

## Covid-19 Evidence Update

### Summarized and appraised resources

06/04/2021

*The following resources are available via electronically or in print. Please follow links to access full text online, or contact the library if you have any difficulties with the links.*

The resources included in this update are summaries or critically appraised articles. If you would like a more specific search conducted please email [kgh-tr.library.service@nhs.net](mailto:kgh-tr.library.service@nhs.net)

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## Royal College/Society Guidance and Point of Care Tools

### Latest information and guidance

<p>NICE</p> <p><a href="#">COVID-19 rapid guideline: managing COVID-19 (NG191)</a> Published 23/03/2021</p> <p><a href="#">Rapid guidelines and evidence summaries</a></p> <p><a href="#">Speciality guides</a> (NHS England and NHS Improvement advice has moved here)</p>	<p>NHS England and NHS Improvement <a href="#">Secondary care</a> (Includes Prevention, Infection control, Assessment, Management, Discharge, Isolation, Estates and facilities, Finance, Workforce, Cancer ...)</p>
<p>Royal College of Emergency Medicine</p> <p><a href="#">Covid-19 resources</a></p>	<p>Association for Palliative Medicine</p> <p><a href="#">Covid 19 and Palliative, End of Life and Beareavement Care</a></p>
<p>Royal College of General Practitioners</p> <p><a href="#">COVID-19</a></p>	<p>Royal College of Obstetrics &amp; Gynaecologists</p> <p><a href="#">Coronavirus (COVID-19), pregnancy and women's health</a></p>
<p>Royal College of Paediatrics and Child Health</p> <p><a href="#">Key topics COVID 19</a></p>	<p>Royal College of Pathologists</p> <p><a href="#">COVID-19 Resources Hub</a></p>
<p>Royal College of Psychiatrists</p> <p><a href="#">COVID-19: Community mental health settings</a></p>	<p>Royal College of Surgeons</p> <p><a href="#">COVID 19 Information Hub</a></p>
<p>Royal Pharmaceutical Society</p> <p><a href="#">COVID-19</a></p>	<p>British Society of Echocardiography</p> <p><a href="#">COVID-19 clinical guidance</a></p>
<p>British Society of Gastroenterology</p> <p><a href="#">COVID 19 updates</a></p>	<p>British Society for Haematology</p> <p><a href="#">COVID-19 Updates</a></p>

British Society for Rheumatology <a href="#">COVID-19 updates for members</a>	Combined Intensive Care Society, Association of Anaesthetists, Royal College of Anaesthetists, Faculty of Intensive Care Medicine guidance <a href="#">Clinical Guidance</a>
BMJ Best Practice <a href="#">Coronavirus disease 2019 (COVID-19)</a> <a href="#">Management of coexisting conditions in the context of COVID-19</a>	DynaMed <a href="#">Covid 19 (Novel Coronavirus)</a> <a href="#">Covid-19 and Pediatric Patients</a> <a href="#">Covid 19 and Special Populations</a> <a href="#">Covid-19 and Patients with Cancer</a> <a href="#">Covid-19 and Cardiovascular Disease Patients</a> <a href="#">Covid-19 and Patients with Chronic Kidney Disease and End-stage renal Disease</a> <a href="#">Covid-19 and Pregnant Patients</a> <a href="#">Covid-19-associated Coagulopathy</a>
Don't forget the bubbles <a href="#">An evidence summary of paediatric Covid-19 literature</a> <a href="#">Covid-19</a> – a selection of evidence based summaries and articles.	

## New NICE Guidance

[Covid-19 rapid guideline: rheumatological autoimmune, inflammatory and metabolic bone disorders \(NG 167\)](#)  
Updated 31/3/2021

[Covid-19 rapid guideline: managing COVID-19 \(NG191\)](#). Published 23/03/21

## New Guidance and Reports from other sources

### [Coronavirus \(COVID-19\): advice for pregnant employees.](#)

Department of Health and Social Care (DHSC); 2020.

<https://www.gov.uk/government/publications/coronavirus-covid-19-advice-for-pregnant-employees/>

[Advice for pregnant employees on risk assessments in the workplace and occupational health during the coronavirus pandemic (29 March 2021: Updated background information section to include information on the next stage of the roadmap)]

*Freely available online*

### [COVID-19 vaccines and medicines: updates for March 2021.](#)

Medicines and Healthcare Products Regulatory Agency (MHRA); 2021.

<https://www.gov.uk/drug-safety-update/covid-19-vaccines-and-medicines-updates-for-march-2021>

[A summary of advice recently issued by the MHRA relating to coronavirus (COVID-19), up to 18 March 2021.]

*Freely available online*

## [Covid-19 Evidence Alerts from McMaster Plus](#)

COVID-19 Evidence Alerts to current best evidence for clinical care of people with threatened, suspected or confirmed COVID-19 infection. Reports are critically appraised for scientific merit, and those with acceptable scientific merit are appraised for relevance and importance by frontline clinicians. The studies listed below meet their criteria for quality. The site also lists other studies published which do not meet their criteria, or do not belong to a study category they appraise. ([More information available](#)).

Diagnosis
<a href="#">A Characteristic Chest Radiographic Pattern in the Setting of the COVID-19 Pandemic.</a> <i>Smith DL, Grenier JP, Batte C, et al.</i> <b>Radiol Cardiothorac Imaging</b>
<a href="#">Diagnostic Accuracy of North America Expert Consensus Statement on Reporting CT Findings in Patients Suspected of Having COVID-19 Infection: An Italian Single-Center Experience.</a> <i>Ciccarese F, Coppola F, Spinelli D, et al.</i> <b>Radiol Cardiothorac Imaging</b>
<a href="#">Saliva for molecular detection of SARS-CoV-2 in school-aged children.</a> <i>Al Suwaidi H, Senok A, Varghese R, et al.</i> <b>Clin Microbiol Infect</b>
<a href="#">Accuracy and Reproducibility of Low-Dose Submillisievert Chest CT for the Diagnosis of COVID-19.</a> <i>Dangis A, Gieraerts C, De Bruecker Y, et al.</i> <b>Radiol Cardiothorac Imaging</b>
<a href="#">Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection.</a> <i>Dinnes J, Deeks JJ, Berhane S, et al.</i> <b>Cochrane Database Syst Rev</b>
<a href="#">Thoracic imaging tests for the diagnosis of COVID-19.</a> <i>Islam N, Ebrahimzadeh S, Salameh JP, et al.</i> <b>Cochrane Database Syst Rev</b>
<a href="#">Nasopharyngeal Panbio COVID-19 Antigen Performed at Point-of-Care Has a High Sensitivity in Symptomatic and Asymptomatic Patients With Higher Risk for Transmission and Older Age.</a> <i>Masia M, Fernandez-Gonzalez M, Sanchez M, et al.</i> <b>Open Forum Infect Dis</b>
Primary Prevention
<a href="#">International travel-related control measures to contain the COVID-19 pandemic: a rapid review.</a> <i>Burns J, Movsisyan A, Stratil JM, et al.</i> <b>Cochrane Database Syst Rev</b>
Etiology
<a href="#">Effect of renin-angiotensin-aldosterone system inhibitors on Covid-19 patients in Korea.</a> <i>Park J, Lee SH, You SC, et al.</i> <b>PLoS One</b>
Clinical Prediction Guide
<a href="#">Nomogram for prediction of fatal outcome in patients with severe COVID-19: a multicenter study.</a> <i>Yang Y, Zhu XF, Huang J, et al.</i> <b>Mil Med Res</b>
<a href="#">CHA2DS2-VASc score and modified CHA2DS2-VASc score can predict mortality and intensive care unit hospitalization in COVID-19 patients.</a> <i>Gunduz R, Yildiz BS, Ozdemir IH, et al.</i> <b>J Thromb Thrombolysis</b>
<a href="#">A biomarker-based age, biomarkers, clinical history, sex (ABCS)-mortality risk score for patients with coronavirus disease 2019.</a> <i>Jiang M, Li C, Zheng L, et al.</i> <b>Ann Transl Med</b>
<a href="#">Early prognostication of COVID-19 to guide hospitalisation versus outpatient monitoring using a point-of-test risk prediction score.</a> <i>Chua F, Vancheeswaran R, Draper A, et al.</i> <b>Thorax</b>
Prognosis
<a href="#">The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis.</a> <i>Wei SQ, Bilodeau-Bertrand M, Liu S, et al.</i> <b>CMAJ</b>
Treatment
<a href="#">The efficacy and safety of hydroxychloroquine (HCQ) in treatment of COVID19 -a systematic review and meta-analysis.</a> <i>Choudhuri AH, Duggal S, Ahuja B, et al.</i> <b>Indian J Med Microbiol</b>
<a href="#">Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure: The HENIVOT Randomized Clinical Trial.</a>

<a href="#">Grieco DL, Menga LS, Cesarano M, et al. <b>JAMA</b></a>
<a href="#">Comparison of Losartan and Amlodipine Effects on the Outcomes of Patient with COVID-19 and Primary Hypertension: A Randomized Clinical Trial.</a>
<a href="#">Nouri-Vaskeh M, Kalami N, Zand R, et al. <b>Int J Clin Pract</b></a>
<a href="#">Safety and efficacy of Favipiravir in moderate to severe SARS-CoV-2 pneumonia.</a>
<a href="#">Solaymani-Dodaran M, Ghanei M, Bagheri M, et al. <b>Int Immunopharmacol</b></a>
<a href="#">Interleukin-6 blocking agents for treating COVID-19: a living systematic review.</a>
<a href="#">Ghosn L, Chaimani A, Evrenoglou T, et al. <b>Cochrane Database Syst Rev</b></a>
<a href="#">Effect of Intermediate-Dose vs Standard-Dose Prophylactic Anticoagulation on Thrombotic Events, Extracorporeal Membrane Oxygenation Treatment, or Mortality Among Patients With COVID-19 Admitted to the Intensive Care Unit: The INSPIRATION Randomized Clinical Trial.</a>
<a href="#">Sadeghipour P, Talasaz AH, Rashidi F, et al. <b>JAMA</b></a>
<a href="#">Current evidence for COVID-19 therapies: a systematic literature review.</a>
<a href="#">Welte T, Ambrose LJ, Sibbring GC, et al. <b>Eur Respir Rev</b></a>
<a href="#">Interventions for treatment of COVID-19: Second edition of a living systematic review with meta-analyses and trial sequential analyses (The LIVING Project).</a>
<a href="#">Juul S, Nielsen EE, Feinberg J, et al. <b>PLoS One</b></a>
<a href="#">Hydroxychloroquine with or without azithromycin for treatment of early SARS-CoV-2 infection among high-risk outpatient adults: A randomized clinical trial.</a>
<a href="#">Johnston C, Brown ER, Stewart J, et al. <b>EClinicalMedicine</b></a>
<a href="#">Chinese Herbal Medicine Used With or Without Conventional Western Therapy for COVID-19: An Evidence Review of Clinical Studies.</a>
<a href="#">Liang SB, Zhang YY, Shen C, et al. <b>Front Pharmacol</b></a>

## Cochrane Evidence on COVID-19: a roundup

### Rapid, point-of-care antigen and molecular-based tests for diagnosis of SARS-CoV-2 infection

Dinnes, J et al (2021) Published 24<sup>th</sup> March 2021

#### **What did we want to find out?**

We wanted to know whether commercially available, rapid point-of-care antigen and molecular tests are accurate enough to diagnose COVID-19 infection reliably, and to find out if accuracy differs in people with and without symptoms.

#### **What did we do?**

We looked for studies that measured the accuracy of any commercially produced, rapid antigen or molecular point-of-care test, in people tested for COVID-19 using RT-PCR. People could be tested in hospital or the community. Studies could test people with or without symptoms.

Tests had to use minimal equipment, be performed safely without risking infection from the sample, and have results available within two hours of the sample being collected.

#### **What we found**

We included 64 studies in the review. They investigated a total of 24,087 nose or throat samples; COVID-19 was confirmed in 7415 of these samples. Studies investigated 16 different antigen tests and five different molecular tests. They took place mainly in Europe and North America.

#### **Main results**

##### ***Antigen tests***

In people with confirmed COVID-19, antigen tests correctly identified COVID-19 infection in an average of 72% of people with symptoms, compared to 58% of people without symptoms. Tests were most accurate when used in the first week after symptoms first developed (an average of 78% of confirmed cases had positive antigen tests). This is likely to be because people have the most virus in their system in the first days after they are infected.

In people who did not have COVID-19, antigen tests correctly ruled out infection in 99.5% of people with symptoms and 98.9% of people without symptoms.

Different brands of tests varied in accuracy. Pooled results for one test (SD Biosensor STANDARD Q) met World Health Organization (WHO) standards as 'acceptable' for confirming and ruling out COVID-19 in people with signs and symptoms of COVID-19. Two more tests met the WHO acceptable standards (Abbott Panbio and BIONOTE NowCheck) in at least one study.

Using summary results for SD Biosensor STANDARD Q, if 1000 people with symptoms had the antigen test, and 50 (5%) of them really had COVID-19:

- 53 people would test positive for COVID-19. Of these, 9 people (17%) would not have COVID-19 (false positive result).
- 947 people would test negative for COVID-19. Of these, 6 people (0.6%) would actually have COVID-19 (false negative result).

In people with no symptoms of COVID-19 the number of confirmed cases is expected to be much lower than in people with symptoms. Using summary results for SD Biosensor STANDARD Q in a bigger population of 10,000 people with no symptoms, where 50 (0.5%) of them really had COVID-19:

- 125 people would test positive for COVID-19. Of these, 90 people (72%) would not have COVID-19 (false positive result).
- 9,875 people would test negative for COVID-19. Of these, 15 people (0.2%) would actually have COVID-19 (false negative result).

### **Molecular tests**

Although overall results for diagnosing and ruling out COVID-19 were good (95.1% of infections correctly diagnosed and 99% correctly ruled out), 69% of the studies used the tests in laboratories instead of at the point-of-care and few studies followed test manufacturer instructions. Most of the data relate to the ID NOW and Xpert Xpress tests. We noted a large difference in COVID-19 detection between the two tests, but we cannot be certain about whether results will remain the same in a real world setting. We could not investigate differences in people with or without symptoms, nor time from when symptoms first showed because the studies did not provide enough information about their participants.

### **How reliable were the results of the studies?**

In general, studies that assessed antigen tests used more rigorous methods than those that assessed molecular tests, particularly when selecting participants and performing the tests. Sometimes studies did not perform the test on the people for whom it was intended and did not follow the manufacturers' instructions for using the test. Sometimes the tests were not carried out at the point-of-care. Nearly all the studies (97%) relied on a single negative RT-PCR result as evidence of no COVID-19 infection. Results from different test brands varied, and few studies directly compared one test brand with another. Finally, not all studies gave enough information about their participants for us to judge how long they had had symptoms, or even whether or not they had symptoms.

### **What does this mean?**

Some antigen tests are accurate enough to replace RT-PCR when used in people with symptoms. This would be most useful when quick decisions are needed about patient care, or if RT-PCR is not available. Antigen tests may be most useful to identify outbreaks, or to select people with symptoms for further testing with PCR, allowing self-isolation or contact tracing and reducing the burden on laboratory services. People who receive a negative antigen test result may still be infected.

Several point-of-care molecular tests show very high accuracy and potential for use, but more evidence of their performance when evaluated in real life settings is required.

We need more evidence on rapid testing in people without symptoms, on the accuracy of repeated testing, testing in non-healthcare settings such as schools (including self-testing), and direct comparisons of test brands, with testers following manufacturers' instructions.

### **How up-to-date is this review?**

This review updates our previous review and includes evidence published up to 30 September 2020.

### **Implications for practice**

We consider the implications for practice for this review separately for symptomatic and for asymptomatic testing.

In the [Role of index test\(s\)](#) section, we suggested that for symptomatic individuals, and if sufficiently accurate, point-of-care testing could be used either to replace laboratory-based RT-PCR or as a triage to RT-PCR. As point-of-care tests are more accessible and provide a result more quickly than RT-PCR, theoretically their use may increase detection and speed up isolation and contact-tracing, leading to reduction in disease spread and reduce the burden on laboratory services.

The evidence included to date suggests that:

1. For diagnosis in symptomatic individuals in the first few days of symptoms, the most accurate rapid antigen tests are a useful alternative to laboratory-based RT-PCR where immediate results are required for

timely patient management or where there are significant logistical or financial challenges in delivering RT-PCR in a timely manner. Rapid antigen tests are only sufficiently sensitive in the first week since onset of symptoms.

Antigen tests vary in sensitivity, and only those shown to meet appropriate criteria, such as WHO's priority target product profiles for COVID-19 diagnostics (i.e. sensitivity  $\geq 80\%$  and specificity  $\geq 97\%$ ; [WHO 2020c](#)), could be considered as a rational substitute for RT-PCR.

Tests had high specificity, thus in symptomatic populations (where prevalence is likely to be high) the risk of false positives is low. At 80% sensitivity compared to RT-PCR, the probability that infected individuals are missed is 20% higher than for RT-PCR. Thus the possibility of false negative results should be considered in those with a high clinical suspicion of COVID-19, particularly if tested several days after onset of symptoms when viral load levels may have fallen.

2. Rapid antigen tests may be used simultaneously in combination with RT-PCR for symptomatic people, particularly where RT-PCR turn-around times are slow, to exploit the benefits of earlier results and consequent contact-tracing and isolation. Given the risk of false-negative results, isolation may be required until RT-PCR-negative results are obtained. Similarly, for investigation of local outbreaks, rapid antigen testing in a clearly defined population may establish cases and contacts that require isolation whilst awaiting results from RT-PCR.

In other circumstances rapid antigen tests may be used to triage to follow-on RT-PCR tests (rather than all receiving PCR tests) dependent on prevalence and the consideration of the consequences of false positive and false negative results.

Where prevalence is low, *positive* rapid test results require confirmatory testing to avoid unnecessary quarantine measures (PPVs around 85% to 90% for antigen assays mean that between 1 in 10 and 1 in 7 positive results will be falsely positive). If unverified, negative rapid test results should be delivered with appropriate advice on self-isolation procedures for the duration of symptoms in order to minimise the effect on transmission of infection from missed cases. RT-PCR tests should still be considered for people with a high clinical suspicion of COVID-19 and negative rapid test..

Where prevalence is higher (i.e. 20% or higher), false positives are less of a concern (PPVs are 96% to 100%) but the impact from false negative results becomes increasingly important and all test *negatives* may be considered for verification. At 20% prevalence, and using data for the more sensitive of our three exemplar assays, between 3% and 6% of those with negative rapid test results are missed cases of SARS-CoV-2 (24 to 50 cases missed out of a total of 200 cases). The lower the NPV the greater the potential effect on transmission of infection from missed cases and greater the impact from delays in commencement of contact tracing. For scenarios in which positive results do not have confirmatory testing, it is important that assays with high specificities (in the range of 99% to 100%) are selected in order to minimise the impact from false positive results at higher prevalences of disease.

3. We identified virtually no evidence for mass screening of asymptomatic individuals using rapid antigen tests in people with no known exposure. A small study screening travellers returning from high-risk countries ([Cerutti 2020](#)), identified only five SARS-CoV-2 infections (prevalence of 3%) with a reported sensitivity of antigen testing for detecting infection of 40%. However, important larger studies have been published since the end of our search, as mentioned above.

The key focus in mass screening is identification of individuals who are or will become infectious. PCR-positives define those who had detectable viral particles on their swab, which will include most of those who are or will become infectious, but also include individuals post-infection with residual viral particles. Without a reference standard for infectiousness, test accuracy studies cannot assess the ability of the test to detect



the infectious subgroup of infections, and cannot provide evidence as to how well rapid antigen tests differentiate between individuals requiring isolation and those who provide no risk. The effectiveness of mass screening using these tests will only be established through outcome studies, such as cluster-randomised community trials.

Given the low false positive rate of rapid tests, when used in a period of outbreak, those found testing positive will have a high chance of being true positives, and thus the test can be used to identify cases requiring isolation. Consideration should be made as to whether test positives should be confirmed with PCR to identify false positives. With a 1% prevalence, a test with 40% sensitivity and 99.6% specificity would yield as many false positives as true positives.

However, the low and variable sensitivity, and lack of evidence that those who test negative are not, or will not become, infectious indicates that those who are rapid antigen test-negative cannot be considered free of risk of being, or of becoming, infectious. In any screening or mass testing programme people testing negative may still have a non-negligible risk of infection.

4. We did not find any evidence of test accuracy in at-risk asymptomatic groups, such as contacts of confirmed cases, hospital workers, or during local outbreaks at schools, workplaces, or care homes. The impact of low-sensitivity tests in these settings is greater than in mass screening, as there will be higher numbers of false negatives, which could either create new outbreaks or will increase the severity of existing outbreaks. Positive cases will be more likely to be true positives than in mass screening settings.

5. We did not find any evidence evaluating the repeated use of tests. Although serial testing (over a number of days), or combinations of different rapid tests (e.g. an antigen test followed by a rapid molecular test) on the same sample are proposed to overcome the limitations of low test sensitivity, they all require validation. Use of multiple tests may increase false positive results, and there are likely to be many individuals with repeated false negative results reducing the expected benefit of subsequent tests. It is unlikely that models will be able to predict how well repeated tests and test combinations would work.

6. Some rapid molecular tests showed promising accuracy levels approximating those of laboratory-based RT-PCR and thus may have a role in small-capacity settings where obtaining test results within two hours will enable appropriate decision making. Results for Xpert Xpress, COVID Nudge and SAMBA II all showed high sensitivity and specificity. However, we identified methodological concerns with many of the evaluations such that we cannot be certain as to how the tests will perform when used in a point-of-care setting. Any application in practice should be accompanied with a proper evaluation to ascertain performance in real-world settings. Rapid molecular tests do not have all the logistical advantage of rapid antigen tests and the resource implications of their use at scale are potentially high, but they may be well suited for some testing scenarios. There is no evidence for use of rapid molecular tests in asymptomatic populations.

Our conclusions are in line with those in the first version of this review despite the increase in the evidence base. Ultimately, decisions around rapid testing will be driven not only by diagnostic accuracy but by acceptable levels of test complexity, time to result, access and acceptability to those being tested, and how test results influence individual behaviour, all of which might vary according to the setting in which the tests are to be used.

## [International travel-related control measures to contain the COVID-19 pandemic: a rapid review](#)

Burns, J et al. Published 25<sup>th</sup> March 2021

### **What did we want to find out?**

We wanted to find out how effective international travel-related control measures are in containing the COVID-19 pandemic.

## **Main results**

Below we summarise the findings of some outcomes.

### **Travel restrictions reducing or stopping cross-border travel (31 modelling studies)**

Most studies showed that travel restrictions reducing or stopping cross-border travel were beneficial, but this beneficial effect ranged from small to large. Additionally, some studies found no effect. Studies also predicted that these restrictions would delay the outbreak, but the delay ranged from one day to 85 days in different studies.

### **Screening at borders (13 modelling studies and 13 observational studies)**

These studies assessed screening at borders, including screening people with symptoms or who had potentially been exposed to COVID-19, or testing people, before or after they travelled.

For screening based on symptoms or potential exposure to COVID-19, modelling studies found that screening reduced imported or exported cases and delayed outbreaks. Modelling studies predicted that 1% to 53% of cases would be detected. Observational studies reported a wide range of cases detected, from 0% to 100%, with the majority of studies reporting less than 54% of cases detected.

For screening based on testing, studies reported that testing travellers reduced imported or exported cases, and cases detected. Observational studies reported that the proportion of cases detected varied from 58% to 90%. This variation might be due to the timing of testing.

### **Quarantine (12 modelling studies)**

All studies suggested that quarantine may be beneficial, but the size of this effect ranged from small to large in the different studies. Modelling studies, for example, predicted that quarantine could lead to between 450 and over 64,000 fewer cases in the community. Differences in effects may depend on how long people were quarantined for and how well they followed the rules.

### **Quarantine and screening at borders (7 modelling studies and 4 observational studies)**

For quarantine and screening at borders, most studies suggested some benefit, however the size of this effect differed between studies. For example, observational studies reported that between 68% and 92% of cases would be detected. Differences in effects may depend on how long people were quarantined for and how often they were tested while in quarantine.

## **How reliable are these results?**

Our confidence in these results is limited. Most studies were based on mathematical predictions (modelling), so we lack real-life evidence. Further, we were not confident that models used correct assumptions, so our confidence in the evidence on travel restrictions and quarantine, in particular, is very low. Some studies were published quickly online as 'preprints'. Preprints do not undergo the normal rigorous checks of published studies, so we are not certain how reliable they are. Also, the studies were very different from each other and their results varied according to the specification of each travel measure (e.g. the type of screening approach), how it was put into practice and enforced, the amount of cross-border travel, levels of community transmission and other types of national measures to control the pandemic.

## **What this means**

Overall, international travel-related control measures may help to limit the spread of COVID-19 across national borders. Restricting cross-border travel can be a helpful measure. Screening travellers only for symptoms at borders is likely to miss many cases; testing may be more effective but may also miss cases if only performed upon arrival. Quarantine that lasts at least 10 days can prevent travellers spreading COVID-19 and may be more effective if combined with another measure such as testing, especially if people follow the rules.

## Evidence Aid

<https://evidenceaid.org/evidence/coronavirus-covid-19/>

This evidence collection contains plain-language summaries of high-quality research which are available in English, and translated into French, Spanish, Portuguese, Arabic and Chinese (simplified and traditional).

The collection includes summaries of systematic reviews that might be relevant to the direct impact of COVID-19 (including reviews of emerging research, as well as existing reviews of relevant interventions) on health and other outcomes, the impact of the COVID-19 response on other conditions, and issues to consider for the recovery period after COVID-19.

### **Environmental measures to prevent transmission of infectious diseases (multiple reviews)**

**What is this?** Environmental measures (including interventions as wide ranging as cleaning of surfaces and border controls) are among the non-pharmaceutical interventions being used to minimise transmission of COVID-19. Several reviews are summarised here, with more details, including citations and links to the full reviews, available further down this page.

**What was found:** Several environmental interventions have been studied for a variety of infectious diseases. These measures include the cleaning of surfaces and other objects, closure of hospital wards, border controls and closure of schools (which is covered in a separate summary, available [here](#)).

The Xiao review (search done in August 2018) did not find evidence of a major effect of surface or object cleaning on transmission of influenza.

The Wong review (search done in July 2014) concluded that it is uncertain whether ward closures are effective at controlling outbreaks of infectious diseases because of the lack of controlled studies.

The Putri review (search done up to April 2020) recommended limited interactions between healthcare departments as a means of preventing the transmission of COVID-19.

The Burns review (search done up to 13 November 2020) found that travel restrictions reducing or stopping cross-border travel were beneficial at reducing the transmission of SARS-CoV-2, screening travellers at borders (including those with symptoms or who had potentially been exposed to COVID-19) would reduce imported or exported cases of COVID-19 and delay outbreaks and that screening based on testing reduced imported or exported cases and cases detected; quarantine may be beneficial for preventing the transmission of SARS-CoV-2 and that quarantine and screening at borders may be beneficial for preventing the transmission of SARS-CoV-2.

Earlier reviews by Saunders-Hasting (search done in July 2016) and Jefferson (search done in October 2010) concluded that it is uncertain whether border controls are effective at controlling outbreaks of infectious diseases and whether screening at ports of entry is effective at controlling outbreaks of infectious diseases, respectively, because of insufficient evidence.

**What are the reviews:** Burns J, Movsisyan A, Stratil JM, et al. International travel-related control measures to contain the COVID-19 pandemic: a rapid review. Cochrane Database of Systematic Reviews. 2021;(3):CD013717.

In this version of the Cochrane rapid review, the authors searched for studies on control measures for international travel during the COVID-19 pandemic. They did not restrict their searches by language of publication and did the search up to 13 November 2020. The review updates an earlier version of the review, which also included data from other pandemics. This version includes 49 modelling studies and 13 observational studies.

**Citation:** Fong MW, Gao H, Wong JY, et al. Nonpharmaceutical measures for pandemic influenza in non-healthcare settings: social distancing measures. Emerging Infectious Diseases. 2020;26(5):976.

In this series of systematic reviews, the authors searched for studies of the effects of social distancing measures for pandemic influenza, and covered six measures: isolating ill individuals, contact tracing, quarantining exposed individuals, school measures or closures, workplace measures or closures, and crowd avoidance, with multiple search periods documented up to November 2018. They included 107 epidemiological studies, 37 simulation studies, 12 observational studies, and one interventional study; and also analyzed archival data from the 1918 influenza pandemic.

**Citation:** Jefferson T, Del Mar CB, Dooley L, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses. Cochrane Database of Systematic Reviews. 2011;(7):CD006207.

In this earlier version of a Cochrane review, the authors searched for randomized trials and observational studies of physical interventions that might prevent respiratory virus transmission. They did not restrict by language of publication and did their searches in October 2010. They identified 67 eligible studies, spread across many different interventions.

**Citation:** Putri SI, Anulus A. Preventive actions to minimizing the coronavirus disease 19 (COVID-19) transmissions among health workers: a systematic review. Journal of the Medical Sciences. 2020;52(3):148-57.

In this rapid review, the authors searched for studies about disease transmission prevention among healthcare workers. The authors restricted their searches to studies published in English or Indonesian between January and April 2020. They included 7 studies.

**Citation:** Saunders-Hastings P, Reisman J, Krewski D. Assessing the state of knowledge regarding the effectiveness of interventions to contain pandemic influenza transmission: a systematic review and narrative synthesis. PLoS One. 2016;11(12):e0168262.

In this systematic overview and narrative syntheses, the authors searched for systematic reviews and meta-analyses of pharmaceutical and non-pharmaceutical interventions for containing pandemic influenza transmission. They did not restrict their searches by date or language of publication and did the search in July 2016. They included 17 reviews.

**Citation:** Wong H, Eso K, Ip A, et al. Use of ward closure to control outbreaks among hospitalized patients in acute care settings: a systematic review. Systematic Reviews. 2015;4(1):152.

In this systematic review, the authors searched for studies in which ward closure was used to control outbreaks of infectious diseases among patients hospitalized in acute care facilities. They did not restrict their searches by date, type or language of publication and did the search in July 2014. They identified 67 case series, 14 case-control studies and 16 studies of other designs. Among these, 11 studies focused on diseases of the respiratory system, including SARS. There were no controlled comparisons of ward closures versus other interventions.

**Citation:** Xiao J, Shiu EY, Gao H, et al. *Nonpharmaceutical Measures for Pandemic Influenza in Nonhealthcare Settings: Personal Protective and Environmental Measures*. Emerging Infectious Diseases 2020;26(5):967-75.

In this systematic review, the authors searched for studies of non-pharmaceutical measures for reducing influenza transmission in community settings. They did not restrict their searches by language of publication and did the search in August 2018. They included studies on hand hygiene (7 randomized trials), face masks (7 randomized trials) or both (6 randomized trials), and surface or object cleaning (1 randomized trial and 1 observational study).

### **Immunotherapy and immunosuppression in COVID-19 patients (multiple reviews)**

**What is this?** Immunotherapy medications have been suggested as possible treatments for COVID-19. In addition, patients with autoimmune disease or those taking immunomodulatory medications may be more at risk of severe COVID-19 disease.

Several reviews are summarized here. More details, including citations and links to the full reviews, are available lower down this page.

#### **What was found:**

At the time of these reviews (with searches largely before June 2020), the available research was insufficient to determine the effects of immunotherapy for treating COVID-19 patients.

The Aziz review (search done on 23 July 2020) suggested that tocilizumab has the potential to reduce mortality rates and the need for mechanical ventilation in COVID-19 patients with severe disease. Earlier, the Yu review (search done in February 2020) found that type I interferons may relieve lung abnormalities, improve respiratory distress and oxygen saturation, and reduce the need for oxygen support without causing life-threatening adverse effects for patients with coronavirus infection.

The Siordia review (search done before July 2020) found that lopinavir/ritonavir, arbidol, hydroxychloroquine and remdesivir did not lead to clinical improvements in COVID-19 patients.

The Russell review (search done before 20 March 2020) reported that low-dose prednisolone and tacrolimus may have beneficial effects for COVID-19 patients and that interleukin-6 peak levels might be associated with severity of pulmonary complications.

The Leisman review (search done on 14 April 2020) reported that the inflammatory cytokine response in COVID-19 patients with severe or critical disease was profoundly lower than in other conditions such as sepsis or Acute Respiratory Distress Syndrome unrelated to COVID-19. The review concluded that the role of inflammatory cytokines in the pathobiology of COVID-19 was unclear.

The Minotti review (search done on 31 March 2020) suggested that children and adults who are immunosuppressed are not at higher risk of severe COVID-19 disease, but the Liu review (search done on 9 May 2020) reported a slightly increased risk of severe COVID-19 disease in patients with autoimmune disease.

#### **What are the reviews:**

**Citation:** AminJafari A, Ghasemi S. *The possible of immunotherapy for COVID-19: A systematic review*. International Immunopharmacology. 2020;83:106455.

In this rapid review, the authors searched for articles on the effects of immunotherapy (e.g. monoclonal antibody, interleukins, vaccines) for coronaviruses (SARS-CoV, MERS-CoV and SARS-CoV-2), which mentioned the potential relevance to COVID-19. They restricted their searches to articles published in English up to 24 March 2020. They included 7 articles.

**Citation:** Antwi-Amoabeng D, Kanji Z, Ford B, et al. *Clinical Outcomes in COVID-19 Patients Treated with Tocilizumab: An Individual Patient Data Systematic Review*. Journal of Medical Virology. 2020;92(11):2516-22.

In this rapid review, the authors searched for studies that reported data on COVID-19 patients who had received tocilizumab, sarilumab or siltuximab. They did not restrict their searches by date, type or language of publication and did the most recent search on 27 April 2020. They included 11 observational studies (total: 29 patients) from China (2 studies), France (2), Italy (2), Switzerland (1) and the USA (4).

**Citation:** Aziz M, Haghbin H, Abu Sitta E, et al. *Efficacy of tocilizumab in COVID-19: A systematic review and meta-analysis*. Journal of Medical Virology. 2021;93(3):1620-30.

In this rapid review, the authors searched for studies of the efficacy of tocilizumab for COVID-19 patients. They did not restrict their searches by language of publication and searched for articles published between 1 January and 23 July 2020. They included 23 observational studies (6279 patients), from Europe (15 studies) and North America (8).

**Citation:** Giuliani F, Gualdi G, Amerio P. *Effect of immunosuppressive drugs in immune-mediated inflammatory disease during the coronavirus pandemic*. Dermatologic Therapy. 2020;33(6):e14204.

In this rapid review, the authors searched for studies on the clinical outcomes of patients with Immune-Mediated Inflammatory Diseases (IMiDs) treated with biologics or conventional disease-modifying anti-rheumatic drugs (DMARDs) who become infected with SARS-CoV-2 or SARS-CoV-1. They restricted their searches to articles published in English and did the search on 14 May 2020. They included 11 studies (57 patients).

**Citation:** Leisman DE, Ronner L, Pinotti R, et al. *Cytokine elevation in severe and critical COVID-19: a rapid systematic review, meta-analysis, and comparison with other inflammatory syndromes*. Lancet Respiratory Medicine. 2020;8(12):1233-44.

In this rapid review, the authors searched for studies with  $\geq 20$  patients that quantified interleukin-6 concentrations in COVID-19 patients with severe or critical disease, and compared the findings to previous published studies on sepsis, cytokine release syndrome and Acute Respiratory Distress Syndrome unrelated to COVID-19. They restricted their searches to articles published in English between 1 November 2019 and 14 April 2020. They included 37 studies, of which 25 were COVID-19 studies (1245 COVID-19 patients).

**Citation:** Liu M, Gao Y, Zhang Y, et al. *The association between severe or dead COVID-19 and autoimmune disease: a systematic review and meta-analysis*. Journal of Infection. 2020;81(3):e93-5.

In this rapid review, the authors searched for studies on the association between severity of COVID-19 and autoimmune disease. They did not restrict their searches by language of publication and did the search on 8 May 2020. They included 6 studies (2091 patients), which were from China (5 studies) and the USA (1).

**Citation:** Minotti C, Tirelli F, Barbieri E, et al. *How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? A systematic review*. Journal of Infection. 2020;81(1):e61-6.

In this rapid review, the authors searched for studies of COVID-19 patients with underlying immunosuppression from a variety of causes. They restricted their searches to articles published in English and did their most recent search on 31 March 2020. They included 16 articles (110 immunosuppressed patients), from Asia (13 articles) and Europe (3).

**Citation:** Russell B, Moss C, George G, et al. Associations between immune-suppressive and stimulating drugs and novel COVID-19: a systematic review of current evidence. *Ecancermedicalscience*. 2020;14:1022.

In this rapid review, the authors searched for research on the impact of immune-suppressing or immune-stimulating drugs on coronaviruses, including but not limited to SARS-CoV-2. The date of the search is not reported but they submitted their manuscript to the journal on 20 March 2020. They included 89 studies covering 10 immunomodulatory medication groups.

**Citation:** Siordia JA, Bernaba M, Yoshino K, et al. Systematic and Statistical Review of Coronavirus Disease 19 Treatment Trials. *SN Comprehensive Clinical Medicine*. 2020;2:1120-31

In this rapid review, the authors searched for COVID-19 clinical trials of any treatment. They did not restrict their searches by date or language of publication and do not report the date of the search (but the article was accepted for publication on 7 July 2020). They included 12 retrospective studies, 10 randomized trials and 4 prospective studies.

**Citation:** Solis-García del Pozo J, Galindo MF, Nava E, et al. A systematic review on the efficacy and safety of IL-6 modulatory drugs in the treatment of COVID-19 patients. *European Review for Medical and Pharmacological Sciences*. 2020;24(13):7475-84.

In this rapid review, the authors searched for studies of treatment of COVID-19 patients with anti-IL-6 drugs. They did not restrict their searches by country or language of publication and completed their search on 18 April 2020. They included 3 case series and 6 case reports. and identified ongoing clinical trials of tocilizumab (8), sarilumab (5) and siltuximab (2).

**Citation:** Yu C, Kang L, Chen J, et al. Evaluation of safety, efficacy, tolerability, and treatment-related outcomes of type I interferons for human coronaviruses (HCoVs) infection in clinical practice: An updated critical systematic review and meta-analysis. *International Immunopharmacology*. 2020;86:106740.

In this rapid review, the authors searched for studies of type I interferon treatment for patients with coronavirus infections. They did not restrict their searches by date, type or language of publication, and did the search in February 2020. They included 15 studies.

**Other relevant reviews of this topic:** Evidence Aid combined summary: Corticosteroids as a treatment for COVID-19

### [Multisystem inflammatory syndrome \(MSIS\) in children with COVID-19 \(multiple reviews\)](#)

**What is this?** Most children with COVID-19 have an asymptomatic or mild course of the disease but rare cases of a serious multisystem inflammatory syndrome (MSIS) have been reported.

The findings of three rapid reviews are summarised here. More details, including citations and links to the full reviews, are available lower down this page.

**What was found:** At the time of these reviews, the included studies reported an overlap in the presentation of MSIS and COVID-19 infection. The most commonly identified symptoms associated with MSIS were fever, gastrointestinal symptoms, conjunctivitis and rash. Most of the affected children required care in an intensive care unit.

The included reviews reported that the following complications occurred frequently in MSIS: hypotension, Kawasaki Disease-like symptoms, circulatory shock, myocarditis, central nervous system involvement, respiratory symptoms and acute kidney injury.

The Ahmed review (search up to 25 July 2020) found that children typically show symptoms of MSIS 3 to 4 weeks after COVID-19 infection and can progress rapidly into shock and cardiorespiratory failure.

#### **What are the reviews:**

**Citation:** Ahmed M, Advani S, Moreira A, et al. Multisystem inflammatory syndrome in children: A systematic review. EClinicalMedicine. 2020;26:100527.

In this rapid review, the authors searched for studies on MSIS in paediatric patients with COVID-19. They searched for articles published between January and 25 July 2020. They included 39 observational studies (662 patients) including 23 case series. The two largest studies were from the USA (total: 285 patients).

**Citation:** Aronoff SC, Hall A, Del Vecchio MT. The Natural History of Severe Acute Respiratory Syndrome Coronavirus 2–Related Multisystem Inflammatory Syndrome in Children: A Systematic Review. Journal of the Pediatric Infectious Diseases Society. 2020;9(6):746-51.

In this rapid review, the authors searched for case reports and case series providing detailed clinical descriptions, laboratory manifestations, complications, natural history and treatment for MSIS in children with COVID-19. They did not restrict their searches by language of publication and searched up to 23 July 2020. They included 16 reports (505 children). The largest case series was from the USA (186 children).

**Citation:** Kaushik A, Gupta S, Sood M, et al. A systematic review of multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection. The Pediatric Infectious Disease Journal. 2020;39(11):e340-6.

In this rapid review, the authors searched for studies reporting the clinical features, treatments and outcomes of MSIS in children with COVID-19. They did not restrict their searches by language of publication and searched for studies published between 1 January and 31 July 2020. They included 16 studies (655 patients).

#### **Oral hygiene care for critically ill patients on mechanical ventilation**

**Citation:** Zhao T, Wu X, Zhang Q, et al. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. Cochrane Database of Systematic Reviews. 2020;(12):CD008367.

**What is this?** Some patients with COVID-19 will become critically ill and require mechanical ventilation in an intensive care unit (ICU). One complication of this is ventilator-associated pneumonia and oral health hygiene, provided by the ICU staff, might help to reduce the risk of this.

In this updated Cochrane review, the authors searched for randomised trials of oral hygiene care in critically ill patients receiving mechanical ventilation for at least 48 hours. They did not restrict their searches by date or language of publication and did the most recent search in March 2020. They included 40 trials (5675 patients) and assessed the risk of bias as high in 31 of these.



**What works:** Chlorhexidine mouthwash or gel probably reduces the incidence of ventilator-associated pneumonia in critically ill patients, when compared to placebo or usual care.

Oral hygiene care including both **antiseptics and toothbrushing** may be more effective than antiseptics alone at reducing the incidence of ventilator-associated pneumonia and length of stay in ICU.

**What doesn't work:** Nothing noted.

**What's uncertain:** The limited evidence available for powered versus manual toothbrushing and for other oral hygiene care agents means that the effects of these are uncertain.

### [Use of healthcare service during the COVID-19 pandemic fell by about a third \(search up to 10 August 2020\)](#)

**Citation:** Moynihan R, Sanders S, Michaleff ZA, et al. *Impact of COVID-19 pandemic on utilisation of healthcare services: a systematic review*. BMJ Open. 2021;11:e045343.

**What is this?** The COVID-19 pandemic has placed a great strain on healthcare services and reduced people's access to them.

In this systematic review, the authors searched for studies that compared use of healthcare services during the COVID-19 pandemic to at least one comparable, earlier period. They did not restrict their searches by language of publication and did the search up to 10 August 2020. They included 81 studies across 20 countries, reporting on more than 11 million services before the pandemic and nearly 7 million during it.

**What was found:** Use of healthcare services decreased by about a third during the pandemic, with considerable variation, and with greater reductions among people with less severe illness.

### [Chloroquine and hydroxychloroquine for COVID-19 \(multiple reviews\)](#)

**What is this?** Chloroquine and hydroxychloroquine have been suggested as possible treatments for COVID-19. Several reviews have been done and details of these are available here, including citations and links to the full reviews.

**What was found:** Currently available research suggests that chloroquine and hydroxychloroquine are not effective as single drug treatments for COVID-19. For example, the Cochrane Review (search up to 15 September 2020) found that hydroxychloroquine does not affect how many COVID-19 patients will die when compared with usual care or placebo (9 studies, 8208 patients; including the findings of the RECOVERY trial).

Currently available research suggests that a combination of hydroxychloroquine and azithromycin does not reduce short-term mortality in patients hospitalized with COVID-19 or risk of hospitalization in outpatients with COVID-19.

**What are the reviews:**

**Citation:** Das RR, Jaiswal N, Dev N, et al. Efficacy and safety of Anti-malarial drugs (Chloroquine and Hydroxychloroquine) in treatment of COVID-19 infection: a systematic review and meta-analysis. Frontiers in Medicine. 2020;7:482.

In this rapid review, the authors searched for clinical trials and observational studies of the safety and efficacy of chloroquine and hydroxychloroquine for COVID-19 patients. They did not restrict their searches by date, type or language of publication and searched up to 5 June 2020. They included 6 clinical trials and 11 observational studies (total: 8071 participants).

**Citation:** Elavarasi A, Prasad M, Seth T, et al. Chloroquine and Hydroxychloroquine for the Treatment of COVID-19: a Systematic Review and Meta-analysis. Journal of General Internal Medicine. 2020;35(11):3308-14.

In this rapid review, the authors searched for studies of the efficacy of chloroquine and hydroxychloroquine for COVID-19 patients. They did not restrict their searches by language of publication and searched for studies published between December 2019 and 8 June 2020. They included 12 cohort studies and 3 randomized trials (total: 10,659 patients).

**Citation:** Elsayah HK, Elsayary MA, Elrazzaz MG, et al. Hydroxychloroquine for treatment of non-severe COVID-19 patients: Systematic review and meta-analysis of controlled clinical trials. Journal of Medical Virology. 2021;93(3):1265-75.

In this rapid review, the authors searched for trials of the efficacy and safety of hydroxychloroquine for COVID-19 patients aged  $\geq 12$  years with non-severe disease. They did their search up to 18 July 2020. They included 6 studies (609 patients).

**Citation:** Hazra S, Chaudhuri AG, Tiwary BK, et al. Matrix metalloproteinase 9 as a host protein target of chloroquine and melatonin for immunoregulation in COVID-19: A network-based meta-analysis. Life Sciences. 2020;257:118096.

In this rapid review, the authors searched for studies examining the use of repurposed drugs for COVID-19 patients. They did not restrict their searches by language of publication and did the search on 23 March 2020. They identified 120 differentially expressed genes and 65 drugs repurposed for COVID-19.

**Citation:** Kashour Z, Riaz R, Garbati MA, et al. Efficacy of chloroquine or hydroxychloroquine in COVID-19 patients: a systematic review and meta-analysis. Journal of Antimicrobial Chemotherapy. 2021;76(1):30-42.

In this rapid review, the authors searched for studies of the effects of chloroquine or hydroxychloroquine for COVID-19 patients. They did not restrict their searches by date or type of publication and did the search on 17 July 2020. They included 7 randomized trials and 14 cohort studies (total: 20,979 patients).

**Citation:** Million M, Gautret P, Colson P, et al. Clinical Efficacy of Chloroquine derivatives in COVID-19 Infection: Comparative meta-analysis between the Big data and the real world. New Microbes and New Infections. 2020;38:100709.

In this meta-analysis, the authors searched for comparative studies of the effects of chloroquine derivatives for COVID-19 patients. They did not restrict their searches by date or language of publication and did the search on 27 May 2020. They included 20 studies (105,040 participants).

**Citation:** Singh B, Ryan H, Kredo T, et al. Chloroquine or hydroxychloroquine for prevention and treatment of COVID-19. Cochrane Database of Systematic Reviews. 2021;(2):CD013587.

In this Cochrane review, the authors searched for randomized trials of chloroquine or hydroxychloroquine for COVID-19 patients, people at risk of exposure to SARS-CoV-2 or people exposed to SARS-CoV-2. They did not restrict their searches by type or language of publication and did the search up to 15 September 2020. They included 12 trials (8569 participants) of the treatment of COVID-19 and 2 trials (3346 participants) for preventing COVID-19 in people exposed to SARS-CoV-2. They found no trials of chloroquine or hydroxychloroquine for preventing COVID-19 disease in people at risk of exposure to SARS-CoV-2. They identified 122 ongoing trials for treatment or prevention of COVID-19.

**Citation:** Siordia JA, Bernaba M, Yoshino K, et al. Systematic and Statistical Review of COVID19 Treatment Trials. SN Comprehensive Clinical Medicine. 2020;2:1120-31.

In this rapid review, the authors searched for studies of drugs to treat COVID-19 patients. They did not restrict their searches by date or language of publication. They do not report the date of their search but the article was accepted for publication on 7 July 2020. The authors included 6 studies of hydroxychloroquine.

**Citation:** Thoguluva Chandrasekar V, Venkatesalu B, Patel HK, et al. Systematic review and meta-analysis of effectiveness of treatment options against SARS-CoV-2 infection. Journal of Medical Virology. 2021;93(2):775-85.

In this rapid review, the authors searched for studies of a variety of interventions for COVID-19 patients. They did not restrict their searches by language of publication and searched for articles published between December 2019 and 11 May 2020. They included 12 studies of hydroxychloroquine-based treatments.

#### **Other reviews relevant to this topic:**

**Citation:** Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients With COVID-19. Clinical Infectious Diseases. 2020;ciaa478.

**Citation:** Cortegiani A, Ingoglia G, Ippolito M, et al. A systematic review on the efficacy and safety of chloroquine for the treatment of COVID-19. Journal of Critical Care. 2020;57:279-83.

**Citation:** Cortegiani A, Ippolito M, Ingoglia G, et al. A systematic review on the efficacy and safety of chloroquine/hydroxychloroquine for the treatment of COVID-19. Journal of Critical Care. 2020;59:176-90.

**Citation:** Gbingie K, Frie K. Should chloroquine and hydroxychloroquine be used to treat COVID-19? A rapid review. BJGP Open. 2020;4(2):bjgpopen20X101069.

**Citation:** Singh AK, Singh A, Shaikh A, et al. 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. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2020;14(3):241-6.

### **Surgical and operating room procedures during the COVID-19 pandemic (multiple reviews)**

**What is this?** The COVID-19 pandemic is affecting the provision of surgery for patients and several relevant reviews have been done. More details of these, including citations and links to their full text are available further down this summary.

#### **What was found:**

**Recommendations for practices relevant to the conduct of surgery** include the use of pre-operative planning, negative pressure ventilation in operating theatres, limited personnel, single-use equipment,

designated donning and doffing areas, dedicated COVID-19 theatres and teams and COVID-free facilities, use of regional anaesthesia to minimise duration of surgery, limited use of electro-cauterization within procedures, limiting the use of endoscopic procedures to emergencies and selected suspected or confirmed cancer patients, and telemedicine for postoperative follow-up.

**Recommendations for staff involved in surgery** include use of appropriate personal protective equipment (PPE), training, screening, showers following procedures and the provision of psychological support.

**Recommendations for surgery patients** include screening for SARS-CoV-2, self-isolation before elective admission and the use of surgical masks during admission.

In the Eichberg review (search done on 5 April 2020) of **neurosurgery, remote telemedicine** was found to be feasible for patients in the pre-hospital, inpatient, outpatient and transfer triage settings, at least in resource-scarce situations.

The Lee review (search done on 1 July 2020) found that most studies which followed the **health of surgical workers** noted no adverse outcomes with proper safety measures including PPE and effective screening and isolation post-operatively. At the time of the review, there was limited information on postoperative complications during pandemics and no information on the clinical impact of delaying surgical care during lockdowns.

#### **What are the reviews:**

**Citation:** De Simone B, Chouillard E, Di Saverio S, et al. *Emergency surgery during the COVID-19 pandemic: what you need to know for practice*. The Annals of The Royal College of Surgeons of England. 2020;102(5):323-32.

In this rapid review, the authors searched for articles on COVID-19 and surgery in an emergency setting. They restricted their searches to articles published in English between 15 December 2019 and 30 March 2020. They included 12 articles.

**Citation:** Eichberg DG, Basil GW, Di L, et al. *Telemedicine in neurosurgery: lessons learned from a systematic review of the literature for the COVID-19 era and beyond*. Neurosurgery. 2021;88(1):e1-e12.

In this systematic review, the authors searched for literature describing telemedicine in the context of neurosurgery. They restricted their searches to articles published from 1995 to 2020 in English and their last literature search was done in April 2020. They included 52 studies (45,801 patients).

**Citation:** Hojaij FC, Chinelatto LA, Boog GH, et al. *Surgical Practice in the Current COVID-19 Pandemic: A Rapid Systematic Review*. Clinics. 2020;75:e1923.

In this rapid review, the authors searched for research or recommendations regarding surgery dynamics, screening of patients and elective procedures during the COVID-19 pandemic. They did not restrict their searches by date, type or language of publication and did the search on 4 April 2020. They included 21 research articles, 5 opinion articles, 4 editorials and 9 other articles.

**Citation:** Lee Y, Kirubarajan A, Patro N, et al. *Impact of hospital lockdown secondary to COVID-19 and past pandemics on surgical practice: A living rapid systematic review*. American Journal of Surgery. 2020 Nov 12.

In this rapid review, the authors searched for studies that assessed postoperative outcomes or protection measures for surgical staff during pandemics. They did not restrict their searches by date or language of publication and did the search on 1 July 2020. They included 61 studies (3948 patients across 17 countries),

56 of which related directly to the COVID-19 pandemic. They also included studies of SARS (3), MERS (1) and Ebola (1).

**Citation:** Pavan N, Crestani A, Abrate A, et al. *Risk of Virus Contamination Through Surgical Smoke During Minimally Invasive Surgery: A Systematic Review of Literature on a Neglected Issue Revived in the COVID-19 Pandemic Era*. European Urology Focus. 2020; 6(5):1058-69.

In this rapid review, the authors searched for clinical and pre-clinical studies evaluating the risk of viral transmission to healthcare workers from any surgical treatment of patients with a viral disease, or studies evaluating the presence of virus remnants in surgical smoke. They did not restrict their searches by language of publication and did the search on 2 April 2020. They included 14 clinical studies, 8 pre-clinical studies and 2 papers reporting both clinical and pre-clinical study data.

**Citation:** Soltany A, Hamouda M, Ghzawi A, et al. *A scoping review of the impact of COVID-19 pandemic on surgical practice*. Annals of Medicine and Surgery. 2020;57:24-36.

In this rapid review, the authors searched for studies of the impact of the COVID-19 pandemic on surgical practice and training or guidelines for surgical practice from accredited institutions or professional associations. They restricted their searches to articles published in English from December 2019 to mid-June 2020. They included 66 articles and reports from North America, South America, Europe and Asia (with most being from the USA).

**Citation:** Spolverato G, Capelli G, Restivo A, et al. *The management of surgical patients during the COVID-19 pandemic*. Surgery. 2020;168(1):4-10.

In this rapid review, the authors searched for research or opinion papers on the epidemiology and diagnosis of COVID-19, the management of cancer and surgical patients, and the safety of healthcare workers during the pandemic. They did not restrict their searches by type or language of publication and searched for articles published between January 1998 and 2 April 2020. They included 28 retrospective studies.

**Citation:** Welsh Surgical Research Initiative (WSRI) Collaborative. *Recommended operating room practice during the COVID-19 pandemic: systematic review*. BJS Open. 2020;4(5):748-56.

In this rapid review, the authors searched for research or recommendations for operating room practices during the COVID-19 pandemic. They did not restrict their search by date, type or language of publication and did the search on 19 March 2020. They included 9 expert opinion articles and 2 observational studies. These were from China (9 articles) and Singapore (2).

#### **Other reviews relevant to this topic:**

**Citation:** Goyal T, Harna B, Taneja A, et al. *Arthroscopy and COVID-19: Impact of the pandemic on our surgical practices*. Journal of Arthroscopy and Joint Surgery 2020;7(2):47-53.

**Citation:** Patterson TJ, Currie PJ, Beck J, et al. *A systematic review of viral transmission risk to healthcare staff comparing laparoscopic and open surgery*. The Surgeon. 2020;18(6):e72-7.

# Dynamed - [COVID-19 \(Novel Coronavirus\)](#)

## Latest updates

**Evidence** Updated 5 Apr 2021

rapid point-of-care antigen tests may have high specificity but low sensitivity for detection of SARS-CoV-2 infection (Cochrane Database Syst Rev 2021 Mar 24) [View in topic](#)

**Evidence** Updated 5 Apr 2021

rapid point-of-care molecular-based tests may have high sensitivity and specificity for detection of SARS-CoV-2 infection (Cochrane Database Syst Rev 2021 Mar 24) [View in topic](#)

**Evidence** Updated 1 Apr 2021

about 80%-83% protection against reinfection with SARS-CoV-2 reported in persons < 65 years old, and 47% protection against reinfection reported in adults ≥ 65 years old in Denmark (Lancet 2021 Mar 27) [View in topic](#)

**Evidence** Updated 1 Apr 2021

in adults with laboratory-confirmed COVID-19, estimated peak prevalence of IgM antibodies about 80% with peak levels at about 20 days after symptom onset, and peak prevalence of IgG antibodies 95% with peak levels at about 25 days (Ann Intern Med 2021 Mar 16 early online) [View in topic](#)

**Evidence** Updated 1 Apr 2021

6.9% seroprevalence of pan-immunoglobulins against SARS-CoV-2 in spring 2020 in Wuhan, China, with about 64% of persons with symptoms seroconverting to have neutralizing antibodies compared to 35% of persons without symptoms (Lancet 2021 Mar 20) [View in topic](#)

**Evidence** Updated 30 Mar 2021

2-dose regimen of ChAdOx1 nCoV-19 vaccine may not be effective against mild-to-moderate Covid-19 due to B.1.351 variant in adults ≤ 64 years old (N Engl J Med 2021 Mar 16 early online) [View in topic](#)

**Evidence** Updated 30 Mar 2021

living with children and adolescents associated with increased risk of SARS-CoV-2 infection and related hospitalization in adults ≤ 65 years old and increased risk of infection and related ICU admission and death in adults (BMJ 2021 Mar 18) [View in topic](#)

**Evidence** Updated 23 Mar 2021

EMA safety committee concludes that benefits of vaccination with AstraZeneca ChAdOx1-S COVID-19 vaccine outweigh risks despite rare cases of thrombosis associated with thrombocytopenia (EMA Press Release 2021 Mar 18) [View in topic](#)

**Evidence** Updated 23 Mar 2021

51% of patients hospitalized with COVID-19 reported symptoms 4 months after discharge from hospital or intensive care (JAMA 2021 Mar 17 early online) [View in topic](#)

## Useful Links

[BMJ – latest news and resources for COVID-19](#)

[Cochrane Library Coronavirus \(COVID-19\): evidence relevant to critical care](#)

[Elsevier - Novel Coronavirus Information Center – Elsevier](#)

[European Centre for Disease Prevention and Control](#)

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[New England Journal of Medicine](#)

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