

UPDATE ALERT

Update Alert 2: Hydroxychloroquine or Chloroquine for the Treatment or Prophylaxis of COVID-19

This report, the second update of a previously published living systematic review (1), focuses on treatment (not prophylaxis) of coronavirus disease 2019 (COVID-19) with hydroxychloroquine or chloroquine. The first update covered evidence available through 1 July 2020 (2); this update evaluates evidence published through 1 August 2020.

No new evidence regarding chloroquine was found. Five new randomized trials (3-7) and 4 new cohort studies (7-10) evaluating hydroxychloroquine were found. None of the studies used zinc; all studies (4-10) except for 1 trial (3) with a hydroxychloroquine group and an azithromycin group evaluated hydroxychloroquine alone. One trial was placebo controlled (5); other studies used "standard care" control groups (3, 4, 6-10). Two (3, 5) of the trials had high risk of bias, whereas 3 trials (4, 6, 7) had some concerns of bias. Three (7, 9, 10) of the cohort studies had critical risks of bias, whereas 1 cohort study (8) had serious risk of bias.

The Supplement Table displays the following for outcomes of all identified trials (3-7, 11, 12, 26, 27) and cohort studies (7-10, 13-25, 28) that addressed treatment with hydroxychloroquine: risk-of-bias assessments, unadjusted estimates of effect, and overall ratings of strength of evidence. Although the strength of evidence was previously rated insufficient regarding effects on mortality, there is now low strength of evidence from trials and cohort studies that hydroxychloroquine has no positive effect on all-cause mortality and need for mechanical ventilation. Trials show low strength of evidence for no positive effect on intubation or death and discharge from the hospital, whereas evidence from cohort studies about these outcomes remains insufficient. Newer trials and cohort studies did not alter the findings for other outcomes that the data are insufficiently strong to support a treatment benefit of hydroxychloroquine.

Of note, 2 of the new trials and 1 cohort study assessed the early prehospitalization administration of hydroxychloroquine in patients with COVID-19; none demonstrated benefits or reductions in hospitalizations (4, 5, 10). The largest trial—the RECOVERY trial (6)—used a much larger dose of hydroxychloroquine (loading dose of 800 mg at 0 and 6 hours, 400 mg at 12 hours; maintenance dose of 400 mg every 12 hours for 9 days or until discharge) than other trials and found no benefits from therapy. Finally, the large SOLIDARITY-WHO and ORCHID-NIH trials have been prematurely discontinued, with press releases citing lack of efficacy (29, 30), but preprints or publications of these trials are still not available.

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