

THE LANCET

Rheumatology

Supplementary appendix

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Supplement to: Gentry CA, Humphrey MB, Thind SK, et al. Long-term hydroxychloroquine use in patients with rheumatic conditions and development of SARS-CoV-2 infection: a retrospective propensity analysis study. *Lancet Rheumatol* 2020; published online Sept 21. [https://doi.org/10.1016/S2665-9913\(20\)30305-2](https://doi.org/10.1016/S2665-9913(20)30305-2).

Supplementary material: Prevention of SARS-CoV-2 infection with hydroxychloroquine in patients with rheumatologic conditions

Table S1. ICD-10 codes included for rheumatoid conditions*

Rheumatoid arthritis: M05.0 –M05.9 and M06.0-M06.9
Systemic lupus: M32.0 – M32.9
Cutaneous lupus: L93.0-L93.2
Systemic Sclerosis: M34.0-M34.9
Mixed connective tissue disease: M35.8, M35.9
Sjogrens: M35.0-M35.09
Undifferentiated connective tissue disease: M35.1, M36.0-M36.8, M65.9
Polyarthritis unspecified: M12.0-M12.9 and M13.0-M13.89
Dermatomyositis: M33.0-M33.9, M60.8-M60.9
Rheumatism, unspec: M79.0
Palindromic Rheumatism: M12.30-M12.39
Arthropathies in other spec diseases: M14.8
Other specific arthropathies, not elsewhere: M12.8

*Diagnoses indicating rheumatoid arthritis, Lupus, polymyositis, connective tissue disease, Inflammatory polyarthritis, Systemic sclerosis, Stills, Palindromic rheumatism, polyarthritis rheumatica, Crest, Sjogren's, Bechet's, Felty's, and Jaccoud's syndromes will be considered specific Rheumatologic conditions. Patients with an ICD10 diagnosis of "arthritis other specified", arthropathy, monoarthritis, polyarthritis, synovitis, myositis, and myalgia will only be included in patients considered having rheumatologic conditions if they also have one of the specific rheumatologic conditions.

Table S2. Baseline univariate variables associated with the selection of hydroxychloroquine among patients with ICD10 codes for rheumatologic conditions.

Baseline variable*	Patients receiving hydroxychloroquine (n=10,703)	Patients not receiving hydroxychloroquine (n=59,567)	Standardized mean difference (95% confidence interval)	p
<u>Rheumatologic condition</u>				
Rheumatoid Arthritis	7193 (67.2)	45047 (75.6)	-0.229 (-0.253, -0.204)	<0.001
Lupus	2642 (24.7)	6406 (10.8)	0.552 (0.524, 0.580)	<0.001
Polymyositis	87 (0.81)	1217 (2.04)	-0.515 (-0.636, -0.395)	<0.001
Polyarthritits	208 (1.94)	927 (1.56)	0.125 (0.041, 0.208)	0.004
Sjogren's Syndrome	398 (3.72)	2239 (3.76)	-0.062 (-0.661, -0.073)	0.84
Bechet's Syndrome	4 (0.04)	117 (0.20)	-0.916 (-1.47, 0.366)	<0.001
Jaccoud's Syndrome	1 (0.01)	10 (0.02)	-0.323 (-1.46, 0.810)	0.99
Connective Tissue Disease	422 (3.94)	932 (1.56)	0.523 (0.459, 0.588)	<0.001
Crest Syndrome	9 (0.08)	58 (0.10)	-0.081 (-0.468, 0.306)	0.68
Felty's Syndrome	12 (0.11)	74 (0.12)	-0.057 (-0.393, 0.280)	0.74
Inflammatory Polyarthritits	346 (3.23)	2161 (3.63)	-0.066 (-0.130, -0.002)	0.040
Systemic Sclerosis	75 (0.70)	702 (1.18)	-0.289 (-0.421, -0.463)	<0.001
Stills Disease	4 (0.04)	31 (0.05)	-0.183 (-0.757, 0.392)	0.65
Palindromic rheumatism	76 (0.71)	248 (0.42)	0.296 (0.154, 0.438)	<0.001
Polyarthralgia	246 (2.30)	2274 (3.82)	-0.288 (-0.362, -0.215)	<0.001
Rheumatica				
<u>Demographics</u>				
Age, mean (SD)	64.8 (12.9)	66.7 (13.2)	-0.149 (-0.169, -0.128)	<0.001
Gender (male)	8029 (75.0)	48517 (81.4)	-0.210 (-0.236, -0.183)	<0.001
Urban (vs. rural) residence	6577 (61.5)	36972 (62.1)	-0.014 (-0.038, 0.009)	0.22
White race	7292 (68.1)	41309 (69.4)	-0.031 (-0.056, -0.007)	0.012
Race				
White	7292 (68.1)	41309 (69.4)		<0.001
Black	2107 (19.7)	10435 (17.5)		
Hispanic	542 (5.06)	3004 (5.04)		

Native	148 (1.38)	703 (1.18)		
American				
Asian/ Pacific islander	168 (1.57)	1007 (1.69)		
Unknown	442 (4.13)	3109 (5.22)		
Body mass index (m²), Mean (SD)	30.0 (6.24)	29.5 (6.09)	0.070 (0.049, 0.091)	<0.001
<25	2206 (21.4)	12156 (22.4)		
25-30	3423 (33.2)	19425 (35.8)		
>30	4671 (45.4)	22683 (41.8)		
Any Tobacco Use	1175 (11.0)	5988 (10.0)	0.054 (0.018, 0.091)	0.004
<u>Rheumatologic prescriptions</u>				
Leflunomide	654 (6.11)	1695 (2.85)	0.440 (0.389, 0.491)	<0.001
Methotrexate	2214 (20.7)	7085 (11.9)	0.363 (0.334, 0.392)	<0.001
Sulfasalazine	947 (8.85)	1580 (2.65)	0.700 (0.455, 0.746)	<0.001
Any other oral DMARD	3388 (31.6)	9665 (16.2)	0.481 (0.455, 0.506)	<0.001
Chronic steroid use	1001 (9.35)	2480 (4.16)	0.477 (0.435, 0.519)	<0.001
Prednisone equivalent >20mg/day	51 (0.48)	206 (0.35)	0.177 (0.008, 0.347)	0.047
Any biologic therapy	1548 (14.5)	7614 (12.8)	0.079 (0.046, 0.111)	<0.001
Other DMARD + biologic	760 (7.10)	2975 (4.99)	0.206 (0.161, 0.252)	<0.001
Methotrexate + biologic	473 (4.42)	2192 (3.68)	0.105 (0.049, 0.161)	<0.001
Methotrexate + other DMARD + biologic	53 (0.50)	126 (0.21)	0.470 (0.293, 0.648)	<0.001
<u>Other prescriptions of interest</u>				
Angiotensin-II receptor blocker	943 (8.81)	3362 (5.64)	0.264 (0.223, 0.306)	<0.001
Angiotensin-II converting enzyme inhibitor	1551 (14.5)	5546 (9.31)	0.276 (0.243, 0.309)	<0.001
Vitamin D	2565 (24.0)	8248 (13.8)	0.371 (0.344, 0.399)	<0.001
Vitamin C	186 (1.74)	667 (1.12)	0.248 (0.156, 0.336)	<0.001
Zinc	14 (0.13)	78 (0.13)	-0.001 (-0.314, 0.313)	0.99
<u>Comorbidities</u>				

Respiratory	2342 (21.9)	11862 (19.9)	0.066 (0.038, 0.093)	<0.001
Renal/Urinary	2636 (24.6)	13318 (22.4)	0.070 (0.043, 0.096)	<0.001
Cardiovascular	4402 (41.1)	23906 (40.1)	0.023 (-0.001, 0.046)	0.053
Gastrointestinal	2487 (23.2)	12650 (21.2)	0.064 (0.037, 0.091)	<0.001
Hepatobiliary	337 (3.15)	1703 (2.86)	0.056 (-0.009, 0.122)	0.10
Neurological	3232 (30.2)	15915 (26.7)	0.094 (0.070, 0.119)	<0.001
Dermatological	1706 (15.9)	8116 (13.6)	0.102 (0.070, 0.133)	<0.001
Metabolic/Endocrine	4547 (42.5)	26228 (44.0)	-0.035 (-0.058, -0.019)	0.003
Hematological	1423 (13.3)	6534 (11.0)	0.121 (0.087, 0.154)	<0.001
Psychiatric	3059 (28.6)	16026 (26.9)	0.046 (0.021, 0.071)	<0.001
Neoplastic	1379 (12.9)	6960 (11.7)	0.061 (0.027, 0.101)	<0.001
<u>Laboratory abnormalities</u>				
Elevated alkaline phosphatase	142 (1.33)	747 (1.25)	0.032 (-0.068, 0.131)	0.54
Elevated alanine aminotransferase	199 (1.86)	1279 (2.15)	-0.081 (-0.164, 0.022)	0.052
Elevated aspartate aminotransferase	459 (4.29)	2371 (3.98)	0.043 (-0.013, 0.099)	0.14
Elevated lactate dehydrogenase	408 (24.2)	1275 (2.14)	0.328 (0.265, 0.390)	<0.001
Low hemoglobin	4790 (44.8)	18467 (31.0)	0.325 (0.302, 0.348)	<0.001
Thrombocytopenia	585 (5.47)	2668 (4.48)	0.115 (0.065, 0.166)	<0.001
Leukocytosis	558 (5.21)	2955 (4.96)	0.029 (-0.022, 0.080)	0.27
Leukopenia	172 (1.61)	500 (0.84)	0.362 (0.266, 0.459)	<0.001
Elevated urea nitrogen	1098 (10.3)	5599 (9.40)	0.054 (0.016, 0.091)	0.006
Elevated creatinine	720 (6.73)	3352 (5.63)	0.105 (0.059, 0.151)	<0.001
Elevated erythrocyte sedimentation rate	1926 (18.0)	6078 (10.2)	0.362 (0.332, 0.394)	<0.001
Elevated C-reactive protein > 10 mcg/ml	691 (6.46)	2360 (3.96)	0.284 (0.236, 0.332)	<0.001

* Data presented are number (percent).

† DMARD = Disease modifying anti-rheumatic drug; hydroxychloroquine, methotrexate, lefunomide, and sulfasalazine. "Other DMARD" refers to agents other than hydroxychloroquine.

Table S3. Baseline univariate variables associated with the development of SARS-CoV-2 infection from the propensity-matched cohorts of patients receiving hydroxychloroquine and patients not receiving hydroxychloroquine.

Baseline variable*	Patients developing active SARS-CoV-2 infection (n=109)	Patients not developing active SARS-CoV-2 infection (n=32,000)	Standardized mean difference (95% confidence interval)	p
<u>Rheumatologic condition</u>				
Rheumatoid Arthritis	79 (72.5)	22163 (69.3)	0.086 (-0.146, 0.319)	0.46
Lupus erythematosus	23 (21.1)	7094 (22.2)	-0.035 (-0.289, 0.219)	0.79
Polymyositis	2 (1.83)	402 (1.26)	0.212 (-0.561, 0.985)	0.40
Polyarthritits	8 (7.34)	600 (1.88)	0.784 (0.385, 1.183)	0.001
Sjogren's Syndrome	1 (0.92)	803 (2.51)	-0.564 (-1.65, 0.523)	0.53
Bechet's Syndrome	0 (0)	6 (0.02)	--	0.99
Jaccoud's Syndrome	0 (0)	4 (0.01)	--	0.99
Connective Tissue Disease	5 (4.59)	1083 (3.38)	0.175 (-0.321, 0.670)	0.42
Crest Syndrome	0 (0)	16 (0.05)	--	0.99
Felty's Syndrome	0 (0)	46 (0.14)	--	0.99
Inflammatory Polyarthritits	1 (0.92)	950 (2.97)	-0.659 (-1.750, 0.427)	0.38
Systemic Sclerosis	0 (0)	223 (0.70)	--	0.99
Stills Disease	0 (0)	15 (0.05)	--	0.99
Palindromic rheumatism	1 (0.92)	237 (0.72)	0.136 (-0.952, 1.220)	0.54
Polyarthralgia	5 (4.59)	815 (2.55)	0.336 (-0.160, 0.832)	0.21
Rheumatica				
<u>Demographics</u>				
Age mean, (SD)	63.6 (12.5)	65.2 (13.2)	-0.117 (-0.305, 0.071)	0.093
Gender (male)	80 (73.4)	24451 (76.4)	-0.088 (-0.323, 0.146)	0.46
Race				
White	54 (49.5)	21459 (67.1)	-0.402 (-0.610, 0.012)	<0.001
Black	42 (38.5)	6529 (20.4)		
Hispanic	6 (5.50)	1581 (4.94)		
Native	3 (2.75)	404 (1.26)		

American				
Asian/ Pacific islander	1 (0.92)	514 (1.61)		
Unknown	3 (2.75)	1513 (4.73)		
Body mass index (m²)	31.7 (7.55)	29.8 (6.20)	0.312 (-0.124, 0.502)	0.010
Any Tobacco Use	9 (8.26)	3463 (10.8)	-0.165 (-0.541, 0.219)	0.39
<u>Rheumatologic prescriptions</u>				
Leflunomide	5 (4.59)	1874 (5.86)	-0.142 (-0.637, 0.353)	0.84
Methotrexate	28 (25.7)	6675 (20.9)	0.150 (-0.088, 0.387)	0.23
Sulfasalazine	4 (3.67)	2321 (7.25)	-0.396 (-0.948, 0.154)	0.19
Any other oral DMARD[†]	35 (32.1)	9852 (30.8)	0.034 (-0.188, 0.256)	0.77
Chronic steroid use	11 (10.1)	2697 (8.43)	0.109 (-0.235, 0.454)	0.54
Prednisone equivalent >20mg/day	0 (0)	140 (0.44)	--	0.49
Any biologic therapy	22 (20.2)	4754 (14.9)	0.205 (-0.054, 0.463)	0.14
Other DMARD + biologic	12 (11.0)	2431 (7.60)	0.225 (-0.106, 0.557)	0.21
Methotrexate + biologic	9 (8.26)	1568 (4.90)	0.308 (-0.070, 0.685)	0.14
Methotrexate + other DMARD + biologic	0 (0)	145 (0.45)	--	0.99
<u>Other prescriptions of interest</u>				
Angiotensin-II receptor blocker	9 (8.26)	2738 (8.56)	-0.021 (-0.398, 0.355)	0.91
Angiotensin-II converting enzyme inhibitor	25 (22.9)	4518 (14.1)	0.327 (-0.080, 0.574)	0.014
Vitamin D	28 (25.7)	7216 (22.6)	0.095 (-0.143, 0.332)	0.44
Vitamin C	7 (6.42)	505 (1.58)	0.802 (0.377, 1.23)	0.002
Zinc	0 (0)	53 (0.17)	--	0.99
<u>Comorbidities</u>				
Respiratory	28 (25.7)	6743 (21.1)	0.142 (-0.095, 0.380)	0.25
Renal/Urinary	33 (30.3)	7599 (23.7)	0.183 (-0.042, 0.409)	0.12
Cardiovascular	51 (46.8)	13246 (41.4)	0.121 (-0.087, 0.329)	0.26

Gastrointestinal	30 (27.5)	7033 (22.0)	0.501 (0.269, 0.733)	0.17
Hepatobiliary	5 (4.59)	983 (3.07)	0.230 (-0.266, 0.726)	0.39
Neurological	46 (42.2)	9232 (28.8)	0.324 (0.114, 0.534)	0.003
Dermatological	12 (11.0)	5005 (15.6)	-0.223 (-0.554, 0.108)	0.16
Metabolic/Endocrine	53 (48.6)	14015 (43.8)	0.107 (-0.100, 0.315)	0.31
Hematological	11 (10.1)	4063 (12.7)	-0.143 (-0.487, 0.201)	0.40
Psychiatric	41 (37.6)	9012 (28.2)	0.237 (0.233, 0.451)	0.033
Neoplastic	15 (13.8)	3925 (12.2)	0.073 (-0.228, 0.374)	0.64
<u>Laboratory abnormalities</u>				
Elevated alkaline phosphatase	3 (2.75)	475 (1.48)	0.348 (-0.287, 0.982)	0.22
Elevated alanine aminotransferase	5 (4.59)	645 (2.02)	0.468 (-0.029, 0.965)	0.071
Elevated aspartate aminotransferase	7 (6.42)	1430 (4.47)	0.211 (-0.212, 0.634)	0.35
Elevated lactate dehydrogenase	8 (7.34)	1041 (3.25)	0.472 (0.074, 0.871)	0.038
Low hemoglobin	60 (55.0)	14020 (43.8)	0.249 (-0.040, 0.457)	0.019
Thrombocytopenia	5 (4.59)	1798 (5.62)	-0.118 (-0.613, 0.378)	0.83
Leukocytosis	7 (6.42)	1818 (5.68)	0.072 (-0.351, 0.494)	0.74
Leukopenia	0 (0)	463 (1.45)	--	0.41
Elevated urea nitrogen	14 (12.8)	3437 (10.7)	0.112 (-0.198, 0.422)	0.49
Elevated creatinine	12 (11.0)	2205 (6.89)	0.283 (-0.048, 0.614)	0.12
Elevated erythrocyte sedimentation rate	35 (32.1)	5392 (16.8)	0.467 (0.245, 0.690)	0.013
Elevated C-reactive protein > 10 mcg/ml	18 (16.5)	1976 (6.18)	0.607 (0.326, 0.887)	0.002

* Data presented are number (percent).

† DMARD = Disease modifying anti-rheumatic drug; hydroxychloroquine, methotrexate, lefunomide, and sulfasalazine. "Other DMARD" refers to agents other than hydroxychloroquine.