ONLINE SUPPLEMENTARY DATA

Supplementary Data 1. Statistical Analysis

Logistic regression models. The main independent variable of interest in this study was subject age, in years, at time of study visit for SERA FDRs. In our adjusted analyses we define age per 1 year increase as a continuous variable, and we had three individual dependent variables of interest, which were anti-CCP3.1, anti-CCP-IgA and anti-CCP-IgG. For this cross-sectional analysis, age and ACPA positivity were collected at the same study visit. Odds ratios (ORs) and 95% confidence intervals (CIs), testing associations between a 1 year increase in age with ACPA outcomes, were obtained from logistic regression. To determine the adjustment variables in the models, we first tested univariate relationships between each potential covariate with the dependent variables (Supplemental Table 1). The potential covariates tested include: gender, race/ethnicity, smoking status, shared epitope positivity, body mass index (BMI), education beyond high school and RF status. If the univariate relationship had a p-value of ≤0.25, then the covariate was considered in a full logistic regression model. Final models were determined on the basis of negative 2 log-likelihood (-2LL) tests.

ACPA positivity by age decade. As discussed in the Methods section, we compared the prevalence of ACPA positivity between age groups as a categorical variable by decade using Chi-square or Fisher's exact testing, with the youngest age decade (18-29 years) serving as the referent group. Of note, subjects 18-19 years were included in the 20-29 year old decade because no subjects <18 years were included in the study. Comparisons were made between the youngest 18-29 year old age decade (referent group) and each of the other age decades (i.e. 30-39, 40-49, 50-59, 60-69 and ≥70 years).

Supplementary Table 1. Univariate relationships between potential covariates and anti-CCP positivity in SERA FDRs		
Anti-CCP3.1		
	OR (95% CI)	**p-value**
Female	0.76 (0.40-1.43)	0.39
Non-Hispanic white	0.85 (0.45-1.61)	0.61
Ever smoker	1.02 (0.60-1.74)	0.92
≥1 shared epitope allele	1.21 (0.72-2.05)	0.47
BMI	1.03 (0.98-1.07)	0.23
Education, > high school	1.39 (0.76-2.54)	0.29
RF positive	2.62 (1.15-5.95)	0.02
Anti-CCP-IgA		
	OR (95% CI)	**p-value**
Female	0.66 (0.33-1.31)	0.23
Non-Hispanic white	1.26 (0.69-2.31)	0.45
Ever smoker	1.57 (0.92-2.70)	0.09
≥1 shared epitope allele	0.78 (0.46-1.34)	0.37
BMI	1.03 (0.98-1.07)	0.18
Education, > high school	1.69 (0.93-3.08)	0.08
RF positive	1.53 (0.57-4.06)	0.39
Anti-CCP-IgG		
	OR (95% CI)	**p-value**
Female	0.93 (0.41-2.10)	0.86
Non-Hispanic white	1.66 (0.79-3.51)	0.18
Ever smoker	0.55 (0.25-1.21)	0.13
≥1 shared epitope allele	1.11 (0.55-2.24)	0.77
BMI	0.98 (0.93-1.05)	0.65
Education, > high school	1.69 (0.79-3.64)	0.17
RF positive	3.87 (1.50-9.99)	0.01

Supplementary Table 2. Prevalence of ACPA positivity by age group in SERA FDRs

Age group	Number of subjects	CCP3.1(+), N (%)	CCP-IgA(+), N (%)	CCP-IgG(+), N (%)	CCP-IgA(+) and CCP-IgG(+), N (%)
18-29 years	115	3 (3)	1 (1)	5 (4)	0 (0)
30-39 years	138	9 (7)	7 (5)	5 (4)	3 (2)
40-49 years	154	9 (6)	10 (7)*	8 (5)	5 (3)
50-59 years	131	16 (12)**	15 (12)**	8 (6)	2 (2)
60-69 years	82	15 (18)**	15 (18)**	4 (5)	2 (2)
≥70 years	58	10 (17)**	10 (17)**	3 (5)	1 (2)
Total	678	62 (9)	58 (9)	33 (5)	13 (2)

*p<0.05 and **p<0.01, calculated in each column using Chi square/Fisher's exact testing to compare anti-CCP positivity in each age group compared to the referent group (18-29 years old).

Supplementary Table 3. Prevalence of ACPA positivity by age group in SERA FDRs

Age group	Number of subjects	CCP3.1(+), N (%)	CCP-IgA(+), N (%)	CCP-IgG(+), N (%)	CCP-IgA(+) and CCP-IgG(+), N (%)
18-39 years	253	12 (5)	8 (3)	10 (4)	3 (1)
40-49 years	154	9 (6)	10 (7)*	8 (5)	5 (3)
50-59 years	131	16 (12)**	15 (12)**	8 (6)	2 (2)
60-69 years	82	15 (18)**	15 (18)**	4 (5)	2 (2)
≥70 years	58	10 (17)**	10 (17)**	3 (5)	1 (2)

*p≤0.05 and **p≤0.01, calculated in each column using Chi square/Fisher's exact testing to compare anti-CCP positivity in each age group compared to the referent group (18-39 years old).