THE LANCET
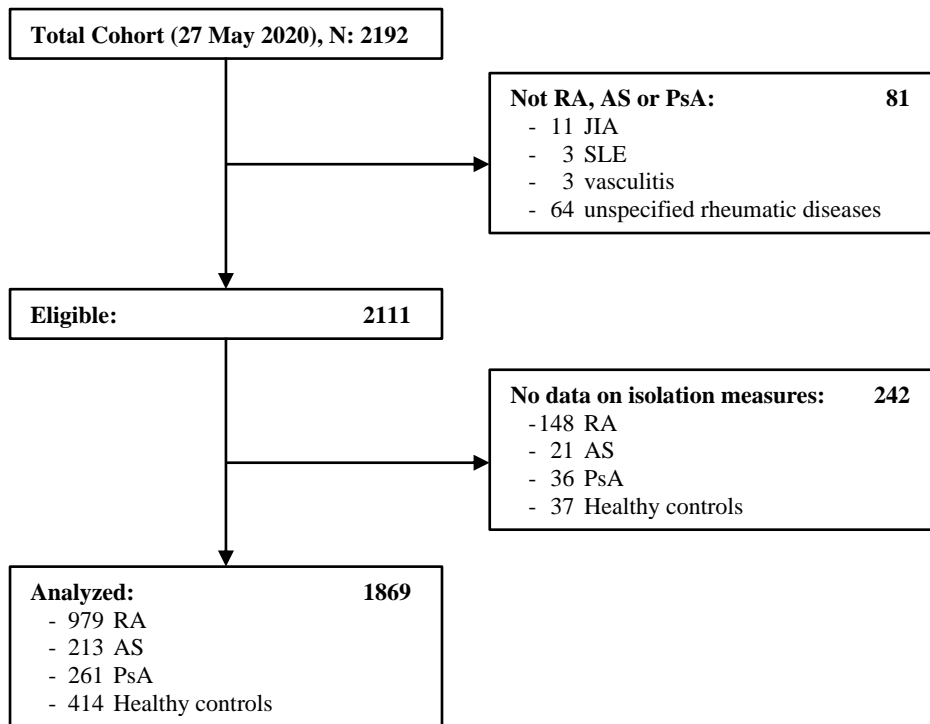## Rheumatology

Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

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┌────────────────────────────────────────┐
│ Total Cohort (27 May 2020), N: 2192     │
└────────────────────────────────────────┘
         │
         │          ┌──────────────────────────────────────────────────┐
         │          │ Not RA, AS or PsA:                        81     │
         ├─────────▶│  -  11 JIA                                        │
         │          │  -   3 SLE                                        │
         │          │  -   3 vasculitis                                 │
         │          │  -  64 unspecified rheumatic diseases             │
         │          └──────────────────────────────────────────────────┘
         ▼
┌────────────────────────────────────────┐
│ Eligible:                    2111       │
└────────────────────────────────────────┘
         │
         │          ┌──────────────────────────────────────────────────┐
         │          │ No data on isolation measures:          242      │
         ├─────────▶│  - 148 RA                                         │
         │          │  -  21 AS                                         │
         │          │  -  36 PsA                                        │
         │          │  -  37 Healthy controls                           │
         │          └──────────────────────────────────────────────────┘
         ▼
┌────────────────────────────────────────┐
│ Analyzed:                    1869       │
│  - 979 RA                               │
│  - 213 AS                               │
│  - 261 PsA                              │
│  - 414 Healthy controls                 │
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Flow chart

Table 1. Baseline characteristics and isolation measures of RA, AS and PsA patients compared to healthy controls.					
Patient characteristics	**All patients (n=1455)**	**RA (n=979)**	**AS (n=215)**	**PsA (n=261)**	**Control (n=414)**
Mean age – yr	55 ± 13	58 ± 12	48 ± 13	55 ± 13	53 ± 13
Female sex – no. (%)	934 (64)*	728 (74)	87 (41)	119 (46)	298 (72)
BMI (IQR)	25 (23-28)*	25 (22-28)	25 (22-28)	26 (24-30)	24 (22-27)
Smoking – no. (%)	178 (12)*	126 (13)	35 (16)	17 (7)	34 (8)
Alcohol consumption – no. (%)	993 (68)**	655 (67)	151 (70)	187 (72)	328 (79)
PCR confirmed COVID-19 – no. (%)	5 (0.3)	5 (0.5)	0	0	2 (0.5)
Coexisting conditions – no. (%)					
Cardiovascular disease	157 (11)*	107 (11)	22 (10)	28 (11)	30 (7)
Chronic pulmonary disease	149 (10)*	108 (11)	20 (9)	21 (8)	22 (5)
Diabetes	92 (6)*	58 (6)	12 (6)	22 (8)	13 (3)
Co-existing immune disorder	61 (4)*	35 (4)	14 (7)	12 (5)	8 (2)
Rheumatic medication – no. (%)					
csDMARDs	877 (60)	712 (73)	17 (8)	148 (57)	N.A.
Methotrexate	736 (51)	595 (61)	6 (3)	135 (52)	N.A.
Hydroxychloroquine	159 (11)	157 (16)	1 (0.4)	1 (0.5)	N.A.
Oral glucocorticoids	161 (11)	139 (14)	5 (2)	17 (7)	2 (0.4)
TNF inhibitor	563 (39)	336 (34)	106 (49)	121 (46)	N.A.
Etanercept	312 (22)	184 (19)	56 (26)	72 (28)	N.A.
Adalimumab	195 13	115 (12)	40 (19)	40 (15)	N.A.
Golimumab	16 (1)	5 (0.5)	7 (3)	4 (2)	N.A.
Infliximab	25 (2)	21 (2)	1 (0.5)	3 (1)	N.A.
Certolizumab pegol	15 (1)	11 (1)	2 (0.9)	2 (0.8)	N.A.
IL-6 inhibitor	19 (1)	19 (2)	0	0	N.A.
IL-17 inhibitor	17 (1)	2 (0.2)	8 (4)	7 (3)	N.A.
Isolation measures* – no. (%)					
None	16 (1)	11 (1)	2 (1)	3 (1)	4 (1)
Hygiene measures	66 (5)	48 (4)	5 (2)	13 (5)	11 (3)
Social distancing	688 (47)	459 (47)	108 (50)	121 (46)	272 (66)
Staying indoors as much as possible	572 (39)	374 (38)	89 (41)	109 (42)	118 (29)
Total isolation	94 (7)	74 (8)	9 (4)	11 (4)	4 (1)

*Table 1. Values are displayed as mean ± standard deviation (SD), median with corresponding interquartile range (IQR) or frequencies with corresponding percentages (%). Patient characteristic of all patients were compared to controls with a Students' t-test, Chi-square test or Mann-Whitney U test depending on the type and distribution of the variable. RA = rheumatoid arthritis, AS = ankylosing spondylitis, PsA = psoriatic arthritis, BMI = body mass index, co-existing immune disorder = a condition caused by disfunctioning of the immune system besides the RA, AS or PsA, such as Sjogren or inflammatory bowel disease; csDMARDs = conventional disease modifying anti-rheumatic drugs, TNF = anti-tumor necrosis factor, IL = interleukin. * p value < 0.05. **p value < 0.001.*

Table 2. Adherence to strict isolation measures in rheumatic patients compared to health controls.						
	Crude model [a]			**Adjusted model** [b]		
All patients	2.0	(1.6 – 2.6)	$p < 0.01$	1.8	(1.5 – 2.4)	$p < 0.01$
RA patients	2.0	(1.6 – 2.6)		1.7	(1.3 – 2.3)	
AS patients	2.0	(1.4 – 2.8)		2.4	(1.7 – 3.6)	
PsA patients	2.1	(1.5 – 2.8)		2.0	(1.4 – 2.8)	
Biological DMARD users	2.3	(1.8 – 3.0)		2.2	(1.6 – 2.9)	
Non-biological DMARD users	1.9	(1.4 – 2.4)		1.7	(1.3 – 2.2)	

Table 2. Values are displayed as odds ratio with corresponding 95% confidence interval and p value. Odds ratios for adherence to strict isolation measures are compared to all healthy control subjects. Strict isolation was defined as staying indoors as much as possible and complete social isolation during the COVID-19 pandemic. RA = rheumatoid arthritis, AS = ankylosing spondylitis, PsA = psoriatic arthritis, DMARD = disease modifying anti-rheumatic drug. [a]*Not adjusted for any covariates.* [b]*Adjusted for gender, age, BMI, current smoking status and presence of comorbidities.*

Table 3. Adherence to strict isolation measures in female and male rheumatic patients compared to health controls; and within rheumatic patients, patients on vs off biological DMARD treatment.						
	Crude model [a]			**Adjusted model** [b]		
Female patients						
All female patients	2.5	(1.9 – 3.3)	$p < 0.01$	2.1	(1.6 – 2.9)	$p < 0.01$
Female RA patients	2.4	(1.8 – 3.2)		2.0	(1.4 – 2.7)	
Female AS patients	2.5	(1.5 – 4.1)		2.9	(1.7 – 4.8)	
Female PsA patients	3.0	(1.9 – 4.6)		2.5	(1.6 – 4.0)	
Female biological DMARD users	2.9	(2.1 – 4.0)		2.5	(1.8 – 3.6)	
Female non-biological DMARD users	2.2	(1.6 – 3.0)		1.8	(1.3 – 2.6)	
Male patients						
All male patients	1.3	(0.9 – 2.0)	$p = 0.17$	1.4	(0.9 – 2.2)	$p = 0.15$
Male RA patients	1.3	(0.8 – 2.1)		1.3	(0.8 – 2.1)	
Male AS patients	1.5	(0.9 – 2.4)		1.8	(1.0 – 3.1)	
Male PsA patients	1.3	(0.8 – 2.2)		1.3	(0.8 – 2.3)	
Male Biological DMARD users	1.4	(0.9 – 2.2)		1.5	(0.9 – 2.5)	
Male Non-biological DMARD users	1.3	(0.8 – 2.0)		1.3	(0.8 – 2.1)	
Rheumatic patients						
Biological DMARD users	1.2	(1.0 – 1.5)	$p = 0.06$	1.3	(1.1 – 1.7)[c]	$p = 0.02$

Table 3. Values are displayed as odds ratio with corresponding 95% confidence interval and p value. Odds ratios for adherence to strict isolation measures of female and male rheumatic patients are compared to female and male healthy controls, respectively. Odds ratios for adherence to strict isolation measures of biological DMARD users are compared to all patients who did not receive biological DMARDs. Strict isolation was defined as staying indoors as much as possible and complete social isolation during the COVID-19 pandemic. RA = rheumatoid arthritis, AS = ankylosing spondylitis, PsA = psoriatic arthritis, DMARD = disease modifying anti-rheumatic drug. [a]*Not adjusted for any covariates.* [b]*Adjusted for gender, age, BMI, current smoking status and presence of comorbidities.* [c]*Adjusted for the above-mentioned covariates and rheumatic diagnosis.*

Data handling procedures

Patient data was collected through a secure webportal, using two-factor authentication as recommended by Dutch security guidelines. The website was designed in line with the requirements of the NEN7512 (security online access in healthcare) and NEN7513 (logging of system access) and is fully compliant with the new European Union's General Data Protection Regulation (GDPR). After completion of the digital questionnaires, the results were stored in an encrypted database. To pseudonymize the data, a study code was assigned to all patients. Questionnaires could be completed from any device with the personal account every participant received on inclusion. Access to and mutations of the database were permanently logged according to Good Clinical Practice guidelines, and again access was only possible with 2-factor authentication. Analysis of the data was performed on planned and pre-defined exports derived from the main database.

Statistical analyses

The distribution of continuous variables of the patient characteristics was explored. Normal distributed variables are displayed as mean ± standard deviation (SD) and variables with a skewed distribution as median with corresponding interquartile range (IQR). It was explored whether patient characteristics of the rheumatic patients differed from control subjects. Depending on the type and distribution of the variable, a Students' t-test, Mann-Whitney U test or Chi-square test was used for this analysis. A threshold of $p < 0.05$ was considered statistically significant. No adjustment was made for multiple testing. Multivariate logistic regression analyses were used to study differences in isolation measures between patients and controls. Age, gender, BMI, current smoking status and the presence of comorbidities were considered potential confounders and added to the analyses. For clarity, it was decided not to perform any selection procedure to investigate whether or not each individual variable could be considered a confounder. For age, gender, presence of comorbidities, and smoking status it was investigated whether they were effect modifiers. A threshold of $p < 0.05$ was used for interaction terms. Lastly, the influence of treatment with biological disease modifying anti-rheumatic drugs (bDMARDs) on adherence to isolation measures by rheumatic patients was investigated. In addition to the before mentioned confounders, this model was also adjusted for the type of rheumatic diagnosis. Again, the same variables were used to investigate effect modification.