Table S1: Univariate and multivariate Cox proportional hazard models comparing RF/ACPA high/low positive vs negative

	NOAR						Leiden EAC					
	Unadjusted		Age & sex adjusted		Multivariate*		Unadjusted		Age & sex adjusted		Multivariate*	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
RF/ACPA negative	ref		ref		ref		ref		ref		ref	
RF/ACPA low positive	0.85	0.61-1.18	0.81	0.59-1.10	0.80	0.57-1.13	2.38	1.67-3.39	1.89	1.13-2.70	1.92	1.30-2.80
RF/ACPA high positive	1.58	1.35-1.84	1.51	1.29-1.77	1.44	1.21-1.70	1.44	1.11-1.86	1.63	1.26-2.12	1.42	1.06-1.91
Female gender	-	-	0.70	0.60-0.81	0.77	0.65-0.91	-	-	0.73	0.57-0.92	0.72	0.54-0.94
Age at onset	-	-	1.10	1.09-1.11	1.11	1.10-1.12	-	-	1.10	1.09-1.11	1.10	1.09-1.12
Smoking *Never*	-	-	-	-	ref		-	-	-	-	ref	
Ever					0.98	0.81-1.18					1.00	0.71-1.42
Current					1.68	1.34-2.10					1.81	1.32-2.49
Inclusion year	-	-	-	-	0.96	0.94-0.98	-	-	-	-	0.95	0.93-1.00
Inflammatory marker	-	-	-	-	1.003	1.002-1.005	-	-	-	-	1.006	1.001-1.011

HR, hazard ratio; CI, confidence interval; RF, rheumatoid factor; ACPA, anti-citrullinated peptide antibodies; inflammatory marker = C-reactive protein in NOAR, = erythrocyte sedimentation rate in EAC
*adjusted for age at symptom onset, sex, baseline smoking status, year of inclusion in cohort & inflammatory marker

Table S2 Univariate and multivariate Cox proportional hazard models comparing RF and ACPA high/low positive vs negative

		NOAR						Leiden EAC					
		Unadjusted		Age & sex adjusted		Multivariate*		Unadjusted		Age & sex adjusted		Multivariate*	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
	RF negative	ref		ref		ref		ref		ref		ref	
	RF low positive	0.90	0.68-1.20	0.81	0.62-1.06	0.80	0.59-1.07	2.13	1.55-2.91	1.67	1.21-2.29	1.62	1.16-2.26
RF	**RF high positive**	1.67	1.41-1.97	1.54	1.29-1.83	1.49	1.23-1.80	1.75	1.33-2.31	1.92	1.46-2.53	1.63	1.19-2.24
	Female gender	-	-	0.71	0.62-0.83	0.78	0.66-0.92	-	-	0.75	0.59-0.95	0.73	0.56-0.97
	Age at onset	-	-	1.10	1.09-1.11	1.11	1.10-1.12	-	-	1.10	1.09-1.11	1.11	1.09-1.12
	Smoking *Never*	-	-	-	-	ref		-	-	-	-	ref	
	Previous					0.98	0.81-1.19					0.99	0.70-1.40
	Current					1.66	1.33-2.08					1.76	1.28-2.42
	Inclusion year	-	-	-	-	0.96	0.94-0.98	-	-	-	-	0.95	0.92-0.99
	Inflammatory marker	-	-	-	-	1.003	1.002-1.005	-	-	-	-	1.006	1.001-1.010
	ACPA negative	ref		ref		ref		ref		ref		ref	
	ACPA low positive	1.05	0.69-1.60	1.16	0.80-1.68	1.38	0.98-1.97	1.65	1.00-2.72	2.52	1.52-4.18	2.21	1.31-3.72
ACPA	**ACPA high positive**	1.49	1.24-1.79	1.41	1.15-1.72	1.38	1.11-1.71	1.17	0.90-1.52	1.45	1.11-1.90	1.25	0.93-1.69
	Female gender	-	-	0.71	0.60-0.84	0.81	0.67-0.98	-	-	0.71	0.55-0.91	0.73	0.55-0.97
	Age at onset	-	-	1.10	1.09-1.11	1.11	1.10-1.12	-	-	1.10	1.09-1.11	1.10	1.09-1.12
	Smoking *Never*	-	-	-	-	ref		-	-	-	-	ref	
	Previous					1.00	0.81-1.24					1.04	0.73-1.48
	Current					1.80	1.40-2.31					1.86	1.35-2.56
	Inclusion year	-	-	-	-	0.96	0.94-0.98	-	-	-	-	0.97	0.93-1.01
	Inflammatory marker	-	-	-	-	1.003	1.001-1.005	-	-	-	-	1.006	1.001-1.011

HR, hazard ratio; CI, confidence interval; RF, rheumatoid factor; ACPA, anti-citrullinated peptide antibodies; inflammatory marker = C-reactive protein in NOAR, = erythrocyte sedimentation rate in EAC
*adjusted for age at symptom onset, sex, baseline smoking status, year of inclusion in cohort & inflammatory marker

Table S3 Comparison of RF or ACPA levels in tertiles

	NOAR				Leiden EAC			
	Total EIA population		2010 ACR/EULAR positive cohort		Total EIA population		2010 ACR/EULAR positive cohort	
RF:	HR	95% CI	HR	95%CI	HR	95% CI	HR	95%CI
Unadjusted [†]								
RF second tertile	0.92	0.69-1.23	0.73	0.47-1.13	1.37	0.96-1.94	1.03	0.65-1.64
RF third tertile	1.39	0.19-1.63	1.21	1.00-1.47	1.91	1.47-2.49	1.40	1.00-1.96
Age & sex adjusted [†]								
RF second tertile	0.83	0.62-1.10	0.85	0.55-1.31	1.49	1.05-2.12	1.46	0.91-2.34
RF third tertile	1.25	1.07-1.47	1.14	0.95-1.38	1.86	1.43-2.42	1.90	1.35-2.67
Multivariate [†][*]								
RF second tertile	1.16	0.85-1.59	1.18	0.74-1.90	1.53	1.05-2.22	1.42	0.87-2.32
RF third tertile	1.29	1.09-1.52	1.25	1.03-1.53	1.66	1.23-2.23	1.68	1.17-2.43
ACPA:								
Unadjusted [§]								
ACPA second tertile	1.04	0.85-1.27	1.25	0.94-1.66	1.22	0.89-1.68	1.18	0.78-1.78
ACPA third tertile	1.29	1.06-1.57	1.31	1.03-1.68	1.26	0.91-1.73	0.82	0.56-1.19
Age & sex adjusted [§]								
ACPA second tertile	0.95	0.77-1.16	1.16	0.87-1.54	1.58	1.15-2.18	1.58	1.04-2.38
ACPA third tertile	1.18	0.97-1.44	1.26	0.99-1.61	1.77	1.28-2.46	1.59	1.08-2.34
Multivariate [§][*]								
ACPA second tertile	1.00	0.81-1.25	1.24	0.91-1.67	1.21	0.84-1.74	1.22	0.76-1.95
ACPA third tertile	1.19	0.97-1.46	1.27	0.98-1.63	1.30	0.90-1.87	1.26	0.81-1.95

HR, hazard ratio; CI, confidence interval; RF, rheumatoid factor; ACPA, anti-citrullinated protein antibodies; inflammatory marker = C-reactive protein in NOAR, = erythrocyte sedimentation rate in EAC

[†]RF first tertile was used as a reference group; [§]ACPA first tertile was used as a reference group

[*]adjusted for age at symptom onset, sex, baseline smoking status, year of inclusion in cohort & inflammatory marker

Table S4 Univariate and multivariate Cox proportional hazard models comparing RF&ACPA positive vs single positive & both antibodies negative

	NOAR						Leiden EAC					
	Unadjusted		Age & sex adjusted		Multivariate*		Unadjusted		Age & sex adjusted		Multivariate*	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Both antibodies negative	ref		ref		ref		ref		ref		ref	
RF positive	1.11	0.83-1.49	1.05	0.78-1.41	1.11	0.82-1.51	1.88	1.29-2.74	1.45	0.99-2.13	1.48	0.99-2.21
ACPA positive	1.27	0.94-1.73	1.40	1.03-1.91	1.35	0.98-1.88	0.63	0.32-1.23	0.96	0.48-1.90	1.05	0.53-2.09
Both antibodies positive	1.51	1.23-1.84	1.38	1.11-1.72	1.35	1.09-1.68	1.59	1.21-2.09	1.82	1.38-2.40	1.57	1.15-2.14
Female gender	-	-	0.72	0.61-0.85	0.81	0.67-0.98	-	-	0.72	0.57-0.93	0.74	0.55-0.98
Age at onset	-	-	1.11	1.10-1.12	1.11	1.10-1.12	-	-	1.10	1.09-1.11	1.10	1.09-1.11
Smoking *Never*	-	-	-	-	ref		-	-	-	-	ref	
Previous					1.00	0.81-1.24					1.00	0.70-1.42
Current					1.76	1.37-2.27					1.82	1.31-2.51
Inclusion year	-	-	-	-	0.96	0.94-0.98	-	-	-	-	0.96	0.93-1.00
Inflammatory marker	-	-	-	-	1.003	1.002-1.005	-	-	-	-	1.005	1.000-1.010

HR, hazard ratio; CI, confidence interval, inflammatory marker = C-reactive protein in NOAR, = erythrocyte sedimentation rate in EAC

*adjusted for age at symptom onset, sex, baseline smoking status, year of inclusion in cohort & inflammatory marker

Table S5 Sensitivity analysis with imputed data

	NOAR		
	Multivariate*		
	HR	**95% CI**	**FMI**
Both antibodies negative	ref	-	-
RF positive	1.12	0.83-1.52	0.153
ACPA positive	1.31	0.95-1.83	0.198
Both antibodies positive	1.38	1.13-1.68	0.101
Female gender	0.76	0.65-0.90	0.002
Age at onset	1.11	1.10-1.12	0.005
Smoking *Never*	ref	-	
Ever	0.97	0.80-1.18	0.001
Current	1.65	1.32-2.07	0.003
Inclusion year	0.96	0.94-0.98	0.002
Inflammatory marker	1.003	1.002-1.005	0.004

HR, hazard ratio; CI, confidence interval; FMI, fraction of missing information;
inflammatory marker = C-reactive protein in NOAR
*adjusted for age at symptom onset, sex, baseline smoking status, year of inclusion in cohort
& inflammatory marker