

Table 3. GRADE evidence profile, Recommendation 3

Question: Hydroxychloroquine compared to no hydroxychloroquine for post-exposure prophylaxis of COVID-19

New evidence profile developed 9/23/2021

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	hydroxychloroquine	no hydroxychloroquine	Relative (95% CI)	Absolute (95% CI)		
Symptomatic SARS-CoV-2 infection (follow up: 14 days) ^a												
3 ^{1,2,3}	randomized trials	not serious	not serious	not serious	serious ^b	none	166/1883 (8.8%)	177/1941 (9.1%)	RR 0.95 (0.77 to 1.16)	5 fewer per 1,000 (from 21 fewer to 15 more)	⊕⊕⊕○ MODERATE	CRITICAL
Hospitalization (follow up: 14 days)												
3 ^{1,2,3}	randomized trials	not serious	not serious	not serious	very serious ^b	none	13/2018 (0.6%)	14/2129 (0.7%)	RR 1.00 (0.47 to 2.12)	0 fewer per 1,000 (from 3 fewer to 7 more)	⊕⊕○○ LOW	CRITICAL
Mortality (follow up: 14 days)												
3 ^{1,2,3}	randomized trials	not serious	not serious	not serious	very serious ^b	none	5/2018 (0.2%)	12/2129 (0.6%)	RR 0.45 (0.16 to 1.28)	3 fewer per 1,000 (from 5 fewer to 2 more)	⊕⊕○○ LOW	CRITICAL
Serious adverse events (follow up: 14 days)												
3 ^{1,2,3}	randomized trials	not serious	not serious	not serious	very serious ^b	none	16/2018 (0.8%)	19/2129 (0.9%)	RR 0.91 (0.47 to 1.76)	1 fewer per 1,000 (from 5 fewer to 7 more)	⊕⊕○○ LOW	CRITICAL
GRADE Working Group grades of evidence												
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect												
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different												
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect												
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect												

Risk of bias: Study limitations

Inconsistency: Unexplained heterogeneity across study findings

Indirectness: Applicability or generalizability to the research question

Imprecision: The confidence in the estimate of an effect to support a particular decision

Publication bias: Selective publication of studies

CI: Confidence interval; **RR:** Risk ratio

Explanations

- a. Boulware included both laboratory-confirmed COVID-19 as well as probable COVID-19; 11/49 patients receiving HCQ were laboratory confirmed and 9/58 receiving placebo were laboratory confirmed .
- b. The 95% CI includes both the potential of benefit and the risk of harm.

References

1. Barnabas RV, Brown ER, Bershteyn A, et al. Hydroxychloroquine as Postexposure Prophylaxis to Prevent Severe Acute Respiratory Syndrome Coronavirus 2 Infection : A Randomized Trial. *Ann Intern Med* **2021**; 174(3): 344-52.
2. Boulware DR, Pullen MF, Bangdiwala AS, et al. A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19. *N Engl J Med* **2020**; 383(6): 517-25.
3. Mitja O, Corbacho-Monne M, Ubals M, et al. A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19. *N Engl J Med* **2021**; 384(5): 417-27.