

A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for COVID-19 In *New England Journal of Medicine* [pdf](#)

Commentary by [Divya Reddy, MBBS, MPH](#), Assistant Professor of Medicine (Pulmonary) and Associate Program Director (Pulmonary and Critical Care Fellowship)



Public health measures to mitigate the ongoing COVID-19 pandemic will need to include pharmacological interventions and vaccines in addition to social distancing, hand hygiene, rapid case identification, and isolation. Chloroquine and Hydroxychloroquine (HCQ) have both shown in vitro activity against SAR-CoV-2; the latter proving to be more efficacious¹. These have been endorsed as possible prophylactic and treatment agents for COVID-19 but conclusive data are lacking.

Boulware² et al report the results of a randomized, double-blind, placebo-controlled clinical trial assessing the preventive role of HCQ (5 day course initiated within 4 days of exposure) among healthy individuals post COVID-19 exposure. Of the 821 participants recruited into the study, the majority, 545 (66%) were healthcare workers and 245 (30%) were household contacts. The incidence of COVID-19 infections (clinical or RT-PCR-proven diagnosis) was not significantly different between the HCQ (49/414, 12%) and the placebo (58/407, 14%) arm. Moreover, participants in the HCQ arm were more likely to develop adverse effects (mild gastrointestinal symptoms) and discontinue the treatment compared to the placebo arm.

The study is a pragmatic study providing time-sensitive and valuable information in the midst of a global pandemic. However, it has several limitations, which were acknowledged by the authors. Participants exposed to COVID-19 patients were recruited mainly via social media outreach. While this resulted in rapid enrollment across United States and Canada, the subjects were younger and healthier, making the findings less generalizable. It also resulted in a delay in initiating HCQ, questioning whether the study assessed its post-exposure or treatment efficacy. Exposure and outcome data were self-reported and prone to significant bias. At the time of the study, due to poor access to lab testing, only 16/109 (15%) of the incident COVID-19 infections among those exposed were RT-PCR proven and the majority (93/109, 85%) were diagnosed based on non-specific clinical symptoms and unvalidated case definitions. This study also does not address asymptomatic COVID-19 infections, which appear to play a significant role in aiding widespread transmission.

In summary, this study shows that HCQ may not be beneficial in reducing the incidence of COVID-19 symptoms in subjects exposed to COVID-19. Its role in pre- and post-exposure prophylaxis, however, still remains unclear.

¹ Yao X., Ye F., Zhang M. et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome

Coronavirus 2 (SARS-CoV-2) Clin Infect Dis. 2020:ciaa237. doi: 10.1093/cid/ciaa237.

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 DOI: 10.1056/NEJMoa2016638.