

## Supplemental file

### Supplemental Methods: PubMed Search Strategy

**Figure S1:** Flowchart of study selection

**Figure S2:** Risk of bias assessment of five randomized controlled trials

**Figure S3:** Detailed risk of bias assessment per randomized controlled trial

**Figure S4:** Effect of prophylaxis with hydroxychloroquine on clinical worsening

**Figure S5:** Effect of prophylaxis with hydroxychloroquine on severe adverse events

**Figure S6:** Effect of prophylaxis with hydroxychloroquine on adverse events

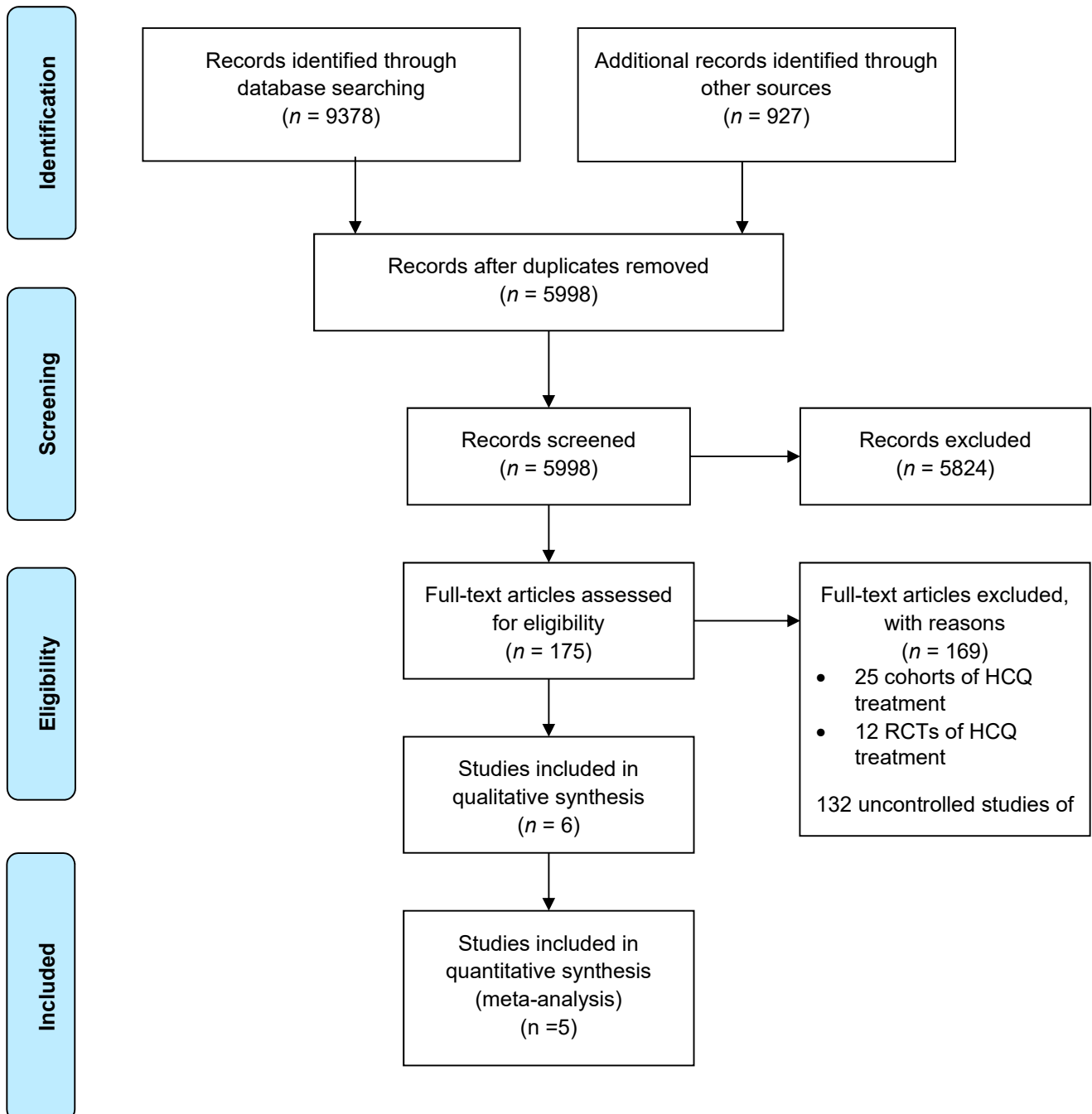
**Figure S7:** Effect of prophylaxis with hydroxychloroquine on diarrhea, abdominal pain or vomiting.

**Figure S8:** Effect of prophylaxis with hydroxychloroquine on headache

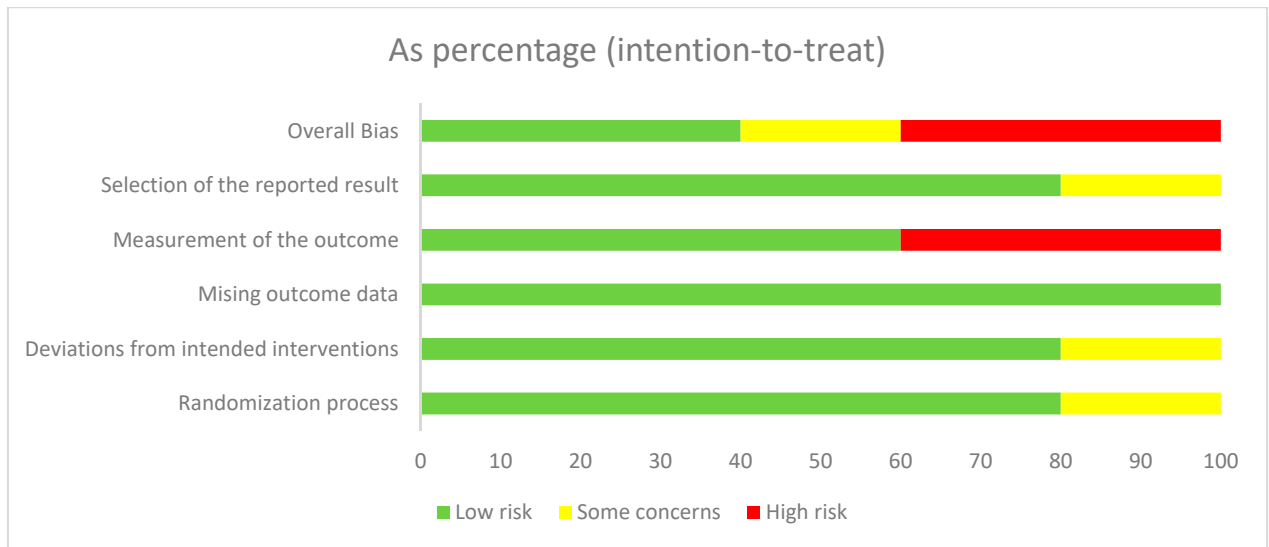
### Supplemental Methods: PubMed Search strategy

("hydroxychloroquine"[MeSH Terms] OR "hydroxychloroquine"[All Fields] OR ("chloroquin"[All Fields] OR "chloroquine"[MeSH Terms] OR "chloroquine"[All Fields] OR "chloroquine s"[All Fields] OR "chloroquines"[All Fields])) AND ("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR "covid 19"[All Fields] OR "sars cov 2"[All Fields] OR ("coronavirus"[All Fields] OR "cov"[All Fields])) AND 2019/11/01:3000/12/31[Date - Publication]) OR ("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "sars cov 2"[All Fields]))

**Figure S1.** Flowchart of study selection.



**Figure S2.** Risk of bias assessment of five randomized controlled trials.



**Figure S3.** Detailed risk of bias assessment per randomized controlled trial.

Study ID	Experimental	Comparator	Outcome	Weight	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall	
1 Boulware	HCQ	Placebo folate	Incidence of confirmed or probable Covid-19 at 14 days	1	+	+	+	N	+	N	+
2 Rajasingham	HCQ twice weekly	Placebo folic acid	Confirmed or probable Covid-19 at 12w	1	+	+	+	N	?	N	?
3 Abella	HCQ	Placebo	Incidence of lab confirmed SARS-CoV-2 infection at 8w	1	?	?	+	+	+	!	
4 Mitja	HCQ	Usual care	PCR-confirmed symptomatic Covid-19 within 14 days	1	+	+	+	+	+	+	+
5 Barnabas	HCQ	Placebo ascorbic acid	SARS-CoV-2 infection at 14 days	1	+	+	+	+	+	+	+

Legend:

- Low risk: + (Green)
- Some concerns: ? (Yellow)
- High risk: N (Red)

Figure S4. Effect of prophylaxis with hydroxychloroquine on clinical worsening.

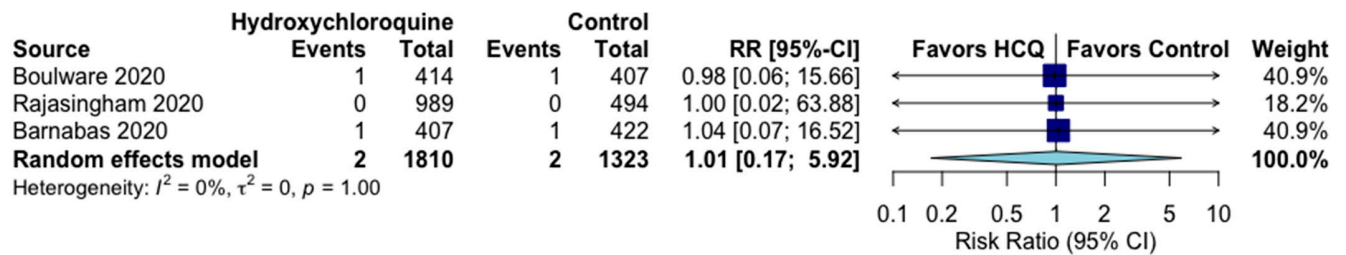


Figure S5. Effect of prophylaxis with hydroxychloroquine on severe adverse events.

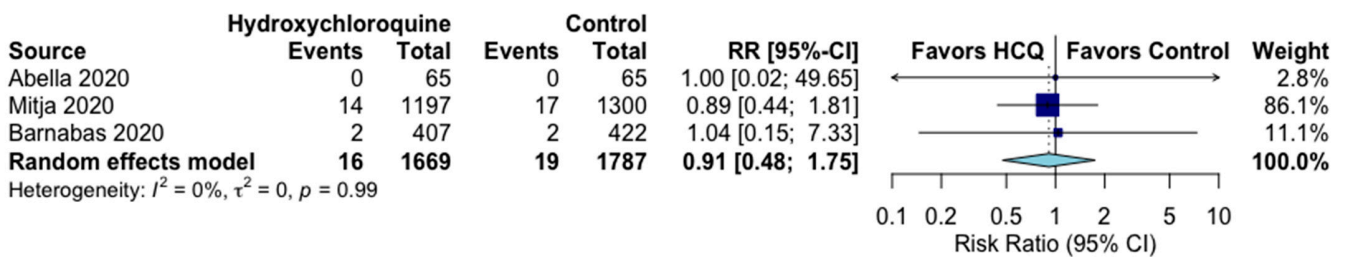


Figure S6. Effect of prophylaxis with hydroxychloroquine on adverse events.

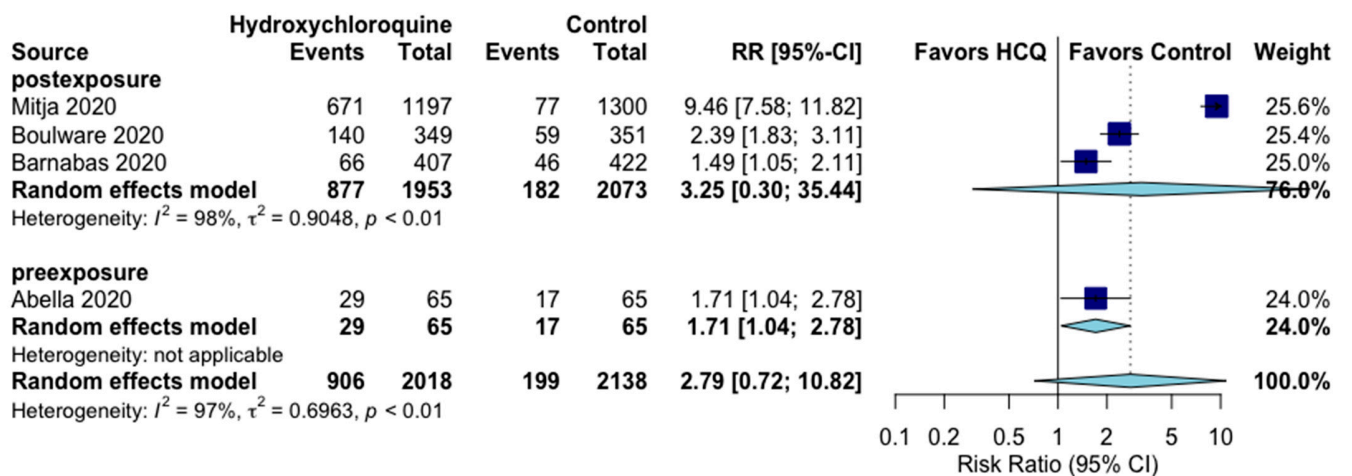


Figure S7. Effect of prophylaxis with hydroxychloroquine on diarrhea, abdominal pain or vomiting.

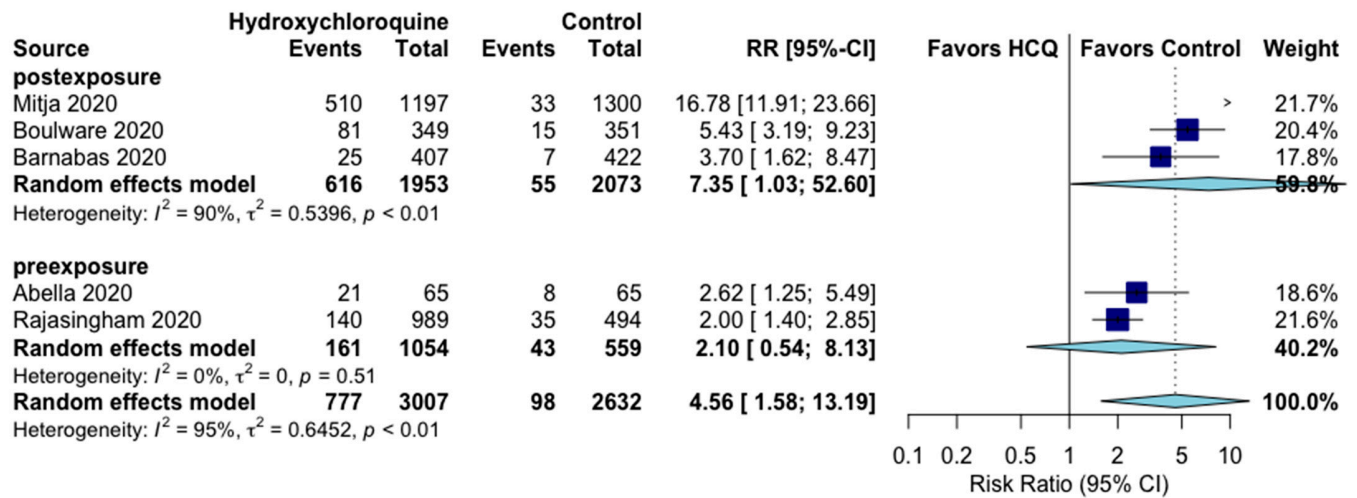
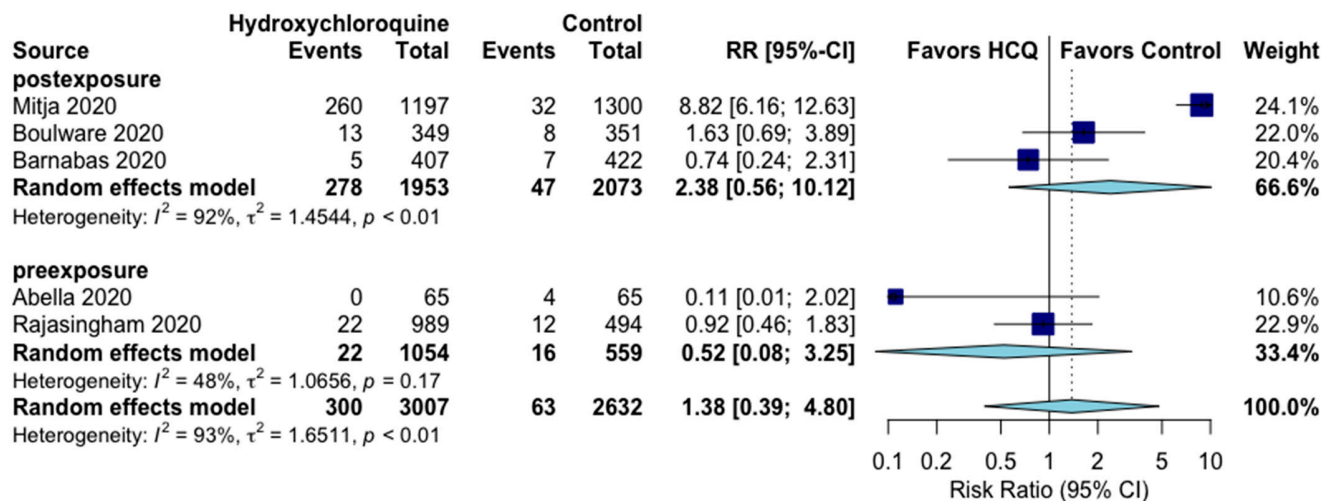


Figure S8. Effect of prophylaxis with hydroxychloroquine on headache.



PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
<b>TITLE</b>			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
<b>ABSTRACT</b>			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
<b>INTRODUCTION</b>			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1,2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
<b>METHODS</b>			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	–
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2, Supplemental file
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$ ) for each meta-analysis.	3

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	3
<b>RESULTS</b>			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	3; Figure S1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6; Figures S3, S4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6-8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6-8; Figures
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6, 8, Table 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	8
<b>DISCUSSION</b>			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-13

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12,13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
<b>FUNDING</b>			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	13