# Evidence Search Service Results of your search request

## Does hydroxychloroquine work in COVID-19 patients?

**ID of request:** 22630  
**Date of request:** 7th April, 2020  
**Date of completion:** 16th April, 2020

If you would like to request any articles or any further help, please contact:  Preeti Puligari at [preeti.puligari1@nhs.net](mailto:preeti.puligari1@nhs.net)

Please acknowledge this work in any resulting paper or presentation as: Evidence search: Does hydroxychloroquine work in COVID-19 patients?. Preeti Puligari. (16th April, 2020). WEST BROMWICH, UK: Sandwell and West Birmingham Hospitals Library Service.

**Sources searched**  
CEBM: Oxford COVID-19 Evidence Service (2)  
Centres for Disease Control and Prevention (1)  
Contagion Live (1)  
Department of Psychiatry, Warneford Hospital, Oxford (1)  
EMBASE (19)  
International Journal of Antimicrobial Agents (1)  
Lancet (1)  
MEDLINE (7)  
Medicines and Healthcare products Regulatory Agency (MHRA) (1)  
MedxRxiv (1)  
New England Journal of Medicine (1)  
The Lancet (1)

**Date range used** (5 years, 10 years): 2015 until present   
**Limits used** (gender, article/study type, etc.): English language; Humans   
**Search terms and notes** (full search strategy for database searches below):

Coronavirus

Novel coronavirus

COVID-19

Hydroxychloroquine

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## Contents

[A. National and International Guidance](#Content1)

Medicines and Healthcare Products Regulatory Agency (MHRA)

[Chloroquine and Hydroxychloroquine not licensed for coronavirus (COVID-19) treatment](#Research621362)

[B. Synopses or Summaries](#Content2)

CEBM Oxford COVID-19 Evidence Service

[Hydroxychloroquine for COVID-19: What do the clinical trials tell us?](#Research625405)

[Hydroxychloroquine or Chloroquine for treating COVID-19 – a PROTOCOL for a systematic review of IPD](#Research625406)

[Chloroquine and hydroxychloroquine: Current evidence for their effectiveness in treating COVID-19](#Research625408)

[C. Institutional Publications](#Content4)

Centres for Disease Control and Prevention

[Information for Clinicians on Therapeutic Options for Patients with COVID-19](#Research621361)

[D. Original Research](#Content5)

1. [Hydroxychloroquine and azithromycin as a treatment of COVID‐19: results of an open‐label non‐randomized clinical trial.](#Research621465)
2. [A Case of Novel Coronavirus Disease 19 in a Chronic Hemodialysis Patient Presenting with Gastroenteritis and Developing Severe Pulmonary Disease](#Research625426)
3. [Audio Interview: New Research on Possible Treatments for Covid-19.](#Research621464)
4. [Cardiovascular risks of hydroxychloroquine in treatment and prophylaxis of COVID-19 patients: A scientific statement from the Indian Heart Rhythm Society](#Research625416)
5. [Chloroquine and hydroxychloroquine in covid-19.](#Research625414)
6. [Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries](#Research625419)
7. [Contentious issues and evolving concepts in the clinical presentation and management of patients with COVID-19 infectionwith reference to use of therapeutic and other drugs used in Co-morbid diseases (Hypertension, diabetes etc)](#Research625418)
8. [Covid-19: A puzzle with many missing pieces](#Research625424)
9. [COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression](#Research625428)
10. [Drug Evaluation during the Covid-19 Pandemic](#Research625432)
11. [Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial](#Research621363)
12. [Emerging prophylaxis strategies against COVID-19.](#Research621462)
13. [Excitement around hydroxychloroquine for treating COVID-19 causes challenges for rheumatology](#Research621359)
14. [Expanded Umbilical Cord Mesenchymal Stem Cells (UC-MSCs) as a Therapeutic Strategy in Managing Critically Ill COVID-19 Patients: The Case for Compassionate Use.](#Research621461)
15. [Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial](#Research625427)
16. [Hydroxychloroquine in the management of critically ill patients with COVID-19: the need for an evidence base](#Research625434)
17. [Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro](#Research621457)
18. [Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro](#Research625425)
19. [Hydroxychloroquine: a potential ethical dilemma for rheumatologists during the COVID-19 pandemic](#Research625417)
20. [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)](#Research621459)
21. [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)](#Research625429)
22. [New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?](#Research625421)
23. [Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): A systematic review](#Research621458)
24. [Potential therapeutic agents against COVID-19: What we know so far](#Research625423)
25. [Race to find COVID-19 treatments accelerates.](#Research621463)
26. [Results from a Controlled Trial of Hydroxychloroquine for COVID-19](#Research625437)
27. [The epidemiology, diagnosis and treatment of COVID-19](#Research625420)
28. [The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): The experience of clinical immunologists from China](#Research625422)
29. [Current and Future Use of Chloroquine and Hydroxychloroquine in Infectious, Immune, Neoplastic, and Neurological Diseases: A Mini-Review.](#Research625415)
30. [Recycling of chloroquine and its hydroxyl analogue to face bacterial, fungal and viral infections in the 21st century](#Research625430)
31. [New insights into the antiviral effects of chloroquine.](#Research621460)
32. [Hydroxychloroquine, aerosolized](#Research625431)

### [E. Search History](#SearchHistory)

## A. National and International Guidance

#### Medicines and Healthcare Products Regulatory Agency (MHRA)

**Chloroquine and Hydroxychloroquine not licensed for coronavirus (COVID-19) treatment** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=46ba03ec690208e972e65f0565f192af)

## B. Synopses or Summaries

#### CEBM Oxford COVID-19 Evidence Service

**Hydroxychloroquine for COVID-19: What do the clinical trials tell us?** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=bf3d8cd98931b9d5245a78df9227a5d3)

VERDICT Current data do not support the use of hydroxychloroquine for prophylaxis or treatment of COVID-19. There are no published trials of prophylaxis. Two trials of hydroxychloroquine treatment that are in the public domain, one non-peer reviewed, are premature analyses of trials whose conduct in both cases diverged from the published skeleton protocols registered on clinical trial sites. Neither they, nor three other negative trials that have since appeared, support the view that hydroxychloroquine is effective in the management of even mild COVID-19 disease.

**Hydroxychloroquine or Chloroquine for treating COVID-19 – a PROTOCOL for a systematic review of IPD** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=89c37f65b2bb1d6f56163a1b2521d811)

**Chloroquine and hydroxychloroquine: Current evidence for their effectiveness in treating COVID-19** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7455e51df5b3e90fe6f540a1266af132)

VERDICT Several in vitro studies report antiviral activity of chloroquine and hydroxychloroquine against SARS-CoV-2. In vivo data, although promising, is currently limited to one study with considerable limitations. On the basis of the weak evidence available to date, treatment guidelines have already incorporated the usage of chloroquine/hydroxychloroquine for certain patients with COVID-19. Further research should address the optimal dose and duration of treatment, and explore side effects and long-term outcomes. There is a higher risk of side effects in the presence of renal and liver impairment, and there have been isolated reports of COVID-19 disease-causing renal and hepatic injury. Over twenty in vivo clinical trials have already been registered to test the use of chloroquine and hydroxychloroquine for the treatment of COVID-19. Contraindications for the use of these drugs must be checked for each individual before treatment. Empirical evidence suggests that hydroxychloroquine has a better safety profile, and it might therefore be preferable to focus research efforts on this less toxic metabolite.

## C. Institutional Publications

#### Centres for Disease Control and Prevention

**Information for Clinicians on Therapeutic Options for Patients with COVID-19** (2020)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=98eabe3d0a6e19c8b46ceda68bea8f4f)

## D. Original Research

1. **Hydroxychloroquine and azithromycin as a treatment of COVID‐19: results of an open‐label non‐randomized clinical trial.**   
   2020;:– In Press 17 March 2020 – DOI : 10.1016/j.ijantimicag.2020.105949 .

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=4097379e1a7b20375e80d9fa7989103b)

1. **A Case of Novel Coronavirus Disease 19 in a Chronic Hemodialysis Patient Presenting with Gastroenteritis and Developing Severe Pulmonary Disease**  
   Ferrey A.J. American journal of nephrology 2020;:1-6.

Novel coronavirus disease 2019 (COVID-19) is a highly infectious, rapidly spreading viral disease with an alarming case fatality rate up to 5%. The risk factors for severe presentations are concentrated in patients with chronic kidney disease, particularly patients with end-stage renal disease (ESRD) who are dialysis dependent. We report the first US case of a 56-year-old nondiabetic male with ESRD secondary to IgA nephropathy undergoing thrice-weekly maintenance hemodialysis for 3 years, who developed COVID-19 infection. He has hypertension controlled with angiotensin receptor blocker losartan 100 mg/day and coronary artery disease status-post stent placement. During the first 5 days of his febrile disease, he presented to an urgent care, 3 emergency rooms, 1 cardiology clinic, and 2 dialysis centers in California and Utah. During this interval, he reported nausea, vomiting, diarrhea, and low-grade fevers but was not suspected of COVID-19 infection until he developed respiratory symptoms and was admitted to the hospital. Imaging studies upon admission were consistent with bilateral interstitial pneumonia. He was placed in droplet-eye precautions while awaiting COVID-19 test results. Within the first 24 h, he deteriorated quickly and developed acute respiratory distress syndrome (ARDS), requiring intubation and increasing respiratory support. Losartan was withheld due to hypotension and septic shock. COVID-19 was reported positive on hospital day 3. He remained in critical condition being treated with hydroxychloroquine and tocilizumab in addition to the standard medical management for septic shock and ARDS. Our case is unique in its atypical initial presentation and highlights the importance of early testing.<br/>Copyright &#xa9; 2020 S. Karger AG, Basel.

1. **Audio Interview: New Research on Possible Treatments for Covid-19.**  
   Rubin Eric J. The New England journal of medicine 2020;382(12):e30.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6f357dca17fe3fdc2900ff9fb3994f9a)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=6c86889bf365169b93109ba6ef722054)

1. **Cardiovascular risks of hydroxychloroquine in treatment and prophylaxis of COVID-19 patients: A scientific statement from the Indian Heart Rhythm Society**  
   Kapoor A. Indian Pacing and Electrophysiology Journal 2020;:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2de10dfce69224437b9f019788e34295)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e35614b7c8487404f83bda6a0a14bd40)

1. **Chloroquine and hydroxychloroquine in covid-19.**  
   Ferner Robin E. BMJ (Clinical research ed.) 2020;369:m1432.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=9d7e68e936619a31b1e0cb0ea6e597f2)

1. **Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries**  
   Singh A.K. Diabetes and Metabolic Syndrome: Clinical Research and Reviews 2020;14(3):241-246.

Background and aims: No drugs are currently approved for Coronavirus Disease-2019 (COVID-19), although some have been tried. In view of recent studies and discussion on chloroquine and hydroxychloroquine (HCQ), we aimed to review existing literature and relevant websites regarding these drugs and COVID-19, adverse effects related to drugs, and related guidelines. Aims and methods: We systematically searched the PubMed database up till March 21, 2020 and retrieved all the articles published on chloroquine and HCQ and COVID-19. <br/>Result(s): Two small human studies have been conducted with both these drugs in COVID-19, and have shown significant improvement in some parameters in patients with COVID-19. <br/>Conclusion(s): Considering minimal risk upon use, a long experience of use in other diseases, cost-effectiveness and easy availability across India, we propose that both these drugs are worthy of fast track clinical trial for treatment, and may be carefully considered for clinical use as experimental drugs. Since HCQ has been approved for treatment of diabetes in India, it should be further researched in diabetes and COVID-19, a subgroup where significant mortality has been shown.<br/>Copyright &#xa9; 2020 Diabetes India

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=1579cfc4411bb4b08520b8dba7241052)

1. **Contentious issues and evolving concepts in the clinical presentation and management of patients with COVID-19 infectionwith reference to use of therapeutic and other drugs used in Co-morbid diseases (Hypertension, diabetes etc)**  
   Gupta R. Diabetes and Metabolic Syndrome: Clinical Research and Reviews 2020;14(3):251-254.

Background and aims: Multiple issues in management of COVID have emerged, but confusion persists regarding rational interpretation. Aim of this brief review is to review these issues based on current literature. <br/>Method(s): This is a narrative review with Pubmed and Google Scholar search till 23 March 2020. Search terms were, COVID-19, treatment of coronavirus, COVID 19 and following terms; chloroquine, hydroxychloroquine, ibuprofen, ACE-inhibitors or angiotensin receptor blockers, cardiovascular disease, diarrhoea, liver, testis and gastrointestinal disease. <br/>Result(s): We discuss evidence regarding role of chloroquine and hydroxychloroquine in treatment and prophylaxis, use of inhibitors of the renin angiotensin system, safety of ibuprofen, unusual clinical features like gastrointestinal symptoms and interpretation of tests for cardiac enzymes and biomarkers. <br/>Conclusion(s): While our conclusions on management of COVID-19 patients with co-morbidities are based on current evidence, however, data is limited and there is immediate need for fast track research.<br/>Copyright &#xa9; 2020 Diabetes India

1. **Covid-19: A puzzle with many missing pieces**  
   Vetter P. The BMJ 2020;368:No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e2e5ccba8c3ccde97974da26cd569011)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=b84ae7494827213793c0219856f872a7)

1. **COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression**  
   Zhou D. The Journal of antimicrobial chemotherapy 2020;:No page numbers.

A novel coronavirus disease (COVID-19), caused by infection with SARS-CoV-2, has swept across 31 provinces in China and over 40 countries worldwide. The transition from first symptoms to acute respiratory distress syndrome (ARDS) is highly likely to be due to uncontrolled cytokine release. There is an urgent need to identify safe and effective drugs for treatment. Chloroquine (CQ) exhibits a promising inhibitory effect. However, the clinical use of CQ can cause severe side effects. We propose that hydroxychloroquine (HCQ), which exhibits an antiviral effect highly similar to that of CQ, could serve as a better therapeutic approach. HCQ is likely to attenuate the severe progression of COVID-19, inhibiting the cytokine storm by suppressing T cell activation. It has a safer clinical profile and is suitable for those who are pregnant. It is cheaper and more readily available in China. We herein strongly urge that clinical trials are performed to assess the preventive effects of HCQ in both disease infection and progression.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved. For permissions, please email: journals.permissions@oup.com.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=74a1a3efa802811a4b63269b521fa576)

1. **Drug Evaluation during the Covid-19 Pandemic**  
   2020;:DOI: 10.1056/NEJMp2009457.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d2ca611b2185d92d68c034fb831ec223)

1. **Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial**  
   2020;:https://doi.org/10.1101/2020.03.22.20040758.

This article is a preprint and has not been peer-reviewed.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=7abd116fab9eb9d2e6fca236f0f34ac4)

1. **Emerging prophylaxis strategies against COVID-19.**  
   Agrawal Sumita Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace 2020;90(1):No page numbers.

The Novel corona virus 2019 which started as an outbreak in China in December 2019 has rapidly spread all over the world, such that on 11th March 2020 WHO declared this disease as pandemic. The emergency that the world faces today demands that we develop urgent and effective measures to protect people at high risk of transmission. WHO has accelerated research in diagnostics, vaccines and therapeutics for this novel coronavirus.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=e2ab71669d96553df6c12aff34f5a80b)

1. **Excitement around hydroxychloroquine for treating COVID-19 causes challenges for rheumatology**  
   2020;:Online.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=f8b4a351a2a32dd4415470a8195006b3)

1. **Expanded Umbilical Cord Mesenchymal Stem Cells (UC-MSCs) as a Therapeutic Strategy in Managing Critically Ill COVID-19 Patients: The Case for Compassionate Use.**  
   Atluri Sairam Pain physician 2020;23(2):E71.

COVID-19 has affected the United States leading to a national emergency with health care and economic impact, propelling the country into a recession with disrupted lifestyles not seen in recent history. COVID-19 is a serious illness leading to multiple deaths in various countries including the United States. Several million Americans satisfy the Center for Disease Control and Prevention (CDC) criteria for being high risk. Unfortunately, the available supply of medical beds and equipment for mechanical ventilation are much less than is projected to be needed. The World Health Organization (WHO) and multiple agencies led by the CDC in the United States have attempted to organize intensive outbreak investigation programs utilizing appropriate preventive measures, evaluation, and treatment. The clinical spectrum of COVID-19 varies from asymptomatic forms to conditions encompassing multiorgan and systemic manifestations in terms of septic shock, and multiple organ dysfunction (MOD) syndromes. The presently approved treatments are supportive but not curative for the disease. There are multiple treatments being studied. These include vaccines, medications Remdesivir and hydroxychloroquine and potentially combination therapy. Finally, expanded umbilical cord mesenchymal stem cells or (UC-MSCs) may have a role and are being studied. The cure of COVID-19 is essentially dependent on the patients' own immune system. When the immune system is over activated in an attempt to kill the virus, this can lead to the production of a large number of inflammatory factors, resulting in severe cytokine storm. The cytokine storm may induce organ damage followed by the edema, dysfunction of air exchange, acute respiratory distress syndrome (ARDS), acute cardiac injury, and secondary infection, which may lead to death. Thus, at this point, the avoidance of the cytokine storm may be the key for the treatment of HCOV-19 infected patients.In China, where there was limited availability of effective modalities to manage COVID-19 several patients were treated with expanded UC-MSCs. Additionally, the Italian College of Anesthesia, Analgesia, Resuscitation and Intensive Care have reported guidelines to treat coronavirus patients with stem cells in the hope of decreasing the number of patients going to the ICU, and, also relatively quickly getting them out of ICU. In this manuscript, we describe the urgent need for various solutions, pathogenesis of coronavirus and the clinical evidence for treatment of COVID-19 with stem cells. The limited but emerging evidence regarding UC MSC in managing COVID-19 suggests that it might be considered for compassionate use in critically ill patients to reduce morbidity and mortality in the United States. The administration and Coronavirus Task Force might wish to approach the potential of expanded UC-MSCs as an evolutionary therapeutic strategy in managing COVID-19 illness with a 3-pronged approach: If proven safe and effective on a specific and limited basis…1. Minimize regulatory burden by all agencies so that critically ill COVID-19 patients will have access regardless of their financial circumstance.2. Institute appropriate safeguards to avoid negative consequences from unscrupulous actors.3. With proper informed consent from patients or proxy when necessary, and subject to accumulation of data in that cohort, allow the procedure to be initiated in critically ill patients who are not responding to conventional therapies.KEY WORDS: Coronavirus, COVID-19, cytokine storm, multiorgan failure, expanded umbilical cord mesenchymal stem cells.

1. **Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial**  
   Gautret P. International journal of antimicrobial agents 2020;:105949.

BACKGROUND: Chloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2, and reported to be efficient in Chinese COV-19 patients. We evaluate the role of hydroxychloroquine on respiratory viral loads. <br/>PATIENTS AND METHODS: French Confirmed COVID-19 patients were included in a single arm protocol from early March to March 16th, to receive 600mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting. Depending on their clinical presentation, azithromycin was added to the treatment. Untreated patients from another center and cases refusing the protocol were included as negative controls. Presence and absence of virus at Day6-post inclusion was considered the end point. <br/>RESULT(S): Six patients were asymptomatic, 22 had upper respiratory tract infection symptoms and eight had lower respiratory tract infection symptoms. Twenty cases were treated in this study and showed a significant reduction of the viral carriage at D6-post inclusion compared to controls, and much lower average carrying duration than reported of untreated patients in the literature. Azithromycin added to hydroxychloroquine was significantly more efficient for virus elimination. <br/>CONCLUSION(S): Despite its small sample size our survey shows that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin.<br/>Copyright &#xa9; 2020. Published by Elsevier B.V.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=916432c3407698a73a7daca048971bb5)

1. **Hydroxychloroquine in the management of critically ill patients with COVID-19: the need for an evidence base**  
   2020;:https://doi.org/10.1016/S2213-2600(20)30172-7.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=2c1127a51ba24be42ef3abf91c914741)

1. **Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro**  
   Liu J. Cell Discovery 2020;6(1):No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8f0197b514d84c99cc568e4fe206cef2)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cb8670076d8bcf49196673645a4baf75)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=40d58db09c07bc1f5eb6948b1532b7d9)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0905191647ef58957f70c129d37630f8)

1. **Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro**  
   Liu J. Cell Discovery 2020;6(1):No page numbers.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=8f0197b514d84c99cc568e4fe206cef2)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=cb8670076d8bcf49196673645a4baf75)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=40d58db09c07bc1f5eb6948b1532b7d9)

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=0905191647ef58957f70c129d37630f8)

1. **Hydroxychloroquine: a potential ethical dilemma for rheumatologists during the COVID-19 pandemic**  
   Scuccimarri R. The Journal of rheumatology 2020;:No page numbers.

Two antimalarial agents, chloroquine (CQ) and hydroxychloroquine (HCQ), have been trusted treatments for a range of rheumatic diseases over the past seventy years [1]. These agents have attracted intense media attention in the past few weeks with suggestions that this category of drugs may have potential in the management of coronavirus (SARS-CoV2) associated disease called COVID-19 [2, 3].

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=15ace42ddb2ab1b2c773fc1faee2e348)

1. **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)**  
   Yao X. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020;:No page numbers.

BACKGROUND: The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) first broke out in Wuhan (China) and subsequently spread worldwide. Chloroquine has been sporadically used in treating SARS-CoV-2 infection. Hydroxychloroquine shares the same mechanism of action as chloroquine, but its more tolerable safety profile makes it the preferred drug to treat malaria and autoimmune conditions. We propose that the immunomodulatory effect of hydroxychloroquine also may be useful in controlling the cytokine storm that occurs late-phase in critically ill SARS-CoV-2 infected patients. Currently, there is no evidence to support the use of hydroxychloroquine in SARS-CoV-2 infection. <br/>METHOD(S): The pharmacological activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2 infected Vero cells. Physiologically-based pharmacokinetic models (PBPK) were implemented for both drugs separately by integrating their in vitro data. Using the PBPK models, hydroxychloroquine concentrations in lung fluid were simulated under 5 different dosing regimens to explore the most effective regimen whilst considering the drug's safety profile. <br/>RESULT(S): Hydroxychloroquine (EC50=0.72 muM) was found to be more potent than chloroquine (EC50=5.47 muM) in vitro. Based on PBPK models results, a loading dose of 400 mg twice daily of hydroxychloroquine sulfate given orally, followed by a maintenance dose of 200 mg given twice daily for 4 days is recommended for SARS-CoV-2 infection, as it reached three times the potency of chloroquine phosphate when given 500 mg twice daily 5 days in advance. <br/>CONCLUSION(S): Hydroxychloroquine was found to be more potent than chloroquine to inhibit SARS-CoV-2 in vitro.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=d2aa3188581d8c371d2e97c2e7493fe9)

1. **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)**  
   Yao X. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America 2020;:No page numbers.

BACKGROUND: The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) first broke out in Wuhan (China) and subsequently spread worldwide. Chloroquine has been sporadically used in treating SARS-CoV-2 infection. Hydroxychloroquine shares the same mechanism of action as chloroquine, but its more tolerable safety profile makes it the preferred drug to treat malaria and autoimmune conditions. We propose that the immunomodulatory effect of hydroxychloroquine also may be useful in controlling the cytokine storm that occurs late-phase in critically ill SARS-CoV-2 infected patients. Currently, there is no evidence to support the use of hydroxychloroquine in SARS-CoV-2 infection. <br/>METHOD(S): The pharmacological activity of chloroquine and hydroxychloroquine was tested using SARS-CoV-2 infected Vero cells. Physiologically-based pharmacokinetic models (PBPK) were implemented for both drugs separately by integrating their in vitro data. Using the PBPK models, hydroxychloroquine concentrations in lung fluid were simulated under 5 different dosing regimens to explore the most effective regimen whilst considering the drug's safety profile. <br/>RESULT(S): Hydroxychloroquine (EC50=0.72 muM) was found to be more potent than chloroquine (EC50=5.47 muM) in vitro. Based on PBPK models results, a loading dose of 400 mg twice daily of hydroxychloroquine sulfate given orally, followed by a maintenance dose of 200 mg given twice daily for 4 days is recommended for SARS-CoV-2 infection, as it reached three times the potency of chloroquine phosphate when given 500 mg twice daily 5 days in advance. <br/>CONCLUSION(S): Hydroxychloroquine was found to be more potent than chloroquine to inhibit SARS-CoV-2 in vitro.<br/>Copyright &#xa9; The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America.

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1. **New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19?**  
   Devaux C.A. International Journal of Antimicrobial Agents 2020;:No page numbers.

Recently, a novel coronavirus (2019-nCoV), officially known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in China. Despite drastic containment measures, the spread of this virus is ongoing. SARS-CoV-2 is the aetiological agent of coronavirus disease 2019 (COVID-19) characterised by pulmonary infection in humans. The efforts of international health authorities have since focused on rapid diagnosis and isolation of patients as well as the search for therapies able to counter the most severe effects of the disease. In the absence of a known efficient therapy and because of the situation of a public-health emergency, it made sense to investigate the possible effect of chloroquine/hydroxychloroquine against SARS-CoV-2 since this molecule was previously described as a potent inhibitor of most coronaviruses, including SARS-CoV-1. Preliminary trials of chloroquine repurposing in the treatment of COVID-19 in China have been encouraging, leading to several new trials. Here we discuss the possible mechanisms of chloroquine interference with the SARS-CoV-2 replication cycle.<br/>Copyright &#xa9; 2020 The Authors

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1. **Potential rapid diagnostics, vaccine and therapeutics for 2019 novel coronavirus (2019-nCoV): A systematic review**  
   Pang J. Journal of Clinical Medicine 2020;9(3):No page numbers.

Rapid diagnostics, vaccines and therapeutics are important interventions for the management of the 2019 novel coronavirus (2019-nCoV) outbreak. It is timely to systematically review the potential of these interventions, including those for Middle East respiratory syndrome-Coronavirus (MERS-CoV) and severe acute respiratory syndrome (SARS)-CoV, to guide policymakers globally on their prioritization of resources for research and development. A systematic search was carried out in three major electronic databases (PubMed, Embase and Cochrane Library) to identify published studies in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Supplementary strategies through Google Search and personal communications were used. A total of 27 studies fulfilled the criteria for review. Several laboratory protocols for confirmation of suspected 2019-nCoV cases using real-time reverse transcription polymerase chain reaction (RT-PCR) have been published. A commercial RT-PCR kit developed by the Beijing Genomic Institute is currently widely used in China and likely in Asia. However, serological assays as well as point-of-care testing kits have not been developed but are likely in the near future. Several vaccine candidates are in the pipeline. The likely earliest Phase 1 vaccine trial is a synthetic DNA-based candidate. A number of novel compounds as well as therapeutics licensed for other conditions appear to have in vitro efficacy against the 2019-nCoV. Some are being tested in clinical trials against MERS-CoV and SARS-CoV, while others have been listed for clinical trials against 2019-nCoV. However, there are currently no effective specific antivirals or drug combinations supported by high-level evidence.<br/>Copyright &#xa9; 2020 by the authors. Licensee MDPI, Basel, Switzerland.

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1. **Potential therapeutic agents against COVID-19: What we know so far**  
   Lu C.-C. Journal of the Chinese Medical Association : JCMA 2020;:No page numbers.

The emerging outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to spread all over the world. Agents or vaccines of proven efficacy to treat or prevent human coronavirus infection are in urgent need and are being investigated vigorously worldwide. This review summarizes the current evidence of potential therapeutic agents, such as lopinavir/ritonavir, remdesivir, favipiravir, chloroquine, hydroxychloroquine, interferon, ribavirin, tocilizumab and sarilumab. More clinical trials are being conducted for further confirmation of the efficacy and safety of these agents in treating COVID-19.

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1. **Race to find COVID-19 treatments accelerates.**  
   Kupferschmidt Kai Science (New York, N.Y.) 2020;367(6485):1412-1413.

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1. **Results from a Controlled Trial of Hydroxychloroquine for COVID-19**  
   2020;:online.

[Available online at this link](https://www.knowledgeshare.nhs.uk/index.php?PageID=link_resolver&link=20163d07a5ccb848f180631d3559c042)

1. **The epidemiology, diagnosis and treatment of COVID-19**  
   Zhai P. International Journal of Antimicrobial Agents 2020;:No page numbers.

In December 2019, the outbreak of the novel coronavirus disease (COVID-19) in China spread worldwide, becoming an emergency of major international concern. SARS-CoV-2 infection causes clusters of severe respiratory illness similar to severe acute respiratory syndrome coronavirus. Human-to-human transmission via droplets, contaminated hands or surfaces has been described, with incubation times of 2-14 days. Early diagnosis, quarantine, and supportive treatments are essential to cure patients. This paper reviews the literature on all available information about the epidemiology, diagnosis, isolation and treatments of COVID-19. Treatments, including antiviral agents, chloroquine and hydroxychloroquine, corticosteroids, antibodies, convalescent plasma transfusion and vaccines, are discussed in this article. In addition, registered trials investigating treatment options for COVID-19 infection are listed.<br/>Copyright &#xa9; 2020 Elsevier Ltd

1. **The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): The experience of clinical immunologists from China**  
   Zhang W. Clinical Immunology 2020;214:No page numbers.

The pandemic outbreak of coronavirus disease 2019 (COVID-19) is rapidly spreading all over the world. Reports from China showed that about 20% of patients developed severe disease, resulting in a fatality of 4%. In the past two months, we clinical immunologists participated in multi-rounds of MDT (multidiscipline team) discussion on the anti-inflammation management of critical COVID-19 patients, with our colleagues dispatched from Chinese leading PUMC Hospital to Wuhan to admit and treat the most severe patients. Here, from the perspective of clinical immunologists, we will discuss the clinical and immunological characteristics of severe patients, and summarize the current evidence and share our experience in anti-inflammation treatment, including glucocorticoids, IL-6 antagonist, JAK inhibitors and choloroquine/hydrocholoroquine, of patients with severe COVID-19 that may have an impaired immune system.<br/>Copyright &#xa9; 2020

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1. **Current and Future Use of Chloroquine and Hydroxychloroquine in Infectious, Immune, Neoplastic, and Neurological Diseases: A Mini-Review.**  
   Plantone Domenico Clinical drug investigation 2018;38(8):653-671.

The process of finding new therapeutic indications for currently used drugs, defined as 'repurposing', is receiving growing attention. Chloroquine and hydroxychloroquine, with an original indication to prevent or cure malaria, have been successfully used to treat several infectious (HIV, Q fever, Whipple's disease, fungal infections), rheumatological (systemic lupus erythematosus, antiphospholipid antibody syndrome, rheumatoid arthritis, Sjögren's syndrome), and other immunological diseases. Indeed, they have anti-inflammatory, immunomodulating, anti-infective, antithrombotic, and metabolic effects. Among the biological effects of chloroquine and hydroxychloroquine, it is important to highlight their antitumoral properties, likely due to their strong antiproliferative, antimutagenic, and inhibiting autophagy capacities. These effects make these drugs a possible option in the treatment of several tumors in association with radiotherapy and chemotherapy. Finally, the repurposing of chloroquine and hydroxychloroquine is currently being examined for neurological diseases such as neurosarcoidosis, chronic lymphocytic inflammation with pontine perivascular enhancement responsive to corticosteroids, and primary progressive multiple sclerosis. Several ongoing clinical trials have been testing these drugs in non-neoplastic and neoplastic diseases. Moreover, the well-demonstrated good tolerability of chloroquine and hydroxychloroquine make them safe even during pregnancy. Gastrointestinal and cutaneous manifestations are considered not to be serious, while retinal, neuromuscular, and cardiac toxicities are classified as serious adverse events.

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1. **Recycling of chloroquine and its hydroxyl analogue to face bacterial, fungal and viral infections in the 21st century**  
   Rolain J.-M. International Journal of Antimicrobial Agents 2007;30(4):297-308.

Chloroquine (CQ) and its hydroxyl analogue hydroxychloroquine (HCQ) are weak bases with a half-century long use as antimalarial agents. Apart from this antimalarial activity, CQ and HCQ have gained interest in the field of other infectious diseases. One of the most interesting mechanisms of action is that CQ leads to alkalinisation of acid vesicles that inhibit the growth of several intracellular bacteria and fungi. The proof of concept of this effect was first used to restore intracellular pH allowing antibiotic efficacy for Coxiella burnetii, the agent of Q fever, and doxycycline plus HCQ is now the reference treatment for chronic Q fever. There is also strong evidence of a similar effect in vitro against Tropheryma whipplei, the agent of Whipple's disease, and a clinical trial is in progress. Other bacteria and fungi multiply in an acidic environment and encouraging in vitro data suggest that this concept may be generalised for all intracellular organisms that multiply in an acidic environment. For viruses, CQ led to inhibition of uncoating and/or alteration of post-translational modifications of newly synthesised proteins, especially inhibition of glycosylation. These effects have been well described in vitro for many viruses, with human immunodeficiency virus (HIV) being the most studied. Preliminary in vivo clinical trials suggest that CQ alone or in combination with antiretroviral drugs might represent an interesting way to treat HIV infection. In conclusion, our review re-emphasises the paradigm that activities mediated by lysosomotropic agents may offer an interesting weapon to face present and future infectious diseases worldwide. &#xa9; 2007 Elsevier B.V. and the International Society of Chemotherapy.

1. **New insights into the antiviral effects of chloroquine.**  
   Savarino Andrea The Lancet. Infectious diseases 2006;6(2):67-69.

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1. **Hydroxychloroquine, aerosolized**  
   Mealy N.E. Drugs of the Future 2005;30(1):82-83.

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| 4. | EMBASE | (2 OR 3) | 21092 |
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| 6. | EMBASE | (1 AND 4 AND 5) | 1 |
| 7. | EMBASE | (treatment outcome OR safety OR efficacy).ti,ab | 1650454 |
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| 7. | EMBASE | exp CORONAVIRINAE/ OR exp CORONAVIRUS/ OR exp "CORONAVIRUS INFECTION"/ OR exp "CORONAVIRUS INFECTIONS"/ | 19316 |
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