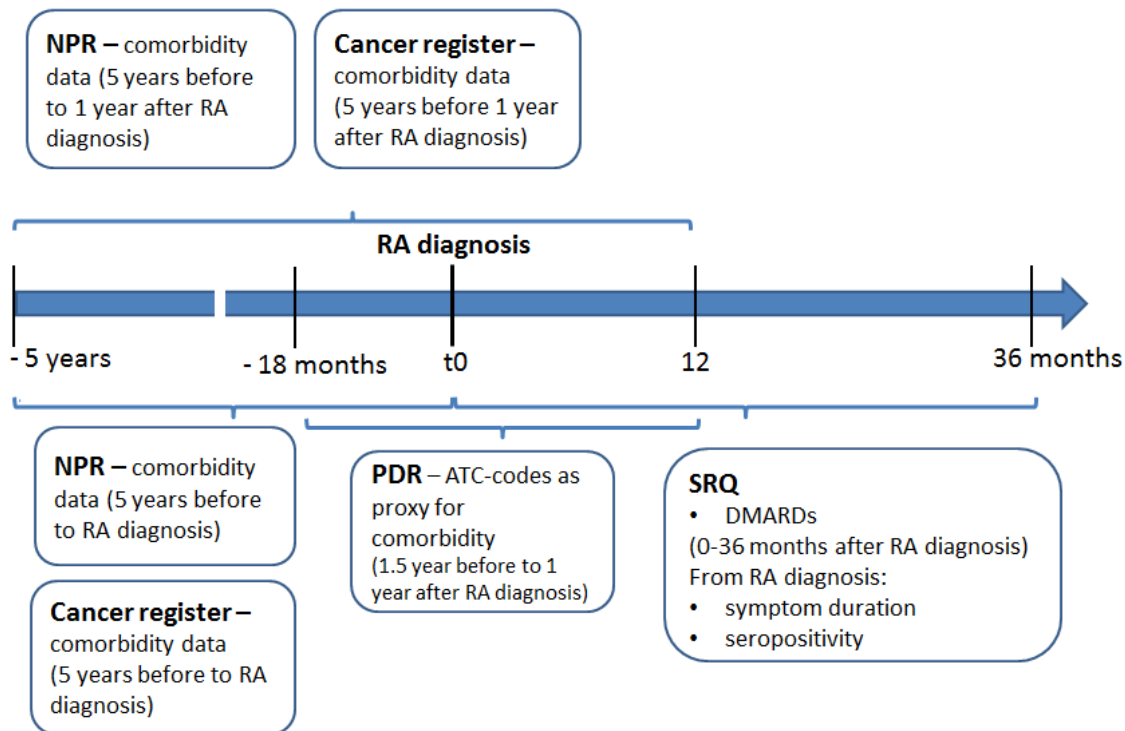
	RA onset n: 13 505	12 months n: 13 373*	36 months n: 13 030*
Cardiovascular n (%)	758 (63.4)	858 (62.1)	698 (54.9)
Non-cardiac vascular n (%)	2549 (69.0)	2802 (64.6)	2299 (55.8)
Malignant n (%)	359 (61.8)	509 (65.3)	388 (54.2)
Endocrine n (%)	1820 (69.4)	1717 (62.1)	1371 (51.7)
Gastrointestinal n (%)	558 (63.5)	632 (58.5)	513 (50.5)
Infectious n (%)	513 (61.7)	631 (56.5)	482 (47.4)
Chronic kidney n (%)	50 (47.6)	65 (42.2)	52 (39.1)
Neurological n (%)	656 (70.6)	686 (60.5)	556 (50.5)
Psychiatric n (%)	1310 (66.7)	1356 (58.6)	1074 (48.0)
Respiratory n (%)	413 (56.8)	450 (48.1)	359 (42.1)
No comorbidity n (%)	4133 (68.3)	3177 (61.7)	2577 (50.5)

*132 died or emigrated up to 12 months after RA onset. An additional 343 died or emigrated up to 36 months after RA onset. Comorbidity data at RA onset refers to reported comorbidities 5 years before to RA diagnosis. Comorbidity data at 12 and 36 months refers to the comorbidity situation 5 years before to 12 months after RA diagnosis.

Supplemental table 14. Comparison of treatment categories at the time of RA diagnosis, based on the Prescribed Drug Register or Swedish Rheumatology Quality register, for patients with the different comorbidity categories.

Comorbidity categories	MTX monotherapy		Non-MTX csDMARDs		MTX + csDMARDs		b/tsDMARDs		No treatment	
	PDR	SRQ	PDR	SRQ	PDR	SRQ	PDR*	SRQ	PDR	SRQ
Cardiovascular n(%)	822 (68.8)	758 (63.4)	87 (7.3)	82 (6.9)	14 (1.2)	9 (0.8)	5 (0.4)	20 (1.7)	267 (22.3)	326 (27.3)
Non-cardiac vascular n(%)	2700 (73.1)	2549 (69.0)	203 (5.5)	189 (5.1)	37 (1.0)	16 (0.4)	27 (0.7)	69 (1.9)	728 (19.7)	872 (23.6)
Malignant n(%)	388 (66.8)	359 (61.8)	50 (8.6)	48 (8.3)	7 (1.2)	5 (0.9)	3 (0.5)	3 (0.5)	133 (22.9)	166 (28.6)
Endocrine n(%)	1917 (73.1)	1820 (69.4)	164 (6.3)	153 (5.8)	26 (1.0)	12 (0.5)	28 (1.1)	60 (2.3)	488 (18.6)	579 (22.1)
Gastrointestinal n(%)	609 (69.3)	558 (63.5)	50 (5.7)	46 (5.2)	9 (1.0)	5 (0.6)	11 (1.3)	20 (2.3)	200 (22.8)	250 (28.4)
Infectious n(%)	559 (67.2)	513 (61.7)	66 (7.9)	62 (7.5)	6 (0.7)	4 (0.5)	8 (1.0)	16 (1.9)	193 (23.2)	237 (28.5)
Chronic kidney disease n(%)	54 (51.4)	50 (47.6)	12 (11.4)	12 (11.4)	1 (1.0)	0	4 (3.8)	4 (3.8)	34 (32.4)	39 (37.1)
Neurological n(%)	702 (75.6)	656 (70.6)	32 (3.4)	31 (3.3)	8 (0.9)	3 (0.3)	9 (1.0)	19 (2.1)	178 (19.2)	220 (23.7)
Psychiatric n(%)	1410 (71.8)	1310 (66.7)	121 (6.2)	108 (5.5)	19 (1.0)	5 (0.3)	15 (0.8)	42 (2.1)	398 (20.3)	498 (25.4)
Respiratory n(%)	442 (60.8)	413 (56.8)	91 (12.5)	84 (11.6)	6 (0.8)	3 (0.4)	6 (0.8)	18 (2.5)	182 (25.0)	209 (28.8)

Total number of patients: 13 505. *Data from PDR does not include bDMARDs given as infusions, only drugs prescribed and dispensed at pharmacies. PDR, Prescribed Drug Register; SRQ, Swedish Rheumatology Quality Register.

Supplemental figure 1. Time periods used for comorbidity and antirheumatic drug data.

Supplemental figure 2. Distribution of different drugs used by RA patients that received different DMARD regimens at diagnosis. The figure shows box plots with median, quartiles and highest numbers of separate ATC-codes that are prescribed and dispensed from 1.5 years before and until RA diagnosis, to capture all prescriptions (renewed once a year).

