

Supplementary Material: Hydroxychloroquine Use and Cardiovascular Events Among Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis

Running Head: Hydroxychloroquine and Cardiovascular Events

Authors: April Jorge, MD¹; Leo Lu, MPH^{1, 2}; Hyon Choi, MD, DrPH¹; John M. Esdaile, MD, MPH^{2,3}; Diane Lacaille, MD, MHS^{2,3}; J. Antonio Avina-Zubieta, MD, PhD^{2,3}

Affiliations:

¹Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital

²Arthritis Research Canada, Richmond, BC, Canada

³Division of Rheumatology, University of British Columbia, Vancouver, BC, Canada

Corresponding Author:

J. Antonio Avina-Zubieta MD, FRCPC MSc, PhD

230-2238 Yukon Street

Vancouver, BC V5Y 3P2

azubieta@arthritisresearch.ca

Supplemental Table 1. Hydroxychloroquine Use and Cardiovascular Events According to Hydroxychloroquine Exposure Status and Rheumatic Disease

	Cases, N	Controls, N	Conditional Odds Ratio (95% CI)	Conditional Adjusted* Odds Ratio (95% CI)
SLE Combined CV Events				
Remote HCQ Users	110	232	1.0 (reference)	1.0 (reference)
Recent HCQ users	32	69	1.05 (0.65-1.72)	1.11 (0.62-2.00)
Current HCQ users	171	386	0.95 (0.71-1.28)	0.90 (0.62-1.29)
HCQ non-users	219	562	0.78 (0.58-1.04)	0.78 (0.55-1.11)
RA Combined CV Events				
Remote HCQ Users	1195	3153	1.0 (reference)	1.0 (reference)
Recent HCQ users	212	566	0.99 (0.84-1.18)	0.90 (0.73-1.11)
Current HCQ users	1011	3063	0.87 (0.79-0.96)	0.86 (0.76-0.96)
HCQ non-users	7318	21938	0.87 (0.81-0.94)	0.96 (0.88-1.05)
SLE Myocardial Infarction				
Remote HCQ Users	36	79	1.0 (reference)	1.0 (reference)
Recent HCQ users	11	22	1.25 (0.53-2.94)	1.40 (0.45-4.42)
Current HCQ users	60	140	0.91 (0.55-1.51)	1.01 (0.52-1.96)
HCQ non-users	91	210	0.86 (0.53-2.37)	1.11 (0.59-2.10)
RA Myocardial Infarction				
Remote HCQ Users	530	1332	1.0 (reference)	1.0 (reference)
Recent HCQ users	87	220	0.98 (0.75-1.28)	1.11 (0.80-1.54)
Current HCQ users	457	1355	0.84 (0.73-0.98)	0.87 (0.73-1.05)
HCQ non-users	3117	9543	0.81 (0.73-1.17)	0.97 (0.85-1.12)
SLE Stroke/TIA				
Remote HCQ Users	47	105	1.0 (reference)	1.0 (reference)
Recent HCQ users	16	35	1.05 (0.53-2.07)	1.01 (0.45-2.28)
Current HCQ users	69	153	1.11 (0.71-1.74)	0.95 (0.55-1.62)
HCQ non-users	80	216	0.83 (0.53-1.29)	0.61 (0.36-1.04)
RA Stroke/TIA				
Remote HCQ Users	489	1369	1.0 (reference)	1.0 (reference)
Recent HCQ users	75	214	0.98 (0.74-1.30)	0.80 (0.58-1.10)
Current HCQ users	399	1248	0.82 (0.70-0.96)	0.84 (0.71-1.00)
HCQ non-users	3098	9124	0.95 (0.85-1.06)	1.01 (0.89-1.15)
SLE Venous Thromboembolism				
Remote HCQ Users	43	94	1.0 (reference)	1.0 (reference)
Recent HCQ users	14	29	1.15 (0.54-2.47)	0.84 (0.30-2.34)
Current HCQ users	55	159	0.75 (0.45-1.24)	0.67 (0.34-1.28)
HCQ non-users	80	204	0.83 (0.52-1.32)	0.89 (0.48-1.64)
RA Venous Thromboembolism				
Remote HCQ Users	278	691	1.0 (reference)	1.0 (reference)
Recent HCQ users	46	126	0.90 (0.62-1.30)	0.63 (0.41-0.99)
Current HCQ users	211	661	0.79 (0.64-0.97)	0.76 (0.59-0.98)
HCQ non-users	1395	4271	0.80 (0.68-0.93)	0.91 (0.75-1.10)

*Additionally adjusted for Charlson comorbidity index, prior CV disease, chronic kidney disease, glucocorticoid use, DMARD use, cardiovascular medication use, anticoagulant use, and healthcare utilization including number of hospitalizations and number of outpatient visits all assessed one year prior to the index date.

Exposure classifications: current use- last prescription date covered <90 days before index date; recent use- last prescription date covered 90-365 days before index date; remote use- >365 days before index date

Supplemental Table 2. Hydroxychloroquine Use and Cardiovascular Events According to Hydroxychloroquine Exposure Status Among Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis, Alternate Exposure Classification

	Cases, N	Controls, N	Conditional Odds Ratio (95% CI)	Conditional Adjusted* Odds Ratio (95% CI)
All Combined CV Events				
Remote HCQ Users	1305	3385	1.0 (reference)	1.0 (reference)
Recent HCQ users	359	857	1.09 (0.95-1.25)	0.99 (0.84-1.18)
Current HCQ users	1067	3327	0.85 (0.78-0.94)	0.85 (0.76-0.95)
HCQ non-users	7537	22500	0.87 (0.81-0.93)	0.96 (0.84-1.18)
All Myocardial Infarction				
Remote HCQ Users	480	1384	1.0 (reference)	1.0 (reference)
Recent HCQ users	135	353	0.94 (0.75-1.18)	1.03 (0.79-1.36)
Current HCQ users	566	1411	0.85 (0.74-0.98)	0.88 (0.74-1.06)
HCQ non-users	3208	9753	0.81 (0.73-0.91)	0.98 (0.85-1.12)
All Stroke/TIA				
Remote HCQ Users	536	1474	1.0 (reference)	1.0 (reference)
Recent HCQ users	121	333	0.99 (0.79-1.25)	0.82 (0.63-1.07)
Current HCQ users	405	1317	0.85 (0.73-0.99)	0.89 (0.75-1.05)
HCQ non-users	3178	9340	0.95 (0.85-1.05)	1.00 (0.88-1.13)
All Venous Thromboembolism				
Remote HCQ Users	321	785	1.0 (reference)	1.0 (reference)
Recent HCQ users	86	202	1.03 (0.77-1.37)	0.75 (0.52-1.06)
Current HCQ users	240	773	0.75 (0.61-0.91)	0.73 (0.57-0.92)
HCQ non-users	1475	4475	0.80 (0.77-1.37)	0.90 (0.75-1.08)

*Additionally adjusted for Charlson comorbidity index, prior CV disease, chronic kidney disease, glucocorticoid use, DMARD use, cardiovascular medication use, anticoagulant use, and healthcare utilization including number of hospitalizations and number of outpatient visits all assessed one year prior to the index date.

CV, cardiovascular; HCQ, hydroxychloroquine; TIA, transient ischemic attack

Exposure classifications: current use- last prescription date covered <30 days before index date; recent use- last prescription date covered 30-365 days before index date; remote use- >365 days before index date

Supplemental Table 3. Hydroxychloroquine Use and Cardiovascular Events According to Hydroxychloroquine Exposure Status Among Patients with Systemic Lupus Erythematosus and Rheumatoid Arthritis: Stratified Analysis by Duration of Hydroxychloroquine Use

All Combined CV Events	Cases, N	Controls, N	Conditional Odds Ratio (95% CI)	Conditional Adjusted* Odds Ratio (95% CI)
Duration of HCQ Use <1 Year				
Remote HCQ Users	733	1816	1.0 (reference)	1.0 (reference)
Recent HCQ users	90	226	0.96 (0.73, 1.26)	0.94 (0.71, 1.24)
Current HCQ users	213	569	0.91 (0.75, 1.10)	0.85 (0.70, 1.04)
HCQ non-users	7537	22500	0.83 (0.75, 0.91)	0.92 (0.84, 1.02)
Duration of HCQ Use ≥ 1 Year				
Remote HCQ Users	150	572	1.0 (reference)	1.0 (reference)
Recent HCQ users	154	409	1.04 (0.84, 1.29)	1.00 (0.80, 1.25)
Current HCQ users	969	2880	0.92 (0.81, 1.04)	0.83 (0.73, 0.94)
HCQ non-users	7537	22500	0.91 (0.82, 1.01)	1.01 (0.91, 1.12)

*Additionally adjusted for Charlson comorbidity index, prior CV disease, chronic kidney disease, glucocorticoid use, DMARD use, cardiovascular medication use, anticoagulant use, and healthcare utilization including number of hospitalizations and number of outpatient visits all assessed one year prior to the index date.

CV, cardiovascular; HCQ, hydroxychloroquine; TIA, transient ischemic attack

Exposure classifications: current use- last prescription date covered <90 days before index date; recent use- last prescription date covered 90-365 days before index date; remote use- >365 days before index date