

Elevated anti-citrullinated protein antibodies prior to rheumatoid arthritis diagnosis and risks for chronic obstructive pulmonary disease or asthma

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Supplemental Material

S1. Supplemental Table 1. Contingency table comparing results from the research ACPA and CCP2 assays among the pre-RA women who had both tests performed in blood banked prior to clinical RA diagnosis (n=167).

S2. Supplemental Table 2. Hazard ratios for incident COPD after blood draw date by pre-RA ACPA serostatus in the Nurses' Health Studies (n=283).

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Supplemental Table 1. Contingency table comparing results from the research ACPA and CCP2 assays among the pre-RA women who had both tests performed in blood banked prior to clinical RA diagnosis (n=167).

	CCP2+	CCP2-	TOTAL
Research ACPA+	36	8	44
Research ACPA-	3	120	123
TOTAL	39	128	167

Kappa statistic=0.82

Concordance=93%

ACPA, anti-citrullinated protein antibody; CCP, 2nd generation cyclic citrullinate peptide.

Supplemental Table 2. Hazard ratios for incident COPD after blood draw date by pre-RA ACPA serostatus in the Nurses' Health Studies (n=283).

	Incident COPD cases/person-years	Unadjusted HR (95%CI)	Multivariable** HR (95%CI)
Pre-RA ACPA+ (n=59)	13/1,030	2.22 (1.13, 4.39)	2.22 (1.12, 4.41)
Pre-RA ACPA- (n=224)	23/4,117	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA+ (n=59)	13/1,030	4.56 (1.03, 21.21)	4.03 (0.90, 18.10)
Pre-RA ACPA- <5 years to diagnosis (n=40)	2/731	1.00 (Ref)	1.00 (Ref)

**Adjusted for smoking (continuous pack-years) and body mass index (continuous, kg/m²).

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; RA, rheumatoid arthritis.

Supplemental Table 3. Hazard ratios for incident asthma after blood draw date by pre-RA ACPA serostatus in the Nurses' Health Studies (n=252).

	Incident COPD cases/person-years	Unadjusted HR (95%CI)	Multivariable** HR (95%CI)
Pre-RA ACPA+ (n=49)	8/890	1.08 (0.50, 2.35)	1.14 (0.52, 2.49)
Pre-RA ACPA- (n=203)	31/3,777	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA+ (n=49)	8/890	2.10 (0.56, 7.93)	2.53 (0.66, 9.72)
Pre-RA ACPA- <5 years to diagnosis (n=36)	3/682	1.00 (Ref)	1.00 (Ref)

**Adjusted for smoking (continuous pack-years) and body mass index (continuous, kg/m²).

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; RA, rheumatoid arthritis.

Supplemental Table 4. Hazard ratios for incident COPD after blood draw date, comparing women who developed RA to their matched controls in the Nurses' Health Studies, among ever smokers (n=557).

	Incident COPD cases/person-years	HR (95%CI) controlling for matching factors*	Multivariable** HR (95%CI)
Pre-RA ACPA+ (n=35)	10/592	2.51 (1.10, 5.73)	2.77 (1.11, 6.95)
Matched controls (n=102)	13/1,947	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA- (n=119)	17/2,172	1.15 (0.65, 2.02)	1.06 (0.59, 1.90)
Matched controls (n=301)	40/5,865	1.00 (Ref)	1.00 (Ref)
All pre-RA (n= 154)	27/2,764	1.44 (0.91, 2.29)	1.34 (0.83, 2.14)
Matched controls (n=403)	53/7,811	1.00 (Ref)	1.00 (Ref)

*Each woman with RA was matched to 3 controls by age, time from blood draw to index date, cohort, calendar year, fasting status/time of day at blood draw, menopausal status, and postmenopausal hormone use.

**Additionally adjusted for body mass index (continuous, kg/m²), and median household income (quartile).

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; RA, rheumatoid arthritis.

Supplemental Table 5. Hazard ratios for incident asthma after blood draw date, comparing women who developed RA to their matched controls in the Nurses' Health Studies, among never smokers (n=483).

	Incident asthma cases/person-years	HR (95%CI) controlling for matching factors*	Multivariable** HR (95%CI)
Pre-RA ACPA+ (n=19)	1/369	0.77 (0.09, 6.92)	0.62 (0.07, 5.69)
Matched controls (n=56)	4/1,110	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA- (n=97)	16/1,806	2.12 (1.13, 3.97)	2.18 (1.16, 4.09)
Matched controls (n=311)	25/6,041	1.00 (Ref)	1.00 (Ref)
All pre-RA (n=116)	17/2,175	1.92 (1.05, 3.49)	1.97 (1.08, 3.60)
Matched controls (n=367)	29/7,151	1.00 (Ref)	1.00 (Ref)

*Each woman with RA was matched to 3 controls by age, time from blood draw to index date, cohort, calendar year, fasting status/time of day at blood draw, menopausal status, and postmenopausal hormone use.

**Additionally adjusted for body mass index (continuous, kg/m²), and median household income (quartile).

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; RA, rheumatoid arthritis.

Supplemental Table 6. Hazard ratios for incident asthma after blood draw date, comparing women who developed RA to their matched controls in the Nurses' Health Studies, among ever smokers (n=468).

	Incident asthma cases/person-years	HR (95%CI) controlling for matching factors*	Multivariable** HR (95%CI)
Pre-RA ACPA+ (n=30)	7/521	2.04 (0.78, 5.37)	2.21 (0.81, 5.98)
Matched controls (n=80)	10/1,549	1.00 (Ref)	1.00 (Ref)
Pre-RA ACPA- (n=106)	15/1,971	1.40 (0.74, 2.63)	1.20 (0.62, 2.29)
Matched controls (n=252)	27/4,998	1.00 (Ref)	1.00 (Ref)
All pre-RA (n=136)	22/2,492	1.55 (0.91, 2.62)	1.43 (0.84, 2.44)
Matched controls (n=332)	37/6,547	1.00 (Ref)	1.00 (Ref)

*Each woman with RA was matched to 3 controls by age, time from blood draw to index date, cohort, calendar year, fasting status/time of day at blood draw, menopausal status, and postmenopausal hormone use.

**Additionally adjusted for smoking (continuous pack-years), body mass index (continuous, kg/m²) and median household income (quartile).

ACPA, anti-citrullinated protein antibodies; CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; RA, rheumatoid arthritis.