THE LANCET
Rheumatology

Supplementary appendix

Supplementary material

Supplementary table 1. Risk of severe COVID-19 and secondary outcomes among patients with rheumatoid arthritis stratified by sex.

	Female		Male	
	Patients with RA n=421	**Comparators** n=2081	**Patients with RA** N=161	**Comparators** n=794
Severe COVID-19, n (%)	93 (22)	248 (12)	33 (21)	115 (14)
Follow-up time, person-days	29,788	165,358	11,623	61,192
Rate, per 1,000 days (95% CI)	3·12 (2·49, 3·76)	1·50 (1·31, 1·69)	2·84 (1·87, 3·81)	1·88 (1·54, 2·22)
Unadjusted, HR (95% CI)	2·03 (1·65, 2·50)	Ref.	1·46 (1·07, 1·98)	Ref.
Adjusted main model, HR (95% CI)	2·03 (1·62, 2·55)	Ref.	1·23 (0·88, 1·74)	Ref.
Adjusted mediators model, HR (95% CI)	1·92 (1·50, 2·46)	Ref.	1·12 (0·78, 1·59)	Ref.
Hospitalization, n (%)	90 (21)	241 (12)	31 (19)	114 (14)
Follow-up time, person-days	29,924	165,942	11,746	61,287
Rate, per 1,000 days (95% CI)	3·01 (2·39, 3·63)	1.45 (1.27, 1.64)	2·64 (1·71, 3·57)	1·86 (1·52, 2·20)
Unadjusted, HR (95% CI)	1·89 (1·55, 2·30)	Ref.	1·30 (0·95, 1·76)	Ref.
Adjusted main model, HR (95% CI)	1·84 (1·49, 2·26)	Ref.	1·11 (0·79, 1·55)	Ref.
Adjusted mediators model, HR (95% CI)	1·81 (1·46, 2·25)	Ref.	1·01 (0·71, 1·43)	Ref.
Death, n (%)	18 (4)	39 (2)	8 (5)	20 (3)
Follow-up time, person-days	36,791	184,491	13,980	70,132
Rate, per 1,000 days (95% CI)	0·49 (0·26, 0·72)	0.21 (0.15, 0.29)	0·57 (0·18, 0·97)	0·29 (0·16, 0·41)
Unadjusted, HR (95% CI)	2·48 (1·51, 4·08)	Ref.	1·99 (0·96, 4·13)	Ref.
Adjusted main model, HR (95% CI)	2·38 (1·36, 4·16)	Ref.	1.04 (0.47, 2.33)	Ref.
Adjusted mediators model, HR (95% CI)	2·25 (1·24, 4·10)	Ref.	0·69 (0·28, 1·73)	Ref.
Mechanical ventilation, n (%)	12 (3)	37 (2)	5 (3)	18 (2)
Follow-up time, person-days	36,882	184,116	14,064	69,974
Rate per 1,000 days, (95% CI)	0·33 (0·14, 0·51)	0.20 (0.14, 0.27)	0·36 (0·04, 0·67)	0·26 (0·14, 0·38)
Unadjusted, HR (95% CI)	1·60 (0·90, 2·83)	Ref.	1·37 (0·58, 3·27)	Ref.
Adjusted main model, HR (95% CI)	1·90 (0·95, 3·80)	Ref.	0·94 (0·37, 2·40)	Ref.
Adjusted mediators model, HR (95% CI)	1·70 (0·76, 3·79)	Ref.	0·50 (0·13, 1·85)	Ref.

CI: confidence interval; HR: hazard ratio.

Adjusted main model for age, sex, race, and smoking. Adjusted mediators model for age, sex, race, smoking, BMI, and Charlson comorbidity index (dichotomized as <2 or ≥ 2).

Supplementary table 2. Risk of severe COVID-19 and secondary outcomes among patients with rheumatoid arthritis who contracted COVID-19 before vaccines were available.

	Patients with RA n=366	Comparators n=1807
Severe COVID-19, n (%)	77 (21)	233 (13)
Follow-up time, person-days	26,290	141,876
Rate, per 1,000 days (95% CI)	2·93 (2·27, 3·58)	1·64 (1·43, 1·85)
Unadjusted, HR (95% CI)	1·72 (1·39, 2·13)	Ref.
Adjusted main model, HR (95% CI)	1·64 (1·30, 2·07)	Ref.
Adjusted mediators model, HR (95% CI)	1·49 (1·16, 1·91)	Ref.
Hospitalization, n (%)	73 (20)	228 (13)
Follow-up time, person-days	26,486	142,356
Rate, per 1,000 days (95% CI)	2·76 (2·12, 3·39)	1·60 (1·39, 1·81)
Unadjusted, HR (95% CI)	1·55 (1·26, 1·92)	Ref.
Adjusted main model, HR (95% CI)	1·49 (1·19, 1·87)	Ref.
Adjusted mediators model, HR (95% CI)	1·36 (1·07, 1·73)	Ref.
Death, n (%)	18 (5)	42 (2)
Follow-up time, person-days	31,793	159,512
Rate, per 1,000 days (95% CI)	0·57 (0·30, 0·83)	0·26 (0·18, 0·34)
Unadjusted, HR (95% CI)	2·20 (1·35, 3·60)	Ref.
Adjusted main model, HR (95% CI)	1·74 (1·01, 2·98)	Ref.
Adjusted mediators model, HR (95% CI)	1·53 (0·85, 2·76)	Ref.
Mechanical ventilation, n (%)	13 (4)	39 (2)
Follow-up time, person-days	31,849	159,346
Rate per 1,000 days, (95% CI)	0·41 (0·19, 0·63)	0·25 (0·17, 0·32)
Unadjusted, HR (95% CI)	1·64 (0·95, 2·82)	Ref.
Adjusted main model, HR (95% CI)	1·75 (0·93, 3·28)	Ref.
Adjusted mediators model, HR (95% CI)	1·44 (0·74, 2·80)	Ref.

CI: confidence interval; HR: hazard ratio.

Adjusted main model for age, sex, race, and smoking. Adjusted mediators model for age, sex, race, smoking, BMI, and Charlson comorbidity index (dichotomized as <2 or ≥ 2).

Supplementary table 3. Risk of severe COVID-19 and secondary outcomes by rheumatoid arthritis (RA) phenotype in comparison to their matched general population.

	RA-ILD n=50	Comparators n=249	Seropositive n=388	Comparators n=1915	Erosive disease n=159	Comparators n=790
Severe COVID-19, n (%)	25 (50)	46 (18)	84 (22)	224 (12)	41 (26)	120 (15)
Follow-up time, person-days	2,285	18,292	27,509	152,483	10,687	60,571
Rate, per 1,000 days (95% CI)	10·90 (6·70, 15·20)	2·50 (1·80, 3·20)	3·10 (2·40, 3·70)	1·50 (1·30, 1·70)	3·80 (2·70, 5·00)	2·00 (1·60, 2·30)
Unadjusted HR (95% CI)	2·89 (2·03, 4·11)	Ref.	2·00 (1·62, 2·47)	Ref.	2·05 (1·54, 2·73)	Ref.
Adjusted main model HR (95% CI)	2·50 (1·66, 3·77)	Ref.	1·97 (1·58, 2·46)	Ref.	1·93 (1·41, 2·63)	Ref.
Adjusted mediators model HR (95% CI)	2·52 (1·52, 4·17)	Ref.	1·89 (1·49, 2·40)	Ref.	2·03 (1·46, 2·84)	Ref.
Hospitalization, n (%)	24 (48)	45 (18)	82 (21)	221 (12)	40 (25)	115 (15)
Follow-up time, person-days	2,368	18,388	27,656	152,739	10,770	60,908
Rate, per 1,000 days, (95% CI)	10·10 (6·10, 14·20)	2·40 (1·70, 3·20)	3·00 (2·30, 3·60)	1·40 (1·30, 1·60)	3·70 (2·60, 4·90)	1·90 (1·50, 2·20)
Unadjusted HR (95% CI)	2·79 (1·97, 3·95)	Ref.	1·85 (1·52, 2·25)	Ref.	1·86 (1·41, 2·44)	Ref.
Adjusted main model HR (95% CI)	2·41 (1·60, 3·62)	Ref.	1·84 (1·49, 2·26)	Ref.	1·77 (1·32, 2·37)	Ref.
Adjusted mediators model HR (95% CI)	2·45 (1·49, 4·02)	Ref.	1·81 (1·46, 2·25)	Ref.	1·89 (1·40, 2·55)	Ref.
Death, n (%)	9 (18)	10 (4)	15 (4)	35 (2)	8 (5)	21 (3)
Follow-up time, person-days	3,877	21,696	33,916	169,998	13,747	69,694
Rate, per 1,000 days, (95% CI)	2·30 (0·80, 3·80)	0·50 (0·20, 0·70)	0·40 (0·20, 0·70)	0·20 (0·10, 0·30)	0·60 (0·20, 1·00)	0·30 (0·20, 0·40)
Unadjusted HR (95% CI)	6·34 (2·72, 14·78)	Ref.	2·34 (1·37, 4·01)	Ref.	2·20 (1·06, 4·56)	Ref.
Adjusted main model HR (95% CI)	5·83 (2·16, 15·70)	Ref.	1·91 (1·07, 3·40)	Ref.	2·16 (0·90, 5·16)	Ref.
Adjusted mediators model HR (95% CI)	5·63 (1·82, 17·45)	Ref.	1·22 (0·61, 2·44)	Ref.	2·44 (0·77, 7·71)	Ref.
Mechanical ventilation, n (%)	5 (10)	6 (2)	12 (3)	31 (2)	5 (3)	14 (2)
Follow-up time, person-days	4,077	21,908	33,920	169,709	13,877	69,926
Rate per 1,000 days, (95% CI)	1·20 (0·20, 2·30)	0·30 (0·10, 0·50)	0·40 (0·20, 0·60)	0·20 (0·10, 0·20)	0·40 (0·00, 0·70)	0·20 (0·10, 0·30)
Unadjusted HR (95% CI)	4·17 (1·54, 11·27)	Ref.	1·90 (1·07, 3·39)	Ref.	1·76 (0·71, 4·38)	Ref.
Adjusted main model HR (95% CI)	2·28 (0·48, 10·82)	Ref.	1·85 (0·95, 3·59)	Ref.	1·28 (0·48, 3·42)	Ref.

Adjusted mediators model HR (95% CI)	2·21 (0·52, 9·47)	Ref.	1·68 (0·82, 3·46)	Ref.	1·02 (0·40, 2·61)	Ref.

CI: confidence interval; HR: hazard ratio.

Adjusted main model for age, sex, race, and smoking. Adjusted mediators model for age, sex, race, smoking, BMI, and Charlson comorbidity index (dichotomized as <2 or ≥ 2).

*Positivity either to rheumatoid factor or anti-CCP.

Supplementary table 4: Risk of severe COVID-19 among patients with mutually exclusive RA phenotypes.

ILD+/Seropositive/Erosion+	Patients with RA N=13	Comparators N=65
Event, n (%)	9 (69)	17 (26)
Follow-up time, person-days	373	4,353
Rate, per 1,000 days (95% CI)	24·13 (8·36, 39·89)	3·91 (2·05, 5·76)
RD, per 1,000 days (95% CI)	20·22 (4·35, 36·10)	-
Unadjusted model, HR (95% CI)	3·12 (1·84, 5·28)	Ref.
Adjusted main model, HR (95% CI)	2·69 (1·20, 6·02)	Ref.

ILD+/Seropositive/Erosion-	Patients with RA N=29	Comparators N=144
Event, n (%)	12 (41)	17 (12)
Follow-up time, person-days	1,550	11,414
Rate, per 1,000 days (95% CI)	7·74 (3·36, 12·12)	1·49 (0·78, 2·20)
RD, per 1,000 days (95% CI)	6·25 (1·82, 10·69)	-
Unadjusted model, HR (95% CI)	3·69 (2·11, 6·44)	Ref.
Adjusted main model, HR (95% CI)	4·95 (2·49, 9·82)	Ref.

ILD+/Seronegative/Erosion+	Patients with RA N=1	Comparators N=5
Not Performed		

ILD+/Seronegative/Erosion-	Patients with RA N=7	Comparators N=35
Event, n (%)	3 (43)	9 (26)
Follow-up time, person-days	362	2,343
Rate, per 1,000 days (95% CI)	8·29 (0·00, 17·67)	3·84 (1·33, 6·35)
RD, per 1,000 days (95% CI)	4·45 (-5·26, 14·15)	-
Unadjusted model, HR (95% CI)	1·43 (0·51, 4·02)	Ref.
Adjusted main model, HR (95% CI)	0·71 (0·12, 4·05)	Ref.

ILD-/Seropositive/Erosion+	Patients with RA N=106	Comparators N=526
Event, n (%)	21 (20)	82 (16)
Follow-up time, person-days	7,682	40,135
Rate, per 1,000 days (95% CI)	2·73 (1·56, 3·90)	2·04 (1·60, 2·49)
RD, per 1,000 days (95% CI)	0·69 (-0·56, 1·94)	-
Unadjusted model, HR (95% CI)	1·48 (0·99, 2·22)	Ref.

Adjusted main model, HR (95% CI)	1·52 (0·98, 2·36)	Ref.
ILD-/Seropositive/Erosion-	**Patients with RA N=240**	**Comparators N=1,180**
Event, n (%)	42 (18)	108 (9)
Follow-up time, person-days	17,904	96,581
Rate, per 1,000 days (95% CI)	2·35 (1·64, 3·06)	1·12 (0·91, 1·33)
RD, per 1,000 days (95% CI)	1·23 (0·49, 1·97)	-
Unadjusted model, HR (95% CI)	1·92 (1·40, 2·65)	Ref.
Adjusted main model, HR (95% CI)	1·91 (1·35, 2·69)	Ref.
ILD-/Seronegative/Erosion+	**Patients with RA N=36**	**Comparators N=179**
Event, n (%)	8 (22)	12 (7)
Follow-up time, person-days	2,542	15,083
Rate, per 1,000 days (95% CI)	3·15 (0·97, 5·33)	0·80 (0·35, 1·25)
RD, per 1,000 days (95% CI)	2·35 (0·12, 4·58)	-
Unadjusted model, HR (95% CI)	3·43 (1·56, 7·54)	Ref.
Adjusted main model, HR (95% CI)	4·45 (1·81, 10·96)	Ref.
ILD-/Seronegative/Erosion-	**Patients with RA N=136**	**Comparators N=672**
Event, n (%)	23 (17)	85 (13)
Follow-up time, person-days	10,304	52,918
Rate, per 1,000 days (95% CI)	2·23 (1·32, 3·14)	1·61 (1·26, 1·95)
RD, per 1,000 days (95% CI)	0·63 (-0·35, 1·60)	-
Unadjusted model, HR (95% CI)	1·40 (0·94, 2·08)	Ref.
Adjusted main model, HR (95% CI)	1·23 (0·80, 1·88)	Ref.

CI: confidence interval; HR: hazard ratio; RD: rate difference.

Adjusted main model for age, sex, race, and smoking.

Seropositivity either to rheumatoid factor or anti-CCP.

Supplementary Table 5. The association of rheumatoid arthritis (RA) phenotypes with the risk of severe COVID-19 and other outcomes.

	Patients with rheumatoid arthritis					
	ILD		Serostatus*		Bone erosions	
	Positive n=50	Negative n=532	Positive n=388	Negative n=180	Positive n=159	Negative n=423
Severe COVID-19, n (%)	25 (50)	101 (19)	84 (22)	35 (19)	41 (26)	85 (20)
Follow-up time, person-days	2,285	39,126	27,509	13,208	10,687	30,724
Rate, per 1,000 days (95% CI)	10·90 (6·70, 15·20)	2·60 (2·10, 3·10)	3·10 (2·40, 3·70)	2·60 (1·80, 3·50)	3·80 (2·70, 5·00)	2·80 (2·20, 3·40)
Unadjusted HR (95% CI)	3·43 (2·19, 5·36)	Ref.	1·21 (0·74, 2·00)	Ref.	1·37 (0·95, 1·97)	Ref.
Adjusted model 1 HR (95% CI)	2·61 (1·52, 4·47)	Ref.	1·21 (0·71, 2·05)	Ref.	1·16 (0·81, 1·66)	Ref.
Adjusted model 2 HR (95% CI)	2·45 (1·55, 3·87)	Ref.	1·11 (0·68, 1·81)	Ref.	1·07 (0·76, 1·50)	Ref.
Hospitalization, n (%)	24 (48)	97 (18)	82 (21)	33 (18)	40 (25)	81 (19)
Follow-up time, person-days	2,368	39,302	27,656	13,294	10,770	30,900
Rate, per 1,000 days, (95% CI)	10·10 (6·10, 14·20)	2·50 (2·00, 3·00)	3·00 (2·30, 3·60)	2·50 (1·60, 3·30)	3·70 (2·60, 4·90)	2·60 (2·10, 3·20)
Unadjusted HR (95% CI)	3·01 (1·89, 4·79)	Ref.	1·18 (0·73, 1·91)	Ref.	1·34 (0·94, 1·92)	Ref.
Adjusted model 1 HR (95% CI)	5·75 (0·69, 47·65)	Ref.	1·17 (0·70, 1·96)	Ref.	1·14 (0·80, 1·63)	Ref.
Adjusted model 2 HR (95% CI)	2·15 (1·29, 3·60)	Ref.	1·07 (0·67, 1·72)	Ref.	1·05 (0·75, 1·49)	Ref.
Death, n (%)	9 (18)	17 (3)	15 (4)	10 (6)	8 (5)	18 (4)
Follow-up time, person-days	3,877	46,894	33,916	15,621	13,747	37,024
Rate, per 1,000 days, (95% CI)	2·30 (0·80, 3·80)	0·40 (0·20, 0·50)	0·40 (0·20, 0·70)	0·60 (0·20, 1·00)	0·60 (0·20, 1·00)	0·50 (0·30, 0·70)
Unadjusted HR (95% CI)	8·81 (3·09, 25·09)	Ref.	0·62 (0·21, 1·82)	Ref.	1·20 (0·52, 2·75)	Ref.
Adjusted model 1 HR (95% CI)	7·71 (2·44, 24·37)	Ref.	0·64 (0·21, 1·82)	Ref.	0·94 (0·40, 2·23)	Ref.
Adjusted model 2 HR (95% CI)	7·16 (2·32, 22·07)	Ref.	0·62 (0·20, 1·99)	Ref.	0·88 (0·37, 2·09)	Ref.
Mechanical ventilation, n (%)	5 (10)	12 (2)	12 (3)	5 (3)	5 (3)	12 (3)
Follow-up time, person-days	4,077	46,869	33,920	15,766	13,877	37,069
Rate per 1,000 days, (95% CI)	1·20 (0·20, 2·30)	0·30 (0·10, 0·40)	0·40 (0·20, 0·60)	0·30 (0·00, 0·60)	0·40 (0·00, 0·70)	0·30 (0·10, 0·50)
Unadjusted HR (95% CI)	4·70	Ref.	1·19	Ref.	1·12	Ref.

	(1·49, 14·80)		(0·36, 3·87)		(0·39, 3·17)	
Adjusted model 1 HR (95% CI)	2·40 (0·76, 7·63)	Ref.	1·06 (0·24, 4·73)	Ref.	0·79 (0·26, 2·40)	Ref.
Adjusted model 2 HR (95% CI)	3·01 (0·90, 10·08)	Ref.	1·05 (0·32, 3·43)	Ref.	0·77 (0·27, 2·19)	Ref.

CI: confidence interval; HR: hazard ratio.

Model 1 adjusted for age, sex, race, and wave of infection. Model 2 adjusted for age, sex, b/tsDMARD (yes/no), and wave of infection.

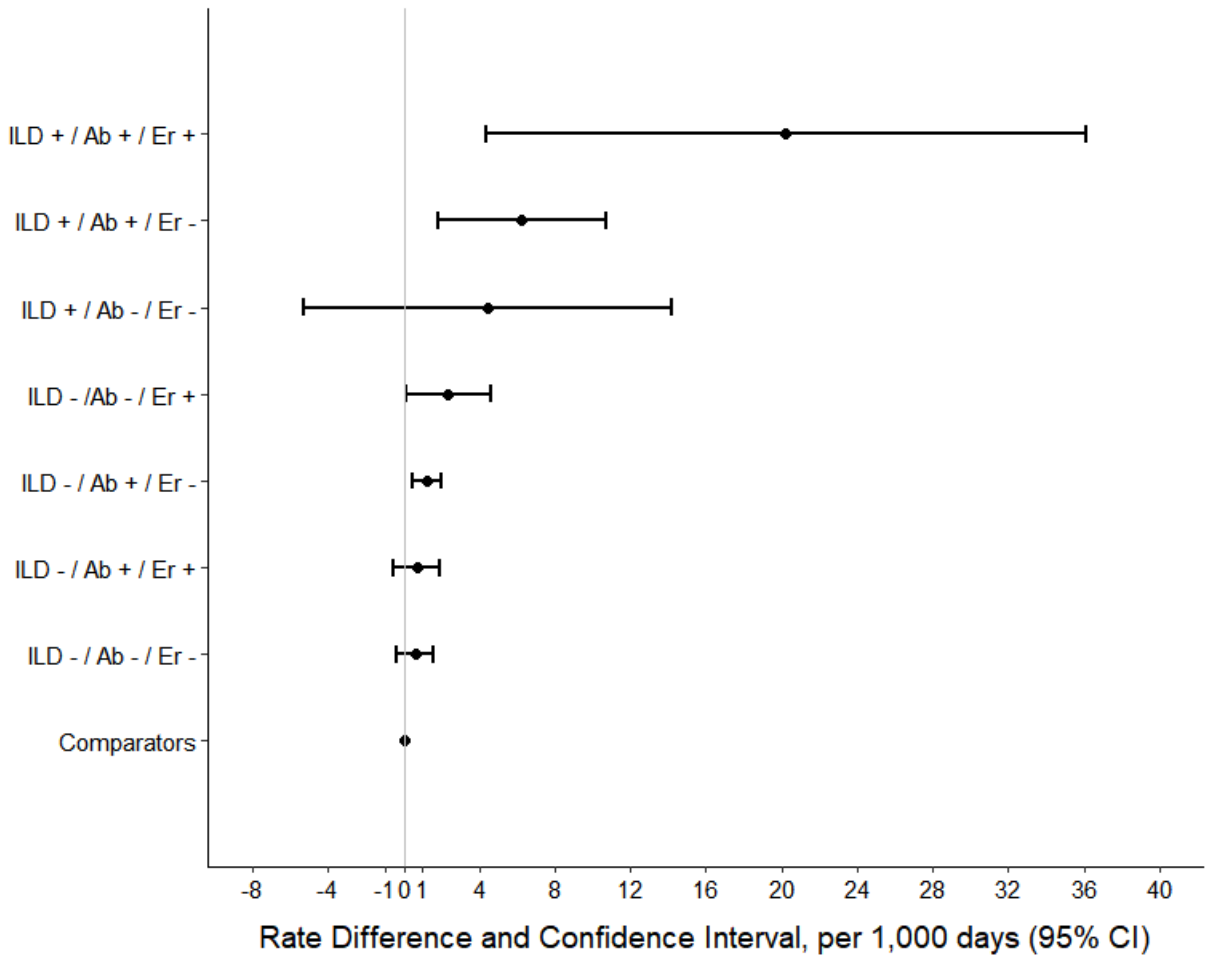*Positivity either to rheumatoid factor or anti-CCP.

Supplementary table 6. Risk of severe COVID-19 and secondary outcomes among patients with rheumatoid arthritis stratified by rheumatoid factor and anti-CCP status.

	Rheumatoid factor		Anti-CCP	
	Positive n=302	Comparators n=1490	Positive n=312	Comparators n=1539
Severe COVID-19, n (%)	70 (23)	188 (13)	61 (20)	168 (11)
Follow-up time, person-days	21,026	117,463	22,684	123,555
Rate, per 1,000 days (95% CI)	3·30 (2·50, 4·10)	1·60 (1·37, 1·83)	2·70 (2·00, 3·40)	1·36 (1·15, 1·57)
Unadjusted, HR (95% CI)	1·99 (1·58, 2·50)	Ref.	1·97 (1·53, 2·53)	Ref.
Adjusted main model, HR (95% CI)	2·03 (1·59, 2·59)	Ref.	1·94 (1·49, 2·54)	Ref.
Adjusted mediators model, HR (95% CI)	1·96 (1·52, 2·55)	Ref.	1·81 (1·36, 2·42)	Ref.
Hospitalization, n (%)	68 (23)	185 (12)	60 (19)	167 (11)
Follow-up time, person-days	21,158	117,713	22,748	123,690
Rate, per 1,000 days (95% CI)	3·20 (2·50, 4·00)	1·57 (1·35, 1·80)	2·60 (2·00, 3·30)	1·35 (1·15, 1·55)
Unadjusted, HR (95% CI)	1·82 (1·46, 2·26)	Ref.	1·82 (1·44, 2·29)	Ref.
Adjusted main model, HR (95% CI)	1·86 (1·48, 2·34)	Ref.	1·82 (1·42, 2·34)	Ref.
Adjusted mediators model, HR (95% CI)	1·88 (1·48, 2·38)	Ref.	1·76 (1·34, 2·30)	Ref.
Death, n (%)	13 (4)	28 (2)	12 (4)	24 (2)
Follow-up time, person-days	26,278	132,180	27,296	136,844
Rate, per 1,000 days (95% CI)	0·50 (0·20, 0·80)	0·21 (0·13, 0·29)	0·40 (0·20, 0·70)	0·18 (0·11, 0·25)
Unadjusted, HR (95% CI)	2·54 (1·42, 4·54)	Ref.	2·67 (1·45, 4·91)	Ref.
Adjusted main model, HR (95% CI)	2·01 (1·03, 3·91)	Ref.	2·16 (1·08, 4·33)	Ref.
Adjusted mediators model, HR (95% CI)	1·22 (0·59, 2·52)	Ref.	1·48 (0·63, 3·46)	Ref.
Mechanical ventilation, n (%)	11 (4)	27 (2)	10 (3)	26 (2)
Follow-up time, person-days	26,266	131,815	27,253	136,310
Rate per 1,000 days, (95% CI)	0·40 (0·20, 0·70)	0·21 (0·13, 0·28)	0·40 (0·10, 0·60)	0·19 (0·12, 0·26)
Unadjusted, HR (95% CI)	2·00 (1·09, 3·66)	Ref.	1·90 (1·01, 3·56)	Ref.
Adjusted main model, HR (95% CI)	1·99 (0·98, 4·03)	Ref.	1·81 (0·82, 3·99)	Ref.
Adjusted mediators model, HR (95% CI)	1·86 (0·84, 4·11)	Ref.	2·22 (0·92, 5·32)	Ref.

CI: confidence interval; HR: hazard ratio.

Adjusted main model for age, race, and smoking. Adjusted mediators model for age, race, smoking, BMI, and Charlson comorbidity index (dichotomized as <2 or ≥ 2).

Supplementary figure 1. Rate difference of RA phenotypic subgroups vs matched comparators for severe outcomes.

Rate Difference and Confidence Interval, per 1,000 days (95% CI)

Ab: Serostatus; Er: Bone erosions; ILD: Interstitial Lung Disease.