

Supplemental Figures

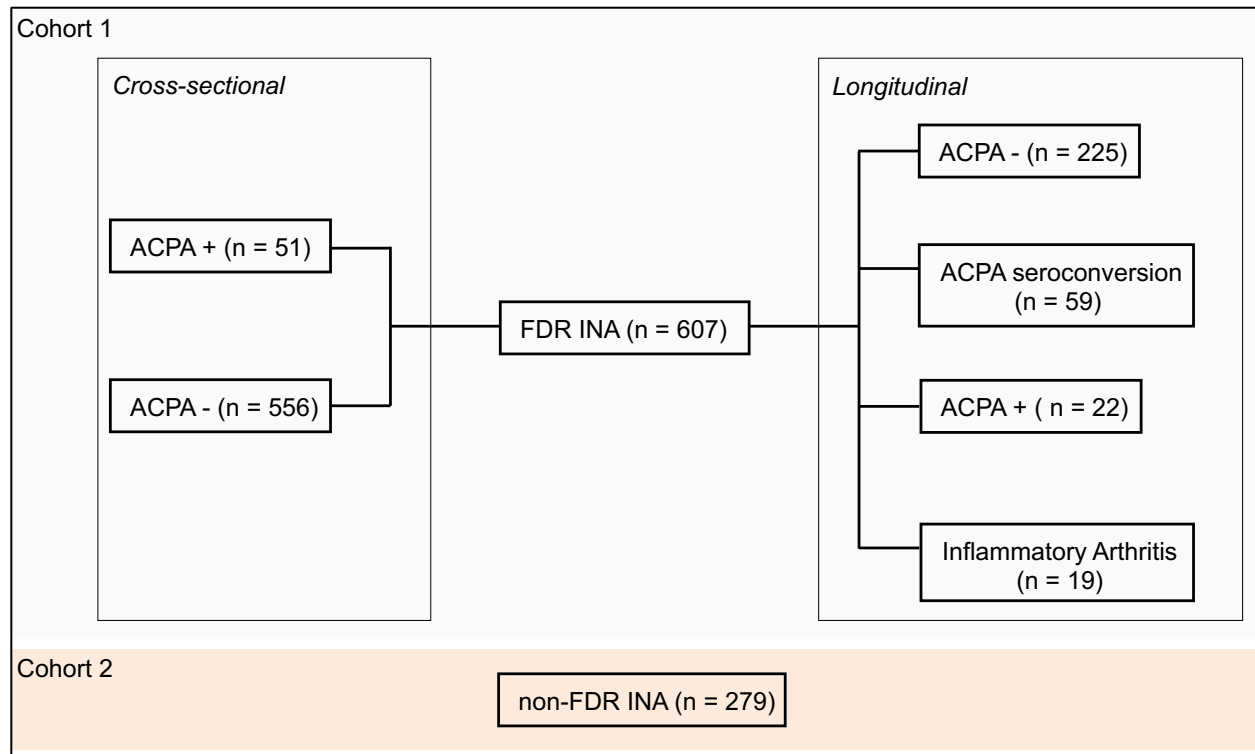


Figure S1: Overview of cohorts used in the study. Cohort 1 is made up of 607 FDR from RA probands who were recruited into a longitudinal study. The cross-sectional analysis focussed on ACPA seropositivity while the longitudinal analysis was restricted to individuals with at least one follow-up visit with serology. Cohort 2 is derived from an oral health study. All participants included in this study were Indigenous North American by self-report.

Patient Arthritis Assessment Questionnaire (PAQ)

The questions below concern your daily activity at this time. Please try to answer each question, even if you do not feel it is related to you or any condition you may have. **There is no right or wrong answer.**

1. Please check (✓) the one best answer, about your abilities at this time.

At this moment, are you able to:	without ANY difficulty	with SOME difficulty	with MUCH difficulty	UNABLE to do
a. Dress yourself, including tying shoelaces and doing buttons?	0	1	2	3
b. Get in and out of bed?	0	1	2	3
c. Lift a full cup or glass to your mouth?	0	1	2	3
d. Walk outdoors on flat ground?	0	1	2	3
e. Wash and dry your entire body?	0	1	2	3
f. Bend down to pick up clothing from the floor?	0	1	2	3
g. Turn regular faucets on and off?	0	1	2	3
h. Get in and out of a car, bus, train or airplane?	0	1	2	3

2. When you get up in the morning, do you feel stiff? Yes No
 If you answered Yes, please enter how many minutes or hours (approximately) it will take until you are as good as you will be, for that day? Hours: _____ Minutes: _____

3. Which of the following best describes you today? (Please check [✓] only one.)
 1: I can do everything I want to do.
 2: I can do most of the things I want to do, but have some limitations.
 3: I can do some, but not all, of the things I want to do, and I have many limitations.
 4: I can hardly do any of the things I want to do.

4. How do you feel today compared to one month ago? (Please check [✓] only one.)
 1: Much better today than one month ago.
 2: Better today than one month ago.
 3: Same today as one month ago.
 4: Worse today than one month ago.
 5: Much worse today than one month ago.

5. How satisfied are you with your ability to do your usual activities? (Please check [✓] only one.)
 1: Very Satisfied.
 2: Somewhat Satisfied.
 3: Somewhat Dissatisfied.
 4: Very Dissatisfied.

6. How much pain have you had, because of your condition, IN THE PAST WEEK?
 Place a vertical mark [|], on the line below, to indicate how severe your pain has been this past week.
 NO PAIN |-----| PAIN AS BAD AS IT COULD BE

7. Considering all the ways your arthritis affects you, place a vertical mark [|], on the scale, for how well you are doing.
 DISEASE NOT ACTIVE |-----| SEVERE ACTIVITY

8. How much of a problem has UNUSUAL fatigue or tiredness been for you OVER THE PAST WEEK?
 Place a vertical mark [|], on the line below, indicating how much of a problem fatigue has been this past week.
 FATIGUE IS NO PROBLEM |-----| FATIGUE IS A MAJOR PROBLEM

Section E – Arthritis Symptoms

We would like to know if you have ever been told you had arthritis, or if you had symptoms that might be due to arthritis.

- Have you ever been diagnosed with rheumatoid arthritis or any other type of arthritis? YES NO
 - If you know your type of arthritis, please write it here. _____
 - When did symptoms of your arthritis first start? _____ / _____
mm yy
 - Do you often have pain in the joints of your hands or fingers, now or in the past? YES NO
 - Do you often have pain in any other joints, now or in the past? YES NO
 - Do you often have swelling of the joints of your hands or fingers, now or in the past? YES NO
 - Do you often have swelling in any other joints, now or in the past? YES NO
 - Do your hands feel stiff in the morning? YES NO
 - Do any of your other joints feel stiff in the morning? YES NO
- Medications:
 1. _____
 2. _____
 3. _____
 4. _____
 5. _____
10. If you answered YES to any of the questions above, then what medications, if any, have you taken for your joint symptoms? (E.g., Tylenol, aspirin, Naproxen, gold, Methotrexate, etc.)

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Figure S2: Patient surveys used to capture patient reported symptoms and functional disability.

Any Difficulty, %	Males			Females		
	non-FDR (n = 133)	FDR (n = 242)	p-value	non-FDR (n = 136)	FDR (n = 365)	p-value
Dressing	3.0	13.2	0.002	4.1	15.1	0.0
Getting out of bed	9.0	20.2	0.008	11.0	33.2	< 0.001
Lifting a glass	3.0	8.7	0.06	4.1	8.8	0.1
Walk on flat ground	6.0	18.6	0.001	7.5	20.0	0.002
Wash and dry body	3.0	14.5	0.001	4.8	12.1	0.02
Bend down	12.8	25.2	0.007	13.7	34.2	< 0.001
Turn Faucet On	3.0	7.9	0.1	4.8	15.3	0.003
Get Out of car	8.3	16.9	0.03	11.0	23.3	0.003

Table S1: Functional disability comparing FDR and non-FDR split by sex. Differences in proportion calculated with chi-square test. FDR: First degree relative.

	FDR	
	(n = 607)	
	ACPA – (n = 556)	ACPA + (n = 51)
Female, %	59.7	64.7
Age	35.0 (21.2)	37.2 (22.1)
Rural*, %	50.1	70.5
Smoker, %	85.6%	88.2%
Pack Years	3.5 (11.1)	4.0 (12.8)
BMI	28.7 (8.8)	27.8 (12.5)

Table S2: Inception demographics of FDR split by ACPA seropositive status. Continuous variables are reported as median (IQR), while proportional variables are reported as %. BMI: Body mass index. ACPA: anti-citrullinated protein antibodies. FDR: First degree relative.

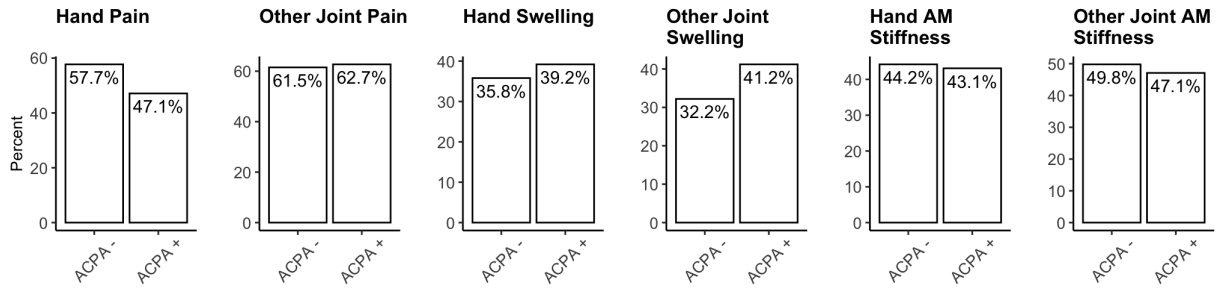


Figure S3: Joint differences between ACPA positive FDR and ACPA negative FDR. Joint symptom survey affirmative responses by self-report. Questions focused primarily on hand, or non-hand (Other) symptomatology.

Any Difficulty, %	FDR ACPA – (n = 556)	FDR ACPA + (n = 51)	p-value
Dressing	14.4	19.6	0.48
Getting out of bed	26.8	39.2	0.17
Lifting a glass	8.1	19.6	0.052
Walk on flat ground	18.0	37.3	0.014
Wash and dry body	12.9	21.6	0.21
Bend down	30.2	37.3	0.49
Turn Faucet On	11.9	15.7	0.57
Get Out of car	20.0	33.3	0.1

Table S3: Functional disability comparing ACPA + FDR and ACPA - FDR. Differences in proportion calculated with chi-square test. ACPA: anti-citrullinated protein antibodies. FDR: First degree relative.

	OR	95% CI
Sex (F)	1.26	0.69 to 2.29
Age	1.01	0.98 to 1.03
Rural	1.36	0.72 to 2.56
HAQ	2.79	1.56 to 5.00

Table S4: Results of a logistic regression model identifying independent risk factors associated with ACPA seropositivity in FDR. ACPA: anti-citrullinated protein antibodies. FDR: First degree relative. OR: Odds ratio, CI: Confidence Interval.

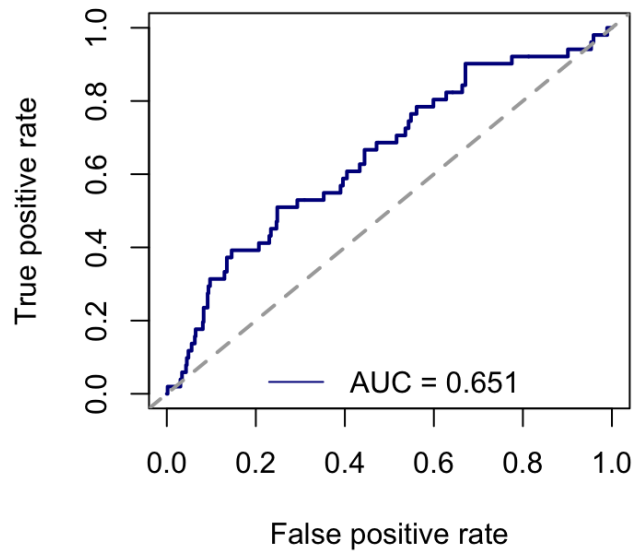


Figure S4: AUC for a logistic regression model that includes age, sex, community and difficulty walking on flat ground.

Tender Joint, %	No Difficulty Walking	Difficulty Walking	p-value
Foot	8.5	19.5	0.02
Ankle	4.2	16.1	0.009
Knee	16.1	33.1	0.009
Hand	22.9	41.5	0.009
Wrist	8.5	20.3	0.02
Elbow	8.5	20.3	0.02
Shoulder	13.6	32.2	0.008

Table S5: Tender joint frequency comparing FDR with difficulty walking and those without difficulty walking. Differences in proportion calculated with chi-square test. FDR: First degree relative.

	Longitudinal Outcome		
Any Difficulty, %	ACPA negative (n = 284)	ACPA positive (n = 22)	ACPA+ RA (n = 19)
Dressing, %	12.7	13.6	10.5
Getting out of bed	26.1	22.7	31.6
Lifting a glass	6.3	13.6	15.8
Walk on flat ground	15.5	36.4	26.3
Wash and dry body	11.3	13.6	15.8
Bend down	26.1	22.7	26.3
Turn Faucet On	12.7	13.6	21.1
Get Out of car	17.6	27.3	26.3

Table S6: Functional impairment comparing longitudinal outcomes in FDR. Differences between groups calculated by Wilcoxon sum-rank test. Difficulty walking p-value = 0.02. ACPA: anti-citrullinated protein antibodies. FDR: First degree relative.

Affirmative Response, %	Longitudinal Outcome		
	ACPA negative (n = 284)	Persistent ACPA positive (n = 22)	ACPA positive RA (n = 19)
Hand Pain, %	52.1	59.1	52.6
Other Joint Pain, %	57.0	63.6	63.2
Hand Swelling, %	35.9	31.8	31.6
Other Joint Swelling, %	28.5	40.9	42.1
Hand AM Stiffness, %	39.4	59.1	42.1
Other Joint AM stiffness, %	41.9	59.1	47.4

Table S7 Joint symptoms comparing longitudinal outcomes in FDR. Differences between groups calculated by Wilcoxon sum-rank test. ACPA: anti-citrullinated protein antibodies. FDR: First degree relative.