Supplementary online content

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Table S1. Description of the creation of the RA population and general population referents.

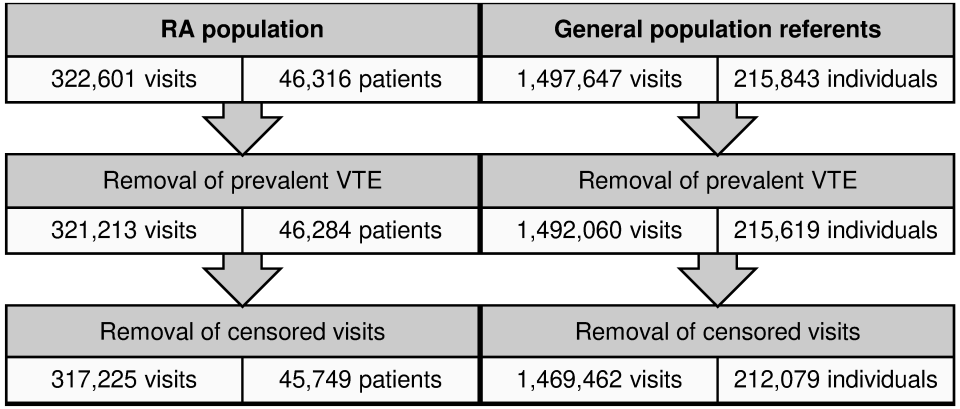


Table S2. Definition of main outcome and sensitivity analyses.

Outcome	Definition	Time period	Exclusion	Codes used
Main outcome	VTE within 1 year after SRQ registered rheumatologist visit.	From date of SRQ visit up until 365 days after	If VTE within 1 year before date of SRQ visit	ICD-10 diagnosis of I26, I80-82 *or* pulmonary embolism listed as the underlying cause of death.
Sensitivity analysis 1	VTE (main outcome) *and* anticoagulant collected at pharmacy within 30 days after diagnosis *OR* death from any cause within 30 days from diagnosis.	As main outcome	As main outcome	As main outcome *and* ATC = B01AA, B01AB, B01AE, B01AF or B01AX
Sensitivity analysis 2	As main outcome but excluding all cases with ever VTE before SRQ visit.	As main outcome	If *ever* VTE before SRQ visit	As main outcome (ICD9 codes for those diagnoses prior to 1997: DVT=451-453 PE=415)
Sensitivity analysis 3	As main outcome *but* "prevalent VTE" defined as VTE within 180 (instead of 365) days before SRQ visit.	As main outcome	As main outcome	As main outcome
Sensitivity analysis 4	As main outcome but time band for VTE assessment ending 180 days instead of 365 days after the visit.	From date of SRQ visit up until 180 days after	As main outcome	As main outcome
Sensitivity analysis 5	As main outcome but ICD codes for unspecified phlebitis and thrombophlebitis excluded from the VTE definition.	As main outcome	As main outcome	As main outcome *except from* I80.0, I80.3, I80.8, I80.9, I82.0 or I82.1
Sensitivity analysis 6	As main outcome	As main outcome	If previous SRQ visit within – 365 days.	As main outcome
Sensitivity analysis 7	As main outcome *but* including only 1 randomly chosen SRQ visit from each patient	As main outcome	As main outcome	As main outcome
Sensitivity analysis 8	As main outcome *but* including only the first visit from each patient	As main outcome	As main outcome	As main outcome
Sensitivity analysis 9	As main outcome *and* applying multiple imputation	As main outcome	As main outcome	As main outcome

Table S3. Degree of missing data, clinical characteristics.

	Percentage missing				
	RA pop	DAS28 category			
Clinical RA data		Remission	Low	Intermediate	High
RA duration	1%	1%	2%	1%	1%
DAS28	17%	0%	0%	0%	0%
DAS28CRP	12%	1%	1%	1%	1%
CRP	4%	1%	1%	1%	1%
ESR	10%	0%	0%	0%	0%
CDAI	90%	87%	89%	90%	90%
CDAI (algorithm)	14%	4%	5%	5%	4%
HAQ	11%	4%	5%	5%	6%
Number of swollen joints	4%	0%	0%	0%	0%
Number of tender joints	4%	0%	0%	0%	0%
VAS global	7%	0%	0%	0%	0%
VAS pain	8%	1%	1%	1%	2%
Smoker	52%	48%	51%	55%	61%

Table S4. Characteristics of underlying RA cohort by first and last visit of study period.

	First visits	Last visits
N	46316	46316
Age at visit, median (IQR)	62 (51-70)	67 (56-75)
Male (%)	29%	29%
RA duration, median (IQR)	4.0 (0.7-13.1)	10.3 (4.4-19.2)
Year of visit, median (IQR)	2010.0 (2007.0-2014.0)	2016.0 (2014.0-2017.0)
Clinical RA data		
DAS28ESR, median (IQR)	4.1 (2.9-5.3)	2.8 (2.0-3.8)
DAS28CRP, median (IQR)	3.8 (2.7-4.9)	2.5 (1.8-3.5)
CRP, median (IQR)	7.0 (4.0-18.0)	4.7 (2.0-8.7)
ESR, median (IQR)	19.0 (10.0-34.0)	14.0 (7.0-26.0)
HAQ, median (IQR)	0.9 (0.4-1.4)	0.8 (0.1-1.3)
Swollen joint count, median (IQR)	3.0 (0.0-7.0)	0.0 (0.0-2.0)
Tender joint count, median (IQR)	3.0 (0.0-7.0)	0.0 (0.0-3.0)
VAS global, median (IQR)	45.0 (21.0-65.0)	30.0 (11.0-54.0)
VAS pain, median (IQR)	44.0 (21.0-66.0)	29.0 (10.0-53.0)
Seropositive, (%)	74%	74%
Seronegative, unknown (%)	26%	27%
Smoker (%)	42%	61%
Comorbidities[a]		
ACS (%)	2%	3%
Other cardiac disease (%)	23%	33%
Prev VTE (%)	1%	2%
Chronic kidney disease (%)	1%	2%
Cancer (in past 10 years) (%)	4%	6%
COPD (%)	14%	17%
Diabetes (%)	9%	12%
Number of hospitalizations, median (IQR)	6 (3-12)	6 (3-12)

Number of specialist care visits, median (IQR)	19 (9-36)	38 (21-66)
Treatments[b]		
Methotrexate (%)	70%	64%
Other csDMARD (%)	17%	16%
TNFi (%)	21%	23%
Other b/tsDMARD (%)	2%	11%
Number previous biologics, median (IQR)	1 (0-1)	1 (1-3)
NSAID/ASA (%)	2%	3%
Anitcoagulant[c] (%)	68%	51%
Oral estrogen[d] (%)	13%	12%
Socioeconomics		
Married/cohabiting partner (%)	47%	48%
Disability pension in previous year (%)	2%	1%
Sick leave in previous year (%)	11%	9%

[a]Registered within the last 5 years unless otherwise stated
[b]RA treatments: at time of visit. Other treatments: Registered within the last year.
[c]Collected anticoagulant drug from pharmacy within one year before VTE event
[d]Oral contraceptive w estrogen *or* hormone replacement therapy

Table S5. Cumulative incidence and risk ratios for DAS28 on the VTE outcomes, stratified by DAS28 category.

Stratification			Relative risk (95% CI)[a], versus remission			
	No. of VTE events (Cumulative incidence, %)	No. of visits	Remission	Low DAS28	Moderate DAS28	High Das28
RA duration <5 years	728 (0.68)	107038	1(ref)	1.35 (1.03, 1.78)	1.45 (1.16, 1.82)	2.09 (1.63, 2.67)
RA duration 5+ years	1481 (0.72)	205200	1(ref)	1.04 (0.85, 1.26)	1.47 (1.26, 1.72)	1.97 (1.59, 2.43)
Never smoker (2012-)	458 (0.69)	66361	1(ref)	1.07 (0.76, 1.52)	1.65 (1.26, 2.16)	2.30 (1.59, 3.31)
Smoker (2012-)	634 (0.75)	84958	1(ref)	1.03 (0.76, 1.38)	1.62 (1.29, 2.02)	2.52 (1.88, 3.39)
Seropositive	1697 (0.70)	242003	1(ref)	1.15 (0.96, 1.38)	1.42 (1.23, 1.65)	1.97 (1.64, 2.37)
Seronegative/unknown	544 (0.73)	74280	1(ref)	1.01 (0.73, 1.40)	1.65 (1.27, 2.14)	2.20 (1.59, 3.04)
CRP <5	738 (0.52)	143191	1(ref)	1.02 (0.80, 1.29)	1.37 (1.12, 1.67)	2.52 (1.83, 3.49)
CRP 5+	1401 (0.88)	159849	1(ref)	1.12 (0.91, 1.38)	1.37 (1.15, 1.64)	1.69 (1.38, 2.07)
No previous VTE	2089 (0.67)	313440	1(ref)	1.12 (0.95, 1.32)	1.49 (1.31, 1.70)	2.01 (1.71, 2.37)
Previous VTE	152 (5.35)	2843	1(ref)	1.02 (0.54, 1.90)	1.01 (0.58, 1.74)	1.79 (0.98, 3.26)
PE	833 (0.26)	316283	1(ref)	1.37 (1.05, 1.80)	1.83 (1.48, 2.27)	3.06 (2.36, 3.97)
DVT	1408 (0.45)	316283	1(ref)	1.01 (0.83, 1.23)	1.32 (1.13, 1.55)	1.59 (1.30, 1.95)
Males	664 (0.80)	82676	1(ref)	1.01 (0.75, 1.36)	1.51 (1.21, 1.88)	1.78 (1.32, 2.41)
Females	1577 (0.68)	233607	1(ref)	1.17 (0.97, 1.42)	1.47 (1.26, 1.72)	2.12 (1.75, 2.56)
Steroid use	1286 (1.00)	128745	1(ref)	1.04 (0.84, 1.30)	1.38 (1.16, 1.63)	1.71 (1.39, 2.09)
No steroid use	955 (0.51)	187538	1(ref)	1.15 (0.92, 1.43)	1.36 (1.13, 1.64)	1.87 (1.44, 2.44)

[a]Models adjusted for age, sex and calendar year of the visit year.

Table S6. Probability in percent (95% CI) of VTE event within 1 year by DAS28 category. Probabilities calculated from the unadjusted and adjusted log-binomial model.

DAS28 category	Unadjusted model	Adjusted model[a]									
		Male					Female				
		40	50	60	70	80	40	50	60	70	80
Remission	0.5 (0.5, 0.6)	0.2 (0.2, 0.3)	0.3 (0.2, 0.3)	0.4 (0.4, 0.5)	0.8 (0.6, 0.9)	1.1 (0.9, 1.3)	0.2 (0.1, 0.2)	0.3 (0.2, 0.3)	0.4 (0.4, 0.5)	0.7 (0.6, 0.8)	1.1 (0.9, 1.2)
Low	0.6 (0.5, 0.7)	0.2 (0.2, 0.3)	0.3 (0.2, 0.4)	0.5 (0.4, 0.6)	0.9 (0.7, 1.0)	1.3 (1.0, 1.5)	0.2 (0.2, 0.3)	0.3 (0.2, 0.4)	0.5 (0.4, 0.5)	0.8 (0.7, 0.9)	1.2 (1.0, 1.4)
Moderate	0.8 (0.7, 0.9)	0.3 (0.2, 0.4)	0.4 (0.3, 0.5)	0.6 (0.5, 0.8)	1.1 (0.9, 1.3)	1.6 (1.4, 1.9)	0.3 (0.2, 0.3)	0.4 (0.3, 0.4)	0.6 (0.5, 0.7)	1.1 (0.9, 1.2)	1.5 (1.3, 1.7)
High	1.1 (0.9, 1.2)	0.4 (0.3, 0.5)	0.5 (0.4, 0.7)	0.9 (0.7, 1.0)	1.5 (1.3, 1.8)	2.2 (1.8, 2.6)	0.4 (0.3, 0.5)	0.5 (0.4, 0.6)	0.8 (0.7, 1.0)	1.4 (1.2, 1.6)	2.1 (1.8, 2.4)

[a]Model adjusted for age and sex.

Table S7. Risk ratios for VTE of DAS28 activity from all sensitivity analyses (SA).

Model[a]	SA description	N model	Remission	Low	Moderate	High
Main exposure		263919	1 (ref)	1.12 (0.96, 1.31)	1.48 (1.30, 1.68)	2.03 (1.73, 2.38)
SA1	Main exposure definition + anticoagulant use *or* death from any cause	263919	1 (ref)	1.14 (0.95, 1.36)	1.45 (1.26, 1.67)	1.98 (1.66, 2.37)
SA2	No previous VTE ever	255875	1 (ref)	1.12 (0.94, 1.33)	1.50 (1.31, 1.72)	2.06 (1.74, 2.44)
SA3	Prevalent VTE defined as 6 instead of 12 months prior to rheumatologist visit	264755	1 (ref)	1.09 (0.94, 1.27)	1.45 (1.28, 1.64)	1.97 (1.69, 2.31)
SA4	Time period for VTE assessment 180 instead of 365 days after visit	263919	1 (ref)	1.30 (1.05, 1.61)	1.58 (1.33, 1.87)	2.02 (1.62, 2.52)
SA5	Excluding less common ICD codes for VTE	263919	1 (ref)	1.18 (0.99, 1.41)	1.48 (1.29, 1.71)	2.00 (1.68, 2.39)
SA6	No overlapping time windows per individual	144919	1 (ref)	1.15 (0.94, 1.42)	1.52 (1.29, 1.79)	2.05 (1.69, 2.49)
SA7	Including only one random visit per individual	36583	1 (ref)	1.29 (0.89, 1.88)	1.88 (1.41, 2.52)	2.59 (1.85, 3.61)
SA8	Including only first visit per individual	37062	1 (ref)	0.84 (0.48, 1.48)	1.40 (0.96, 2.05)	1.86 (1.27, 2.71)
SA9	Multiple imputation of main exposure	316200	1 (ref)	1.13 (0.96, 1.32)	1.46 (1.28, 1.65)	2.02 (1.72, 2.37)
	Multiple imputation of DVT	316200	1 (ref)	1.03 (0.85, 1.24)	1.31 (1.12, 1.54)	1.62 (1.33, 1.98)
	Multiple imputation of PE	316200	1 (ref)	1.35 (1.01, 1.81)	1.78 (1.42, 2.23)	2.98 (2.29, 3.87)

[a]Models adjusted for age, sex and calendar year of the visit year.

Table S8: Cumulative incidence of VTE and relative risks from main definition and sensitivity analyses (SA) in Swedish patients with RA during 1-year follow-up after rheumatologist visit vs. matched general population referents (1:5), followed from first visit registered after 2006 until 2018.

		No. of VTE events (Cumulative incidence, %)		Risk ratio (95% CI)[a]
	SA description	RA pop	Gen pop	
Main exp		2241 (0.71)	5301 (0.36)	1.88 (1.65-2.15)
SA1	Main exposure definition + anticoagulant use *or* death from any cause	1754 (0.55)	3985 (0.27)	1.92 (1.64, 2.23)
SA2	No previous VTE ever	1849 (0.60)	4420 (0.31)	2.02 (1.76, 2.32)
SA3	Prevalent VTE defined as 6 instead of 12 months prior to rheumatologist visit	2381 (0.75)	5561 (0.38)	1.89 (1.66, 2.16)
SA5	Excluding 1less common ICD codes for VTE	1793 (0.57)	4078 (0.28)	1.97 (1.69, 2.28)

[a]Risk ratios adjusted for age, sex and calendar year of the visit year.

Figure S1. Overview of study design. If a VTE event was registered within one year before the visit in question, that visit (but not the individual) was excluded.

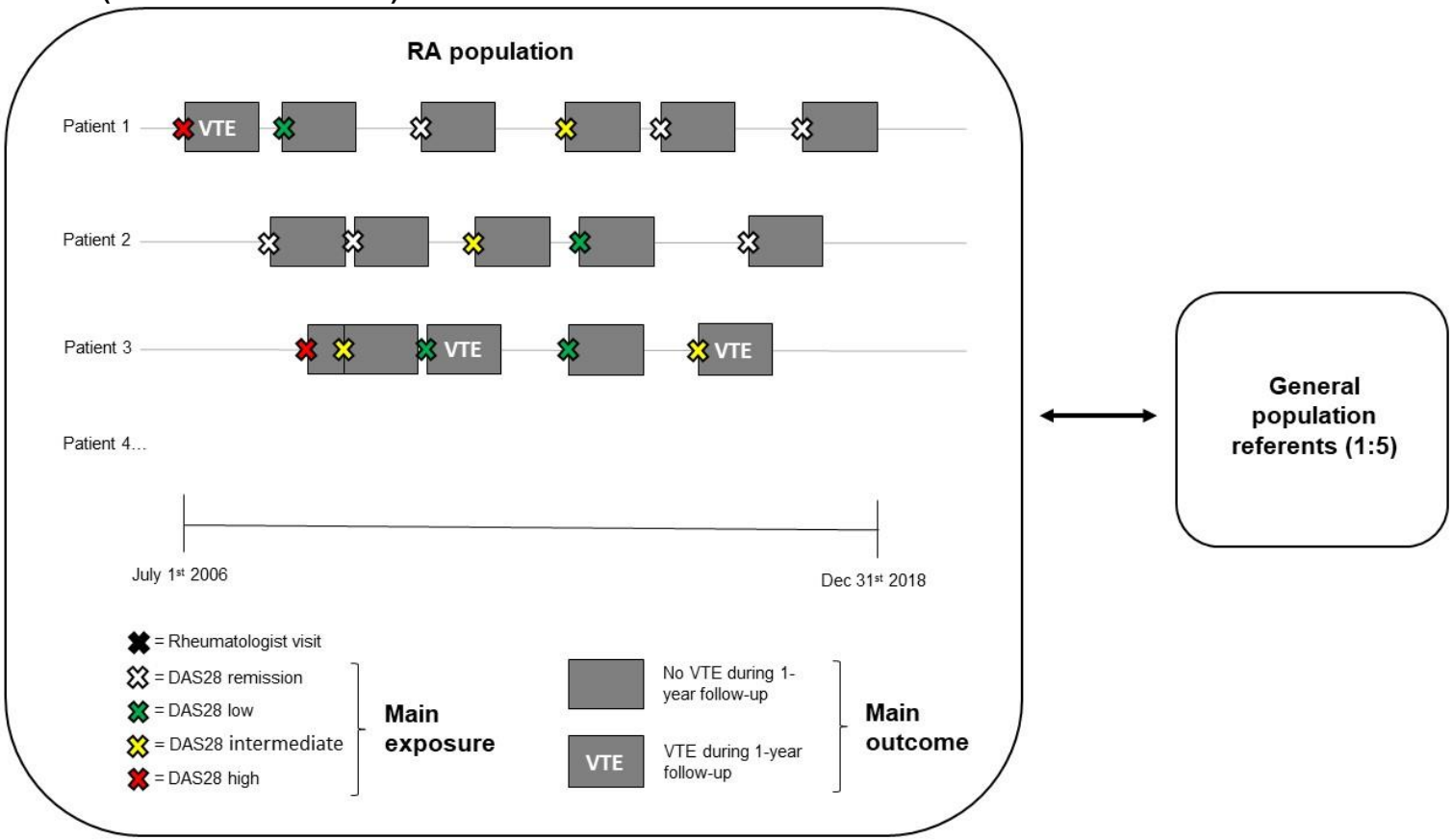
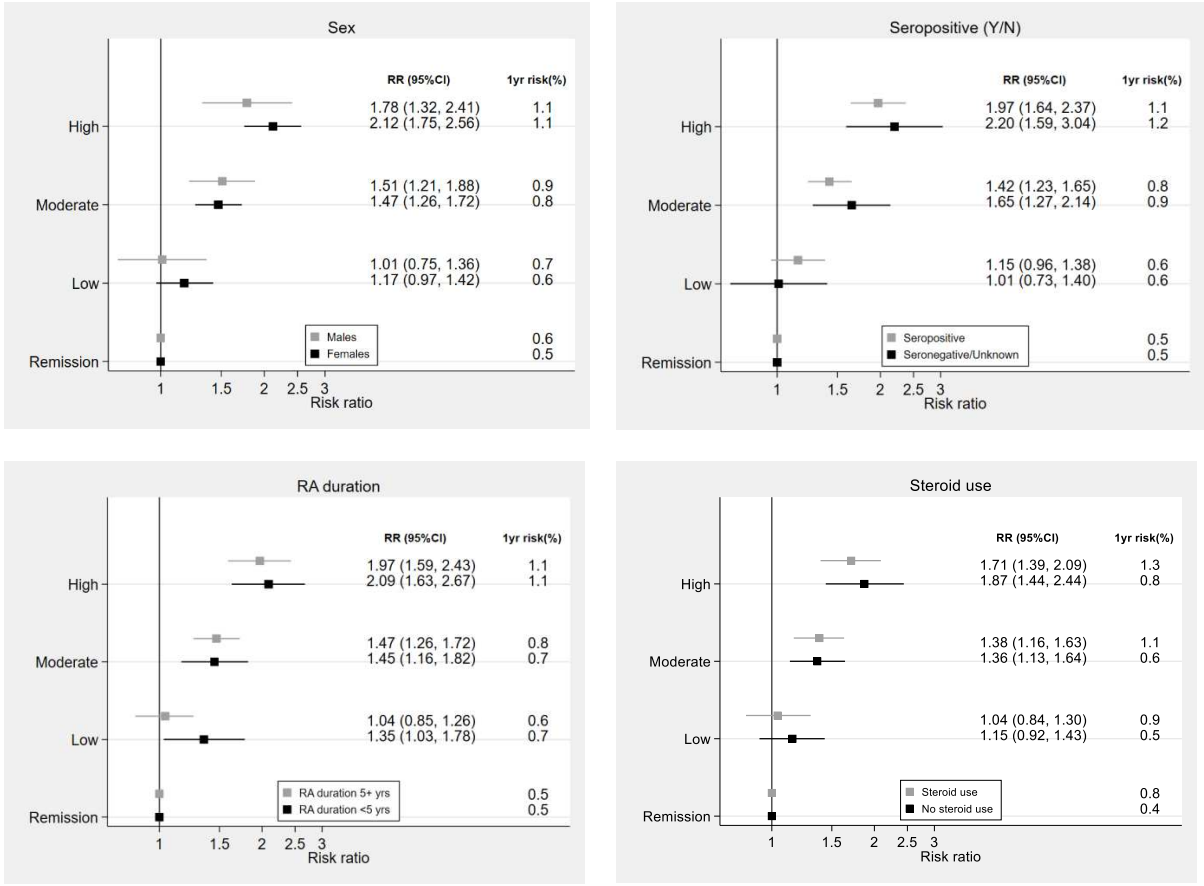
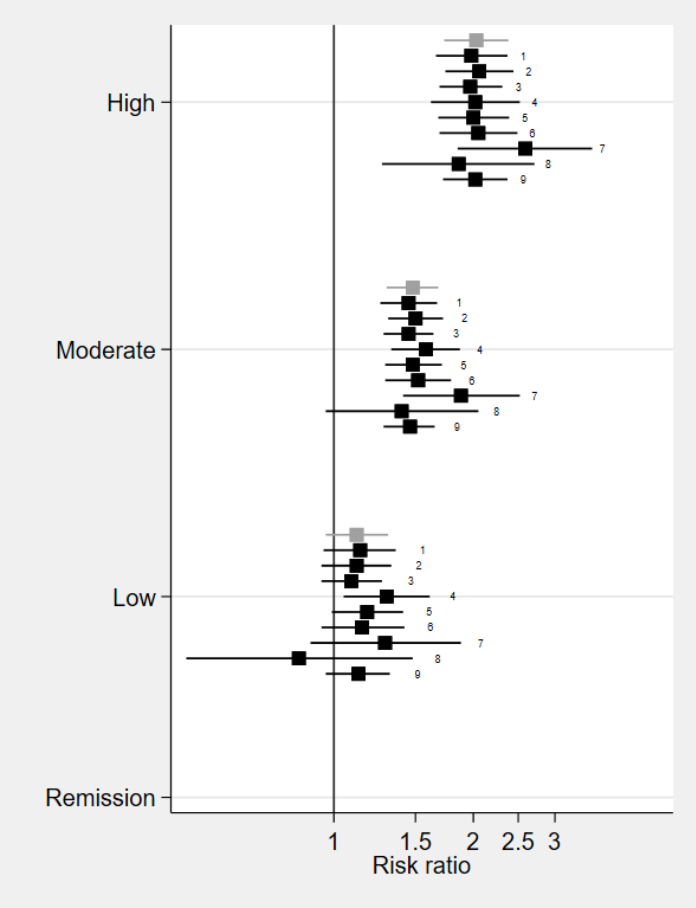


Figure S2. Risk ratios for the association between DAS28 and VTE stratified by sex, by seropositive (yes vs. no), by RA duration (≥5 vs.<5 years)) and by oral steroid use (yes vs. no) within one year among Swedish patients with RA. Absolute one-year risks are calculated from observed data.



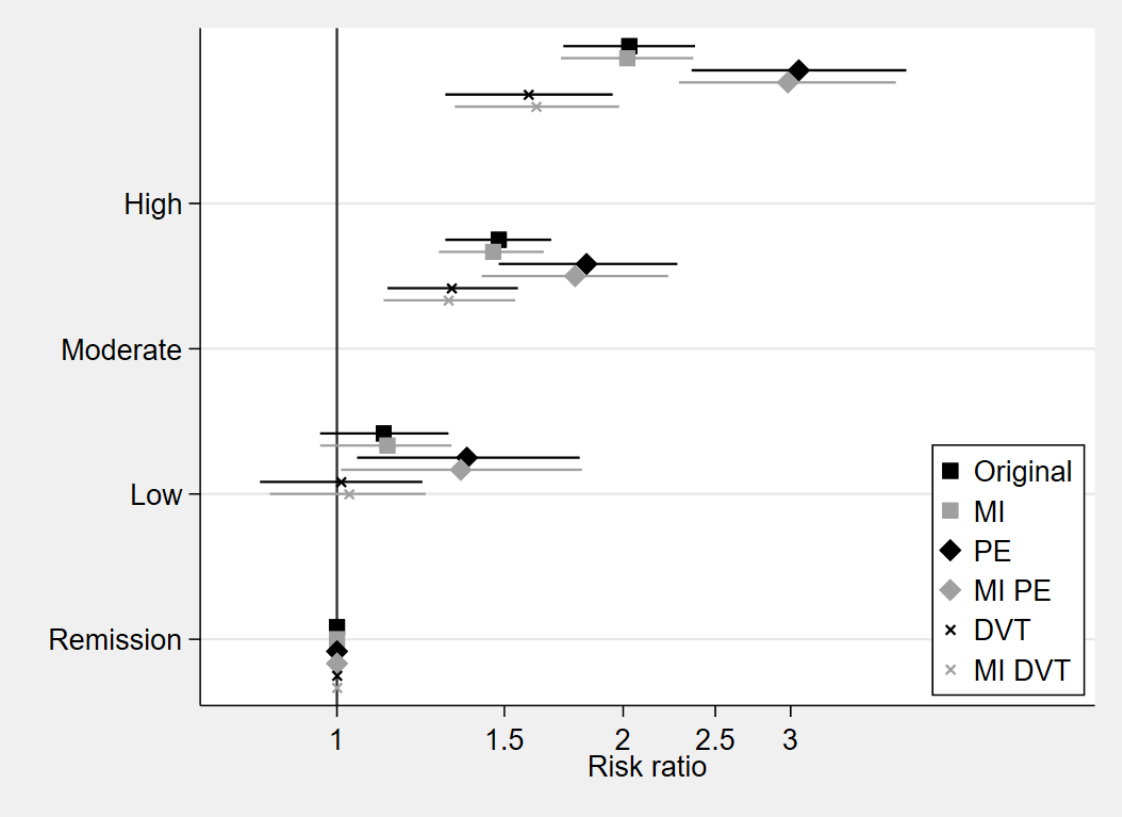
[a]Risk ratios adjusted for age, sex and calendar year of the visit year.

Figure S3. Risk ratios from all sensitivity analyses for the association between DAS28 category and risk of VTE. Grey estimates represent main exposure, for comparison.



[a]Risk ratios adjusted for age, sex and calendar year of the visit year.

Figure S4. Risk ratios for the association between DAS28 category and VTE, PE and DVT after multiple imputation. Black estimates represent corresponding risk ratios before multiple imputation for comparison.



[a]Risk ratios adjusted for age, sex and calendar year of the visit year.