

SUPPLEMENTARY MATERIAL

Supplementary Table 1. ATC codes for conventional synthetic DMARD

Conventional synthetic DMARD	ATC Code
Methotrexate	L04AX03 / L01BA01
Sulfasalazine	A07EC01
Hydroxychloroquine	P01BA02
Leflunomide	L04AA13
Ciclosporin	L04AD01 / L04AA01
Gold	MC01CB
Azathioprine	L04AX01

DMARD, disease-modifying anti-rheumatic drug.

ATC, Anatomical Therapeutic Chemical

Supplementary Table 2. Demographic description of incident rheumatoid arthritis (RA) cases based on Criterion B in Denmark, divided in three calendar periods

	Calendar period		
	1998-2004	2005-2011	2012-2018
N	10 533	12 002	13 295
Age (years), median (2.5 to 97.5 percentile)	59.9 (25.7 to 83.6)	60.0 (27.1 to 84.5)	61.9 (25.9 to 84.9)
Female	7470 (70.9)	8443 (70.3)	9029 (67.9)
Region within Denmark			
Capital Region	3641 (34.6)	3508 (29.2)	3756 (28.3)
Central Region	1858 (17.6)	1733 (14.4)	2687 (20.2)
Northern Region	1374 (13.0)	1617 (13.5)	1399 (10.5)
Southern Region	1995 (18.9)	3128 (26.1)	3393 (25.5)
Zealand Region	1665 (15.8)	2016 (16.8)	2060 (15.5)
csDMARD use in previous year	5757 (54.7)	7261 (60.5)	7498 (56.4)
At least two prednisolone prescriptions in past year	1979 (18.8)	2403 (20.0)	2295 (17.3)
NSAID use in previous year	8264 (78.5)	8349 (69.6)	7677 (57.7)
Chronic obstructive pulmonary disease	474 (4.5)	631 (5.3)	780 (5.9)
Diabetes mellitus	440 (4.2)	706 (5.9)	847 (6.4)
Cardiovascular disease	1154 (11.0)	1517 (12.6)	1631 (12.3)
Previous hip or knee replacement surgery	441 (4.2)	801 (6.7)	1168 (8.8)
Mean 5 year household income above mean national household (per year), %	41	43	42

Data are shown as n (%) unless otherwise indicated.

Criterion B was defined as an RA diagnosis recorded twice in the Danish National Patient Registry within 90 days of each other, and with both records originating from a department of rheumatology or general internal medicine.

csDMARD, conventional synthetic disease-modifying anti-rheumatic drug

NSAID, non-steroidal anti-inflammatory drug.

Supplementary Table 3. Demographic description of incident rheumatoid arthritis (RA) cases based on Criterion C in Denmark, divided in three calendar periods

	Calendar period		
	1998-2004	2005-2011	2012-2018
N	10 973	12 408	13 053
Age (years), median (2.5 to 97.5 percentile)	60.1 (26.1 to 83.2)	59.9 (26.9 to 84.0)	62.0 (25.8 to 84.9)
Female	7778 (70.9)	8684 (70.0)	8820 (67.6)
Region within Denmark			
Capital Region	3445 (31.4)	3452 (27.8)	3734 (28.6)
Central Region	1952 (17.8)	1992 (16.1)	2686 (20.6)
Northern Region	1438 (13.1)	1580 (12.7)	1316 (10.1)
Southern Region	2362 (21.5)	3260 (26.3)	3343 (25.6)
Zealand Region	1766 (16.1)	2068 (16.7)	1967 (15.1)
csDMARD use in previous year	10 894 (99.3)	12 398 (99.9)	13 040 (99.9)
At least two prednisolone prescriptions in past year	2384 (21.7)	2674 (21.6)	2498 (19.1)
NSAID use in previous year	8685 (79.1)	8739 (70.4)	7711 (59.1)
Chronic obstructive pulmonary disease	469 (4.3)	650 (5.2)	745 (5.7)
Diabetes mellitus	449 (4.1)	711 (5.7)	866 (6.6)
Cardiovascular disease	1168 (10.6)	1513 (12.2)	1619 (12.4)
Previous hip or knee replacement surgery	474 (4.3)	812 (6.5)	1131 (8.7)
Mean 5 year household income above mean national household (per year), %	41	44	42

Data are shown as n (%) unless otherwise indicated.

Criterion C was defined as a single RA diagnosis recorded at any time with a redeemed conventional synthetic disease-modifying anti-rheumatic drug (csDMARD) prescription in the year before or after the diagnosis was recorded in the Danish National Patient Registry.

NSAID, non-steroidal anti-inflammatory drug.

Supplementary Table 4. Demographic description of incident rheumatoid arthritis (RA) cases based on Criterion D in Denmark, divided in three calendar periods

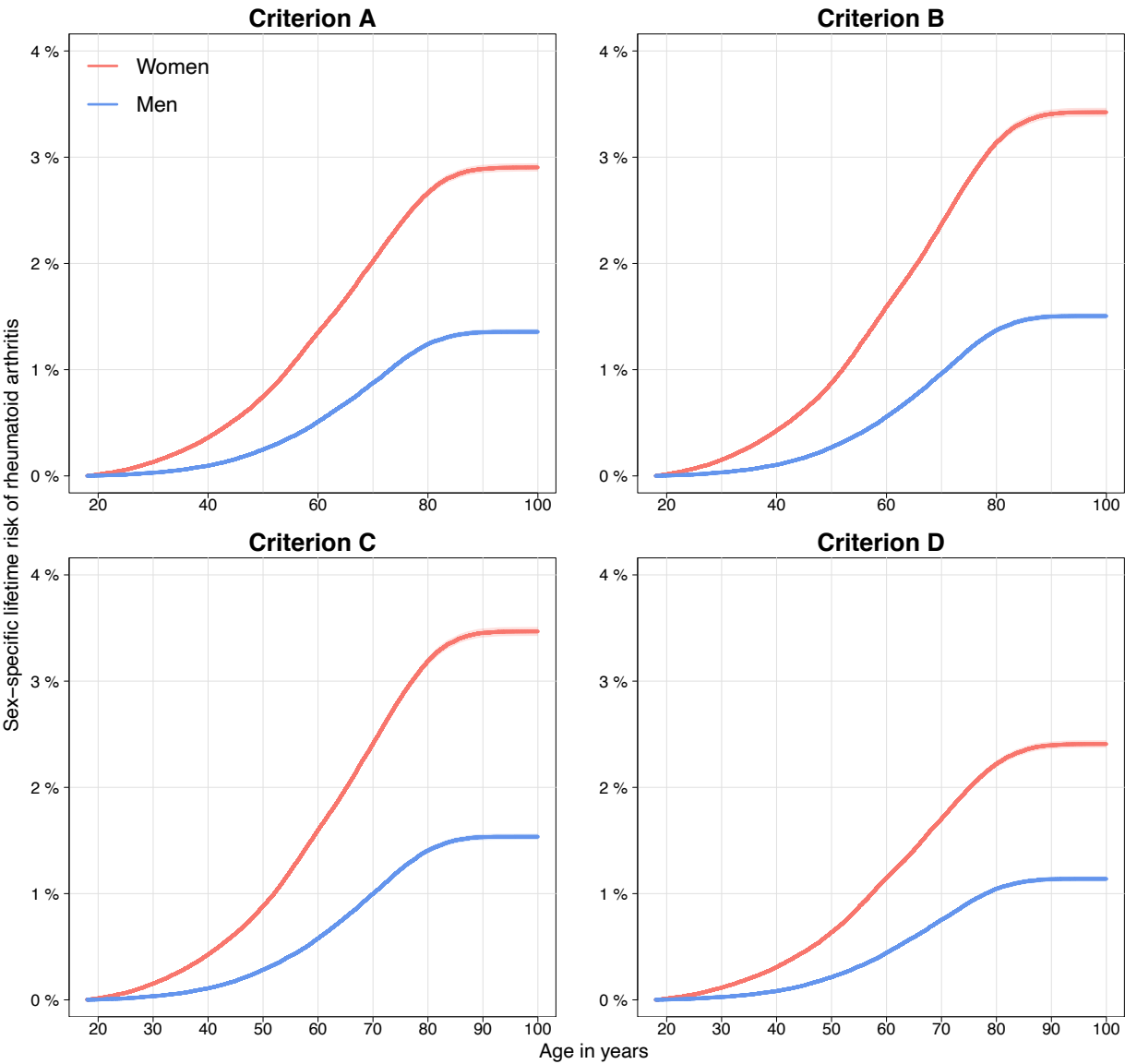
	Calendar period		
	1998-2004	2005-2011	2012-2018
N	7344	9052	9504
Age (years), median (2.5 to 97.5 percentile)	59.8 (25.5 to 83.5)	59.3 (26.2 to 83.8)	61.3 (25.4 to 84.8)
Female	5105 (69.5)	6208 (68.6)	6294 (66.2)
Region within Denmark			
Capital Region	2196 (29.9)	2463 (27.2)	2665 (28.0)
Central Region	1277 (17.4)	1454 (16.1)	1991 (20.9)
Northern Region	969 (13.2)	1173 (13.0)	961 (10.1)
Southern Region	1640 (22.3)	2413 (26.7)	2402 (25.3)
Zealand Region	1257 (17.1)	1517 (16.8)	1479 (15.6)
csDMARD use in previous year	7316 (99.6)	9047 (99.9)	9498 (99.9)
At least two prednisolone prescriptions in past year	1424 (19.4)	1709 (18.9)	1524 (16.0)
NSAID use in previous year	6088 (82.9)	6635 (73.3)	5863 (61.7)
Chronic obstructive pulmonary disease	305 (4.2)	435 (4.8)	493 (5.2)
Diabetes mellitus	280 (3.8)	465 (5.1)	573 (6.0)
Cardiovascular disease	741 (10.1)	1038 (11.5)	1060 (11.2)
Previous hip or knee replacement surgery	238 (3.2)	519 (5.7)	743 (7.8)
Mean 5 year household income above mean national household (per year), %	42	44	43

Data are shown as n (%) unless otherwise indicated.

Criterion D was defined as a first-time RA diagnosis code registered in the Danish National Patient Registry, a redeemed prescription of a conventional synthetic disease-modifying anti-rheumatic drug (csDMARD) in the following year, and with no ICD code for psoriatic or enteropathic arthropathies, systemic connective tissue disorders, inflammatory bowel diseases, or sarcoidosis recorded prior to the RA diagnosis in the Danish National Patient Registry.

NSAID, non-steroidal anti-inflammatory drug.

Supplementary Figure 1: Cumulative lifetime risk of rheumatoid arthritis for women and men at various ages in Denmark



Supplementary Table 5. Coefficients from log-linear Poisson regression with robust sandwich variance estimator

		Trend from 2000 to 2018	2000 (reference) compared to 2009	2011 (reference) compared to 2018
Criterion A	Overall coefficients (95%CI), p-value	0.0310 (0.0286 to 0.0335), <0.0001	0.2381 (0.2381 to 0.2381), <0.0001	0.2370 (0.2370 to 0.2370), <0.0001
	Women coefficients (95%CI), p-value	0.0304 (0.0287 to 0.0320), <0.0001	0.2425 (0.2425 to 0.2425), <0.0001	0.2230 (0.2230 to 0.2230), <0.0001
	Men coefficients (95%CI), p-value	0.0334 (0.0294 to 0.0375), <0.0001	0.2389 (0.2389 to 0.2389), <0.0001	0.2733 (0.2733 to 0.2733), <0.0001
Criterion B	Overall coefficients (95%CI), p-value	0.0286 (0.0263 to 0.0308), <0.0001	0.2195 (0.2195 to 0.2195), <0.0001	0.2191 (0.2191 to 0.2191), <0.0001
	Women coefficients (95%CI), p-value	0.0284 (0.0271 to 0.0298), <0.0001	0.2308 (0.2308 to 0.2308), <0.0001	0.2080 (0.2080 to 0.2080), <0.0001
	Men coefficients (95%CI), p-value	0.0297 (0.0254 to 0.0340), <0.0001	0.2019 (0.2019 to 0.2019), <0.0001	0.2506 (0.2506 to 0.2506), <0.0001
Criterion C	Overall coefficients (95%CI), p-value	0.0309 (0.0299 to 0.0319), <0.0001	0.2568 (0.2568 to 0.2568), <0.0001	0.2197 (0.2197 to 0.2197), <0.0001
	Women coefficients (95%CI), p-value	0.0307 (0.0305 to 0.0309), <0.0001	0.2675 (0.2675 to 0.2675), <0.0001	0.2089 (0.2089 to 0.2089), <0.0001
	Men coefficients (95%CI), p-value	0.0322 (0.0292 to 0.0351), <0.0001	0.2408 (0.2408 to 0.2408), <0.0001	0.2500 (0.2500 to 0.2500), <0.0001
Criterion D	Overall coefficients (95%CI), p-value	0.0230 (0.0194 to 0.0266), <0.0001	0.1507 (0.1507 to 0.1507), <0.0001	0.1959 (0.1959 to 0.1959), <0.0001
	Women coefficients (95%CI), p-value	0.0225 (0.0197 to 0.0252), <0.0001	0.1573 (0.1573 to 0.1573), <0.0001	0.1821 (0.1821 to 0.1821), <0.0001
	Men coefficients (95%CI), p-value	0.0251 (0.0198 to 0.0304), <0.0001	0.1468 (0.1468 to 0.1468), <0.0001	0.2312 (0.2312 to 0.2312), <0.0001