

## General context: vocabulary for the query

### Chloroquine and hydroxychloroquine during the COVID-19 pandemic

[https://en.wikipedia.org/wiki/Chloroquine\\_and\\_hydroxychloroquine\\_during\\_the\\_COVID-19\\_pandemic](https://en.wikipedia.org/wiki/Chloroquine_and_hydroxychloroquine_during_the_COVID-19_pandemic)

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[Chloroquine](#) and [hydroxychloroquine](#) are [anti-malarial](#) medications also used against some [auto-immune](#) diseases.<sup>[1]</sup> Chloroquine, along with hydroxychloroquine, was an early failed experimental treatment for [COVID-19](#).<sup>[2]</sup> They are not effective for preventing infection.<sup>[3][4][5][6][7]</sup>

Several countries initially used chloroquine or hydroxychloroquine for treatment of persons hospitalized with COVID-19 (as of March 2020), though the drug was not formally approved through clinical trials.<sup>[8][9]</sup> From April to June 2020, there was an [emergency use authorization](#) for their use in the United States,<sup>[10]</sup> and was used [off label](#) for potential treatment of the disease.<sup>[11]</sup> On 24 April 2020, citing the risk of "serious heart rhythm problems", the FDA posted a caution against using the drug for COVID-19 "outside of the hospital setting or a clinical trial".<sup>[12]</sup>

Their use was withdrawn as a possible treatment for COVID-19 infection when it proved to have no benefit for hospitalized patients with severe COVID-19 illness in the international [Solidarity trial](#) and UK [RECOVERY Trial](#).<sup>[13][14]</sup> On 15 June, the FDA revoked its emergency use authorization, stating that it was "no longer reasonable to believe" that the drug was effective against COVID-19 or that its benefits outweighed "known and potential risks".<sup>[15][16][17]</sup> In fall of 2020, the [National Institutes of Health](#) issued treatment guidelines recommending against the use of hydroxychloroquine for COVID-19 except as part of a [clinical trial](#).<sup>[1]</sup>

#### Background

[Chloroquine](#) is an [anti-malarial](#) medication that is also used against some [auto-immune](#) diseases. Hydroxychloroquine is more commonly available than chloroquine in the United States.<sup>[8]</sup> Hydroxychloroquine is used as a [prophylactic](#) in India.<sup>[18][19]</sup>

Hydroxychloroquine and chloroquine have numerous, potentially serious, [side effects](#), such as [retinopathy](#), [hypoglycemia](#), or life-threatening [arrhythmia](#) and [cardiomyopathy](#).<sup>[20]</sup> Both drugs have [extensive interactions](#) with prescription drugs, affecting the therapeutic dose and disease mitigation.<sup>[20][21]</sup> Some people have [allergic reactions](#) to these drugs.<sup>[20][21]</sup> The NIH recommended against the use of a combination of hydroxychloroquine and azithromycin because of the resulting increased risk of sudden cardiac death.<sup>[22]</sup>

## Timeline

Chloroquine was initially recommended by Indian, Chinese, South Korean and Italian health authorities for the treatment of COVID-19,<sup>[23]</sup> although these agencies and the US CDC noted [contraindications](#) for people with [heart disease](#) or [diabetes](#).<sup>[8][24]</sup> In February 2020, both drugs were shown to effectively reduce COVID-19 illness, but a further study concluded that hydroxychloroquine was more potent than chloroquine and had a more tolerable safety profile.<sup>[25][26]</sup>

On 18 March, the [World Health Organization](#) (WHO) announced that chloroquine and the related [hydroxychloroquine](#) would be among the four drugs studied as part of the multinational [Solidarity clinical trial](#).<sup>[27]</sup>

On 19 March, US President [Donald Trump](#) encouraged the use of chloroquine and hydroxychloroquine during a national press conference. These endorsements led to massive increases in public demand for the drugs in the United States.<sup>[28]</sup> Beginning in March 2020, Trump began promoting hydroxychloroquine to prevent or treat [COVID-19](#), citing small numbers of [anecdotal reports](#).<sup>[29]</sup> Trump stated in June that he was taking the drug as a preventive measure,<sup>[16]</sup> stimulating unprecedented worldwide demand and causing shortages of hydroxychloroquine for its prescribed purpose of preventing [malaria](#).<sup>[29]</sup>

[...]

On 28 March 2020, the FDA authorized the use of [hydroxychloroquine](#) and chloroquine under an [emergency use authorization](#) (EUA).<sup>[2]</sup> The experimental treatment was first authorized only for emergency use for people hospitalized but unable to receive treatment in a clinical trial.<sup>[32]</sup>

On 1 April 2020, the [European Medicines Agency](#) (EMA) issued guidance that chloroquine and hydroxychloroquine are only to be used in clinical trials or emergency use programs.<sup>[35]</sup>

[...]

On 5 June, use of hydroxychloroquine in the UK [RECOVERY Trial](#) was discontinued when an interim analysis of 1,542 treatments showed it provided no mortality benefit to people hospitalized with severe COVID-19 infection over 28 days of observation.<sup>[14]</sup>

On 15 June, the FDA revoked the emergency use authorization for hydroxychloroquine and chloroquine, stating that although the evaluation of both these drugs under clinical trials continues, the FDA (after interagency consultation with the [Biomedical Advanced Research and Development Authority](#) (BARDA)) concluded that, based on new information and other information discussed "... it is no longer reasonable to believe that oral formulations of **hydroxychloroquine (HCQ) and chloroquine (CQ)** may be effective in treating COVID-19, nor is it reasonable to believe that the known and potential benefits of these products outweigh their known and potential risks".<sup>[15][42][43][17]</sup>

[...]

In November 2020, a U.S. National Institutes of Health clinical trial evaluating the safety and effectiveness of hydroxychloroquine for the treatment of adults with COVID-19 formally

concluded that the drug provided no clinical benefit for COVID-19 treatment and recommended against its use.<sup>[46][47][1]</sup>

## WHO trial

Due to safety concerns and evidence of [heart arrhythmias](#) leading to higher death rates, the WHO suspended the hydroxychloroquine arm of the multinational [Solidarity trial](#) in May 2020.<sup>[59][60][61]</sup> The WHO had enrolled 3,500 patients from 17 countries in the Solidarity trial.<sup>[59]</sup> The research surrounding this suspension, provided by a company called [Surgisphere](#) based in [Chicago](#), came into question due to errors in the underlying data set.<sup>[62][63][64]</sup> The authors of the study corrected errors in the data later but initially remained firm on their conclusions.<sup>[62]</sup> **Subsequently, a retraction of the study by three of its authors was published by *The Lancet* on 4 June, 2020.**<sup>[65]</sup> The authors stated that their reason behind the retraction was because Surgisphere had failed to cooperate with an independent review of the data used for the study by not allowing any such review to take place.<sup>[66][67]</sup>

The WHO decided to resume the trial on 3 June, after reviewing the safety concerns which had been raised. Speaking at a press briefing, WHO's director-general, [Tedros Adhanom Ghebreyesus](#) stated that the board had reviewed the available mortality data and had found "no reasons to modify the trial".<sup>[68][69]</sup>

On 4 July, the WHO discontinued the hydroxychloroquine trial based on evidence presented at the July WHO Summit on COVID-19 research and innovation. The WHO stated that "These interim trial results show that hydroxychloroquine and lopinavir/ritonavir produce little or no reduction in the mortality of hospitalized COVID-19 patients when compared to standard of care."<sup>[70]</sup>

**[65]Mehra MR, Ruschitzka F, Patel AN (June 2020). "Retraction-Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis". *Lancet*. 395 (10240): 1820. doi:10.1016/S0140-6736(20)31324-6. PMC 7274621. PMID 32511943.**

## Keywords selection

1. Chloroquine
2. Chloroquinine
3. Hydroxychloroquine

The chemical formula has been tried, but was not present in the articles without mentioning one of the three terms above.

Two acronyms are used, mostly added in parenthesis:

- HCQ for Hydroxychloroquine
- QC for Chloroquine