

Support for steroid use in severe cases

- A meta-analysis of 8 studies with 4,051 patients
 - Evaluated steroids use in patients with coronavirus infections.
 - 3,416 had dx with SARS, 360 patients with MERS, and 275 with COVID-19;
 - 60% patients were administered steroids.
 - Meta-analyses no differences overall in terms of mortality (OR=1.15; 95% CI 0.63-2.10).
 - Some studies the steroid group had more severe symptoms than those in the control group.
 - When the meta-analysis was performed restricting only to studies that used appropriate adjustment (e.g., time, disease severity), use of steroids was associated with a lower risk of mortality (HR=0.38; 95% CI 0.22-0.65).
 - Lee et al. (July 2020). Efficacy of Corticosteroids in Patients with SARS, MERS and COVID-19: A Systematic Review and Meta-Analysis. Journal of Clinical Medicine. <https://doi.org/10.3390/jcm9082392>

Interferon -Timing is everything

- Retrospective cohort study of COVID-19 patients in Hubei, China (n=446),
- Early administration of interferon-a2b was associated with lower likelihood of in-hospital mortality versus no interferon
 - OR=0.05, 95% CI: 0.01-0.37,
- Late interferon therapy was associated with greater likelihood of mortality OR=6.82, 95% CI: 1.14-40.8.
- Most of the patients in also received the antiviral agents umifenovir or lopinavir boosted with ritonavir.
- Wang et al. (July 18, 2020). Retrospective Multicenter Cohort Study Shows Early Interferon Therapy Is Associated with Favorable Clinical Responses in COVID-19 Patients. Cell Host & Microbe.
<https://doi.org/10.1016/j.chom.2020.07.005>

FDA Vaccine Approval Criteria-June 30th

- FDA Commissioner Stephen Hahn, MD, on vaccine approval criteria
- Prevent or lessen severity in at least 50 percent of people who receive it.
- Post development safety & monitoring monitoring system in place post approval
- Clinical trial participants are expected to be diverse in race and age.
 - Disease hitting minorities and elderly hardest
- Agency may do temporary approvals on a case-by-case basis.

Vaccine Distribution and Cost

- Currently there is not a COVID 19 vaccine approved by FDA
 - Over 170 vaccines are in development
 - Phase 3 clinical trials are starting
 - Require 30,000+ may take 3-6 months, difficulty recruiting minority participants
 - Human challenge trials
 - Require <200 can deliver results in 4-6 weeks
- New York Post Poll Refusal Rates n=7,632
 - 35% of Americans
 - 41% of minorities; 30% of Senior Citizens; 24% aged 18-29
 - Democrats- 19% vs Republicans- 53%; independents- 41%
- Moderna- Perceived vaccine leader \$32-\$37/dose
- Gates Foundation partnering with Serum Institute of India \$3/dose

ACE Vs ARB

- BMJ July 2020
- Meta Analysis- 10 studies N= 9890
- ACE/ARB or both vs Naïve patients
- Risk of severe disease/death-0.9 ACE
0.92-ARB
- Authors suggest that ACE/ARB treatment beneficial in COVID cases and should be continued unless clinically contraindicated



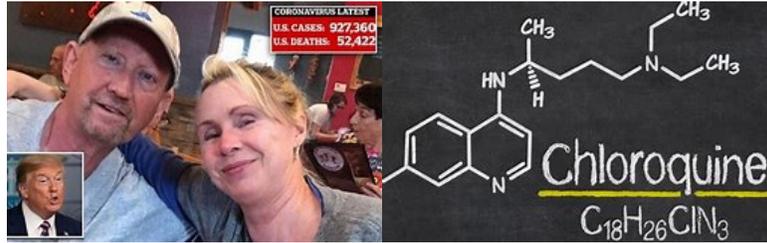
Live Vaccine may lessen COVID sx review

- <https://mbio.asm.org/content/11/3/e00907-20>
- Same theory as BCG vaccination
 - Live vaccines temporarily provide temporary change to bone marrow to create leukocytes that are more active against acute infectious events.
 - 6 ongoing trials in Europe looking at BCG
 - Trial in USA will use MMR- New Orleans HCW & 1st Responders are subjects
- Rationale:
 - Children milder COVID infections—most have received MMR/varicella
 - USS Roosevelt 955 sailors with mild symptoms had recent MMR
- Not a COVID cure, but a booster to lessen disease severity until effective COVID-19 vaccines are available

Hydroxychloroquine, a
tale as mysterious as JR
Ewing's demise!



March



- **March 20** — [Anti-malaria drug touted as COVID-19 'game changer' already in short supply](#)
After President Donald Trump says hydroxychloroquine and chloroquine are possible treatments for COVID-19 during his daily televised news briefings, demand skyrockets, and the drugs quickly go into shortage.
- **March 23** — [Physicians found hoarding experimental COVID-19 treatments for relatives](#)
Ohio's pharmacy board blocks pharmacists from dispensing hydroxychloroquine and chloroquine unless a person has tested positive for the virus.
- **March 24** — [Man dies after ingesting fish tank cleaner containing chloroquine for COVID-19](#)
A man in Arizona dies after ingesting a non-medication form of chloroquine phosphate in an attempt to prevent himself from contracting COVID-19.
- **March 26** — [India bans exports of potential COVID-19 drug](#)
India bans exports of hydroxychloroquine to ensure the country has its own stable supply of the drug.
- **March 28** — [FDA issues emergency use authorization](#)
The FDA grants emergency use authorization to allow patients with COVID-19 to be treated with hydroxychloroquine and chloroquine.

April

- **April 6** — [20 states try to stop hoarding of potential COVID-19 treatments](#)

At least 20 states across the U.S. take measures to prevent hoarding of hydroxychloroquine and chloroquine after both drugs are listed on the FDA's drug shortage list.

- **April 7** — [India lifts ban on hydroxychloroquine exports](#)

India lifts its export ban on hydroxychloroquine after President Donald Trump threatens retaliation against the country.

- **April 9** — [CDC deletes advice on front-running COVID-19 drugs from website](#)

The CDC deletes most of its guidelines for hydroxychloroquine and chloroquine from its website. The agency previously had a section on its website detailing how some U.S. healthcare providers have used hydroxychloroquine for COVID-19 patients and how the drug was "reportedly well-tolerated."

April

- **April 10** — [Physicians cast doubt on drug touted as COVID-19 game changer](#)

Some physicians on the front lines of the COVID-19 pandemic express concern that using hydroxychloroquine could do more harm than good.

- **April 13** — [Chloroquine study halted after patients develop heart complications](#)

A small study in Brazil testing the effectiveness of chloroquine in treating COVID-19 patients ends after patients taking a higher dose of the drug develop irregular heart rates.

- **April 21** — [Novartis to test malaria drug in 440 hospitalized COVID-19 patients](#)

Novartis says it plans to conduct a 440-person clinical trial to determine the effectiveness of hydroxychloroquine against COVID-19.

- **April 22** — [Largest hydroxychloroquine study to date finds no benefit for COVID-19](#)

Hydroxychloroquine shows no benefit for patients hospitalized with COVID-19 in a study conducted by the Veterans Health Administration.

April- more bad news

- **April 24** — [FDA warns against hydroxychloroquine use outside of hospital settings](#)
The FDA issues a warning against using hydroxychloroquine outside of a hospital setting or clinical trial due to the risk of serious heart problems.
- **April 27** — [Despite FDA warning, states stockpiling potential COVID-19 treatment](#)
States and local governments stockpiling hydroxychloroquine have obtained about 30 million doses of it.
- **April 29** — [Demand for malaria drug to treat COVID-19 falls amid warnings of serious side effects](#)
Demand for hydroxychloroquine falls significantly as hospitals become more wary of using the drug after more public health officials warn of serious side effects.
 - Internet searches jump 1300% higher

May- HCQ falls on its own sword

- **May 5:** Rick Bright, PhD, former director of an HHS agency at the center of the government's coronavirus pandemic response, [filed a whistleblower complaint](#) claiming he was fired after he resisted a push from HHS officials for widespread hydroxychloroquine use because claims of its benefits lacked "scientific merit."
- **May 7:** A study [became available](#) in the *The New England Journal of Medicine* showing COVID-19 patients who were treated with hydroxychloroquine did not experience lower risk of death compared to coronavirus patients who received other treatments.
- **May 18:** President Donald Trump [announced](#) he was taking hydroxychloroquine as a preventive measure against COVID-19, after the FDA's late April safety warnings that hydroxychloroquine could cause serious heart rhythm problems and should not be taken for COVID-19 outside of clinical trials or hospitals.
- **May 25:** The World Health Organization [announced the temporary discontinuation](#) of its global study testing the effectiveness of hydroxychloroquine as a COVID-19 treatment. The decision came after *The Lancet* published a study May 22 claiming COVID-19 patients who received hydroxychloroquine experienced a significantly higher risk of dying than those who didn't receive it.

May- Cleaning HQC house?

- **May 27:** Anthony Fauci, MD, the nation's top infectious disease physician, [reported a lack of confidence](#) in hydroxychloroquine's ability to treat COVID-19 during a *CNN* interview. "The scientific data is really quite evident now about the lack of efficacy for it," Dr. Fauci said.
- **May 28:** Research published in *The Lancet* [showed](#) that cancer patients with COVID-19 who received hydroxychloroquine and azithromycin experienced a risk of death 2.89 times greater within 30 days than those who did not receive the drugs.
- **June 2:** Richard Horton, editor of *The Lancet*, [tweeted about the validity](#) of the study the medical journal published May 22 claiming a higher risk of death for patients who received hydroxychloroquine. "Serious questions have been raised about the reliability of the findings reported in this paper," he said.
- **June 3:** The World Health Organization [announced the resumption](#) of its international trial analyzing the effectiveness of hydroxychloroquine in treating COVID-19 during a news conference held at WHO headquarters in Geneva.
- On the same day, the Minneapolis-based University of Minnesota Medical School [released a study](#) claiming hydroxychloroquine is no more effective than a vitamin placebo in preventing COVID-19 in individuals who have been exposed to the disease.

June- THE HQC purge

- **June 2:** Tucson, Ariz.-based Association of American Physicians and Surgeons [sued HHS](#) for preventing physicians from prescribing hydroxychloroquine as a COVID-19 preventative.
- **June 4:** *The Lancet* [retracted the study](#) it published May 22 that claimed hydroxychloroquine was linked to higher mortality rates in COVID-19 patients.
- On the same day, *The New England Journal of Medicine* retracted a separate study showing that blood pressure medications were safe to take for COVID-19 patients. Both studies used data from analytics company Surgispher, which refused to share its raw data with study authors or a third-party auditor after questions about its accuracy arose.
- **June 5:** A U.K.-based, non-peer-reviewed study [showed no significant difference](#) in the death rate at 28 days between COVID-19 patients who received the drug and those who did not.
- On the same day, Salt Lake City-based University of Utah [terminated its faculty appointment](#) of Amit Patel, MD, who co-authored the two medical papers on hydroxychloroquine that had been recently retracted by *The Lancet* and *The New England Journal of Medicine*.

June- Camps at both extremes emerge

- **June 15:** The FDA [wrote a letter](#) to withdraw its emergency use authorizations for hydroxychloroquine and related drug chloroquine.
- **June 17:** WHO [announced it had pulled hydroxychloroquine](#) from its global study assessing possible treatments for COVID-19.
- **June 19:** Novartis [announced that it discontinued](#) its hydroxychloroquine trial, as the drugmaker was unable to collect meaningful data in a reasonable time frame to determine the effectiveness of the drug in treating COVID-19 patients due to slow enrollment.
- **June 20:** The National Institutes of Health [stopped its hydroxychloroquine trial](#) that was taking place at the Nashville, Tenn.-based Vanderbilt University Medical Center.
- **July 2:** *The International Journal of Infectious Diseases* [published a study](#) conducted by researchers at Detroit-based Henry Ford Health System that claimed COVID-19 patients who received a small dose of hydroxychloroquine within the first two days of their hospital stay were more likely to survive.

July so you are saying there's a chance?



- **July 8:** *STAT* [published an article](#) highlighting the viewpoint of many clinical experts quick to point out the flaws in Henry Ford Health System's study.
 - **July 29:** Vizient's July 2020 Drug Price Forecast [revealed](#) that hydroxychloroquine saw a 1,132 percent increase in spend during March and April.
 - On the same day, Ohio's board of pharmacy [prohibited pharmacists](#) from dispensing or selling hydroxychloroquine to treat COVID-19.
 - **July 30:** After a request from Ohio Gov. Mike DeWine, the state's board of pharmacy [reversed its ban](#) on hydroxychloroquine for use in COVID-19 patients and said it will reexamine the issue.
- Aug. 3:** Two Henry Ford Health System executives [wrote in an open letter](#) that the persisting political climate has made any objective discussion about hydroxychloroquine "impossible."

Live Vaccine follow up

- <https://mbio.asm.org/content/11/3/e00907-20>
- Same theory as BCG vaccination
 - Live vaccines temporarily provide temporary change to bone marrow to create leukocytes that are more active against acute infectious events.
 - 6 ongoing trials in Europe looking at BCG
 - Trial in USA will use MMR- New Orleans HCW & 1st Responders are subjects
- Rationale:
 - Children milder COVID infections—most have received MMR/varicella
 - USS Roosevelt 955 sailors with mild symptoms had recent MMR
- Not a COVID cure, but a booster to lessen disease severity until effective COVID-19 vaccines are available